



US 20060003340A1

(19) **United States**(12) **Patent Application Publication**
Kostrikis(10) **Pub. No.: US 2006/0003340 A1**(43) **Pub. Date: Jan. 5, 2006**(54) **MULTI-ALLELIC MOLECULAR
DETECTION OF SARS-ASSOCIATED
CORONAVIRUS**(75) **Inventor: Leondios G. Kostrikis, Limassol (CY)**

Correspondence Address:

VENABLE LLP**P.O. BOX 34385****WASHINGTON, DC 20045-9998 (US)**(73) **Assignee: Birch Biomedical Research, LLC, New
York, NY (US)**(21) **Appl. No.: 10/917,421**(22) **Filed: Aug. 13, 2004****Related U.S. Application Data**(60) **Provisional application No. 60/496,995, filed on Aug.
22, 2003. Provisional application No. 60/576,314,
filed on Jun. 3, 2004.****Publication Classification**(51) **Int. Cl.****C12Q 1/70** (2006.01)**C12Q 1/68** (2006.01)**G01N 33/53** (2006.01)**C12N 7/00** (2006.01)**C12N 7/01** (2006.01)(52) **U.S. Cl. 435/6; 435/7.1**(57) **ABSTRACT**

The subject invention relates to a multiple-allelic RT-real-time polymerase chain reaction (PCR) assay for coronaviruses including the SARS virus. Multiple target sequences within the SARS-CoV, S, E, M and N genes are identified. The use of the four different targets enhances the likelihood that the fundamental genetic drift of the virus will not lead to a false negative result. Multiplex assays format for the assay are envisioned. Thus, the present invention allows for early diagnosis of a SARS infection. The assay would be useful in the context of monitoring treatment regimens, screening potential anti SARS agents, and similar applications requiring qualitative and quantitative determinations.

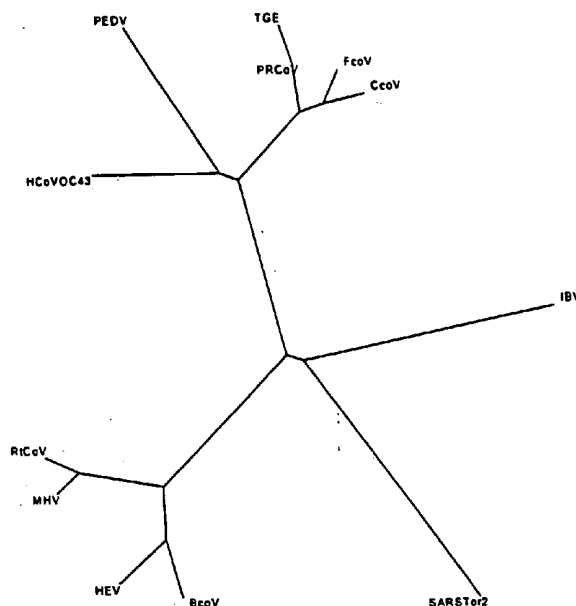
Phylogenetic Analysis of S Gene

Figure 1: CLUSTAL W (1.81) multiple DNA sequence alignment of coronavirus S genes from strains isolated from different species

CcoV	ATGATTGTGCTTACATTGTGCCTTTTCTTGTT---TTGTACAGTAGTGTGAGCTGTACA
FcoV	ATGATTGTGCTCGTAACCTGCTCTTGTTGTTATGTTCATACCACACAGTTTTGAGTACA
TGE	ATGAAAAAACTATTTGTGTTTTGGTCGTAATGCCATTGATTATGGAGACAATTTTCCT
PRCoV	-----
HCoVOC43	-----
PEDV	-----
SARSUrba	-----
SARSTor2	-----
BcoV	-----
HEV	-----
MHV	-----
RtCoV	-----
IBV	-----
CcoV	TCAAACAATGACTGTGTACAAGTTAATGTGACACAACCTGCCTGGCAATGAAAATATTATC
FcoV	ACAAATAATGAATGCATACAAGTTAACGTAACACAATTGGCTGGCAATGAAAACCTTATC
TGE	TGTTCTAAATTGACTAATAGAACTATAGGCAACCAGTGGAAATCTCATTGAAACCTTCCTT
PRCoV	-----
HCoVOC43	-----
PEDV	-----ATGAGGTCTTTAATTTACTTCTGGTTGCTCTT
SARSUrba	-----ATGTTT
SARSTor2	-----ATGTTT
BcoV	-----ATGTTTTTGATACTT
HEV	-----ATGTTTTTTTATACTT
MHV	-----ATGCTATTTCGTGTTT
RtCoV	-----ATGCTATTTCGTGTTT
IBV	-----
CcoV	AAAGATTTTCTATTTTCAGAACTTTAAAGAAGAAGGAAGTTTAGTTGTTGGTGGTTATTAC
FcoV	AGAGATTTTCTGTTTAGTAACCTTTAAAGAAGAAGGAAGTGTAGTTGTTGGTGGTTATTAC
TGE	CTAAACTATAGTAGTAGGTTACCACCTAATTCAGATGTGGTGTAGGTGATTATTTTCCT
PRCoV	-----
HCoVOC43	-----
PEDV	ACCAGTACTTCCAACACTCAGCCTACCACAAGATGTCAGTAGGTGCCAGTCTACTACTAA
SARSUrba	ATTTTCTTATTATTTCTTACTCTCACTAGTGGTAGTGACCTTGACCGGTGCACCACCTTTT
SARSTor2	ATTTTCTTATTATTTCTTACTCTCACTAGTGGTAGTGACCTTGACCGGTGCACCACCTTTT
BcoV	TTAATTTCCCTTACCAATGGCTTTTGCTGTTATAGGAGATTTAAAGTGTAACGGTTTCC
HEV	TTAATCTCCCTGCCTTCTGCTTTTGCAAGTTATAGGGGATTTAAAGTGTAACCTTCATTA
MHV	TTAACCTTGTTGCCCTCTTCTCAAGGTATATTGGTGATTTTAGATGTATCCAACCTTGTA
RtCoV	TTAACCTATTGCCCTCTTGTCTAGGTATATTGGTGATTTTAGATGTATCAACCTTGTA
IBV	-----
CcoV	CCCACAGAGGTGTGGTATAACTGTTCCACAACCTCAACAACTACCGCTTATAAGTATTTT
FcoV	CCTACAGAGGTGTGGTACAACCTGCTCTAGAACAGCTCGAACTACTGCCTTTTCACTATTTT
TGE	ACTGTACAACCTTGGTTAATTGCATTGCAATGATAGTAATGACCTTTATGTTACACTG
PRCoV	-----
HCoVOC43	-----
PEDV	CTTTAGGCGGTTCTTTTCAA--AATTTAATGTTTCAGGCACCTGCCGTCGTTTGGGT
SARSUrba	GA-----TGATGTTCAAGCTCCTA--ATTACACTCAACATACTTCAT---CT
SARSTor2	GA-----TGATGTTCAAGCTCCTA--ATTACACTCAACATACTTCAT---CT
BcoV	ATTAATGATGT---TGACACCGGTGCTCCCTCTATTAGCACTGATATTGTGCGATGTTACT
HEV	ATTAATGACGT---TGACACTGGTGTGCCATCTATTAGCTCTGAAGTTGTTGATGTCACT
MHV	AATACCGACACCTCTAATGCCAGCGCTCCAAGCGTTAGTACAGAGGTAGTTGATGTTTCC

RtCoV
IBVAACACCCGCATTTCTAATGCGCGCGCACCCAGTGTAGCACAGAGGTAGTTGATGTTTCT
-----CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBVAGTAATATACATGCATTTTATTTTGATATGGAAGCCATGGAGAATAGTACTGGCAATGCA
AATAATATACATGCCTTTTATTTGTATGGAAGCCATGGAAAAATAGCACTGGTAATGCA
GAAAACTCTAAAGCATTGTATTGGGATT---ATGCTACAGAAAAATATCACTTGGAAAT---

GGTTACCTACCTAGTATGAACTCTTCTAGCTGGTACTGTGGCACAGGCATTGAAACTGCT
ATGAG---GGGGGTTTACTATCCT---GATGAAATT---TTTAGATCAGACACTCTT---
ATGAG---GGGGGTTTACTATCCT---GATGAAATT---TTTAGATCAGACACTCTT---
AATGGTTTAGGTACTTATTATGTTTTAGATCGTGTGTATTTAAATACTACGTTGTGTG---
AATGGTTTGGGGACTTTCTATGTTTTAGATCGTGTCTATTTAAATACCACATTGTGTG---
AAAGGGATTGGTACTTATTATGTTTTAGATCGAGTCTATTTAAATGCCACACTATTG---
AAAGGTCTTGGTACATATTACGTTTTAGATCGTGTATTATTTAAATGCCACGTTATTG---
-----CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBVCGTGGTAAACCTTTACTAGTACATGTTTCATGGTAATCCTGTAGTATCATTGTTTACATA
CGTGGTAAACCATTTATTATTTTCATGTGCATGGTGAGCCTGTAGTGTATT-----ATA
CACAGACAACGGTTAAACGTAGTCGTTAATGGATACCCATACTCCATCACAGTT---ACA

AGTGGCGTTTCATGGTATTTTCTCAGCTACATCGATTCTGGTCAGGGCTTTGAGA---TTG
-----TATTTA---ACTCAGGATTTATTTCTTC-CATTTTATTCTAATGTTACAGG---GTT
-----TATTTA---ACTCAGGATTTATTTCTTC-CATTTTATTCTAATGTTACAGG---GTT
CTTAATGGTTACTACCCTACTTCAGGTTCTACATATCGTAATATGGCACTGAAGG---GAA
CTCAATGGTTATTACCCAATTTTCAGGTGCTACATTTTCGTAATATGGCTCTGAAAG---GAA
CTTACTGGTTATTACCCTGTAGATGGGTCCATGTATAGAAACATGGCTCTAACGG---GAA
CTTACTGGTTACTACCCTGTAGATGGGTCCATGTATCGTAACATGGCTCTAATGG---GTA
-----CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBVTCAGCTTATAGAGATGATGTGCAATTTAGGCCGCTTTTAAAGCATGGTTTATTGTGTATA
TCGGCTTATAGGGATGATGTGCAACAAAGGCCCTTTTAAACATGGGTTAGTGTGCATA
ACAACCCGCAATTTTAAT-TCTGCTGAAGGTGCTATTATATGCATTTGTAAGGGCTCACC

GCATTTGCAAGAGCCGT-TTGATCCTAGTGGTTACCAGCTTTATTTACATAAGGCCACT
TCATACTATTAATCATAC---GTTTGG---CAACCTGTGCAT-ACCTTTTAAGGATGGTA
TCATACTATTAATCATAC---GTTTGG---CAACCTGTGCAT-ACCTTTTAAGGATGGTA
CTTTACTATTGAGCAGACTATGGTTTAAACCACCTTTTCTTCTGATTTTATTAATGGTA
CTCGATTATTGAGCACCTTGTGGTTTAAAGCCGCTTTTATCACCTTTTAAATGATGGTA
TTAATACCATAAGCCCTTAATTGGTACAAACCACCTTTTATCAGAGTTTAAATGATGGCA
CTAATACCTTAAGCCCTTAATTGGTTGAACCGCCCTTTTATCAGAGTTTAAACGATGGCA
-----CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBVACTAAAAATGACACCGTTGACTATAATAGCTTTACAATTAACCAATGGCGAGACATATGT
ACTAAAAATCGCCATATTAACATGAACAATTCACCTCCAACCAAGTGGAAATCCACATGT
ACCTACTACCACCACAGAATCTA-----GTTTGACTTGCAATTGGGGTAGTGAGTGCAAG

AATGGTAACACTAATGCTATTGCACGACTGCGCATTTGCCAGTTTCCCGATAATAAAACA
TTTA-TTTTGCTGCCACAGAGAAATCAAATGTTGTCCGTGGTTGGGTTTTGGTTCTTACC
TTTA-TTTTGCTGCCACAGAGAAATCAAATGTTGTCCGTGGTTGGGTTTTGGTTCTTACC
TTT---TTGCTAAGGTCAAAAAACAGCAGATTTTCTAAAGATGGTGTATTTATAGTGAG
TTT---TTGCCAAGGTAAAAACAGCAGATTTTCTAAAGATGGTGTATTTATAGTGAG
TAT---TTGCTAAGGTAAAGAACCTTAAAGCATCTTTGCCCAAAGATTCTATTTATAT
TAT---ATGCTAAGGTAAAGAACCTTAAAGCATCTTTGCCCATAGGCTCGGCTTCATAC

CcoV TTGGGTGACGACAGAAAAATACCATTCTCTGTAGTACCCACAGATAATGGTACGAAATTA
FcoV ACGGGTGCTGACAGAAAAATTCCTTTCTCTGTACATACCCACGGACAATGGAACAAAAATC
TGE TTAAACCATAAGTTCCTATATGTCTCTTAATTGAGAGGCAATTTGGTAAATATGCTG

PRCoV
HCoVOC43
PEDV TTGGGCCCTACTGTTAATGATGTTACAACAGGTCGTAACCTGCCTATTCAACAAAGCCATT
SARSUrba ATGAACAACA-AGTCACAGTCGGTGATTA--TTATTAACAATTCTACTAATGTTGTTATA
SARSTor2 ATGAACAACA-AGTCACAGTCGGTGATTA--TTATTAACAATTCTACTAATGTTGTTATA
BcoV TTTCCTGCTATAACTATAGGTAGTACTT---TTGTAAATACATCCTATAGTGTGGTAGTA
HEV TTTCCTGCTATTACTATAGGTAGTACTT---TTGTAAATCTTCTATAGCATAGTAGTA
MHV TTCCCTACTATAATTATAGGTAGTAATT---TTGTCAACCTTCTCTATAGTGTAGTATTG
RtCoV TTTCCTACTATAATTATAGGTAGTAATT---TTGTAAATCTTCTCTATAGTGTAGTATTG
IBV -----

CcoV TTTGGTCTTGAGTGGGAATGATGACTATGTTACAGCCTATATTAGTGATGAGTCTCACCGT
FcoV TATGGTCTTGAGTGGGAATGATGACTTTGTTACAGCTTATATTAGTGGTCTGTTCTATCAC
TGE TATGGCCTACAATGGTTTGAGATGAGGTTGTTGCTTATTTACATGGTGCTAGTTACCGT

PRCoV
HCoVOC43
PEDV CCAGCTTATATGCGTGATGGAAGATAATTGTTGTCGGCATAACATGGGATAATGATCGT
SARSUrba CGAGCATGTA-----ACTTTGAAT-----TGTGTGACAACCCCTTTCTTTGC
SARSTor2 CGAGCATGTA-----ACTTTGAAT-----TGTGTGACAACCCCTTTCTTTGC
BcoV CAACCACATACTACCAATTGGGATAATAAATTACAAGGTCTCTTAGAGATCTCTGTTTGC
HEV GAGCCTCATACCTCACTTATTAATGGTAATTTACAAGGTTGTTGCAAATTTCTGTTTGT
MHV GAACCGTATA-----ATGGTA-----TAATTAT-GGCATCCATTTGC
RtCoV GAACCATA-----ATGGTA-----TTATTAT-GGCATCTATTTGC
IBV -----

CcoV TTGAATATCAATAAATAATTGGTTTAAACAATGTTACACTC--CTATACTCACGTACAAGCA
FcoV TTGAACATCAATACTAATTGGTTTAAACAATGTCACACTT--TTGTATTACGCTCAAGCA
TGE ATTAGTTTGAATAATCAATGGTCTGGCACTGTCACATTTGGTGATATGCGTGCGACAACA

PRCoV
HCoVOC43
PEDV GTCACTGTTTTTGCTGACAAGATCTATCATTTTTATCTT--AAAAATGATTGGTCCCGCG
SARSUrba TGTTTCTAAACCCATGGGTACACAGACACATACTATGAT---ATTGCA---TAATGCA
SARSTor2 TGTTTCTAAACCCATGGGTACACAGACACATACTATGAT---ATTGCA---TAATGCA
BcoV CAGTATACTATGTGCGAGTACCCACATAAGATTGTCATCCTAAGCTGGG---TAATAAA
HEV CAATACACTATGTGTGAATACCCACATACTATTTGTCATCCTAATTGGG---TAATCAA
MHV CAGTATACCATTGTCAACTACCGTACACGGATTGCAAACCGAATACGGGCGGTAATAAG
RtCoV CAGTATACCATTGTCAATTACCGCACACGGATTGCAAACCTAACCGGCGGTAACAGG
IBV -----

CcoV CCGCCACGTGGCAACACA-GTGCTGCATATGTTTA---TCAAGGTGTTTCAAATTTTACT
FcoV CTGCTACCTGGGAATACA-GTGCTGCATATGCTTA---CCAAGGTGTTTCTAACTTCACT
TGE TTAGAAGTCGCTGGCAGCCTTTGTAGACCTTTGGTGGTTAATCCTGTTTATGATGTCAGT
PRCoV -----ATGAAAAAATTATTTG---TGGTCTTGGTTGTAATGCCATT
HCoVOC43 -----ATGTT-TGTT-TTGCTTGTGTC--ATATGCCTTGT
PEDV TTGCGACAAGATGTTACAATCGCAGAAGTTTGCT-ATGCAATATGTTTATACACCTACC
SARSUrba TTTAATTGCACTTTTCGAGTACATATCTGATGCCTTTTCGCTTGATGTTTCAGAA-----A
SARSTor2 TTTAATTGCACTTTTCGAGTACATATCTGATGCCTTTTCGCTTGATGTTTCAGAA-----A
BcoV CG-CGTAGAACTATGGCATTGGGATACAGGTGTTGTTTCTGTTTATATAAGCG-----T
HEV CG-CATAGAATTATGGCATTATGACACAGATGTTGTTTCTGTTTATACAGGCG-----T
MHV TT-AATTGGCTTTTGGCACACAGAGCTAAAATCCCCTGTGTGCATTTTAAAGCG-----T
RtCoV CT-AATTGGTTTTGGCACACAGATTAAAGGCTCCGGTGTGCATTTTAAAGCG-----T
IBV -----ATGTTGGTAACACCTCTTTTACTAGTGACTCTTTTGTGTGCACTATGT

CcoV TATTACAAGTTAAATAAAACCGCTGGCTTAAAAAGCTATGAATTGTGTGAAGATTATG-A
FcoV TATTACAAGTTAAATAACACCAATGGTCTAAAAACCTATGAATTATGTGAAGATTATG-A

TGE	TATTATAGGGTTAATAATAAAATGGT-----ACTACCGTAGTTTCCAATTGCACTG-A
PRCoV	GATTTATGGA-----GACAAGTTTCCT-----ACTTCGGTAGTTTCCAATTGCACTG-A
HCoVOC43	TGCATATTGCTGGTTGTCAA-ACTACAAATGGGCTGAACACTAGTTACT--CTGTTTGCA
PEDV	TACTACATGCTTAATGTTACTAGTGCAGGTGAGGATGGCATTATTATGAACCTGTACA
SARSurba	AGT----CAGGTAATTTTAAAC---ACTTACGAGAGTTTGTGTTAAAAATAAAGATGGG
SARSTor2	AGT----CAGGTAATTTTAAAC---ACTTACGAGAGTTTGTGTTAAAAATAAAGATGGG
BCoV	AATTTACATATGATGTGAATGCTGATTACTTGTATTTCATTTTTATCAAGAAGGTGGT
HEV	AATTTACATATGATGTGAATGCTGATTATTTATATTTTCACTTTTATCAGGAAGGTGGC
MHV	AATTTACGTTTAAATGTTAATGCCGAATGGCTTTATTTTCATTTTTACCAGCAGGGTGGT
RtCoV	AATTTACGTTTAAATGTTAATGCCGAATGGCTTTATTTTCATTTTTACCAGCAGGGTGGT
IBV	AGTGCTGTTTGTATGACAGTAGTTCTTACGTTTACTACTACCAAAGTGCTTCAGACCA
*	
CcCoV	AT--ACTGCACTGGCTATGCAACCAATGTGTTTGCTCCGACATCAGGTGGTTATATACCT
FCoV	AC--ATTGCACTGGCTATGCTACCAATGTATTGCTCCGACATCAGGTGGTTACATACCT
TGE	TC--AATGTGCTAGTTATGTGGCTAATGTTTTACTACACAGCCAGGAGGTTTTATACCA
PRCoV	TC--AATGTGCTAGTTATGTGGCTAATGTTTTACTATACTACCAGGAGGTTTTATACCA
HCoVOC43	AC--GGCTGTGTTGGTTATTACAGAAATGTATTGCTGTTGAGAGTGGTGGTTATATACCC
PEDV	GCTAATTGCACTGGTTACGCTGCCAATGTATTGCACTGATTCCAATGGCCATATACCA
SARSurba	TTTCTCTATG-----TTTATAAGGGCTAT-----CAACCTATAGATGTAGTTCGTGA
SARSTor2	TTTCTCTATG-----TTTATAAGGGCTAT-----CAACCTATAGATGTAGTTCGTGA
BCoV	ACTTTTATGCATATTTTACAGACTGGTGTGTTACTAAGTTTCTGTTTAAAGTTTAT
HEV	ACTTTTATGCATATTTTACAGACTGGTGTGTTACTAAGTTTCTGTTTAAAGTTTAT
MHV	ACTTTTATGCGTATTATGCGGATGTTTCTTCTGCTACTACGTTTTGTTTAGTATGTAT
RtCoV	ACTTTTATGCGTATTATGCGATGTTTCTTCTGCCACTACGTTTTGTTTAGTTCGTAT
IBV	CCTAGTGGTTGGCATTACAAAGGGGTGCTTATGCGGTAGTTAACATTTCTAGCGAATTT
*	
CcCoV	GATGGATTGAGTTTTAACAAATGGTTTATGCTTACAAACAGCTCCACTTTTGTAGTGGC
FCoV	GATGGATTGAGTTTTAACAAATGGTTTCTTGCTTACAAATAGTTCCTTTTGTAGTGGC
TGE	TCAGATTTTAGTTTTAAATTTGGTTCTTCTAACTAATAGCTCCAGTTGGTTAGTGGT
PRCoV	TCAGATTTTAGTTTTAAATTTGGTTCTTCTAACTAATAGCTCCAGTTGGTTAGTGGT
HCoVOC43	TCCGACTTTGCATTCAATAATGGTTCTTCTAACTAATACCTCATCTGTTGATAGTGGT
PEDV	GAAGGTTTAGTTTTAAATTTGGTTCTTTTATCCAATGACTCCACTTTGTTGCATGGT
SARSurba	TCTACCTTCTGGTTTTAACACT--TTGAAACCTATTTTTAAGTTGCCTCTT-----
SARSTor2	TCTACCTTCTGGTTTTAACACT--TTGAAACCTATTTTTAAGTTGCCTCTT-----
BCoV	TTAGGCACGGTGCTTTCACATTATTATGTTATGCTGCTTGTGCTTGTCT-----
HEV	TTAGGCACGTGCTGTCACATTATTATGTTATGCCATTGACTTGTAAAT-----
MHV	ATTGGTGATGTGTTAACACAATATTTTGTGTTGCCTTATATGTGTACTCTCACTACAACA
RtCoV	ATTGGTGCTGTGTTAACACAGTATTTTGTGTTGCCTTATATGTGTAGTCCCACTACCTCA
IBV	AATAATGCAGGCTCTTCATCAGGGTGACTGTTGGTATTATTTCATGGTGGTGGTGGT
*	
CcCoV	AGATTGTAAACAAATCAACCGCTGCTAGT--TAATTGCTTGTGGCCAGTGC--CCAGTTT
FCoV	AGGTTTGTAAACAAATCAACCATTTATGAT--TAATTGCTTGTGGCCAGTGC--CCAGTTT
TGE	AAATTAGTTACCAACAGCCGTTATTAGT--TAATTGCTTATGGCCAGTGC--CTAGCTT
PRCoV	AAATTAGTTACCAACAGCCCTATTAGT--TAATTGCTTATGGCCAGTGC--CTAGCTT
HCoVOC43	GTTGTGAGGAGTTTTAGCCTTTGTTGCT--TAATTGCTTATGGTCTGTTT--CT--GGC
PEDV	AAAGTGGTTTTCAACCAACCTTGTGGT--CAATTGCTTTTGGCCATTG--CTAAGAT
SARSurba	GGTATTAAACATTACAAATTTAGAGCCATTCTTACAGCCTTTTCACC--TGC--TCAAGAC
SARSTor2	GGTATTAAACATTACAAATTTAGAGCCATTCTTACAGCCTTTTCACC--TGC--TCAAGAC
BCoV	AGTGCTATGACTTTAGAATATTGGGTTACACCTCTCACTTCTAAACAATAT--TTACTAG
HEV	AGCGCTTATCTTTAGAATACTGGGTTACACCTCTCACTACTAGACAATTT--CTTCTAG
MHV	GGTGTCTTTTACCAGCAGTATTGGGTTACACCTCTTGTCAAGCGCCAATAT--TTATTTA
RtCoV	GGTGTCTTCTCACCAGTATTGGGTTACACCACTTGTTAAGCGCCAATAT--TTATTTA
IBV	AATGCTTCTTCTATAGCTATGACGGCACCGTCATCAGGTATGGCTTGGTCTAGCAGTCAG
*	
CcCoV	TGGCGTCGCAGCACAGAATT--TTGTTTTGAAGGTGCTCAGTTTAGCCAAATGTAACGGT
FCoV	TGGGTAGCAGCACAGAATT--TTGTTTTGAAGGTGACAGTTTAGCCAAATGTAATGGT
TGE	TGAAGAAGCAGCTTCTACATT--TTGTTTTGAAGGTGCTGGCTTTGATCAATGTAATGGT
PRCoV	TGAAGAAGTAGCTTCTACATT--TTGTTTTGAAGGTGCTGACTTTGATCAATGTAATGGT
HCoVOC43	TTGCGGTTTACTACTGGTTTTGTCTATTTTAAATGGTACTGGGAGAGGTGATTGTAAGGT

PEDV TTAGGACTAG-GCCAATTTT-TCTCATTCAATCACACGATGGATGGCGTTTGTAAATGGA
SARSurba ATTTGGGGCAC-GTCAGC--TGCAGCCTATTTTGTGGCTATTTAAAGCCAACTACATTT
SARSTor2 ATTTGGGGCAC-GTCAGC--TGCAGCCTATTTTGTGGCTATTTAAAGCCAACTACATTT
BcoV CTTTCAATCAA-GATGGTGTATTTTAAATGCTGTTGATTGTAAGAGTGATTTTATGAGT
HEV CCTTTGACCAG-GATGGTGTATTTTATACCATGCTGTTGATTGTGCTAGTAGTTTATGAGT
MHV ATTTTAAATCAA-AAGGGTATTATTACTAGTGCTGTTGATTGTGCTAGTAGTTATACCAGC
RtCoV ATTTTAAACCAA-AAGGGTATTATTACTAGCGCTGTTGATTGTGCTAGTAGTTATACCAGT
IBV TTTTGTACTGCACACTGTAATTTTCAGATACTACAGTGTGTTGTACACATTGTTATAAA

CcoV GTTTCCTTTAAATAATACAGTAGATGTTATTAGATTTAACCTTAATTTCACTACAGATGTA
FcoV GTGCTCTTTAAATAACACAGTGGATGTTATTAGATTCAACCTTAATTTCACTGCAGATGTA
TGE GCTGTTTTTAAATAAATCTGTAGACGTCATTAGGTTCAACCTTAATTTTACTACAAATGTA
PRCoV GCTGTTTTTAAATAACACTGTAGACGTCATTAGGTTTAACTTAATTTTACTACAAATGTA
HCoV43 TTTTCCTCAGATGTTTGTCTGATGTCATACGTTACAACCTCAATTTTGAA-----GAA
PEDV GCTGCTGTGGATCGTGCCCGAGAGGCTCTGAGGTTTAAATTAATGACACCTC---CGTC
SARSurba ATGCTCAAGTATGATGAAATGGTACAATCACAGATGCTGTTGATTGT-----T
SARSTor2 ATGCTCAAGTATGATGAAATGGTACAATCACAGATGCTGTTGATTGT-----T
BcoV GAGATTAAGTGTAAACACTATCTATAGCACCCTACTGGTGTATGAATTAACCGGT
HEV GAGATTATGTGTAAACTCTTCAATTACACCACCTACTGGTGTATGAATTAACCGGT
MHV GAAATAAAGTGTAAAGACCAAGTATGAATCCCAATACGGGAGTTTATGATTATCCGGT
RtCoV GAAATAAAGTGTAAAGTCTAAAGTATGAATCCCAATACGGGAGTCTATGATTATCCGGT
IBV CATGGTGGGTGTCCTTTAACTGGCATGCTTCAACAGAATCTTATACGT-----GTT

CcoV CAATCTGGCATGGGTGCTACAGTATTTTCACTGAATACAACAGGCGGTGTCATTCTTGAG
FcoV CAATCTGGTATGGGTGCTACAGTATTTTCACTGAATACAACAGGCGGTGTCATTCTTGAA
TGE CAATCAGGTAAGGGTGCCACAGTGTTTTCATTGAACACAACGGGTGGTGTCACTCTTGAA
PRCoV CAATCAGGTAAGGGTGCTACAGTGTTTTTCATTGAACACAACGGGTGGTGTCACTCTTGAA
HCoV43 AACCTTAGACGTGGAACCAATTTGTTT-----AAAACATCTTATGGTGTGTTGTTT
PEDV ATTCTTGCTGAAGGCTCAATTGTACTT-----CATACTGCTTAGGAACAATCTTCT
SARSurba CTCAAAATCCA-CTTGCTGAACCTCAAAATGCT---CTGTTAAGAGCTT---TGAGATTGAC
SARSTor2 CTCAAAATCCA-CTTGCTGAACCTCAAAATGCT---CTGTTAAGAGCTT---TGAGATTGAC
BcoV TACACTGTTAGCCCAATGTCAGATGTTTACCGAGTATACCTAATCTTCCCGATTGTAAT
HEV TACACAGTCAACCTGTTGCCACTGTATATCGTAGAATACCTGATTACCCAATTGCGAT
MHV TACACCGTCCAACCTGTAGGATTAGTGTACCGGCGTGTAGAAATTTGCCTGATTGTAAA
RtCoV TACACCGTCCAACCTGTAGGATTAGTGTACCGGCGTGTAGAAATTTGCCTGATTGTAAA
IBV TCTGCTATGAAAAATGGCCAGCTTTTCTATAATTTAACAGTTAGTGTAGCTAAGTACCCT

CcoV ATTTCTTGTTATAATGACACAGTGAAGTGAAGTCTAGT-TTCTACAGTTATGGTGAATTC
FcoV ATTTCTTGTTATAATGACACAGTGAAGTGAAGTCTAGT-TTCTACAGTTATGGTGAATTC
TGE ATTTCTTGTTATA-----CAGTGAAGTGAAGTCTAGT-TTCTACAGTTATGGTGAATTC
PRCoV ATTTCTTGTTATAATGACACAGTGAAGTGAAGTCTAGT-TTCTACAGTTATGGTGAATTC
HCoV43 TATTGTACCAACCACTTTAGTTTC-----AGGTGATGCTACATACCAATTTGGTACA
PEDV TTTGTTTGCAGTAATTCCTCAGATCCTCATTAGCCATCTTGCCATACCTCTGGGTGCT
SARSurba AAAGGAATTTACCAGACCTCTAATTTAGGGTGTGTTCC-CTCAGGAGATGTTGTGAGATT
SARSTor2 AAAGGAATTTACCAGACCTCTAATTTAGGGTGTGTTCC-CTCAGGAGATGTTGTGAGATT
BcoV ATAGAGGCTTGGCTTAATGATAAGTCCGTGTCCTCTCCATTAAATTTGGGAACGTAAAGAC
HEV ATCGAAGCTTGGCTTAATTTAGAGACCTTTCTTGCCTCTTAATTTGGGAACGTAAAGAC
MHV ATCGAAGCTTGGCTTAATTTAGAGACCTTTCTTGCCTCTTAATTTGGGAACGTAAAGAC
RtCoV ATTGAGGAATGGTGGCTGCTAACACAGTACCCTCTCTCTCAATTTGGGAGCGCAAAACA
IBV ACTTTTAGATCATTTAGTGTGTTAATAATTTAACATCCGTATATTTAAATGGTGAATCTT

CcoV ATTCGGCGTAACTGATG-GACCAGTACTGTTATGTACTCT-ACAATGGCACAGCTCTT
FcoV GTTCGGCATAACTGACG-GACCAGTACTGTTATGTACTCT-ACAATGGCACAGCTCTT
TGE GTTCGGCGTAACTGATG-GACCAGTACTGTTACGTACTCT-ATAATGGCACAGCTCTT
PRCoV GTTCGGCGTAACTGATG-GACCAGTACTGTTACGTACTCT-ATAATGGCACAGCTCTT
HCoV43 GTTTTGGGCAATTTT---ATTGCTTTGTAAATACTACTATTGGCAATGAACTACGTCT
PEDV ACTGAAGTACCCTACT---ATTGCTTTCTTAAAGTGGATACTTACAATCCACTGTTTAT
SARSurba CCTTAATATTACAA-----ACTTGTGCTCTTTTGGAGAGGTTTAAATGCTACTAAATTC
SARSTor2 CCTTAATATTACAA-----ACTTGTGCTCTTTTGGAGAGGTTTAAATGCTACTAAATTC

BcoV TTTTCAAATTGTAATTTTAAATATGAGCAGCCTGATGTCTTTTATTCAAGGCAGACTCATT
HEV TTTTCTAATTGTAATTTTAAATATGAGCAGCCTGATGTCTTTTATTCAAGGCAGACTCTTT
MHV TTTCAAATTTGTAACCTCGACCTGAGCAGTCTATTAAGATTGTTCAAGGCTGAGTCACTC
RtCoV TTTCAAATTTGTAACCTCAACCTGAGCAGTCTATTAAGATTGTTCAAGGCTGAGTCACTC
IBV GTTACACCTCTAATGAGACCATAGATGTTACATCTGCAGGTGTTATTTTAAAGCTGGT

CcoV AAGTATT-TAGGAACATTACCACCTAGTGTCAAGGAAATTGCTATTAGTAAGTGG-----
FcoV AAATATT-TAGGAACATTACCACCTAGTGTCAAGGAAATTGCTATTAGTAAGTGG-----
TGE AAGTATT-TAGGAACATTACCACCTAGTGTCAAGGAGATTGCTATTAGTAAGTGG-----
PRCoV AAGTATC-TAGGAACATTACCACCTAGTGTCAAGGAGATTGCTATTAGTAAGTGG-----
HCoVOC43 GCTTTTG-TGGGTGCACCTACCTAAGACAGTTCGTGAGTTTGTATT-TCACGCACA-----
PEDV AAATTCT-TGGCTGTTTACCTCCTACTGTCAAGGAAATTGTCATCAACCAAGTAT-----
SARSurba CCTTCTG-----TCTATGCATGGGAGAGAAAAAAAT---TTCTAATTGTGTGTCT---
SARSTor2 CCTTCTG-----TCTATGCATGGGAGAGAAAAAAAT---TTCTAATTGTGTGTCT---
BcoV ACTTGTAATAATATTGATGCTGCTAAGATATATGGTATGTGTTTTCCAGCATAACTATA
HEV GGTGTGAACAATATTGATGCTTCTCGCTTATATGGTATGTGTTTTGGTAGCATTACTATT
MHV TCATGTAGTAATATAGATGCTTCCAAGGTTTATGGTATGTGCTTTGGTAGTATATCTATA
RtCoV TCATGTAGTAATATAGATGCTTCCAAGGTTTATGGTATGTGCTTTGGTAGCATATCTATA
IBV GGACCTA-TAACTTATAAAGTTATGAGAGAAGTTAAA---GCCCTGGCTTATTTT-----

CcoV GGACATTTTATATTAATGGTTACAATTTCTTTAGCACGTTTCTATTGATTGTATAGCT
FcoV GGCCATTTTATATTAATGGTTACAATTTCTTTAGCACATTTCTATTGTTGTATATCT
TGE GGCCATTTTATATTAATGGTTACAATTTCTTTAGCACATTTCTATTGATTGTATATCT
PRCoV GGCCATTTTATATTAATGGTTACAATTTCTTTAGCACATTTCTATTGATTGTATATCT
HCoVOC43 GGACATTTTATATTAATGGCTATCGCTATTTCACTTTAGGTAATGTAGAAGCCGT----
PEDV GGTGATGTTTATGTCAATGGGTTTGGCTATTGTCATCTCGGTTTGTGGATGCTGTGACA
SARSurba GATTACTCTGTCTCTACAAC--TCAACATTTTTTCAACCTTTAAGTGTATGGCGTTT
SARSTor2 GATTACTCTGTCTCTACAAC--TCAACATTTTTTCAACCTTTAAGTGTATGGCGTTT
BcoV GATAAGTTTGCTATACCAATGGTAGGAAGGTTGACCTACAATTGGGCAATTTGGGCTAT
HEV GATAAGTTTGCTATACCAATAGACGCGGAGTTGATTGTCAGCTAGGCAACTCTGGGTTT
MHV GACAAGTTTGGGATACCAATAGACGCGGAGTTGATTGTCAGCTAGGCAACTCTGGGTTT
RtCoV GATAAATTTGCAATACCAACAGTTCGCGTGTGATCTTCAGCTAGGTAATCGGGTCTT
IBV GTTAATGGTACTGCACAAGATGTTATTTTGTGTGATGGATCACCTAGAGGCTTGTTAGCA

CcoV TTTAATTTAA-----CCACTGGTGTAGTGGAGCAT-TTTGGACAATTGCTTA
FcoV TTTAATTTAA-----CCACTGGTGTAGTGGAGCTT-TTTGGACAATTGCTTA
TGE TTTAATTTGA-----CCACTGGTGATAGTGACGTTT-TCTGGACAATAGCTTA
PRCoV TTTAATTTGA-----CTACTGGTGATAGTGACGTTT-TCTGGACAATAGCTTA
HCoVOC43 --TAATTTCA-----ATGTCACTACTGCAGAAACCACTGATT-TTTGTAAGTGTGCGTT
PEDV ATTAATTTCACTGGTGTGCTGACGATGACGTTTTCAGGTT-TCTGGACCATAGCATC
SARSurba CTGC---CAC-----TAAGTTGAATGATCTTTGCTT-CTCCAATGTCTATGCA
SARSTor2 CTGC---CAC-----TAAGTTGAATGATCTTTGCTT-CTCCAATGTCTATGCA
BcoV TTGCAGTCTT-----TTAACTATAGAATTGATACTA-CTGCTACAAGT-TGTC
HEV TTACAATCTT-----TTAATTATAAGATTGACACTG-CTGTTAGCAGT-TGTC
MHV TTGCAATCCT-----TTAATTACAAAATAGATACAA-GAGCTACTTCG-TGTC
RtCoV TTGCAATCTT-----TTAATTATAAAATGATACAA-GAGCGACCTCG-TGTC
IBV TGCCAGTATA-----ATACTGGCAATTTTTCAGATGGCTTTTATCCTTTTACT

CcoV TACG-TCGTACACAGAAGCATTAGTACAA-GTTGAAAACACAGCTATTAAAAAGGTGACG
FcoV CACA-TCGTATACTGAAGCATTAGTACAA-GTTGAAAACACAGCTATTAAAAATGTGACG
TGE CACA-TCGTACACTGAAGCATTAGTACAA-GTTGAAAACACAGCTATTACAAAGGTGACG
PRCoV CACA-TCGTACACTGAAGCATTAGTACAA-GTTGAAAACACAGCTATTACAAATGTGACG
HCoVOC43 AGCT-TCTTATGCTGACGTTTGGTTAAT-GTGTCACAAACCTCTATTGCTAATATAATT
PEDV GACT-AATTTTGTGATGCACTCATCGAG-GTTCAAGGAACCTCCATTGAGCGTATTCTT
SARSurba GATTCTTTTGTAGTCAAG--GGAGATGAT-GTAAG-ACAAATAGCGCCAGGACAACTGG
SARSTor2 GATTCTTTTGTAGTCAAG--GGAGATGAT-GTAAG-ACAAATAGCGCCAGGACAACTGG
BcoV AGTTGTATTATAATTTACCTGCTGCTAAT-GTTTCTGTTAGCAGGTTAATCCTTCTACT
HEV AACTCTATTATAGTTGCTGACGAAAC-GTATCTGTCACTCATTATAATCCTTCTACT
MHV AGCTCTATTATAGTCTTGCAAAAAATAAT-GTCACTGTCAATAACCATTAACCCGCTCTCT

RtCoV IBV	AGCTCTATTACAGTCTTGACACAAGATAAT-GTCACTGTCATTAACCACAACCCATCCTCC AATAGTAGTTTAGTTAAGCAGAAGTTTATTGTCTATCGTGAAATAGTGTTAATACTACT * **
CcoV FcoV TGE PRCoV HCoVOC43 PEDV SARSUrba SARSor2 BcoV HEV MHV RtCoV IBV	TATT-GTAACAGTCAC--ATTAATAACATCAAATGTTCTCAACTTACTG---CTAATTT TATT-GTAACAGTCAC--ATTAATAACATTAATGTTCTCAACTTACTG---CTAATTT TATT-GTAATAGTCAC--GTTAATAACATTAATGCTCTCAACTTACTG---CTAATTT TATT-GTAATAGTTAT--GTTAATAACATTAATGCTCTCAACTTACTG---CTAATTT TATT-GCAACTCTGTT--ATTAACAGACTGAGATGTGACCAGTTGTCCT---TTGATGT TATT-GTGATGATCCT--GTTAGCCAACCTCAAGTGTCTCAGGTTGCTT---TTGACCT TGTT-ATTGCTGATTATAATT-----ATAAATGCCAGATGATTTCAT-----GG--- TGTT-ATTGCTGATTATAATT-----ATAAATGCCAGATGATTTCAT-----GG--- TGGA-ATAGGAGATTTGGTTTTACAGAACAATTTGTTTTAAGCCTCAACCTGTAGGTGT TGGA-ATAGAAGGTATGGGTTT---AATAATCAGAGTTTGGTTCCAG---AGG--- TGGA-ACAGGCGTTATGGGTTT---AATGATGTGGCTACATTTGGAAC---TGG--- TGGA-ATAGGCGTTATGGATTT---AATGACGTGGCTACATTTTCATAG---TGG--- TGTCAGTTACACAATTTTCATTTTT--CATAATGAGACTGGCGCCAACCC----- * **
CcoV FcoV TGE PRCoV HCoVOC43 PEDV SARSUrba SARSor2 BcoV HEV MHV RtCoV IBV	GCAAAATGGTTTTTACCCTGTTG---CTTCAAGTGAAGTTGGTCTTGTCATAAAGAGTGT GAATAATGGATTTTATCCTGTTG---CTTCAAGTGAAGTAGGTTTCGTTAATAAGAGTGT GAATAATGGATTTTATCCTGTTT---CTTCAAGTGAAGTTGGTCTTGTCATAAAGAGTGT GAATAATGGATTTTATCCTGTTT---CTTCAAGTGAAGTTGGTCTTGTCATAAAGAGTGT ACCAGATGGTTTTTATCTACAA---GCCCTATTCAATCCGTTGAGCTACCTGTGTCTAT TGACGATGGTTTTTACCCCATCT---CTTCTAGA-AACCTTCTGAGTCACGAACAGCCAA -----GTTGTGTCCTTGCTTGGAAATACTAGGAACATTGATGCTACTTCAACTGGTAA -----GTTGTGTCCTTGCTTGGAAATACTAGGAACATTGATGCTACTTCAACTGGTAA TTTTACTCATCATGATGTTGTTT---ATGCACAACATTGTTTTAAAGCTCCCAAAATTT -----CCTTCATGATGCTGTTT---ATTCACAGCAATGTTTTAATACACCTAACACATA -----TAAACATGACGTTGCTT---ATGCTGAGGCTTGTTTTACCGTGGGAGCATCATA -----TGAACATGACGTTGCTT---ATGCAGAGGCATGTTTCACTGTTGGAGCTTCATA -----TAATCCTAGTGGTGTTT---AGAATATTCAAACCTTACCAACAAAAACAGCTCA *
CcoV FcoV TGE PRCoV HCoVOC43 PEDV SARSUrba SARSor2 BcoV HEV MHV RtCoV IBV	TGTGTTACTACCTAGTTTCTATTC---ACATACCAGTGTTAATATAACTATTGATCTTGG TGTGTTATTACCTAGCTTTTTTAC---ATACACCGCTGTCAATATAACCATTGATCTTGG TGTGTTACTACCTAGCTTTTTACAC---ACATACCATTGTTAACATAACTATTGGTCTTGG TGTGTTACTACCTAGCTTTCTGAC---ACATACCATTGTTAACATAACTATTGGTCTTGG TGTGTCGCTACCTGTTTATCATAA---ACATACGTTTATTGTTGTGTACGTTGACTTCAA TTTCTT-TTGTTACTTTTGCCATCA---TTAATGATCATTCTTTTGTAAAT--ATTACTG T-TATAATTATAAAT---ATAG-----GTATCTTAGACATGGCAAGCTTAG T-TATAATTATAAAT---ATAG-----GTATCTTAGACATGGCAAGCTTAG C-TGTCCGTGTAAATGGATGG-----GTCTTTGTGTGATAGGTAATGGTCTTGGTATAG T-TGTCCCTGTAGA---ACAA-----GTCA--ATGCATAGGTGGTG---CAGGCACAG T-TGCCCTTGCGCGAAGCCAGCATAGTGTGCGCATGTACCACTGGAAACCTAAGTTTG T-TGCCCTTGCGGAAGCCAGCACAGTCTATTTCATGTGTACAGGTAACCTAAGTCTG G-AGTGGTTATTATAATTTTAA-----TTTTCTCTTCTGAGTAGTTTTGTTTATAAGG *
CcoV FcoV TGE PRCoV HCoVOC43 PEDV SARSUrba SARSor2 BcoV HEV MHV RtCoV IBV	TATGAAGCGTAGTG-TTACGGTCA--CCATAGCCTCACCATTAAAGTAACATCACACTACC TATGAAGCTTAGTGGTTATGGTCAACCCATAGCCTCGACACTAAGTAACATCACACTACC TATGAAGCGTAGTGGTTATGGTCAACCCATAGCCTCAACATTAAGTAACATCACACTACC TATGAAGCGTAGTGGTTATGGTCAACCCATAGCCTCAACGCTAAGTAACATCACACTACC ACCTCAGAGTGGCGGTGGCAAGTG-----CTTAACTGTTATCCTGCT--- TCTCT-----GCGGCTTTTGGTG-----GTCTTAGTAGTGCCAATCT--- GCCCTT-TGAGAGAGACATATCTAAT----GTGCCTTTCT-----CCCCTGA-- GCCCTT-TGAGAGAGACATATCTAAT----GTGCCTTTCT-----CCCCTGA-- ATGCTGGTTATAAAATAGTGGTATAGGCACTTGTCTGCA--GGTACTAATTATTAAAC GAACCTGTCTGTAGGCAACCATGTGCGCAAGTGTGCT--G---CAGTTACAAA-- CCAATTGCCCTACAGGCACCTCGAATCGTGAGTGCACTGTTATGCCATTGGCTAATAAT- CTAATTGCCCAACAGGTACCTCGAATCGTGAGTGTAAATGTTCAAGGCTTCAGGTTTTAA- AGTCTAATTTTATGTATGGATCTTAT-----CACCCAAGTTGTAATTTAGAC-

CcoV AATGCAGGATAATAACATAGACGTGTACTGTATTTCGTTCTAACCAATTCTCAGTTTATGT
FcoV AATGCAGGATAACAATACTGATGTGTACTGTATTTCGTTCTAACCAATTCTCAGTTTATGT
TGE AATGCAGGATCACAACACCGATGTGTACTGTATTTCGTTCTGACCAATTTTCAGTTTATGT
PRCoV AATGCAGGATAACAACAACGATGTGTACTGTGTTCGTTCTGACCAATTTTCAGTTTATGT
HCoVOC43 --GGTGTAAATATTACACTGGCCAATTTT--AATGAACTAAAGGGCCTT--TGTGTGT
PEDV --CGT-TGCATCTGACACT----ACTATC--AATGGGTTA--GTTCTT--TCTGTGT
SARSUrba -----TGGCAAACCTTGCACCCACCTGCTCTTA--ATTGT-----TATTG
SARSTor2 -----TGGCAAACCTTGCACCCACCTGCTCTTA--ATTGT-----TATTG
BcoV TTGCCATAATGCTGCCCAATGTGATTGTTGTGCACTCCCG--ACCCATTACATCTAA
HEV -----GCTACTAAGTGTACTTGTGGTGTCAACCAG--ATCCTTCCACATATAA
MHV -----CAATTTAAGTGTGATTGCACTTGTAAACCCTA--GTCC-----TCTAA
RtCoV -----GTCTAAGTGCGATTGCACATGTAAACCCTA--GTCC-----TCTAA
IBV -----TAGAACTATTAAATAATGGCTTGTGGTTTA--ATTC-----ACTTTC

CcoV TCATTCCACTTGCAAAAGTTCTTTATGGGATAACAATTTTAATTTCAGCATGTACCGACGT
FcoV TCATTCCACTTGCAAAAGTTCTTTATGGGACAATATTTTAACTCAAGACTGCACGGATGT
TGE TCATTCTACTTGCAAAAGTGCTTTATGGGACAATATTTTAAAGCGAAACTGCACGGACGT
PRCoV TCATTCTACTTGCAAAAGTGTTTATGGGACAATGTTTAAAGCGAAACTGCACGGACGT
HCoVOC43 TGACACATC-----ACACTTCACTACCAATACGTTGCT-----GTTTATGCCAATGT
PEDV TGACACTAG-----ACAATTTACCATTACACTGTTTTAT-----AATGTTACAAACAG
SARSUrba GCCATTAAATGATTATG--GTTTTTACAC-----CACTACTGGCATTGGCTACCAACC
SARSTor2 GCCATTAAATGATTATG--GTTTTTACAC-----CACTACTGGCATTGGCTACCAACC
BcoV ATCTACAGGGCCTTACAAGTGCCCCCAACTAAATACTTAGTTGGCATAGGTGAGCACTG
HEV AGGTGTAAACGCGCTGGACTTGTCCGCAATCTAAAGTTTCTATACAACAGGTGAGCATTG
MHV CCACCTATGATCTTAGA--TGTCTCAAGCAAGAAGCATGCTTGGCGTAGGTGATCATTG
RtCoV CCACCTATGATCTTAGA--TGTCTCAAGCGCGGAGCATGCTTGGCGTAGGTGATCATTG
IBV AGTTTCAATTGCTTACGGTCTCTTCAAGGTGGTTGCAA----GCAATCTGCTTTTAAAG

CcoV TT-TAGACGCCACAGCTGTTATAAAAACTGGTACTTGTC---CTTTCTCATTTGATAAAT
FcoV TT-TAGAGGCTACAGCTGTTATAAAAACTGGTACTTGTC---CTTTCTCATTTGATAAAT
TGE TT-TAGATGCCACAGCTGTTATAAAAACTGGTACTTGTC---CTTTCTCATTTGATAAAT
PRCoV TT-TAGATGCCACAGCTGTTATAAAAACTGGTACTTGTC---CTTTCTCATTTGATAAAT
HCoVOC43 TGGTAGGTGGAGTGCTAGTATTA-ACACGGGAAATTGCC---CTTTTCTTTTGGCAAAG
PEDV TTAT-GGTTATGTGTCTAAATCACAGGATAGTAATTGTC---CTTTCACCTTGCAATCTG
SARSUrba TT-ACAG-----AGTTGTAGTACTTTCTTTTGA-----ACTTTTAAATGCACCGGC
SARSTor2 TT-ACAG-----AGTTGTAGTACTTTCTTTTGA-----ACTTTTAAATGCACCGGC
BcoV TT-CGGGTCTTGCTATTAAAGTGATTATTGTGGAGGTA---ATCCTTGACTTGCCAAAC
HEV CC-CTGGTTTGGGCTTTGTGGAGGATGATTGCTCTGGCA---ACCCTTGCACTTGTAAC
MHV TG-AAGGTCTAGGAGTTTGAAGATAAATGTGGTGGCAGCAACACCTGCAATTGTTCTG
RtCoV TG-AAGGTCTAGGATTTTGAAGATAAATGTGGTGGCAGCAACATATGCAATTGTTCTG
IBV GT--AGAGCAACTTGTGTTATGCTTATTATATGAGG-----TCCTTCGCTGTG

CcoV TGAATAATTACTTAACCTTTTAAACAAGTTCTGTTTGTGCGTTGAATCCCGTTGGTGCCAACT
FcoV TGAACAATTACTTGACTTTTAAACAAGTTCTGTTTGTGCGTTGAGTCCTGTTGGTGCTAATT
TGE TGAACAATTACTTAACCTTTTAAACAAGTTCTGTTTGTGCGTTGAGTCCTGTTGGTGCTAATT
PRCoV TGAACAATTACTTAACCTTTTAAACAAGTTCTGTTTGTGCGTTGAGTCCCGTTGGTGCTAATT
HCoVOC43 TTAATAACTTTGTTAAATTTGGCAGTGTATGTTTTTCGCTAAAGGATATACCCGGTGGTT
PEDV TTAATGATTACCTGTCTTTTAGCAAATTTGTGTTTCAACCAGCCTTTTGGCTGGTGCTT
SARSUrba CACGG---TTTGTGGACCAAAT-TATCCACTGACCTTATTAAGAACCAGTGTGTCAATT
SARSTor2 CACGG---TTTGTGGACCAAAT-TATCCACTGACCTTATTAAGAACCAGTGTGTCAATT
BcoV CACAAGCATTTTGGGTTGGTCTGTTGACTCTTGTTTACAAGGGGATAGGTGTAATATTT
HEV CACAGGCTTTTATAGGCTGGAGTTCAGAACTTGTGTTGCAAAATGGTAGGTGTAATATTT
MHV CTCATGCCTTTGTTGGCTGGGCTAAGGATAGTTGCTTGGCTAATGGCCGCTGTACATTT
RtCoV CTGATGCCTTTGTTGGCTGGGCTATGGACAGCTGTCTATCTAATGCCCGCTGCCATATTT
IBV TAAAGGTGTTTATTAGGTGAGTTAGATCATAATTTGAATGTGACTGTTA-GTTTTATG

CcoV GTAAGTTAGATGTTGCCGCCGTACAAGAACCAATGAGCAGGTTTTTGAAGTT---TAT
FcoV GCAAGTTTATGTTGCTGCACGTACAAGAACCAATGAGCAGGTTGTTAGAAGTC---TAT

TGE
PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV

GTAAGTTTGATGTAGCTGCCGTACAAGAACCAATGAGCAGGTTGTTAGAAGTT---TGT
GTAAGTTTGATGTAGCTGCCGTACAAGAACCAATGATCAGGTTGTTAGAAGTT---TGT
GCGCAATGCCTATAGTGGCTAATTGGGCTTATAGTAAGTACTATACTATAGGCTCATGT
GTACCATAGATCTTTTGGTTACCCTGCGTTCGGTAGTGGTGTAACTCCTTCTTCAAAGAGAT---TTC
TTAATTTTAATGGACTCACTGGTACTGGTGTGTTAACTCCTTCTTCAAAGAGAT---TTC
TTAATTTTAATGGACTCACTGGTACTGGTGTGTTAACTCCTTCTTCAAAGAGAT---TTC
TTGCTAATTTTATTTTTCATGATGTTAATAGTGGTACTACTTGTCTACTGATT---TAC
TTGCTAATTTTATTTTTCATGATGTTAATAGTGGTACTACTTGTCTACTGATT---TAC
TTAGTAATTTTGATGTTAAATGGCATTAAATAGTGGTACTACATGTTCCATGGATT---TGC
TTAGTAATTTTGATGTTAAATGGCATTAAATAGTGGTACTACATGTTCCACGGATT---TTC
TTACTAAGAGCGGTGGCTCTCGTATACAAACAGCCACTGAACCGCCAGTTATAA---CTC

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV

ATGTAATATATGAAGAAGGAGACAACATAGTGGGTGTACCGTCTGATAATAGTGGTTT-G
ATGTAATATATGAAGAAGGAGACAACATAGTGGGTGTACCGTCTGATAATAGCGGTCT-G
ATGTAATATATGAAGAAGGAGACAACATAGTGGGTGTACCGTCTGATAATAGTGGTGT-G
ATGTAATATATGAAGAAGGAGACAGCATAGTGGGTGTACCGTCTGACAAATAGTGGTTT-G
ATGTTTCTTGGAGTGATGGTGATGGAATTACTGGCGTCCCAACCTGTTGAGGGTGTTA
ATTTTCAATTCACAAAAGGTGAGTTGATTACTGGCACGCTAAACCACTTGAAGGTATCA
AACCATTT--CAACAATTTGGCCG-TGATGTTTCTG---ATTTCAGTGATTCCGTTTGA
AACCATTT--CAACAATTTGGCCG-TGATGTTTCTG---ATTTCAGTGATTCCGTTTGA
AAAAATCAACACAGACATAATTCTTGGTGTGTTGTTAATTATGATCTTTATGGTATTA
AACAGGGTAATACTATTACTACTGATGTTTGTGTTAATTATGACCTATATGGCATT
AATTGCCTAATACTGAAGTGGTCACTGGCGTCTGCGTCAAATATGACCTCTACGGTATAA
AATTGCCTAATACTGAAGTGGTCACTGGCGTCTGCGTCAAATATGACCTCTACGGTATTA
AAAACAATTATAATAATATTACTTTAAATACTTGTGTTGATTATAATATATATGCGAGAA

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV

CACGATTTGTCTAGTGTGCACTTAGACTCTTGT-ACAGATTACAATATATATGGTAGAAC
CACGATTTGTCTGTGCTACACCTAGACTCCTGT-ACAGATTACAATATATATGGTAGAAC
CACGATTTGTCTAGTGTGCTACACCTAGACTCCTGT-ACAGATTACAATATATATGGTAGAAC
CACGATTTGTCTAGTGTGCTACACCTAGACTCCTGT-ACAGATTACAATATATATGGTAGAAC
GTTCCCTTATGAATGTTACAT-TGGACAAATGT-ACTAAATATAATATTTATGATGTATC
CAGACGTTTCTTTATGACTC-TGGATGTGTGT-ACCAAGTATACTATCTATGGCTTTAA
GATCCTAAAACATCT-----G-AAAT-----ATTA-GACATTTACCTTGCTC
GATCCTAAAACATCT-----G-AAAT-----ATTA-GACATTTACCTTGCGC
CAGGCCAAGGTATTTTGTG--AGGTTAATGCGACTTATTATAATAGTTGGCAGAACCT
CAGGCCAAGGTATTTTATAG--AAGTTAATGCCACTTATTATAATAGTTGGCAGAATCT
CAGGCCAAGGTATTTTAAAG--AGGTTAAGGCTGACTATTATCATAGTTGGCAGAACT
CAGGCCAAGGTATTTTAAAG--AGGTTAAGGCTGATTATTACAATAGTTGGCAGAACCT
CTGGCCAAGGTATTTATT-----ACTAATGTGACCGACTCAGCTGTTAGTTATAATTA

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV

TGGTGTGGTATTATTAGAAAACTAACAGCACACTACTTAGTGGCTTATATT-ACACAT
TGGTGTGGTATTATTAGACGAACCTAACAGTACGCTACTTAGTGGCTTATATT-ACACAT
TGGTGTGGTATTATTAGACAACTAACAGGACGCTACTTAGTGGCTTATATT-ACACAT
TGGTGTGGTATTATTAGACAACTAACAGGACGATACTTAGTGGCTTATATT-ACACAT
TGGTGTGGGTGTTATTCGCTTAGCAATGACACCTTTCTTAATGGAATTACGT-ACACAT
AGGTGAGGGTATTATTACCTTACAAATCTAGCATTTTGGCAGGTGTTTATT-ATACAT
TTTTGGGGGTGTAAGTG-TAATTACACCTGGAACAAATGCTTCATCTGAAGTT-GCTGTT
TTTTGGGGGTGTAAGTG-TAATTACACCTGGAACAAATGCTTCATCTGAAGTT-GCTGTT
TTTATATGATTCTAATGGTAACTCTCTATGGTTTATAGAGACTACTTAACAAACA-GAAGTT
TCTTTATGATTCTAGTGGTAACTCTCTATGGCTTATAGAGATTATTATCAAATA-GAAGTT
CTTATATGATGTTAATGGTAACTTAAATGGTTTCCGTGACATTGTTACCAATA-AGAGTT
CTTATATGATGTTAATGGTAACTTAAATGGTTTCCGTGACATTGTTACCAATA-AGAGTT
TCTAGCAGACGAGGT-----TTGGCTATTTTAGATACATCTGGTTCCATAGACATCT

CcoV
FcoV
TGE
PRCoV
HCoVOC43

CACTATCAGGTGATTTGTTAGGTTTTAAAAATGTTAGTGATGGTGTGTTCTACTCTGTAA
CACTATCAGGTGATTTGTTAGGTTTTAAAAATGTTAGTGATGGTGTGTTCTACTCTGTAA
CACTATCAGGTGATTTGTTAGGTTTTAAAAATGTTAGTGATGGTGTGTTCTACTCTGTAA
CACTATCTGGTGATTTGTTAGGTTTTACAAATGTTAGTGATGGTGTGTTCTACTCTGTAA
CAACTTCAGGTAACTTCTGGGTTTTAAAGATGTTACTAAGGGCACCCTACTCTATCA

PEDV	CTGATTCTGGACAGTTGTTAGCCTTTAAGAATGTCACTAGTGGTGTGTTTATTCTGTCA
SARSUrba	CTATATCAAGATGTTA--ACTGCACTGATGTTTCTACAGCAATTCAATGCAGATCAACTCA
SARSTor2	CTATATCAAGATGTTA--ACTGCACTGATGTTTCTACAGCAATTCAATGCAGATCAACTCA
BcoV	TTATGATTCTAGTTGCTATAGCGGTCTGTTTTCAGCGGCCTTTTATGCTAACTCTTCCG
HEV	TTCTTATTCTAGCTGCTATAGTGGGAGAGTTTTCAGCAGTTTTCATGCTAACTCATCTG
MHV	ATACTATTGAAAGTTGCTATAGTGGGCGGGTCTCGGCTGCATATCATCAAGATGCACCAG
RtCoV	ATTTATTAAGAAGTTGCTATAGTGGGCGCGTTTTCGGCTGCATATCATCAAGATGCACCTG
IBV	TTGTTGTACAAGGTGAATATGGTCTTAATTATTATAAGGTAAACCTTGCGAAGATGTCA
CcoV	CGCCATGTGATGTAAGTGCACAAGCTGCTGT-TATTGATGGTGCCATAGTTGGAGCTATG
FcoV	CGCCATGTGATGTAAGCGCACAAGCGGCTGT-TATTGATGGTGCCATAGTTGGAGCTATG
TGE	CGCCATGTGATGTAAGCGCACAAGCAGCTGT-TATTGATGGTACCATAGTTGGGGCTATC
PRCoV	CGCCATGTGATGTTAGCGCACAAGCAGCTAT-TATTGATGGTACCATAGTTGGGGCTATC
HCoVOC43	CTCCTTGTAACCCACCAGATCAGCTTGTGTTTATCAGCAA-GCTGTTGTTGGTGCTATG
PEDV	CGCCATGTTCTTTTTTTCAGAGCAGGCTGC-ATATGTTAATGATGATATAGTGGGTGTTATT
SARSUrba	CACCA-GCTT-----GGCGCATATATTCTACTGGAACAATG-TATT
SARSTor2	CACCA-GCTT-----GGCGCATATATTCTACTGGAACAATG-TATT
BcoV	AACCA-GCATTGCTATTTTGGGAATATTAAATGCAATTACGTTTTTAATAATACTC-TTTC
HEV	AACCA-GCTTTGATGTTTTCGTAATCTTAAATGCAGCCACGTTTTTAATAATACCA-TTTT
MHV	AACCA-GCGCTACTATATCGCAATTTAAATGTGACTATGCTTTTAACAACAACA-TATC
RtCoV	AACCA-GCGCTACTATATCGCAATTTAAATGTGATTATGTTTAAATAACAACA-TATC
IBV	-ACCAGCAGTTGTAGTTTCTGGTGGTAAATTAGTAGGTATTCTACTTCACGTAATGAG
CcoV	ACTTCCATTAAATAGTGAAGTGTAGGT--CTAACTCATTGGACAACAACACCTAATTTTT
FcoV	ACTTCCATTAAACAGTGAAGTGTAGGT--CTAACACATTGGACAACGACACCTAATTTTT
TGE	ACTTCCATTAAACAGTGAAGTGTAGGT--CTAACACATTGGACAACAACACCTAATTTTT
PRCoV	ACTTCCATTAAACAGTGAATTTGTTAGGT--CTAACACATTGGACAACAACACCTAATTTTT
HCoVOC43	TTGTCTGAAATT-----TACTAGTT--ACGGC---TTTTCTAATGTTGTAGAACTGCC
PEDV	TCT-----AGTT-----TGTCTAACT--CCACT---TTTAACTACTAGGGAGTTGCC
SARSUrba	CC-----AGTT-----AGACTCAAGCAGGCTGTCTTAT-AGGAGCTG
SARSTor2	CC-----AGTT-----AGACTCAAGCAGGCTGTCTTAT-AGGAGCTG
BcoV	ACGACAGCTGCAACCTATTAACTATTTTGATAGTTATCTTGGTTGTGTTGT-CAATGCTG
HEV	AAGACAAATACAGCTTGTAACTATTTTGATAGTTACCTTGGTTGTGTTGT-TAATGCTT
MHV	CCGTGAGGAGACACCACTTAATTTTCGATAGTTATCTTGGTTGTGTTGT-TAATGCTG
RtCoV	CCGTGAGGAGACACCACTTAATTTTGATAGTTATTTGGTTGTGTTAT-TAATGCTG
IBV	AC-----TGGTTCTCAGCTTCTT-GAGAACCAAGTTTACATCAAAATCACTAATGG
CcoV	ATTACTACTCCATATATAATTATACAAATGTGATGAATCGTGGCAGGCAATTGA---TA
FcoV	ATTACTACTCTATATATAATTACACAAGTGAGAGGACTCGTGGCACTGCAATTGACAGTA
TGE	ATTACTACTCTATATATAATTACACAAGTGATAGGACTCGTGGCACTGCAATTGACAGTA
PRCoV	ATTACTACTCTATATATAATTACACAAGTGATAAGACTCGTGGCACTCCAATTGGCAGTA
HCoVOC43	GAAATTTTTCTATGCGT-----CCAATGGCAC-----TTATAAATTGC-----
PEDV	TGGTTTCTTCTACCACT-----CTAATGACGG-----CTCCAATTGT-----
SARSUrba	AGCAT-----GTCGACACTT-----CTTATGAGTGGCAGATTCTTATTGGAGCTGGCATT
SARSTor2	AGCAT-----GTCGACACTT-----CTTATGAGTGGCAGATTCTTATTGGAGCTGGCATT
BcoV	ATAATAGTACTTCTAGTGTG-----TTCAACATGTGATCTCACAGTAGGTAGTGGTTACT
HEV	ATAATAATACAGCTAGTGTG-----TAAGTACTTGTGATTTAACCGTTGGTAGCGGCTATT
MHV	ACAACCTCAACTGAAGAAGCTG-----TTGACGCGTGTGATTTGCGTATGGGTAGTGGGCTTT
RtCoV	ATAACCTCAACTGAGCAGTCTG-----TTGACGCGTGTGATTTGCGTATGGGTAGTGGGCTTT
IBV	AACACGTCGTTTTAGACGTTT-TATTACTGAAATG-----TTGCAAATTGCCCTT
CcoV	ATGATATTGATTGTGAACCTATCATAACATATTCTAATATAGGTGTTTGTAAAAATGGAG
FcoV	ACGATGTTGATTGTGAACCTGTCTAACCTATTCTAATATAGGTGTTTGTAAAAATGGTG
TGE	ATGATGTTGATTGTGAACCTGTCTAACCTATTCTAATATAGGTGTTTGTAAAAATGGTG
PRCoV	ATGACGTTGATTGTGAACCTGTCTAACCTATTCTAATATAGGTGTTTGTAAAAATGGTG
HCoVOC43	---ACA-----GAGCGTGTTTTAACTTATTCTAGTTTGGCGTTTGTGCAGATGGTT
PEDV	---ACA-----GAGCGTGTGTGTTGTTATAGTAACATAGGTGTTTGTAAATCTGGCA
SARSUrba	GTGCTAGTTACCATACAGTTTCTTTATTACGTAG-----TACTAGCCAAAAATCTA
SARSTor2	GTGCTAGTTACCATACAGTTTCTTTATTACGTAG-----TACTAGCCAAAAATCTA

BcoV GTGTGGATTACTCTACAAAAGACGAAGTCGTAGAGCGATTACCACTGGTTATCGGTTTA
HEV GTGTGGATTATGTTACAGCACTTAGATCACGTAGATCTTTTACTACAGGTTATCGCTTTA
MHV GTGTCAACTATTCAACGTCTCACC GCGCTCGCAGCTCTGT CAGCACGGGTTATAAATTAA
RtCoV GTGTCAACTATTCAATCGCTCACC GTGCGCGCAGGTCTGT CAGTACGGGTTATAAATTAA
IBV ATGTTAGTTATGGTAAGTTTTGTATAAAACCTGATGGCT----CAATTGCCACAATAGTA *

CcoV CTTTGGTTTTTATT--AACGTCACACATTCTG-ATGGAGACGTTCAACCAATTAGCACCG
FcoV CTTTGGTTTTTATT--AACGTCACACATTCTG-ACGGAGACGTGCAACCAATTAGCACTG
TGE CTTTGTTTTTTATT--AACGTCACACATTCTG-ATGGAGACGTGCAACCAATTAGCACTG
PRCoV CTTTGGTTTTTATT--AACGTCACACATTCTG-ATGGAGACGTGCAACCAATTAGCACTG
HCoVOC43 CTATAATTGCTGTTCAACCACGTAATGTTTCATATGATAGTGTTTCAGCTATCGTCACAG
PEDV GTATTGGCTATGTTCCATCTCAGTATGGCC---AAGTCAAGATTGCACCCACGGTTACTG
SARSUrba -----TTGTGGCTTATACTATGCTCTTTAGGTGCTGATAGTTC--AATTGCTTACTCTAA
SARSTor2 -----TTGTGGCTTATACTATGCTCTTTAGGTGCTGATAGTTC--AATTGCTTACTCTAA
BcoV CTAATTTTGAGCCATTTACTGTTAATTCAGTAAATGATAGTTTAGAACCTGTAGGTGGTT
HEV CTAATTTTGAACCATTTGCCGCTAATTTGGTAAATGATAGTATAGAACCTGTTGGTGGTT
MHV CTACTTTTGAACCATTTACAGTCCGCATTGTCAATGATAGTGTTGAGTCTGTTGATGGGT
RtCoV CTACTTTTGAACCATTTACAGTCAGCATTGTCAATGATAGTGTTGAGTCTGTTGGTGGAT
IBV -----CCAAAACAATTGGAACAGTTTGTGGCACCTTT--ATTTAATGTTACTG *

CcoV ---GTAATGTCACGATACCCACAAATTTTACTATATCTGTGCAAGTCGAATATATTACAGG
FcoV ---GTAATGTCACGATACCTACAAATTTTACTATATCTGTGCAAGTTGAATACATGCAGG
TGE ---GTAATGTCACGATACCTACAACTTTTACCATATCCGTGCAAGTCGAATATATTACAGG
PRCoV ---GTAACGTACGATACCTACTAATTTTACTATATCCGTGCAAGTCGAATACATTACAGG
HCoVOC43 ---CTAATTTGTCTATACCTTCCAATTTGGACCACTTCGGTCCAGGTTGAGTATTTACAAA
PEDV ---GGAATATTAGTATTTCCACCAACTTTAGTATGAGTATTAGAACAGAAATTTACAGC
SARSUrba TA-ACACCATTGCTATACCTACTAATTTTCAATTAGCATTACTACAGAAGTAATGCCTG
SARSTor2 TA-ACACCATTGCTATACCTACTAATTTTCAATTAGCATTACTACAGAAGTAATGCCTG
BcoV TGTATGAAATTCAAATACCTTCAGAGTTTACTATAGGTAATATGGAGGTTTATTCAA
HEV TGTATGAAATACAGATACCTTCAGAGTTTACCATTGGTAATTTAGAAGAGTTCATTCAA
MHV TATATGAGCTGCAAATACCAACCACTTTACTATAGCTAGCCATCAGGAGTTCGTTCAA
RtCoV TATATGAGATGCAAATACCTACTAATTTTACTATAGCTAGCCATCAGGAGTTCATTCAA
IBV ---AAAATGTGCTCATACCTAACAGTTTCAACTTAAGTGTACAGATGAGTACATACAAA
* ** *

CcoV TTTACACTACACCAGTTTCAATAGACTGTGCAAGATACGTTTGCAATGGTAACCCAAGAT
FcoV TTTACACTACACCAGTATCAATAGATTGTGCAAGATACGTTTGTAATGGTAACCTAGAT
TGE TTTACACTACACCAGTGTCAATAGACTGTTCAAGATATGTTTGTAATGGTAACCTAGGT
PRCoV TTTACACTACACCAGTGTCAATAGACTGTTCAAGATATGTTTGTAATGGTAACCTAGGT
HCoVOC43 TTACAAGTACACCTATCGTAGTTGATTGCTCCACTTATGTTTGCAATGGTAATGTGCGCT
PEDV TTTACAACACGCCTGTTAGTTGATTGCTGCTACATATGTTTGTAATGGTAACCTCTCGTT
SARSUrba TTTCTATGGCTAAAACCTCCGTAGATTGTAATATGTACATCTGCGGAGATTCTACTGAAT
SARSTor2 TTTCTATGGCTAAAACCTCCGTAGATTGTAATATGTACATCTGCGGAGATTCTACTGAAT
BcoV CAAGCTCTCCTAAAGTTACTATTGATTGTTCTGCTTTTGTCTGTGGTGATTATGCAGCAT
HEV CGAGATCCCCTAAGGTTACTATAGACTGTGCTACATTTGTTTGTGGTGACTATGCAGCAT
MHV CGAGGTCTCCAAAGGTTACTATAGACTGTGCTGCATTTGTCTGTGGTGCCACACAGCAT
RtCoV CGAGGTCTCCGAAGGTTACTATAGATTGTGCTGCATTTGTCTGTGGTGATTATACAGCGT
IBV CCGCTATGGATAAGGTCAAATTAATTGCTGCAGTATGTTTGTGGCAGTTCTCTGGATT
* * * *

CcoV GCAATAAGTTATTAACACAATACGTTTCTGCATGTCAAATATTGAGCAAGCGCTTGCAA
FcoV GTAACAAATTGTTAACACAATATGTGCTGCATGTCAAATATTGAACAAGCACTTGCAA
TGE GTAACAAATTGTTAACACAATACGTTTCTGCATGTCAAATATTGAGCAAGCACTTGCAA
PRCoV GTAACAACTGTTAACACAATACGTTTCTGCATGTCAAATATTGAGCAAGCACTTGCAA
HCoVOC43 GTGTTGAATTGCTTAAGCAGTATACTTCTGCTTGTAACAACTATTGAAGACGCCCTTAAGAA
PEDV GTAAACAATTACTCACCCAGTACACTGCAGCATGTAAGACCATAGAGTCAGCATTACAAC
SARSUrba GTGCTAATTTGCTTCTCCAATATGGTAGCTTTTGACACAACCTAAATCGTGCACTCTCAG
SARSTor2 GTGCTAATTTGCTTCTCCAATATGGTAGCTTTTGACACAACCTAAATCGTGCACTCTCAG
BcoV GTAAATCACAGTTGGTTGAATATGGTAGCTTTGTGACAATATTAATGCTATACTCACAG
HEV GTAGACAACAGTTAGCTGAGTATGGTAGTTTTTGTGAGAACATTAATGCTATACTCACAG
MHV CCCGTCAGCAGTTGGTTGAGTACGGCTCATTCTGTGATAATATTAATGCCATTCTTGCGC

RtCoV IBV	GTAGACAACAGTTGGTTGATTATGGCTCTTTTGTGATAATATTAATGCCATTCTTGGCG GTAGAAAGTTGTTTCAACAATATGGGCCTGTTTGGGACAACATATTGTCTGTAGTAAATA *
CcOV FcoV TGE PRCoV HCoVOC43 PEDV SARSurba SARSTor2 BcoV HEV MHV RtCoV IBV	TGGGTGCCAG---ACTTGAAAACATGGAGATTGATTCCATGTTATTTGTTTCGGAAAAATG TGGGTGCCAG---ACTTGAAAACATGGAGTTGATTCCATGTTGTTTGTCTCGGAAAAATG TGGGTGCCAG---ACTTGAAAACATGGAGTTGATTCCATGTTGTTTGTCTGAAAAATG TGGGTGCCAG---ACTTGAAAACATGGAAGTTGATTCCATGTTATTTGTTTCTGAAAAATG ATAGCGCCAG---GCTGGAGTCTGCAGATGTTAGTGAGATGCTCACTTTTGACAAGAAAG TCAGCGCTAG---GCTTGAGTCTGTTGAAGTTAACTCTATGCTTACCATTCTGAAGAGG GTATTG-----CTGCTGAACAGGATCGCAACACACGTGAAGTGTTCGCTCAAGTCAACA GTATTG-----CTGCTGAACAGGATCGCAACACACGTGAAGTGTTCGCTCAAGTCAACA AAGTAAATGAACACTTGACACTACACAGTTGCAAGT-AGCTAATAGTTTAAATGAATGTT AAGTAAATGAACACTTGACACTACACAGTTGCAAGT-AGCTAATAGTTTAAATGAATGTT AGGTAAATAACCTCATAGATACTATGCAACTTCAAGT-TGCAAGTGCTTTAATCCAAGGT AGGTGAATAACCTCATAGATACTATGCAATTCAAGT-TGCTAGTGCTCTGATCCAAGGT GTGTTGGTCA---AAAAGAAGATATGGAACCTTTGAATTTCTATTCTTCTACTAAACCGG
CcOV FcoV TGE PRCoV HCoVOC43 PEDV SARSurba SARSTor2 BcoV HEV MHV RtCoV IBV	CCCTTA-AATTGGCATCTGTTGAAGCATTCAATAGTACGGAATAATTTAGACCCTATTAT CCCTTA-AATTGGCATCTGTTGAGGCGTTCAATAGTACAGAAAATTTAGATCCTATTAC CCCTTA-AATTGGCATCTGTTGAAGCATTCAATAGTTTCAAGAACTTTAGACCCTATTAC CCCTTA-AATTGGCTTCTGTGCAAGCATTCAATAGTTTCAAGAACTTTAGATCCTATTAC CGTTTACACTT-GCTAATGTTAGT-----AGTTTT---GGTGACTACAACCTTAGC--- C-TTTACAGTTAGTACCATCAGTTGCTTTAATGGT---GATGGATATAACTTTACT--- AATGTACAAAACCCCACTTTGAAA-----TATTTTGGTGGTTTTAATT--- AATGTACAAAACCCCACTTTGAAA-----TATTTTGGTGGTTTTAATT--- GTCACCTTTAGCACTAAGCTTAAAGATGGCGTTAATTTCAATGTAGACGACATCAATT-- GTCACCTTTAGTACCAAGATTAAGGATGGCATTAAATTTCAATGTTGACGATATCAACT-- GTCACGTTAAGCTCAGCTTATCGGATGGCATTGGTGGTCAAATAGATGATATTAATT-- GTCACGCTAAGTTTACGCTTGGCAGATGGCATCTCAGGTGAGATTGATGATATTAATT-- CTGGTTTTAATACACCACTTCTTAG-----TAATGTTAGCACTGGTGAGTTAATA--
CcOV FcoV TGE PRCoV HCoVOC43 PEDV SARSurba SARSTor2 BcoV HEV MHV RtCoV IBV	AAAGAATGGCCTAACATTGGTGGTTCTTGGCTAGGAGGTTTAAAGATATATTGCCATCT AAAGAATGGCCTAGCATAGGTGGTTCTTGGCTAGGAGGTTTAAAGATATACTACCGTCC AAAGAATGGCCTAATATAGGTGGTTCTTGGCTAGAAGGTTTAAATACATACTTCCGTCC AAAGAATGGCCTAATATAGGTGGCTTTTGGCTAGAAGGTTTAAATACATACTTCCGTCC ---AGCGTCATA---CCTAGCTTG-----CCCACA ---AATGTGCTG---GGTGCTTCCGTGTACGA-----TCCTGCA ---TTTCACAAATATTACCTGACCCT-----CTAAAGCCAA--- ---TTTCACAAATATTACCTGACCCT-----CTAAAGCCAA--- ---TTTCCCCTGTATTAGGTTGTTAGGAAGCGC-----TTGTAATAAAGTT ---TCTCCCCTGTATTAGGTTGTTAGGAAGCGA-----ATGTAATAGAGCT ---TTAGTCTCTGCTTGGTTGTTTAGGTTCTGA-----CTGTGGCGAAGTT ---TTAGTCTCTCTAGGTTGCTTGGCTCAGA-----TTGTAGCGAAGGC ---TTTCTCTTCTGTTAACAATCCT-----AGTAGT
CcOV FcoV TGE PRCoV HCoVOC43 PEDV SARSurba SARSTor2 BcoV HEV MHV RtCoV IBV	CATAATAGCAAACGTAAGTACCGCTCGGCTATAGAAGACTTGCTTTTTGATAAGGTTGTA CATAATAGCAAACGTAAGTATGGTTCTGCTATAGAAGATTGCTTTTTGATAAGGTTGTA CATAATAGCAAACGTAAGTATCGTTTCAGCTATAGAGGACTTGCTTTTTGATAAGGTTGTA GATAATAGCAAACGTAAGTATCGTTTCAGCTATAGAGGACTTGCTTTTTGATAAGGTTGTA AGTGGTAGTAGAGTGCTGGTGGCAGTGCATAGAAGACATACTTTTTAGCAAACCTGTT AGTGGCAGGTTGGTACAAAAAAGGCTGTTATTGAAGACTTGCTTTTTAATAAAGTGTT -CTAAGA-----GGTCTTTTATTGAGGACTTGCTCTTTAATAAAGTGACA -CTAAGA-----GGTCTTTTATTGAGGACTTGCTCTTTAATAAAGTGACA TCCAGCA-----G---ATCTGCTATAGAGGATTACTTTTTTCTAAAGTAAAG TCCACTA-----G---ATCTGCTATAGAGGATTACTTTTTGATAAAGTAAAG ACCATGGCAGCTCAAACCGGACGATCTGCTATAGAGGATGATTATTTGATAAAGTCAAA ACCAAGGCAGCGCAA---GGGCGATCTGCTATAGAGGATGATTATTTGATAAAGTCAAA CGTAGAA-----AGCGTTCTCTATTGAAGACCTTCTATTTACAAGCGTTGAA *

CcoV ACATCTGGCTTAGGTACAGTTGACGAAGATTACAAACGTTCTGCAGGTGGTTATGACA--
 FcoV ACATCTGGTTTAGGTACAGTTGATGAAGATTATAAACGTTGTACTGGTGGTTACGACA--
 TGE ACATCTGGTTTAGGTACAGTTGATGAAGATTATAAACGTTGTACAGGTGGTTATGACA--
 PRCoV ACATCTGGTTTAGGTACAGTTGATGAAGATTATAAACGTTGTACAGGTGGTTATGACA--
 HCoVOC43 ACTTCTGGACTTGGCACTGTGGACGCAGACTACAAAAGTGCACTAAGGGTCTTTCCA--
 PEDV ACTAATGGCCTTGGTACTGTTGATGAAGACTATAAGCGCTGTTCTAATGGTCGCTCTG--
 SARSUrba CTCGCTGATGCTGGCTTCATGAA---GCAATATGGCGAATGCCTAGGTGATATTAATG--
 SARSTor2 CTCGCTGATGCTGGCTTCATGAA---GCAATATGGCGAATGCCTAGGTGATATTAATG--
 BcoV TTATCTGATGCTGGCTTCGTTGA---GGCTTATAAATTTGACTGGAGGTGCCGAAA--
 HEV TTGTCTGATGCTGGCTTTGTACA---GGCTTATAAATGCACTGGAGGTGCCGAAA--
 MHV CTCTCTGATGTTGGCTTTGTGCA---AGCATATAACAATTGCACTGGAGGTCAAGAAG--
 RtCoV CTCTCTGATGTTGGCTTTGTGCA---ATCATATAAATTTGCACTGGAGGTCAAGAAG--
 IBV TCTGTTGGACTACCAACAAATGA---CGCATATAAAAAATGCACTGCAGGACCTTAGGC

CcoV ----TAGCTGACTTAGTGTGTGTCACGATATTACAATGGCATCATGGTCTACCTGGTGTA
 FcoV ----TAGCAGACTTGGTGTGTGCTCAATATTACAATGGCATCATGGTCTACCTGGTGTA
 TGE ----TAGCTGACTTAGTATGTGCTCAATACTATAATGGCATCATGGTCTACCTGGTGTA
 PRCoV ----TAGCTGACTTAGTATGTGCTCAATACTATAATGGCATCATGGTCTACCTGGTGTA
 HCoVOC43 ----TTGCTGACTTGGCTTTGTGCTCAATATTATAATGGCATTATGGTCTTGGCTGGCGTC
 PEDV ----TGGCTGATCTAGTCTGTGCGCAGTATTACTCTGGTGTCTAGTACTACCTGGCGTC
 SARSUrba ----CTAGAGATCTCATTGTGTGCGCAGAAGTTCAATGGACTTACAGTGTGGCCACCTCTG
 SARSTor2 ----CTAGAGATCTCATTGTGTGCGCAGAAGTTCAATGGACTTACAGTGTGGCCACCTCTG
 BcoV ----TTAGGGACCTCATTGTGTGCGCAGAAGTTCAATGGATCAAAGTGTGGCTCCACTG
 HEV ----TTAGGGATCTCATTGTGTGCGCAGAAGTTCAATGGATCAAAGTGTGGCTCCACTG
 MHV ----TTAGAGACCTACTTTGTGTGCAATCTTTAATGGCATCAAAGTGTACCGCCTGTG
 RtCoV ----TTAGAGACCTACTTTGTGTGCAATCTTTAATGGCATCAAAGTGTACCGCCTGTG
 IBV TTTTAAAGGACCTTGGCTGTGCTCGTGAATATAATGGTTGTGCTTGTGTGCTCCTATC

CcoV GCTAATGATGACAAAGATGACTATGTACACTGCATCTCTTACAGGTGGTATAACATTAGGT
 FcoV GCTAATGCTGACAAAGATGACTATGTACACAGCATCACTTGCAGGTGGTATAACATTAGGT
 TGE GCTAATGCTGACAAATGACTATGTACACAGCATCCCTGCGAGGTGGTATAACATTAGGT
 PRCoV GCTAATGCTGACAAATGACTATGTACACAGCATCCCTGCGAGGTGGTATAACATTAGGT
 HCoVOC43 GCTGATGCTGAACGAATGGCCATGTATACAGGTTCTTTAATGGTGAATGTCTTAGGA
 PEDV GTTGACGCTGAGAAGCTTCACATGTACAGTGCCTCTCTCATAGGTGGTATGCGCTAGGA
 SARSUrba CTCCTGATGATATGATTGCTGCCTACACTGCTGCTCTAGTTAGTGGTACTGCCACTGCT
 SARSTor2 CTCCTGATGATATGATTGCTGCCTACACTGCTGCTCTAGTTAGTGGTACTGCCACTGCT
 BcoV CTCTCAGTAAATCAGATCAGTGGATACACTTTGGCTGCCACCTCTGCTAGTCTGTTTCCT
 HEV TTATCTGAAATCAGATCAGTGGCTACACTTTGGCAGCCACCGCTGCTAGCTTATTCCT
 MHV TTGTCTGAGAAATCAAATTTCTGGTTATACAGCGGGAGCTACTGTATCTGCTATGTTCCCT
 RtCoV TTATCCGAGAGTCAAATCTCTGGTTATACAGCGGGAGCTACTGCATCTGCTATGTTCCCT
 IBV ATAACAGCAGAAATGCAAGCTTTGTATAGTCTCTAGTAGCTTCTATGGCTTTTGGT

CcoV GCACTTAGTGGTGGCGCAGTGGC-----TATACCTTTTGCAGTAGCAGTTCAGGCT
 FcoV GCACTTGGTGGTGGCGCGTGGC-----TATACCTTTTGCAGTAGCAGTTCAGGCT
 TGE GCACTTGGTGGAGGCGCGTGGC-----TATACCTTTTGCAGTAGCAGTTCAGGCT
 PRCoV GCACTTGGTGGAGGCGCGTGGC-----TATACCTTTTGCAGTAGCAGTTCAGGCT
 HCoVOC43 GGTCTAACATCAG---CCGTTTC-----AATACCATTTTATTAGCAATTCAGGCA
 PEDV GGTATAACTGCTG---CAGCGGC-----ATTGCCTTTTAGCTATGCTGTTCAAGCG
 SARSUrba GGATGGACATTTGGTGTGCGCTGCTCTTCAAATACCTTTTGCTATGCAAATGGCATAT
 SARSTor2 GGATGGACATTTGGTGTGCGCTGCTCTTCAAATACCTTTTGCTATGCAAATGGCATAT
 BcoV CCTTTGTGACGACGAGTAGGTG-----TACCATTTTATTAAATGTTCAAGTAT
 HEV CCTTTGTGACGACGAGTAGGTG-----TACCATTTTATTAAATGTTCAAGTAT
 MHV --ATGGTCTGCAGCTGCAGGTG-----TGCCATTTTCTTAAAGTGTTCATAT
 RtCoV CCATGGTCTGCAGCTGCAGGTG-----TGCCATTTTCTTAAAGTGTTCATAT
 IBV GGTATTACTGCAG---CTGGTGC-----TATACCTTTTGCCACACAACCTGCAGGCT

CcoV AGACTTAATTATGTTGCTCTACAACTGATGTATTGAACAAAAACCAAAATCTTGGCT
 FcoV AGACTTAATTATGTTGCTCTACAACTGATGTATTGAATAAAAAACCAAGATCCTGGCT

TGE
PRCoV
HCoVOC43
PEDV
SARSUrb
SARSor2
BcoV
HEV
MHV
RtCoV
IBV

AGACTTAATTATGTTGCTCTACAACTGATGTATTGAACAAAAACCAGCAGATTCTGGCT
AGACTTAATTATGTTGCTCTACAACTGATGTATTGAACAAAAACCAGCAGATCCTGGCT
CGTTTAAATTATGTTGCTTGCAGACTGATGTTTACAAGAAAATCAGAAAATCTTGCT
AGACTCAATTATCTTGCTTTACAGACGGATGTTCTACAGCGGAACCAGCAATTGCTTGCT
AGGTTCAATGGCATTGGAGTTACCCAAAATGTTCTCTATGAGAACCAAAAACAATCGCC
AGGTTCAATGGCATTGGAGTTACCCAAAATGTTCTCTATGAGAACCAAAAACAATCGCC
CGTATAATGGGATTGGTGTACCATGGATGTGTTAAGTCAAAATCAAAAGCTTATTGCT
CGTATAATGGGCTTGGCGTCACTATGGATGTGCTAAGTCAAAACCAAAAGCTTATTGCT
AGAATTAATGGTCTTGGTGTCACTATGAATGTTCTTAGTGAAAATCAGAAAATGATAGCA
AGAATTAATGGTCTTGGTGTCACTATGAATGTTCTTAGTGAAAACCAAGAAAATGATAGCT
AGAATTAATCACTTGGGTATTACCCAGTCACCTTTGTTGAAGAATCAAGAAAAATTTGCT
* * * * *

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrb
SARSor2
BcoV
HEV
MHV
RtCoV
IBV

AATGCTTTCAATCAAGCTATTGGTAACATTACACAGGCATTTGGTAAGGTTAATGAGCT
AATGCTTTCAATCAAGCTATTGGTAACATTACACAGGCATTTGGTAAGGTTAATGATGCT
AGTGCTTTCAATCAAGCTATTGGTAACATTACACAGTCATTTGGTAAGGTTAATGATGCT
AGTGCTTTTAAATCAAGCTATTGGTAACATTACACAGTCATTTGGTAAGGTTAATGATGCT
GCATCTTTTAAACAAAGCAATGACCAACATAGTAGATGCCTTTACTGGTGTAAATGATGCT
GAGTCTTTTAACTCTGCTATTGGTAATATACTTCAGCCTTTGAGAGTGTAAAGAGGCT
AACCAATTTAACAAGGCGATTAGTCAAAT-----
AACCAATTTAACAAGGCGATTAGTCAAAT-----
AATGCATTAAACAATGCTCTTGATGCTAT-----
AGTGCAATTTAACAATGCTCTTGATGCTAT-----
AGTGCAATTTAACAACGCGATAGGTGCTAT-----
AGTTCATTAAACAACGCGATAGGTGCTAT-----
GCTTCCTTTAATAAGGCCATTGGTCATAT-----
* * * * *

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrb
SARSor2
BcoV
HEV
MHV
RtCoV
IBV

ATACATCAACATCAAAAGGTCTTGCTACTGTTGCTAAAGCATTGGCAAAGGTGCAAGAT
ATACATCAACATCACAAGGTCTTGCCACTGTTGCTAAAGCATTGGCAAAGGTGCAAGAT
ATACATCAACATCAGGAGTCTTGCTACTGTTGCTAAAGCATTGGCAAAGGTGCAAGAT
ATACATCAACATCAGGAGTCTTACAACCTGTTGCTAAAGCATTGGCAAAGGTGCAAGAT
ATTACACAACCTTACAAGCCCTACAAACAGTTGCTACTGCCTTAAACAAGATCCAGGAT
ATTAGTCAAACTTCCAAGGGTTTGAACACTGTGGCTCATGCGCTTACTAAGGTTCAAGAG
-----TCAAG-----AATCACTTACAACAACATCACTGCATTGGGCAAGCTGCAAGAC
-----TCAAG-----AATCACTTACAACAACATCACTGCATTGGGCAAGCTGCAAGAC
-----TCAGG-----AAGGGTTTGATGCTACCAATTCTGCTTTAGTAAAATTCAAGCT
-----CCAGG-----AAGGGTTTGAAGCTTACCAATTCTGCTTTAGTAAAATTCAAGCT
-----ACAGG-----AAGGGTTTGCTGCAACCAATTCTGCCTTAGCAAAAATGCAAGTTC
-----ACAGG-----AAGGGTTTGCATGCAACCAATTCTGCTTTAGCGAAAATTCAGTCC
-----GCAGG-----AAGGTTTGTAGAAGTACATCTCTAGCATTACAACAATTCAGAT
* * * * *

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrb
SARSor2
BcoV
HEV
MHV
RtCoV
IBV

GTTGTTAACACGCAAGGTCAAGCTTTAAGCCACCTAACAGTACAATTGCAAAACAATTTT
GTTGTCAACACACAAGGGCAAGCTTTAAGTCACCTTACAGTACAATTGCAAAATAATTTT
GTTGTCAACACACAAGGGCAAGCTTTAAGCCACCTAACAGTACAATTGCAAAATAATTTT
GTTGTTAATCAACAAGGCAACTCATTGAACCAATTTAACTTCTCAGTTGAGGCGAATTTT
GTTGTTAATTCGAGGGTTCAGCTTTGAACCAACTTACCGTACAGCTGCAACACAACCTTC
GTTGTTAACCAGAATGCTCAAGCATTAAACACACTTGTAAACAACCTTAGCTCTAATTTT
GTTGTTAACCAGAATGCTCAAGCATTAAACACACTTGTAAACAACCTTAGCTCTAATTTT
GTTGTTAATGCAAAATGCTGAAGCTCTTAATAACTTATTGCAACAACCTCTAATAGATTT
GTTGTTAATGCAAAATGCTGAAGCACTTAATAACTTATTGCAACAACCTCTAATAGATTT
GTTGTCAATGCAAAATGCGGAAGCACTCAATAATTTTAAACAGCTTTCCAATAGGTTT
GTTGTCAACGCAAAATGCAAGCACTCAATAACCTTTTGAATCAGCTTTCCAATAGGTTT
GTTGTTAGTAAACAGAGTGCTATTCTTACTGAGACTATGGCATCACTTAATAAAATTTT

CcoV
FcoV
TGE
PRCoV
HCoVOC43

CAAGCCATTAGCAGTTCTATTAGTGACATTTATAACAGGCTTGATGAATTGAGTGCTGAT
CAAGCCATTAGTAGTTCTATTAGTGATATTTATAACAGGCTTGACGAAGTGAAGTGCTGAT
CAAGCCATTAGTAGTTCTATTAGTGACATTTATAATAGGCTTGACGAATTGAGTGCTGAT
CAAGCCATTAGTAGTTCTATTAGTGACATTTATAATAGGCTTGATGAATTGAGTGCTGAT
CAAGCTATCTTAGCTCTATTAGGCTATCTATGACAGACTTGACACTATTAGGCTGAT

PEDV
 SARSUrb
 SARSTor2
 BCoV
 HEV
 MHV
 RtCoV
 IBV

CAAGCCATTTCTAGTCTATTGATGACATTTATCCCGACTGGACATTTCTTCACGCCGAT
 GGTGCAATTTCAAGTGTGCTAAATGATATCTTTTCGCGACTTGATAAAGTCGAGGCGGAG
 GGTGCAATTTCAAGTGTGCTAAATGATATCTTTTCGCGACTTGATAAAGTCGAGGCGGAG
 GGTGCTATAAGTTCTTTCTTTACAAGAAATTTCTATCTAGACTGGATGCTCTTTGAAGCGCAA
 GGTGCCATAAGTGCCTCTTTACAAGAAATTTTATCCAGGCTCGATGCTCTTTGAAGCTAA
 GGTGCAATTAGTGCTTTCTTTACAAGAAATTTCTATCTCGCTAGATGCTCTTTGAAGCGCAG
 GGTGCAATTAGTGCTTTCTTTACAAGAAATTTCTATCTCGCTCGATGCTCTTTGAAGCTCAG
 GGTGCTATTTCTTCTGTGATTCAAGAAATCTACCAGCAATTTGACGCCATACAAGCAAT

CCoV
 FCoV
 TGE
 PRCoV
 HCoVOC43
 PEDV
 SARSUrb
 SARSTor2
 BCoV
 HEV
 MHV
 RtCoV
 IBV

GCACAAGTTGACAGGCTGATTACAGGACGACTTACAGCACTTAATGCATTTGTGTCTCAG
 GCACAAGTTGATAGGCTGATTACAGGTAGACTTACAGCACTTAATGCATTTGTGTCTCAG
 GCACAAGTTGACAGGCTGATCACAGGAAGACTTACAGCACTTAATGCATTTGTGTCTCAG
 GCACAAGTCGACAGGCTGATCACAGGAAGACTTACAGCACTTAATGCATTTGTGTCTCAG
 CAACAAGTAGATAGGCTGATTACTGGTAGATTGGCTGCTTTGAATGTATTCTGTTCTCAT
 GTTACAGGTTGATCGTCTCATCACCAGGAGATTATCAGCACTTAATGCATTTGTGTGCCAA
 GTACAAATTGACAGGTTAATTACAGGAGACTTCAAAGCCTTCAAACCTATGTAACACAA
 GTACAAATTGACAGGTTAATTACAGGAGACTTCAAAGCCTTCAAACCTATGTAACACAA
 GCTCAGATAGACAGACTTATTAAATGGGCGTCTTACCGCTCTTAATGTTTATGTTTCTCAA
 GCTCAGATAGACAGACTTATTAAATGGGCGTCTTACCGCTCTTAATGTTTATGTTTCTCAA
 GCTCAGATAGACCGTCTTATTAAATGGCAGATTAACTGCACTTAATGCATATGTCTCTAAG
 GCTCAGATAGACCGTCTTATTAAATGGCAGATTAACTGCACTTAATGCATATGTCTCTAAG
 GCTCAAGTGGATCGTCTTATAACTGGTAGATTGTCTCACTTTCTGTTTAGCATCTGCT

CCoV
 FCoV
 TGE
 PRCoV
 HCoVOC43
 PEDV
 SARSUrb
 SARSTor2
 BCoV
 HEV
 MHV
 RtCoV
 IBV

ACTTTAACCAGACAAGCAGAGGTTAGGGCTAGTAGACAACCTTGCTAAAGACAAGGTTAAT
 ACTCTAACCAGACAAGCAGAGGTTAGGGCTAGTAGACAACCTTGCCAAAGACAAGGTTAAT
 ACTCTAACCAGACAAGCGGAGGTTAGGGCTAGTAGACAACCTTGCCAAAGACAAGGTTAAT
 ACTCTAACCAGACAAGCGGAGGTTAGGGCTAGTAGACAACCTTGCTAAAGACAAGGTTAAT
 ACATTGACTAAGTACTAGCTGAAGTTCTGCTTCCAGACAGCTTGCAACAACAAAAGTGAAT
 ACCCTCACTAAGTACTAGGTTTACGGCTAGCAGGAAGCTAGCAGCAAAAAGGTTAAT
 CAACTAATCAGGGCTGCTGAAATCAGGGCTTCTGCTAATCTTGCTGCTACTAAAATGTCT
 CAACTAATCAGGGCTGCTGAAATCAGGGCTTCTGCTAATCTTGCTGCTACTAAAATGTCT
 CAGCTTAGTGATTCTACACTAGTAAATTTAGTGCAGCACAAGCTATTGAGAAAGTTAAT
 CAGCTTAGTGATTCTACACTAGTAAATTTAGTGCAGCACAAGCTATTGAGAAAGTTAAT
 CAGCTGAGTGACATGACCCCTTGTAAAGGTGAGTGCTGCCAGGCTATAGAGAAAGTTAAT
 CAGCTGAGCGACATGACCCCTTATTAAAGGTGAGTGCTGCCAGGCTATAGAGAAAGTTAAT
 AAGCAGGCGGAGTATATTAGAGTGTCAACAACAGCGTGAGTTAGCTACTCAGAAATTAAT

CCoV
 FCoV
 TGE
 PRCoV
 HCoVOC43
 PEDV
 SARSUrb
 SARSTor2
 BCoV
 HEV
 MHV
 RtCoV
 IBV

GAATGCGTTAGGTCTCAATCCCAGAGATTGGATTCTGTGGTA---ATGGTACACATTTG
 GAATGTGTTAGGTCTCAGTCTCAGAGATTTCGGATTCTGTGGTA---ATGGTACACATTTG
 GAATGCGTTAGGTCTCAGTCTCAGAGATTTCGGATTCTGTGGTA---ATGGTACACATTTG
 GAATGCGTTAGGTCTCAGTCTCAGAGATTTCGGATTCTGTGGTA---ATGGTACACATTTG
 GAGTGTGTTCAAAATCCCAGTCTAAGCGTTATGGCTTCTGTGGAA---ATGGCACTCACATT
 GAGTGCCTCAAAATCGCAATCTCAGCGTTACGGTTTTTGTGGTGTGATGGCGAGCAGATT
 GAGTGTGTTCTTGGACAATCAAAAAGAGTTGACTTTTGTGGAA---AGGGCTACCACTT
 GAGTGTGTTCTTGGACAATCAAAAAGAGTTGACTTTTGTGGAA---AGGGCTACCACTT
 GAATGTGTTCAAAAGCCAATCATCTAGGATAAATTTTGTGGTA---ATGGTAATCATATT
 GAATGTGTTCAAAAGCCAATCATCTAGGATAAATTTTGTGGTA---ATGGTAATCATATT
 GAGTGTGTTAAAGGCCAATCATCTAGGATAAATTTTGTGGCA---ATGGCAATCATATA
 GAGTGTGTTAAAGGCCAATCACCTAGGATAAATTTTGTGGCA---ATGGCAATCATATA
 GAGTGTGTTAAGTCACAGTCTATTAGGTACTCCTTTTGTGGTA---ATGGACGACATGTT

CCoV
 FCoV
 TGE
 PRCoV
 HCoVOC43
 PEDV
 SARSUrb
 SARSTor2
 BCoV
 HEV
 MHV
 RtCoV
 IBV

TTTTCACTTGCAAATGCGGCACCAATGGCATGATTTTCTTTACACAGTGCTATTACCA
 TTTTCACTAGCAAATGCAGCACCAATGGCATGATTTTCTTTACACAGTGCTATTACCA
 TTTTCACTCGCAAATGCAGCACCAATGGCATGATTTTCTTTACACAGTGCTATTACCA
 TTTTCACTCGCAAATGCAGCACCAATGGCATGATTTTCTTTACACAGTGCTATTACCA
 TTCTCAATTGTTAATGCTGCTCCTGAGGGGCTGTTTCTTCCACACTGTCTTGTGCGG
 TTCTCTCTGTACAGGCGGCACTCAGGGCCTGCTGTTCTTACATACAGTACTGTACCG
 ATGTCCTTCCCAACAGCAGCCCGCATGGTGTGTCTTCTACATGTCACGTATGTGCCA
 ATGTCCTTCCCAACAGCAGCCCGCATGGTGTGTCTTCTACATGTCACGTATGTGCCA

BcoV
HEV
MHV
RtCoV
IBV

ATATCATTAGTGCAGAATGCTCCATATGGTTTGTATTTATCCACTTTAGCTATGTCCCT
ATATCATTAGTACAGAATGCTCCATATGGTTTGTATTTATCCATTTTAGCTATGTCCCT
TTGTCATTAGTCCAGAATGCGCCTTATGGTTTATATTTTATTCATTTAGCTATGTCCCT
TTGTCATTAGTCCAGAATGCGCCTTACGGTTTATATTTTATTCATTTAGCTATGTCCCT
CTAACCATACCGCAAAATGCACCTAATGGTATAGTGTATACACTTTTCTTATACTCCA
* * * * *

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSurba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV

ACAGCTTATGAACTGTGACGGCCTGGTCAGGTATTTGTGCGT---CAGATGGCAGTCGC
ACAGCTTATGAACTGTAAACAGCTTGGTCAGGTATTTGTGCTT---CAGATGGCGATCGC
ACGGCTTATGAACTGTGACTGCTTGGCCAGGTATTTGTGCTT---CAGATGGTGATCGC
ACGGCTATGAACTGTGACTGCTTGGTCAGGTATTTGTGCTT---TAGATGTTGATCGC
ACACAATATAAGGATGTTGAAGCGTGGTCTGGGTTGTGCGTTG---ATGGTACAAACGGT
GGTGATTTTGTAAATGTTCTTGCCATCGCTGGCTTATGCGTTA---ATGGTGAATGTC
TCCCAGGAGAGGAACTTACCACAGCGCCAGCAATTTGTCTATG---AAGGCAAAGCATAC
TCCCAGGAGAGGAACTTACCACAGCGCCAGCAATTTGTCTATG---AAGGCAAAGCATAC
ACTAAGTATGTCACTGCGAAGGTTAGTCCCGTCTGTGCATTG---CTGGTGATAGAGGT
ACCAAGTATGTTACAGCAAAGGTTAGTCTGGTTTGTGCATTG---CTGGCGATATAGGA
ACTTCCTTTACAACGGCAAATGTGAGTCTGGGCTATGCATT---CTGGTGATAGAGGA
ACATCCTTTACAACGGTAAATGTGAGTCTGGGCTATGCATT---CTGGTGATAGAGGA
GATAGTTTTGTTAATGTTACTGCAATAGTGGGTTTTTGTGTAAAGCCAGCTAATGCTAGT
* * * * *

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSurba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV

ACTTTTGGACTTGTGTTGAGGATGTCCAGCTGACGC-TATTTGCGAA-----TTAGAT
ACTTTTGGACTTGTGTTGAGGATGTCCAGTTGACGT-TGTTTCGTAA-----TCTAGAT
ACTTTTGGACTTGTGTTGAGGATGTCCAGTTGACTT-TGTTTCGTAA-----TCTAGAT
ACTTTTGGACTTGTGTTGAGGATGTCCAGTTGACTT-TATTTGCGTA-----TCTAGAT
TATGTGTTGCGCAACCTAATCTTGCTCT--TTACAAAGAAGGCA-----ATTATT
TTGACTCTACGTGAGCCTGGCTTAGTCTTGTGTTACGCATGAACCTCAAACCTTATACTGCG
TTCCCT-----CGTGAAGGTGTTTTTGTGTTTAAATG-----GCACCTT
TTCCCT-----CGTGAAGGTGTTTTTGTGTTTAAATG-----GCACCTT
ATAGCC-----CCTAAGAGTGGTTATTTTGTGTTAATGTA-----ATAATA
ATATCG-----CCTAAGAGTGGTTATTTTATTAATGTA-----ATAATT
TTAGCA-----CCTAAGAGTGGATATTTTGTGTTCAAGATG-----ATGGAG
TTAGCA-----CCTAAGAGTGGATATTTTGTGTTCAAGATC-----ATGGAG
CAGTATGCAATAGTGCCCGCTAATGGTAGGGTATTTTATACAA-----GTTAAT
* * * * *

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSurba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV

GAAAAATTTTATTTGACGCCCAGAACTATGTATCAGCCAGAGTTGCAACTAGTTCTGAT
GACAAGTTCTATTTGACCCCCAGAACTATGTATCAGCCTAGAGTTGCAACTAGTTCTGAT
GACAAGTTCTATTTGACCCCCAGAACTATGTATCAGCCTAGAGTTGCAACTAGTTCTGAT
GACAAGTTCTATTTGACCCCCAGAACTATGTATCAGCCTAGAGTTGCAACTAGTTCTGAT
ATAGAAT-----CACATCTCGCATAATGTTTGAACCACGTATTCCTACCATTGGCAGAT
ACGGAATATTTGTTTCACTGCGACGTATGTTGAACCTAGAAAACCTACCGTTAGTGAT
CTTGGTTTAT----TACACAGAGGAACTTCTTTTCTCCACAAATAATTACTACAGACAAT
CTTGGTTTAT----TACACAGAGGAACTTCTTTTCTCCACAAATAATTACTACAGACAAT
CTTGGATGTT----CACTGGTAGTGGTTATTACTACCTGAACCCATACTGGAATAAT
CTTGGATGTT----CACTGGTAGTGGTTATTACTACCTGAACCCATACTGGAATAAT
AGTGGAAGTT----CACAGGTAGTAATTATTACTACCTGAACCCATACTGGAATAAT
AATGGAAGTT----CACAGGTAGTAATTATTACTACCTGAATCCATTACAGATAAAAAAC
GGTAGTTACTACATCACTGCACGAGATATGTATATGCCAAGAGCTATTACTGCAGGAGAT
* * * * *

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSurba
SARSTor2
BcoV
HEV
MHV

TTTGTTCAAATAGAAGGCTGTGATGTGTTGTTTGTAAATGGAACGTGAATTGAATTGCCT
TTTGTTCAAATTGAAGGGTGTGATGTGTTGTTTGTCAACGCGACTGTAATTGATTGCCT
TTTGTTCAAATTGAAGGGTGTGATGTGTTGTTTGTAAATGCAACTGTAAGTGATTGCCT
TTTGTTCAAATTGAAGGGTGTGATGTGTTGTTTGTAAATGCAACTGTAAGTGATTGCCT
TTTGTTCAAATTGAGAGTTGTGTTGTTTGTAAATGCAACTGTAAGTGATTGCCT
ACATTGTCTCAGGAAATTTGTGATGTGTTTGTAAATGCAACTGTAAGTGATTGCCT
ACATTGTCTCAGGAAATTTGTGATGTGTTTGTAAATGCAACTGTAAGTGATTGCCT
GTTGTTGTTATGAGTACCTGTGCTGTTTAACTATACTAAAGCGCGGATGTAATGCTGAAC
GTTGTTGTTATGAGTACCTGTGCTGTTTAACTATACTAAAGCGCGGATGTAATGCTGAAC
AGTGTCGTGATGAGTAGTTGCGCAGCAAACTACACAAAGGCACCTGAAGTTCCTTGAAC
* * * * *

RtCoV
IBV
AGTGTCTGATGAGTAGTTGCGCAGTAACTACACAAAGGCACCTGAAGTTTTCTTGAAC
GTAGTTACGCTTACTTCTTGTCAAGCAAATTATGTAAGTGTAATAAGACCGTCATTACT
* * *

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSurba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV
AGTATCATA---CCTGACTATATCGATATTAATCAAACCTGTTCCAGGACATATTAGAAAAAT
AGTATTATA---CCTGACTATATTGACATTAATCAAACCTGTTCAAGACATATTAGAAAAAT
AGTATTATA---CCTGATTATATTGATATTAATCAGACTGTTCAAGACATATTAGAAAAAT
AGTATTATA---CCTGATTATATTGATATTAATCAGACTGTTCAAGACATATTAGAAAAAT
ACCATTGTG---CCAGAGTATATTGATGTTAATAAGACGCT--GCAAGAAATTAAGTTACA
GATGTAATC---CCAGATTACATCGATGTTAACAACAACTTGATGAGATTTTAGCTTCT
CCTCTGCAA---CCTGAGCTCGACTCATTCAAAGAAGAGCTGGACAAGTACTTCAAAAAAT
CCTCTGCAA---CCTGAGCTTGACTCATTCAAAGAAGAGCTGGACAAGTACTTCAAAAAAT
ATTTCAACA---CCCAACCTCCATGATTTTAAGGAAGAGTTGGATCAATGGTTTAAAAAC
ACATCGACA---CCCAACCTTCTGACTTCAAGGAAGAATTGTATCAATGGTTTAAAAAC
ACTTCAATA---CCTAATCTACCCGACTTTAAGGAGGAGTTAGATAAATGGTTTAAAAAT
ACTTCAATA---ACTAATCTACCCGACTTTAAGGAGGAGTTAGATAAATGGTTTAAAAAT
ACATTCGTAGACAATGATGATTTTGATTTAATGACGAATTGTCAAAATGGTGGATGAT
* * *

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSurba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV
TTCAGACCAAATTGGACTGTACCCGAGTTGCCACTTGACATTTTTCATGCAACCTACTTA
TACAGACCAAATTGGACTGTACCTGAATTTACACTTGATATTTTCAACGCAACCTATTTA
TTTAGACCAAATTGGACTGTACCTGAGTTGACATTTTACATTTTAAACGCAACCTATTTA
TTTAGACCAAATTGGACTGTACCTGAGCTGACATTTGGACGTTTAAACGCAACCTATTTA
AATTG-CCAAATTACACTGTTCCAGACCTAGTTGTCGAACAGTACAACCAAGACTATTTTG
--CTG-CCCAATAGAACTGGTCCAAAGTCTTCCCCTAGATGTTTAAATGCCACTTATCTT
CATACATCACCAGATGTTGATCT-TGGCGACATTTCAAGGCA--TTAACGCTTCTGTGCTC
CATACATCACCAGATGTTGATCT-TGGCGACATTTCAAGGCA--TTAACGCTTCTGTGCTC
CAAACATCAGTGGCACCAGATTTGTCACTTGATTATA-----TAAATGTTACATTTCTTG
CAATCTTCAGTGGCACCAGATTTGTCACTTGATTATA-----TAAATGTTACGTTCTTG
CAGACGTCTATTGCGCCTGATTATCTCTCGATTTGAGAAATTAACGTTACCTCTCTG
CAGACGTCTATTGTCCTGATTATCTTTCGATATCGGGAATTAATGTTACATTCCTT
-ACTAAGCATGAGCTACCAGACTTTGAC--AAATTCAATTA---CACAGTACCTATACTT
* *

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSurba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV
AACCTGACTGGTGAAATTATGACTTAGAATTTAGGTCAGAAAAGTTACATAACACCACA
AATCTGACTGGTGAAATTGATGACTTAGAGTTTAGGTCAGAAAAGCTACATAACCACTACA
AACCTGACTGGTGAAATTGATGACTTAGAATTTAGGTCAGAAAAGCTACATAACCACTACT
AACCTGACTGGTGAAATTGATGACTTAGAATTTAGGTCAGAAAAGCTACATAACCACTACT
AATTGACCAAGTAAATTAGCACCCTTGAAATAAATCTGCGGAGCTTAATTACACTGTT
AATCTTACTGGTGAAATTGAGATCTAGAGCAGCGTTAGAGTCTCTCCGTAATACTACA
AACATTCAAAAAGAAATTGACCGCCTCAATGAGG-----
AACATTCAAAAAGAAATTGACCGCCTCAATGAGG-----
GACCTACAAGATGAAATGAATAGGTTACAGGAGG-----
GACCTACAAGATGAAATGAATAGGTTACAGGAGG-----
GACCTGACTGATGAGATGAACAGGATTCAAGGAG-----
GACCTGCTCTATGAGATGAACAGGATTCAAGGAG-----
GACATTGATAGTGAATTTGATCGTATTCAAGGCG-----
* * *

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSurba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV
GTAGAACTTGCTATTCTCATTGATAATATTAATAACACATTAGTCAATCTTGAATGGCTC
GTAGAACTTGCCATTCTCATTGATAACATTAATAATACATTAGTCAATCTTGAATGGCTC
GTAGAACTTGCCATTCTCATTGACAACATTAACAATACATTAGTCAATCTTGAATGGCTC
GTAGAACTTGCCATTCTCATTGACAACATTAACAATACATTAGTCAATCTTGAATGGCTC
CAAAAATTGCAAACTCTGATTGACAACATAAATAGCACATTAGTCGACTTAAAGTGGCTC
GAAGAGCTCCGAAGTCTCATTAAACAACATCAACAACACACTTGTGACCTTGAGTGGCTC
-----TCGCTAAAAATTTAAATGAATCACTCATTGACCTTCAAGAAATTG
-----TCGCTAAAAATTTAAATGAATCACTCATTGACCTTCAAGAAATTG
-----CAATAAAAGTTTTAAATCAGAGCTACATCAATCTCAAGGACATT
-----CTATAAAAGTTTTAAATCAGAGCTACATCAATCTCAAGGACATT
-----CAATTAAGAAGTTAAATGAGAGTTACATCAACCTCAAGGACGTT
-----CAATTAAGAAGTTTTAAATGAGAGTTACATCAACCTCAAGGAAATT
-----TTATACAGGCTCTTAATGACTCTTAATAGACCTTGAAAACTT
* * *

CcoV AACAGAATTGAACTTATGTAAAATGGCCTTGGTATGTTTGGCTACTAATTGGATTAGTA
 FcoV AATAGAATTGAACTTATGTAAAATGGCCTTGGTATGTGTGGCTACTGATAGGTTTAGTA
 TGE AATAGAATTGAACTTATGTAAAATGGCCTTGGTATGTGTGGCTACTAATAGGCTTAGTA
 PRCoV AATAGAATTGAACTTATGTAAAATGGCCTTGGTATGTGTGGCTACTAATAGGCTTAGTA
 HCoVOC43 AACCGGGTTGAGACTTACATCAAGTGGCCGTTGGTGGGTTGGTTGATCATTTGATCGTG
 PEDV AACCGAGTTGAGACATACATCAAGTGGCCGTTGGTGGGTTGGTTGATCATTTGATCGTG
 SARSUrba GGAAAAATATGAGCAATATATTAATGGCCTTGGTATGTTTGGCTCGGCTTCA---TTGCT
 SARSTor2 GGAAAAATATGAGCAATATATTAATGGCCTTGGTATGTTTGGCTCGGCTTCA---TTGCT
 BcoV GGTACATATGAGTATTATGTAAAATGGCCTTGGTATGTATGGCTTTAATGGCTTTGCT
 HEV GGTACATATGAGTATTATGTAAAATGGCCTTGGTATGTATGGCTTTAATGGCTTTGCT
 MHV GGCACATATGAAATGTATGTAAAATGGCCTTGGTATGTGTGGTTGCTAATGGATTAGCT
 RtCoV GGCACATATGAGTATTATGTAAAATGGCCTTGGTATGTGTGGTTGCTAATGGATTAGCT
 IBV TCAATACTCAAACTTATATTAAGTGGCCTTGGTATGTGTGGTTAGCCATAGCTTTTGCC

* * * * *

CcoV GTAATATTCTGCATACCCATATTGCTATTTTGTGTTGTAGTACTGGTTGTTGTGGATGT
 FcoV GTAGTATTTTGCATACCATTAAGTCTATTTTGTGTTTGTAGTACAGGTTGTTGTGGATGC
 TGE GTAATATTTTGCATACCATTAAGTCTATTTTGTGTTTGTAGTACAGGTTGTTGTGGATGC
 PRCoV GTAATATTTTGCATACCATTAAGTCTATTTTGTGTTTGTAGTACAGGTTGTTGTGGATGC
 HCoVOC43 CTCATCTTTGTGGTGAAGTATGTTGCTATTATGTTGTTGTTCTACTGGTTGCTGGCTTC
 PEDV CTCATCTTTGTGTTGCTATTACTAGTGTCTGCTGCAATTTCCACGGGTTGTTGTGGATGC
 SARSUrba GGACTAATTGCCATCGTCATGGTTACAATCTTGCTTTGTTGCTAGTGTGTTGCTAGT
 SARSTor2 GGACTAATTGCCATCGTCATGGTTACAATCTTGCTTTGTTGCTAGTGTGTTGCTAGT
 BcoV GGTGTAGCTATGCTTGTGTTTACTATTCTTCATATGCTGCTGTACAGGATGTGGGACTAGT
 HEV GGTGTAGCTATGCTTGTGTTTACTATTCTTCATATGCTGCTGTACAGGATGTGGGACTAGT
 MHV GGTGTAGCTGTTTGTGTTGTTTATTTTTCATATGTTGCTGCACGGGTTGTGGCTCATGT
 RtCoV GGTGTAGCTGTTTGTGTTTGTGTTTATTTTTCATATGTTGCTGCACAGGTTGTGGCTCTGT
 IBV ACTATATCTTCATCTTAATACTAGGATGGGTTTCTTCATGACTGGTTGTTGTGGTTGT

* * *

CcoV ATCGGGTGTTTAGGAAGCTGTTGTCTATTCCATAT-GTAGTAGAGGCCA---ATTTGAAAG
 FcoV ATAGGTTGTTTAGGAAGTGTGTTGCTACTCTATAT-GTAGTAGAAGACA---ATTTGAAAA
 TGE ATAGGTTGTTTAGGAAGTGTGTTGCTACTCTATAT-GTAGTAGAAGACA---ATTTGAAAA
 PRCoV ATAGGTTGTTTAGGAAGTGTGTTGCTACTCTATAT-TCAGTAGAAGACA---ATTTGAAAA
 HCoVOC43 TTTAGTTGTTTGTGATCTTCTATTAGAGGTTGTT-GTGAATCAACTAA---ACTTCCTTA
 PEDV TGCAGGTTGCTGCGGTGCTTGTGTTTTCAGGTTGTT-GTAGGGTCTAG---ACTTCAACC
 SARSUrba TGCCTCAAGGGTGCATGCTCTTGTGGTTCTTGCT-GCAAGTTTGATGA---GGATGACTC
 SARSTor2 TGCCTCAAGGGTGCATGCTCTTGTGGTTCTTGCT-GCAAGTTTGATGA---GGATGACTC
 BcoV TGTTTTAAGAT---ATG---TGGTGGTTGTTGTG-ATGATTATACTGG---ACACCAGG-
 HEV TGTTTTAAGAA---ATG---TGGCGGTTGTTGTG-ATGATTATACTGG---ACACCAGG-
 MHV TGTTTTCAAGAA---GTG---TGGAATTGTTGTG-ATGAGTGTGGAGG---ACACCAGGA
 RtCoV TGTTTTAAGAA---ATG---TGGAATTGTTGTG-ATGAGTGTGGAGG---ACGTCAGGC
 IBV TGTGTGGATGC-TTGCCATTATGCCTCTAATGAGTAAGTGTGGTAAGAAATCTTCTTA

*

CcoV TTATGAACCTATTGAAAAAGTTCATGTTCACTGA-----
 FcoV TTATGAACCAATTGAAAAAGTGCATGTCCACTAA-----
 TGE TTACGAACCAATTGAAAAAGTGCACGTCCATTAA-----
 PRCoV TTATGAACCTATTGAAAAAGTGCACGTCCATTAA-----
 HCoVOC43 TTACGACG---TTGAAAAGATCCACATACAGTAA-----
 PEDV TTACGAAGCTTTGAAAAGTCCACGTGCAGTGA-----
 SARSUrba TGAGCCAGTTCTCAAGGGTGTCAAATTACATTACACATAA-----
 SARSTor2 TGAGCCAGTTCTCAAGGGTGTCAAATTACATTACACATAA-----
 BcoV -AGT-TAGTAAT-TAAAA---CATCACATGACGACTAA-----
 HEV -AGT-TTGTAAAT-CAAAA---CTTCACATGACGATTAA-----
 MHV CAGTATTGTGATACATAATATTTCCTCTCATGAGGATTGA-----
 RtCoV AGGTATTGTGATACATAATATTTCCTCTCATGAGGATTGA-----
 IBV TTACACGACTTTTGATAACGATGTGGTAACTGAACAATACAGACCTAAAAAGTCTGTTTG

* * *

CcoV
 FcoV

TGE	-
PRCoV	-
HCoVOC43	-
PEDV	-
SARSUrba	-
SARSTor2	-
BCoV	-
HEV	-
MHV	-
RtCoV	-
IBV	A

Figure 2: Phylogenetic Analysis of S Gene

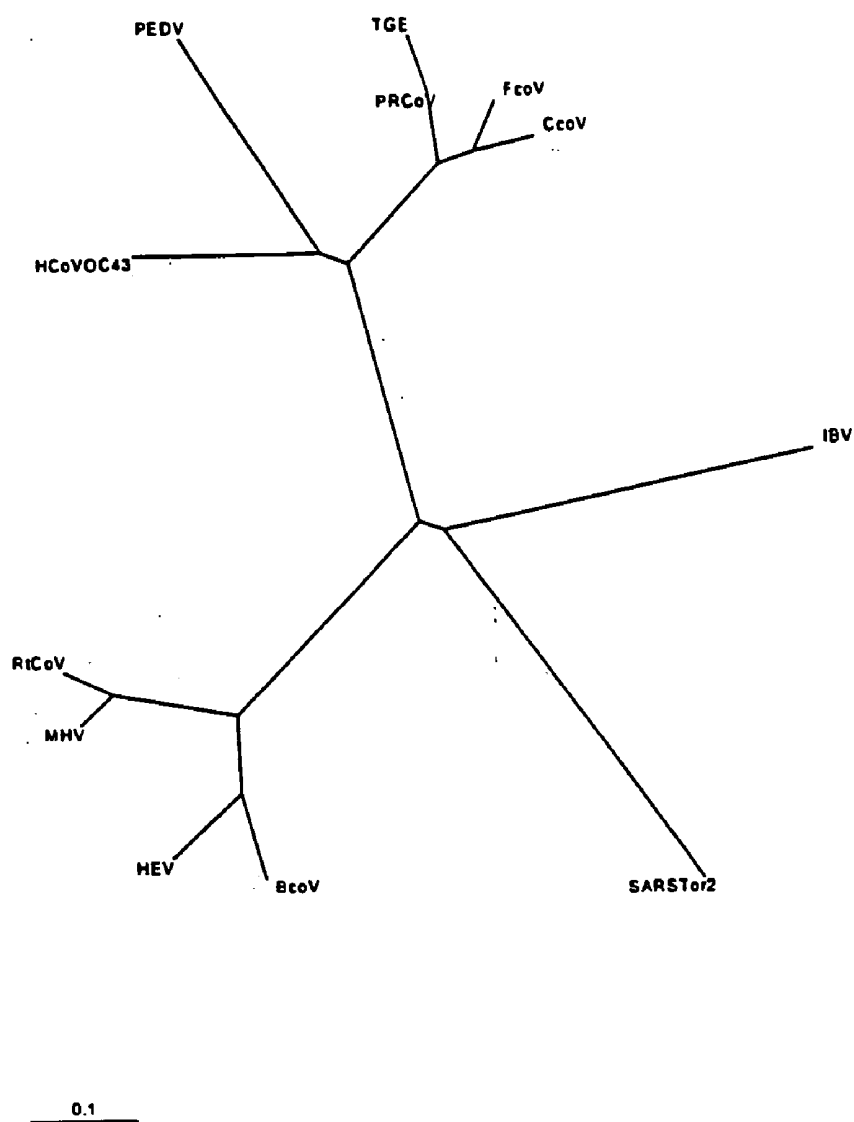
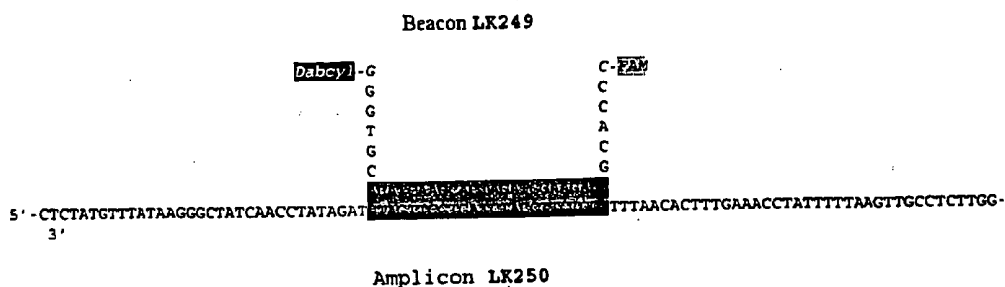


Figure 3: Molecular Designs for SARS-Associated S Gene LK249 (Molecular Beacon) LK250 (Amplicon) and LK251 & LK252 (PCR Primers)

NOTE: LK249 is a TET-molecular beacon, which recognizes the *S* gene of coronavirus (SARS Tor2 and SARS urbani human pathogenic strains). It will be used in a real-time PCR diagnostic for the identification of SARS-associated coronavirus RNA/DNA.



LK249

A. Target recognition sequence:	24 nucleotides (11 G/C)
B. Length of the arms:	6 nucleotides (5 G/C)
C. Melting temperature of the beacon:	dG = -2.37 dH = -46.3 dS = -135.9 Tm = 67.7 °C
D. Melting temperature of target:	°C

LK251 5'-CTCTATGTTTATAAGGGCTATCAACC-3'

Length: 26 nucleotides (10 G/C)
 Tm: °C
 Position: (see alignment below)

LK252 5'-CCAAGAGGCAACTTAAAAATAGGTTTC-3'

Length: 27 nucleotides (10 G/C)
 Tm: °C
 Position: (see alignment below)

S-RT 5'-AGGCTGTAAGAA-3'

Length: 14 nucleotides (6 G/C)
 Tm: 47 °C
 Position: (see alignment below)

LK250 Amplicon (95 nucleotides)

5' - CTCTATGTTTATAAGGGCTATCAACCTATAGATGTAGTTCGTGATCTA
CCTTCTGGTTTTAACACTTTGAAACCTATTTTAAAGTTGCCTCTTGG -3'

DNA sequence alignment of complete
S genes from corona virus strains

CcoV	ATGATTGTGCTTACATTGTGCCTTTTCTTGTT---TTTGTACAGTAGTGTGAGCTGTACA
FcoV	ATGATTGTGCTCGTAACTTGCCCTCTTGTTGTTATGTTCATACCACACAGTTTGTGAGTACA
TGE	ATGAAAAAACTATTTGTGGTTTTGGTCGTAATGCCATTGATTATGGAGACAATTTTCCT
PRCoV	-----
HCoVOC43	-----
PEDV	-----
SARSurba	-----
SARSTor2	-----
BcoV	-----
HEV	-----
MHV	-----
RtCoV	-----
IBV	-----
CcoV	TCAAACAATGACTGTGTACAAGTTAATGTGACACAAGTGCCTGGCAATGAAAATATTATC
FcoV	ACAAATAATGAATGCATACAAGTTAACGTAACACAATTGGCTGGCAATGAAAACCTTATC
TGE	TGTTCTAAATTGACTAATAGAACTATAGGCAACCAAGTGAATCTCATGAAACCTTCCTT
PRCoV	-----
HCoVOC43	-----
PEDV	-----ATGAGGTCTTTAATTTACTTCTGGTTGCTCTT
SARSurba	-----ATGTTT
SARSTor2	-----ATGTTT
BcoV	-----ATGTTTTTGATACTT
HEV	-----ATGTTTTTTATACTT
MHV	-----ATGCTATTCTGTGTTT
RtCoV	-----ATGCTATTCTGTGTTT
IBV	-----
CcoV	AAAGATTTTCTATTTTCAGAACTTTAAAGAAGAAGGAAGTTTAGTTGTTGGTGGTTATTAC
FcoV	AGAGATTTTCTGTTTAGTAACTTTAAAGAAGAAGGAAGTGTAGTTGTTGGTGGTTATTAC
TGE	CTAAACTATAGTAGTAGGTTACCACCTAATTCAGATGTGGTGTAGGTGATTATTTTCCT
PRCoV	-----
HCoVOC43	-----
PEDV	ACCAGTACTTCCAACACTCAGCCTACCACAAGATGTCACTAGGTGCCAGTCTACTACTAA
SARSurba	ATTTTCTTATTATTTCTTACTCTCACTAGTGGTAGTGACCTTGACCGGTGCACCACTTTT
SARSTor2	ATTTTCTTATTATTTCTTACTCTCACTAGTGGTAGTGACCTTGACCGGTGCACCACTTTT
BcoV	TAAATTTCTTACCAATGGCTTTTGCTGTTATAGGAGATTTAAAGTGTACTACGGTTTCC
HEV	TAAATCTCCCTGCCCTCTGCTTTTGCACTTATAGGGGATTTAAAGTGTACTACTTCATTA
MHV	TAAACCTTGTGGCCTCTTCTAGGGTATATTGGTGATTTTAGATGTATCCAACCTTGTA
RtCoV	TAAACCTTATGGCCTCTTGTCTAGGGTATATTGGTGATTTTAGATGTATCAACCTTGTA
IBV	-----
CcoV	CCCACAGAGGTGTGGTATAACTGTTCCACAACCTCAACAACTACCGCTTATAAGTATTTT
FcoV	CCTACAGAGGTGTGGTACAACCTGCTCTAGAACAGCTCGAACTACTGCTTTTCACTATTTT
TGE	ACTGTACAACCTTGGTTTAAATTCATTGCAATGATAGTAATGACCTTTATGTTACACTG

PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV

CTTTAGGCGGTTCTTTTCAA--AATTTAATGTTCAGGCACCTGCCGTCGTCGTTTGGGT
GA-----TGATGTTCAAGCTCCTA--ATTACACTCAACATACTTCAT----CT
GA-----TGATGTTCAAGCTCCTA--ATTACACTCAACATACTTCAT----CT
ATTAATGATGT---TGACACCGGTGCTCCCTCTATTAGCACTGATATTGTCGATGTTACT
ATTAATGACGT---TGACACTGGTGTGCCATCTATTAGCTCTGAAGTTGTTGATGTCAC
AATACCGACACCTCTAATGCCAGCGCTCCAAGCGTTAGTACAGAGGTAGTTGATGTTTCC
AACACCCGCATTTCTAATGCGCGCGCACCCAGTGTTAGCACAGAGGTAGTTGATGTTTCT

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV

AGTAATATACATGCATTTTATTTTGATATGGAAGCCATGGAGAATAGTACTGGCAATGCA
AATAATATACATGCCTTTTATTTTGTTATGGAAGCCATGGAAAATAGCACTGGTAATGCA
GAAAATCTTAAAGCATGTATTGGGATT---ATGCTACAGAAAATATCACTTGGAAAT---

GGTTACCTACCTAGTATGAACTCTTCTAGCTGGTACTGTGGCACAGGCATTGAAACTGCT
ATGAG---GGGGGTTTACTATCCT---GATGAAATT---TTTAGATCAGACACTCTT----
ATGAG---GGGGGTTTACTATCCT---GATGAAATT---TTTAGATCAGACACTCTT----
AATGGTTTAGGTACTTATTATGTTTATAGATCGTGTGATTAAATACTACGTTGTTG---
AATGGTTTGGGGACTTTCTATGTTTATAGATCGTGTCTATTTAAATACCACATTGTTG---
AAAGGGATTGGTACTTATTATGTTTATAGATCGAGTCTATTTAAATGCCACACTATTG---
AAAGGTCTTGGTACATATTACGTTTATAGATCGTGTATTATTTAAATGCCACGTTATTG---

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV

CGTGGTAAACCTTTACTAGTACATGTTTATGGTAATCCTGTTAGTATCATTGTTTACATA
CGTGGTAAACCATTTATTATTTTATGTCATGGTGAGCCTGTTAGTGTATT-----ATA
CACAGACAACGGTTAAACGTAGTCGTTAATGGATAACCCATACTCCATCAGATT---ACA

AGTGGCGTTTATGTTATTTTCTCAGCTACATCGATTCTGGTCAGGGCTTTGAGA--TTG
-----TATTTA--ACTCAGGATTTATTTCTTC-CATTTTATTCTAATGTTACAGG--GTT
-----TATTTA--ACTCAGGATTTATTTCTTC-CATTTTATTCTAATGTTACAGG--GTT
CTTAATGGTTACTACCCTACTTCAGGTTCTACATATCGTAATATGGCACTGAAGG--GAA
CTCAATGGTTATTACCCAATTTAGGTCATACATTTCTGTAATATGGCTCTGAAAG--GAA
CTTACTGGTTATTACCCTGTAGATGGGTCCATGTATAGAAACATGGCTCTAACGG--GAA
CTTACTGGTTACTACCCTGTAGATGGGTCCATGTATCGTAACATGGCTCTAATGG--GTA

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV
SARSUrba
SARSTor2
BcoV
HEV
MHV
RtCoV
IBV

TCAGCTTATAGAGATGATGTGCAATTTAGGCCGCTTTTAAAGCATGTTTATTGTGTATA
TCGGCTTATAGGGATGATGTGCAACAAAGGCCCTTTTAAACATGGGTTAGTGTGCATA
ACAACCCGCAATTTTAAAT-TCTGCTGAAGGTGCTATTATATGCATTTGTAAGGGCTCACC

GCATTTGCGAAGAGCCGT-TTGATCCTAGTGGTTACCAGCTTTATTTACATAAGGCCACT
TCATACTATTAATCATAC----GTTTGG--CAACCCTGTCAT-ACCTTTTAAGGATGGTA
TCATACTATTAATCATAC----GTTTGG--CAACCCTGTCAT-ACCTTTTAAGGATGGTA
CTTTACTATTGAGCAGACTATGGTTTAAACCACCTTTTCTTTCTGATTTTATTATGGTA
CTCGATTATTGAGCACCTTGTGGTTTAAAGCCGCTTTTATACCTTTTAAATGATGGTA
TTAATACCATAAGCCTTAATTGGTACAAACCACCTTTTATCAGAGTTTAAATGATGGCA
CTAATACCTTAAGCCTTAATTGGTTTGAACCGCCCTTTTATCAGAGTTTAAACGATGGCA

CcoV
FcoV
TGE
PRCoV
HCoVOC43
PEDV

ACTAAAAATGACACCGTTGACTATAATAGCTTTACAATTAACCAATGGCGAGACATATGT
ACTAAAAATCGCCATATTAATCATGAACAATCACCTCCAACAGTGGAAATCCACATGT
ACCTACTACCACCACAGAATCTA-----GTTTGACTTGCAATTGGGGTAGTGAGTGCAGG

AATGGTAACACTAATGCTATTGCACGACTGCGCATTGCCCAGTTTCCCGATAATAAAACA

SARSurba	TTTA-TTTTGCTGCCACAGAGAAATCAAATGTTGTCCGTGGTTGGGTTTTGGTTCTACC
SARSTor2	TTTA-TTTTGCTGCCACAGAGAAATCAAATGTTGTCCGTGGTTGGGTTTTGGTTCTACC
BcoV	TTT---TTGCTAAGGTCAAAAATACCAAGGTTATTAAGGTTGTAATGTATAGTGAG
HEV	TTT---TTGCCAAGGTTAAAAACAGCAGATTTTCTAAAGATGGTGTATTATATAGTGAG
MHV	TAT---TTGCTAAGGTAAAGAACCTTAAAGCATCTTTGCCCAAAGATTCTATTTTCATAT
RtCoV	TAT---ATGCTAAGGTAAAGAACCTCAAAGCATCTTTGCCCATAGGCTCGGCTTCATAC
IBV	-----
CcoV	TTGGGTGACGACAGAAAAATACCATTCTCTGTAGTACCCACAGATAATGGTACGAAATTA
FcoV	ACGGGTGCTGACAGAAAAATTCCTTTCTCTGTATACCCACGACAATGGAACAAAAATC
TGE	TTAAACCATAAGTTCCCTATATGTCTTCTAATTAGAGGCAAATTGTGGTAATATGCTG
PRCoV	-----
HCoVOC43	-----
PEDV	TTGGGCCCTACTGTTAATGATGTTACAACAGGTCGTAAGTGCCTATTCAACAAAGCCATT
SARSurba	ATGAACAACA-AGTCACAGTCGGTGATTA--TTATTAACAATTCTACTAATGTTGTTATA
SARSTor2	ATGAACAACA-AGTCACAGTCGGTGATTA--TTATTAACAATTCTACTAATGTTGTTATA
BcoV	TTTCCTGCTATAACTATAGGTAGTACTT---TTGTAATACATCCTATAGTGTGGTAGTA
HEV	TTTCCTGCTATTACTATAGGTAGTACTT---TTGTAATACTTCTATAGCATAGTAGTA
MHV	TTCCCTACTATAATTATAGGTAGTAATT---TTGTCACCACTTCTATAGTATAGTATTG
RtCoV	TTTCCTACTATAATTATAGGTAGTAATT---TTGTTAATACTTCTATAGTATAGTATTG
IBV	-----
CcoV	TTTGGTCTTGAGTGGAATGATGACTATGTTACAGCCTATATTAGTGATGAGTCTCACCGT
FcoV	TATGGTCTTGAGTGGAATGATGACTTTGTTACAGCTTATATTAGTGGTCGTTCTTATCAC
TGE	TATGGCCTACAATGGTTTGAGATGAGGTTGTTGCTTATTTACATGGTGCTAGTTACCGT
PRCoV	-----
HCoVOC43	-----
PEDV	CCAGCTTATATGCGTGATGGAAGATATTGTTGTGCGGCATAACATGGGATAATGATCGT
SARSurba	CGAGCATGTA-----ACTTTGAAT-----TGTTGACAACCCCTTTCTTTGC
SARSTor2	CGAGCATGTA-----ACTTTGAAT-----TGTTGACAACCCCTTTCTTTGC
BcoV	CAACCACATACTACCAATTTGGATAATAATTACAAGGTCCTTAGAGATCTCTGTTTGC
HEV	GAGCCTCATACCTCACTTATTAATGGTAATTTACAAGGTTGTTGCAAATTTCTGTTTGT
MHV	GAACCGTATA-----ATGGTA-----TAATTAT-GGCATCCATTTGC
RtCoV	GAACCATACA-----ATGGTA-----TTATTAT-GGCATCTATTTGC
IBV	-----
CcoV	TTGAATATCAATAATAATTGGTTTAAACAATGTTACACTC--CTATACTCACGTACAAGCA
FcoV	TTGAACATCAATACTAATTGGTTTAAACAATGTCACACTT--TTGTATTACGCTCAAGCA
TGE	ATTAGTTTGAATAATCAATGGTCTGGCACTGTCACATTGTTGATATGCGTGCGACAACA
PRCoV	-----
HCoVOC43	-----
PEDV	GTCAGTGTTTTTGCTGACAAGATCTATCATTTTTATCTT--AAAAATGATTGGTCCCGG
SARSurba	TGTTTCTAAACCCATGGGTACACAGACACATACTATGAT---ATTCTGA---TAATGCA
SARSTor2	TGTTTCTAAACCCATGGGTACACAGACACATACTATGAT---ATTCTGA---TAATGCA
BcoV	CAGTATACTATGTGCGAGTACCCACATACGATTGTTCATCCTAAGCTGGG---TAATAAA
HEV	CAATACACTATGTGTGAATACCCACATACTATTTGTCTATCCTAATTTGGG---TAATCAA
MHV	CAGTATACCATTTGTCAACTACCGTACACGGATTGCAAACCGAATACGGGCGGTAATAAG
RtCoV	CAGTATACCATTTGTCAATTACCGCACACGGATTGCAAACCTAACACGGGCGGTAACAGC
IBV	-----
CcoV	CCGCCACGTGGCAACACA-GTGCTGCATATGTTTA---TCAAGGTGTTTCAAATTTTACT
FcoV	CTGCTACCTGGGAATACA-GTGCTGCATATGCTTA---CCAAGGTGTTTCTAACTTCACT
TGE	TTAGAAGTCGCTGGCAGCTTGTAGACCTTTGGTGGTTAATCCTGTTTATGATGTCAGT
PRCoV	-----ATGAAAAAATTATTG---TGGTCTTGGTTGTAATGCCATT
HCoVOC43	-----ATGTT-TGTT-TTGCTTGTGTC-ATATGCCTTGT
PEDV	TTGCGACAAGATGTTACAATCGCAGAAGTTGTGCT-ATGCAATATGTTTATACACCTACC
SARSurba	TTTAATTGCACCTTTTCGAGTACATATCTGATGCCTTTTCGCTTGATGTTTCAGAA-----A
SARSTor2	TTTAATTGCACCTTTTCGAGTACATATCTGATGCCTTTTCGCTTGATGTTTCAGAA-----A
BcoV	CG-CGTAGAACTATGGCATTGGGATACAGGTGTTGTTTCTGTTTATATAAGCG-----T

HEV
MHV
RtCoV
IBV

AGCGCTTTATCTTTAGAATACTGGGTTACACCTCTCACTACTAGACAATTT--CTTCTAG
GGTGTCTTTTCCACGCGAGTATTGGGTTACACCTCTTGTCAGCGCCAATAT--TTATTTA
AAGTGTTTCTTCACCGCAGTATTGGGTTACACCACTTGTTAAGCGCCAATAT--TTATTTA
GATGCTTCTCTATAGCTATGACGGCACCGTCATCAGGTATGGCTTGGCTAGCAGTCAG

CC-5' LK252

3'-GTAAGAATGTCGGA-5' S-RT

~~~~~

CcOV  
FcOV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcOV  
HEV  
MHV  
RtCoV  
IBV

TGGCGTCGCAGCACAGAATT--TTGTTTGAAGGTGCTCAGTTTAGCCAATGTAACGGT  
TGGTGTAGCAGCACAAGAATT--TTGTTTGAAGGTGCACAGTTTAGCCAATGTAATGGT  
TGAAGAAGCAGCTTCTACATT--TTGTTTGAAGGTGCTGGCTTTGATCAATGTAATGGT  
TGAAGAAGTAGCTTCTACATT--TTGTTTGAAGGTGCTGACTTTGATCAATGTAATGGT  
TTGCGGTTTACTACTGGTTTGTCTATTTAATGGTACTGGGAGAGGTTGATTGAAGGT  
TTATGGACTAG-GCCAAATT-TCTCATTCAATCACAGTAGGATGGCGTTTGTAAATGGA  
ATTTGGGGCAC-GTCAGC--TTCAGCCTATTTGTGGCTATTTAAAGCCAACCTACATTT  
ATTTGGGGCAC-GTCAGC--TGCAGCCTATTTGTGGCTATTTAAAGCCAACCTACATTT  
CCTTCAATCAA-GATGGTGTATTTTTAATGCTGTTGATTGTAAGAGTGATTTTTATGAGT  
CCTTTGACCAG-GATGGTGTTTATACCATGCTGTTGATTGTGCTAGTAGTTTTATGAGT  
ATTTAATCAA-AAGGGTATTATTACTAGTGCTGTTGATTGTGCTAGTAGTTATACCAGC  
ATTTTAACCAA-AAGGGTATTATTACTAGCGCTGTTGATTGTGCTAGTAGTTATACCAGT  
TTTTTACTGCACACTGTAATTTTTCAGATACTACAGTGTTTGTACACATTTGTATAAA

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

GTTTCCTTTAAATAATACAGTAGATGTTATTAGATTTAACTTAATTTCACTACAGATGTA  
GTGCTCTTTAAATAACACAGTGGATGTTATTAGATTTCAACCTTAATTTCACTGCAGATGTA  
GCTGTTTTAAATAACTCTGTAGACGTCATTAGGTTCAACCTTAATTTTACTACAAATGTA  
GCTGTTTTAAATAACACTGTAGACGTCATTAGGTTTAACTTAATTTTACTACAAATGTA  
TTTTCTCAGATGTTTTGTCTGATGTCATACGTTTACAACCTCAATTTTGAA-----GAA  
GCTGCTGTGGATCGTGCCCCAGAGGCTCTGAGGTTTAAATATTATGACACCTC-----CGTC  
ATGCTCAAGTATGATGAAATGGTACAATCACAGATGCTGTTGATTGT-----T  
ATGCTCAAGTATGATGAAATGGTACAATCACAGATGCTGTTGATTGT-----T  
GAGATTAAGTGTA AACACTATCTATAGACCACTACTGCTGTTTATGAATTAACCGGT  
GAGATTAAGTGTA AACACTTCTTCAATTAACCACTTCTGCTGTTTATGAATTAACCGGT  
GAAATAAAGTGTAAGACCCAAAGTATGAATCCCAATACGGGAGTTTATGATTTATCCGGT  
GAAATAAAGTGTAAGACTCAAAGTATGAATCCCAATACGGGAGTCTATGATTTATCCGGT  
CATGGTGGGTGTCCTTTAACTGGCATGCTTCAACAGAATCTTATACGT-----GTT

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

CAATCTGGCATGGGTGCTACAGTATTTTCACTGAATACAACAGGCGGTGTCATTCTTGAG  
CAATCTGGTATGGGTGCTACAGTATTTTCACTGAATACAACAGGTGGTGTCACTCTTGAA  
CAATCAGGTAAGGGTGCCACAGTGTTTTTCAATTGAACACAACGGGTGGTGTCACTCTTGAA  
CAATCAGGTAAGGGTGCTACAGTGTTTTTCAATTGAACACAACGGGTGGTGTCACTCTTGAA  
AACCTTAGACGTGGAACCATTTTGTTT-----AAAACATCTTATGGTGTGTTGGTGT  
ATTCTTGCTGAAGGCTCAATTGTACT-----CATACTGTTTAGGAACAAATCTTTCT  
CTCAAAATCCA-CTTGCTGAAC TCAAATGCT---CTGTTAAGAGCTT---TGAGATTGAC  
CTCAAAATCCA-CTTGCTGAAC TCAAATGCT---CTGTTAAGAGCTT---TGAGATTGAC  
TACACTGTTTCAAGCAATTCAGATGTTTTACCGCAGTATACCTTAATCTCCCGATTGTAAT  
TACACAGTTCAACCTGTTGCCACTGTATACGTAGAACCTGATTACCAACCAATGGCAT  
TACACCGTCCAACTGTAGGATTAGTGATCCGGCGTGTAGAAATTTGCCTGATTGTAAT  
TACACCGTCCAACTGTAGGACTAGTGATCCGGCGTGTAGAAATTTGCCTGATTGTAAT  
TCTGCTATGAAAAATGGCCAGCTTTTCTATAATTTAACAGTTAGTGATGCTAAGTACCTT

CCoV  
FCoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSurba  
SARSTor2  
BCoV  
HEV

ATTTCTTGTTATAATGACACAGTGAGTGAAGTCGAGT-TTCTACAGTTATGGTGAAATTC  
ATTTTCATGTTATAAGTGACACAGTGAGTGAAGTCAGT-TCTTACAGTTATGGTGAAATCCC  
ATTTTCATGTTATA- ----CAGTGAGTGACTCGAGC-TTTTTCAGTTACCGTGAAATTC  
ATCTCATGTTATAATGATACAGTGAGTGATTGAGC-TTTTCCAGTTACCGTGAAATTC  
TATTGTACCAACAACACTTTAGTTT- ----AGGTGATGCTCACATACCAATTTGGTAC  
TTTGTTTGCAGTAATTCTCTAGATCTCATTTAGCCATTTGCCATACCTCTGGGTGCT  
AAAGGAATTTACCAGACCTCTAATTTCAAGGTTGTTCC-CTCAGGAGATGTTGTGAGATT  
AAAGGAATTTACCAGACCTCTAATTTCAAGGTTGTTCC-CTCAGGAGATGTTGTGAGATT  
ATAGAGGCTTGGCTTAATGATAAGTCGGTGCCCTCTCCATTAAATTTGGGAACGTAAGAC  
ATCGAAGCTTGGCTTAATTTCAAGACCGTTTCTTCGCCCTCTAATTTGGGAACGTAAGATT

MHV  
RtCoV  
IBV  
ATTGAGGAATGGCTAACTGCTAAGTCTGTACCTTCTCTCTCAATTGGGAGCGCAAAACA  
ATTGAGGAATGGTTGGCTGCTAACACAGTACCCTCTCTCTCAATTGGGAGCGCAAAACA  
ACTTTTAGATCATTTCAGTGTGTTAATAATTAAACATCCGTATATTTAAATGGTGATCTT

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV  
ATTCGGCGTAACTGATG-GACCACGTTACTGTTATGTACTCT-ACAATGGCACAGCTCTT  
GTTCCGCATAACTGACG-GACCACGATACTGTTATGTACTTT-ACAATGGCACAGCTCTT  
GTTCCGGCGTAACTGATG-GACCACGGTACTGTTACGTACACT-ATAATGGCACAGCTCTT  
GTTCCGGCGTAACTAATG-GACCACGGTACTGTTACGTACTCT-ATAATGGCACAGCTCTT  
GTTTTGGGCAATTTTT---ATTGCTTTGTAAATACTACTATTGGCAATGAACTACGTCT  
ACTGAAGTACCCTACT---ATTGCTTTCTTAAAGTGGATACTTACAACCTCACTGTTTAT  
CCCTAATATTACAA-----ACTTGTGTCCTTTTGGAGAGGTTTTTAATGCTACTAAATTC  
CCCTAATATTACAA-----ACTTGTGTCCTTTTGGAGAGGTTTTTAATGCTACTAAATTC  
TTTTCAAATTGTAATTTTAAATATGAGCAGCCTGATGTCTTTTATTTCAGGCAGACTCAATT  
TTTTCTAATTGTAATTTTAAATATGAGCAGCCTGATGTCTTTTATTTCAGGCAGACTCTTTT  
TTTCAAATTTGTAACCTTCGACCTGAGCAGTCTATTAAGATTGGTTCAGGCTGAGTCACTC  
TTTCAAATTTGTAACCTTCAACCTGAGCAGTCTATTAAGATTGGTTCAGGCTGAGTCACTC  
GTTTACACCTCTAATGAGACCATAGATGTTACATCTGCAGGTGTTTATTTTAAAGCTGGT

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV  
AAGTATT-TAGGAACATTACCACCTAGTGTCAAGGAAATTGCTATTAGTAAGTGG-----  
AAATATT-TAGGAACATTACCACCTAGTGTCAAGGAAATTGCTATTAGTAAGTGG-----  
AAGTATT-TAGGAACATTACCACCTAGTGTCAAGGAAATTGCTATTAGTAAGTGG-----  
AAGTATC-TAGGAACATTACCACCTAGTGTCAAGGAAATTGCTATTAGTAAGTGG-----  
GCTTTTG-TGGGTGCACTACCTAAGACAGTTCGTGAGTTTGTATT-TCACGCACA-----  
AAATTCT-TGGCTGTTTTACCTCCTACTGTCAAGGAAATTGCTATCACCAAGTAT-----  
CCTTCTG-----TCTATGCATGGGAGAGAAAAAAT---TTCTAATTGTGTTGCT---  
CCTTCTG-----TCTATGCATGGGAGAGAAAAAAT---TTCTAATTGTGTTGCT---  
ACTTGTAAATAATTGATGCTGCTAAGATATATGGTATGTGTTTTCCAGCATAACTATA  
GGTTGTAACAATATTGATGCTTCTCGCTTATATGGTATGTGTTTTGGTAGCACTACTATT  
TCATGTAGTAATATAGATGCTTCCAAGGTTTATGGTATGTGCTTTGGTAGTATATCTATA  
TCATGTAGTAATATAGATGCTTCCAAGGTTTATGGTATGTGCTTTGGTAGCATATCTATA  
GGACCTA-TAACTATAAAGTTATGAGAGAAGTTAA---GCCCTGGCTTATTTT-----

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV  
GGACATTTTATATTAATGGTTACAATTTCTTTAGCACGTTTCTTATTGATTGTATAGCT  
GGCCATTTTATATTAATGGTTACAATTTCTTTAGCACATTTCTTATTGGTTGTATATCT  
GGCCATTTTATATTAATGGTTACAATTTCTTTAGCACATTTCTTATTGATTGTATATCT  
GGCCATTTTATATTAATGGTTACAATTTCTTTAGCACATTTCTTATTGATTGTATATCT  
GGACATTTTATATTAATGGCTATCGCTATTTCACTTTAGGTAATGTAGAGCCGT----  
GGTGATGTTTATGTCAATGGGTTTGGCTATTTGCATCTCGGTTTGTGGATGCTGTGACA  
GATTACTCTGTGCTCTACAAC--TCAACATTTTTTTCAACCTTTAAGTGCTATGGCGTTT  
GATTACTCTGTGCTCTACAAC--TCAACATTTTTTTCAACCTTTAAGTGCTATGGCGTTT  
GATAAGTTTGTCTATACCCAATAGTAGAAGGTTGACCTACAATTGGGCAATTTGGGCTAT  
GATAAGTTTGTCTATACCCAATAGTAGAAGGTTGATCTGCAAGTGGGTAATCTGGTTAT  
GACAAGTTTGGGATACCCAATAGACGCGGAGTTGATTGTCAGCTAGGCAACTCTGGGTTT  
GATAAATTTGCAATACCCAACAGTCGCGGTTGATCTTCAGCTAGGTAATCGGGTCTT  
GTTAATGGTACTGCACAAGATGTTATTTTGTGTGATGGATCACCTAGAGGCTTGTAGCA

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV  
TTTAATTTAA-----CCACTGGTGCTAGTGGAGCAT-TTTGGACAATTGCTTA  
TTTAATTTAA-----CCACTGGTGTTAGTGGAGCTT-TTTGGACAATTGCTTA  
TTTAATTTGA-----CCACTGGTGATAGTGACGTTT-TCTGGACAATAGCTTA  
TTTAATTTGA-----CTACTGGTGATAGTGACGTTT-TCTGGACAATAGCTTA  
--TAATTTCA-----ATGTCACACTGTCAGAAACCACTGATT-TTTGTACTGTGCGTT  
ATTAATTTCACTGGTCATGGCACTGACGATGACGTTTTCAGGTT-TCTGGACCATAGCATC  
CTGC---CAC-----TAAGTTGAATGATCTTTGCTT-CTCCAATGTCTATGCA  
CTGC---CAC-----TAAGTTGAATGATCTTTGCTT-CTCCAATGTCTATGCA  
TTGCAATCTT-----TTAATATAGAATTGATACTA-CTGCTACAAGT-TGTC  
TTGCAATCTT-----TTAATATAGAATTGATACTA-CTGCTACAAGT-TGTC  
TTGCAATCTT-----TTAATTACAAAATAGATACAA-GAGCTACTTCG-TGTC  
TTGCAATCTT-----TTAATTACAAAATAGATACAA-GAGCGACCTCG-TGTC  
TGCCAGTATA-----ATACTGGCAATTTTTCAGATGGCTTTTATCCTTTTACT

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

TACG-TCGTACACAGAAGCATTAGTACAA-GTTGAAAAACACAGCTATTAAAAAGGTGACG  
CACA-TCGTATACTGAAGCATTAGTACAA-GTTGAAAAACACAGCTATTAAAAAGGTGACG  
CACA-TCGTACACTGAAGCATTAGTACAA-GTTGAAAAACACAGCTATTACAAAGGTGACG  
CACA-TCGTACACTGAAGCATTAGTACAA-GTTGAAAAACACAGCTATTACAAATGTGACG  
AGCT-TCCTATGCTGACGTTTGGTTAAT-GTGTCAAAACCTCTATTGCTAATATAATT  
GACT-AAATTTGTTGATGCACTCATCGAG-GTTCAAGGAACCTCCATTGAGCGTATTCTT  
GATTCTTTTGTAGTCAAG--GGAGATGAT-GTAAG-ACAAATAGCGCCAGGACAACTGG  
GATTCTTTTGTAGTCAAG--GGAGATGAT-GTAAG-ACAAATAGCGCCAGGACAACTGG  
AGTTGTATTATAATTTACCTGCTGCTAAT-GTTTCTGTAGCAGGTTTAACTCTTCTACT  
AACTCTATTATAGTTTGCCTGCAGCAAC-GTATCTGTCACTCATTATAATCCTTCTACT  
AGCTCTATTATAGTCTTGCAAAAAATAAT-GTCACTGTCAATAACCATAACCCGCTCTCT  
AGCTCTATTACAGTCTTGCAAGATAAT-GTCACTGTCAATAACCACAACCCATCTCTC  
AATAGTAGTTTAGTTAAGCAGAAGTTTATTGTCTATCGTGAAAAATAGTGTTAATACTACT

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

TATT-GTAACAGTCAC--ATTAATAACATCAAATGTTCTCAACTTACTG----CTAATTT  
TATT-GTAACAGTCAC--ATTAATAACATCAAATGTTCTCAACTTACTG----CTAATTT  
TATT-GTAATAGTCAC--GTTAATAACATCAAATGCTCTCAAATTACTG----CTAATTT  
TATT-GTAATAGTTAT--GTTAATAACATCAAATGCTCTCAAATTACTG----CTAATTT  
TATT-GCAACTCTGTT--ATTAACAGACTGAGATGTGACCAGTTGTCCT----TTGATGT  
TATT-GTGATGATCCT--GTTAGCCAACCTCAAGTGTCTCAGGTTGCTT----TTGACCT  
TGTT-ATTGCTGATTATAATT-----ATAAATTGCCAGATGATTTCAT-----GG---  
TGTT-ATTGCTGATTATAATT-----ATAAATTGCCAGATGATTTCAT-----GG---  
TGGA-ATAGGAGATTGGTTTACAGAACAATTTGTTTAAAGCCTCAACCTGTAGGTGT  
TGGA-ATAGAAGGTATGGGTTT-----AATAATCAGAGTTTGGTCCAG-----AGG---  
TGGA-ACAGGCGTTATGGGTTT-----AATGATGTGGCTACATTGGAAC-----TGG---  
TGGA-ATAGGCGTTATGGATT-----AATGACGTGGCTACATTTCATAG-----TGG---  
TGTACGTTACACAATTTCAATTTT--CATAATGAGACTGGCGCCAACCC-----

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

GCAAAATGGTTTTTACCCTGTTG---CTTCAAGTGAAGTTGGTCTTGTCAATAAGAGTGT  
GAATAATGGATTTTATCCTGTTG---CTTCAAGTGAAGTAGGTTTCGTTAATAAGAGTGT  
GAATAATGGATTTTATCCTGTTT---CTTCAAGTGAAGTTGGTCTTGTCAATAAGAGTGT  
GAATAATGGATTTTATCCTGTTT---CTTCAAGTGAAGTTGGTCTTGTCAATAAGAGTGT  
ACCAGATGGTTTTTATCTACAA--GCCCTATTCAATCCGTTGAGCTACCTGTGTCTAT  
TGACGATGGTTTTTACCCCATCT---CTTCTAGA-AACCTTCTGAGTCACGAACAGCCAA  
-----GTTGTGCTTGTCTTGAATACTAGGAACATTGATGCTACTTCAACTGGTAA  
-----GTTGTGCTTGTCTTGAATACTAGGAACATTGATGCTACTTCAACTGGTAA  
TTTTACTCATCATGATGTTGTTT---ATGCACAACATTGTTTAAAGCTCCCAAAATTT  
-----CCTTCATGATGCTGTTT---ATTCACAGCAATGTTTAAACACCTAACACATA  
-----TAAACATGACGTTGCTT---ATGCTGAGGCTTGTTTTACCGTGGGAGCATCATA  
-----TGAACATGACGTTGCTT---ATGCAGAGGCATGTTTCACTGTTGGAGCTTCATA  
-----TAATCCTAGTGGTGTTC---AGAAATATTCAAACCTACCAACAAAAACAGCTCA

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

TGTGTTACTACCTAGTTTCTATTC--ACATACCAGTGTTAATATAACTATTGATCTTGG  
TGTGTTATTACCTAGCTTTTTCAC--ATACACCGCTGTCAATATAACCAATTGATCTTGG  
TGTGTTACTACCTAGCTTTTACAC--ACATACCATTGTTAACATAACTATTGGTCTTGG  
TGTGTTACTACCTAGCTTTCTGAC--ACATACCATTGTTAACATAACTATTGGTCTTGG  
TGTGTCGCTACCTGTTTATCATAA--ACATACGTTTATTGTGTTGTACGTTGACTTCAA  
TTTCTT-TTGTACTTTGCCATCA--TTTAATGATCATTCTTTTGTTAAT--ATTACTG  
T-TATAATTATAAAT--ATAG-----GTATCTTAGACATGGCAAGCTTAG  
T-TATAATTATAAAT--ATAG-----GTATCTTAGACATGGCAAGCTTAG  
C-TGTCCGTGTAAATTGGATGG-----GTCTTTGTGTGTAGGTAATGGTCTGGTATAG  
T-TGTCCTTGTAGA--ACAA-----GTCA--ATGCATAGGTGGT---CAGGCACAG  
T-TGCCCTTGCGGAACCCAGCATAGTGTGCGCATGTACCACTGGAAAACTAATTTG  
T-TGCCCTTGTGCGGAAGCCAGCAGCTATTCTATGTGTACAGGTAACCTAAGTCTG  
G-AGTGGTTATTATAATTTTAA-----TTTTTCCTTCTGAGTAGTTTGTATTATAAGG

CcoV

TATGAAGCGTAGTG-TTACGGTCA--CCATAGCCTCACCATTAAAGTAACATCACACTACC

FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

TATGAAGCTTAGTGGTTATGGTCAACCCATAGCCTCGACACTAAGTAACATCACACTACC  
TATGAAGCGTAGTGGTTATGGTCAACCCATAGCCTCAACATTAAGTAACATCACACTACC  
TATGAAGCGTAGTGGTTATGGTCAACCCATAGCCTCAACGCTAAGTAACATTACACTACC  
ACCTCAGAGTGGCGGTGGCAAGTG-----CTTTAACTGTTATCCTGCT---  
TCTCT-----GCGGCTTTTGGTG-----GTCTTAGTAGTGCCAATCT---  
GCCCTT-TGAGAGAGACATATCTAAT-----GTGCCTTTCT-----CCCCTGA--  
GCCCTT-TGAGAGAGACATATCTAAT-----GTGCCTTTCT-----CCCCTGA--  
ATGCTGGTTATAAAAAATAGTGGTATAGGCACCTGTCTCTGCA--GGTACTAATTATTAAAC  
GAACTTGTCTGTAGGCACCACTGTGCGCAAGTGTTTGTCT--G----CAGTTACAAAA-  
CCAATTGCCCTACAGGCACCTCGAATCGTGAGTGCACTGTTATGCCATTGGCTAATAAT-  
CTAATTGCCCAACAGGTACCTCGAATCGTGAGTGAATGTTTCAGGCTTCAGGTTTTAA--  
AGTCTAATTTTATGTATGGATCTTAT-----CACCCAAGTTGTAAATTTAGAC-

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

AATGCAGGATAATAACATAGACGTGTACTGTATTGTTTCTAACCAATTCTCAGTTTATGT  
AATGCAGGATAACAATACTGTACTGTATTGTTTCTAACCAATTCTCAGTTTATGT  
AATGCAGGATCACAACACCGATGTGTACTGTATTGTTTCTGACCAATTTTCAGTTTATGT  
AATGCAGGATAACAACACGATGTGTACTGTGTTCTGCTGACCAATTTTCAGTTTATGT  
--GGTGTTAATATTACTGCGCAATTTT--AATGAACTAAAGGGCCTT--TGTGTGT  
--CGT-TGCATCTGACACT-----ACTATC--AATGGGTTTA--GTTCTT--TCTGTGT  
-----TGGCAAACCTTGCACCCACCTGCTCTTA--ATTGT-----TATTG  
-----TGGCAAACCTTGCACCCACCTGCTCTTA--ATTGT-----TATTG  
TTGCCATAATGCTGCCAATGTGATTGTTTGTGCACTCCCG--ACCCATTACATCTAA  
-----GCTACTAAGTGTACTTGTGCTGGTGTCAACCAG--ATCCTTCCACATATAA  
-----CAATTTAAGTGTGATTGCACTTGTAAACCCTA--GTCC-----TCTAA  
-----GTCTAAGTGCAGATTGCACATGTAAACCCTA--GTCC-----TCTAA  
-----TAGAACTATTAAATAGGCTTGTGTTTA--ATTC-----ACTTTC

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

TCATTCCACTTGCAAAAGTTCCTTATGGGATAACAATTTTAATTAGCATGTACCGACGT  
TCATTCCACTTGCAAAAGTTCCTTATGGGACAATATTTTAATCAAGACTGCACGGATGT  
TCATTCTACTTGCAAAAGTGCTTTATGGGACAATATTTTAAGCGAACTGCACGGACGT  
TCATTCTACTTGCAAAAGTGCTTTTATGGGACAATGTTTTTAAGCGAACTGCACGGACGT  
TGACACATC-----ACACTTCACTACCAAAATACGTTGCT-----GTTTATGCCAATGT  
TGACACTAG-----ACAATTTACCATTACACTGTTTTAT-----AATGTTACAAACAG  
GCCATTAAATGATTATG---GTTTTTACAC-----CACTACTGGCATTGGCTACCAACC  
GCCATTAAATGATTATG---GTTTTTACAC-----CACTACTGGCATTGGCTACCAACC  
ATCTACAGGGCCTTACAAGTGCCCCCAAACTAAATACTTAGTTGGCATAGGTGAGCACTG  
AGGTGTAAACGCCTGGACTTGTCCGCAATCTAAAGTTTCTATACACCAGGTGAGCATTTG  
CCACCTATGATCTTAGA--TGTCTCAAGCAAGAAGCATGCTTGGCGTAGGTGATCATTG  
CCACCTATGATCCTAGA--TGTCTTCAAGCGCGGAGCATGCTTGGCGTAGGTGATCATTG  
AGTTTCAATTGCTTACGGTCTCTTCAAGGTGGTTGCAA---GCAATCTGCTTTAAAG

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

TT-TAGACGCCACAGCTGTTATAAAAACTGGTACTTGTC---CTTTCTCATTGATAAAT  
TT-TAGAGGCTACAGCTGTTATAAAAACTGGTACTTGTC---CTTTCTCATTGATAAAT  
TT-TAGATGCCACAGCTGTTATAAAAACTGGTACTTGTC---CTTTCTCATTGATAAAT  
TT-TAGATGCCACAGCTGTTATAAAAACTGGTACTTGTC---CTTTCTCATTGATAAAT  
TGGTAGGTGGAGTGCTAGTATTA-ACACGGGAAATTGCC---CTTTTTCTTTGGCAAAG  
TTAT-GGTTATGTGTCTAAATCACAGGATAGTAATTGTC---CTTTACCTTGCAATCTG  
TT-ACAG-----AGTTGTAGTACTTTCTTTTGA-----ACTTTTAAATGCACCGGC  
TT-ACAG-----AGTTGTAGTACTTTCTTTTGA-----ACTTTTAAATGCACCGGC  
TT-CGGGTCTTGCTATTAAAGTGATTATGTGGAGGTA--ATCCTTGTAATTGCCAAC  
CC-CTGGTTTGGGCTTGTGGAGGATGATTGCTCTGGCA--ACCCTTGCACTGTAAAC  
TG-AAGGTCTAGGAGTTTATAGAAGATAAATGTGGTGGCAGCAACACCTGCAATTGTTCTG  
TG-AAGGTCTAGGATTTTATAGAAGATAAATGTGGTGGCAGCAACATATGCAATTGTTCTG  
GT--AGAGCAACTTGTTGTTATGCTTATTCATATGGAGG-----TCCTTCGCTGTG

CcoV  
FcoV  
TGE  
PRCoV

TGAATAATTACTTAACTTTTAAACAAGTTCTGTTTGTGCGTTGAATCCCGTTGGTGCCAACT  
TGAACAATTACTTGACTTTTAAACAAGTTCTGTTTGTGCGTTGAGTCCGTGTTGGTGCTAATT  
TGAACAATTACTTAACTTTTAAACAAGTTCTGTTTGTGCGTTGAGTCCGTGTTGGTGCTAATT  
TGAACAATTACTTAACTTTTAAACAAGTTCTGTTTGTGCGTTGAGTCCCGTTGGTGCTAATT

HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

TTAATAACTTTGTTAAATTTGGCAGTGTATGTTTTTCGCTAAAGGATATACCCGGTGGTT  
TTAATGATTACCTGTCTTTTAGCAAAATTTGTGTTTCAACCAGCCTTTTGGCTGGTGCTT  
CACGG---TTTGTGGACCAAAAT-TATCCACTGACCTTATTAAGAACCAGTGTGTCAATT  
CACGG---TTTGTGGACCAAAAT-TATCCACTGACCTTATTAAGAACCAGTGTGTCAATT  
CACAAAGCATTTTGGGTTGGTCTGTGACTCTTGTTTACAAGGGGATAGGTGTAATATTT  
CACAGGCTTTCATAGGCTGGAGTTCAGAAACTTGTTCGAAAATGGTAGGTGTAATATTT  
CTCATGCCCTTTGTTGGCTGGGCTAAGGATAGTTGCTTGGCTAATGGCCGCTGTCAATTT  
CTGATGCCCTTTGTTGGCTGGGCTATGGACAGCTGTCTATCTAATGCCCGCTGCCATATTT  
TAAAGGTGTTTATTCAGGTGAGTTAGATCATAATTTTGAATGTGGACTGTTA-GTTTATG

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

GTAAGTTAGATGTTGCCGCCCGTACAAGAACCAATGAGCAGGTTTTTGGGAAGTT---TAT  
GCAAGTTTGATGTTGCTGCACGTACAAGAACCAATGAGCAGGTTGTTAGAAGTC---TAT  
GTAAGTTTGATGTAGCTGCCCGTACAAGAACCAATGAGCAGGTTGTTAGAAGTT---TGT  
GTAAGTTTGATGTAGCTGCCCGTACAAGAACCAATGATCAGGTTGTTAGAAGTT---TGT  
GCGCAATGCCATATAGTGGCTAATGGGCTTATAGTAAGTACTATACTATAGGCTCATTGT  
GTACCATAGATCTTTTGGTTACCTGCGTTCGGTAGTGGTGTAAAGTTGACGTCCCTTT  
TTAATTTTAATGGACTCACTGGTACTGGTGTGTTAACTCCTTCTTCAAAGAGAT---TTC  
TTAATTTTAATGGACTCACTGGTACTGGTGTGTTAACTCCTTCTTCAAAGAGAT---TTC  
TTGCTAATTTTATTTTTCATGATGTTAATAGTGGTACTACTTGTCTACTGATT---TAC  
TTGCTAATTTTATTTCTGAATGATGTTAATAGCGGTACAACCTGTTCTACTGATT---TAC  
TTAGTAATTTGATGTTAATGGCATTAAATAGTGGTACTACATGTTCCATGGATT---TGC  
TTAGTAATTTGATGTTAATGGCATTAAATAGTGGTACTACATGTTCCACGGATT---TTC  
TTACTAAGAGCGGTGGCTCTCGTATACAAACAGCCACTGAACCGCCAGTTATAA---CTC

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

ATGTAATATATGAAGAAGGAGACAACATAGTGGGTGTACCGTCTGATAATAGTGGTTT-G  
ATGTAATATATGAAGAAGGAGACAACATAGTGGGTGTACCGTCTGATAATAGCGGTCT-G  
ATGTAATATATGAAGAAGGAGACAACATAGTGGGTGTACCGTCTGATAATAGTGGTGT-G  
ATGTAATATATGAAGAAGGAGACAGCATAGTGGGTGTACCGTCTGACAATAGTGGTTT-G  
ATGTTTCTTGGAGTGATGGTGTGGAATTACTGGCGTCCCACAACCTGTTGAGGGTGTTA  
ATTTTCAATTACAAAAGGTGAGTTGATTACTGGCAGCGCTAAACCACTTGAAGGTATCA  
AACCATTT--CAACAATTTGGCCG-TGATGTTTCTG---ATTTCACTGATTCCGTTTGA  
AACCATTT--CAACAATTTGGCCG-TGATGTTTCTG---ATTTCACTGATTCCGTTTGA  
AAAAATCAAACACAGACATAATTCTTGGTGTGTTGTTAATTATGATCTTTATGGTATTA  
AACAGGGTAATACTATTATTACTACTGATGTTTGTGTTAATTATGACCTATATGGCATT  
AATTGCCTAATACTGAAGTGGTCACTGGCGTCTGCGTCAAATATGACCTCTACGGTATAA  
AATTGCCTAATACTGAAGTGGTCACTGGCGTCTGCGTCAAATATGACCTCTACGGTAGTA  
AAACAATTATAATAATATTACTTTAAATACTTGTGTTGATTATAATATATATGGCAGAA

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba  
SARSTor2  
BcoV  
HEV  
MHV  
RtCoV  
IBV

CACGATTTGTCAGTGTGCACTTAGACTCTGT-ACAGATTACAATATATATGGTAGAAC  
CACGATTTGTCAGTGTGCTACACCTAGACTCCTGT-ACAGATTACAATATATATGGTAGAAC  
CACGATTTGTCAGTGTGCTACACCTAGACTCCTGT-ACAGATTACAATATATATGGTAGAAC  
CACGATTTGTCAGTGTGCTACACCTAGACTCCTGT-ACAGATTACAATATATATGGTAGAAC  
GTTCCCTTATGAATGTTACAT-TGGACAAATGT-ACTAAATATAATATTTATGATGTATC  
CAGACGTTTCTTTATGACTC-TGGATGTGTGT-ACCAAGTATACTATCTATGGCTTTAA  
GATCCTAAACATCT-----G--AAAT-----ATTA-GACATTTACCTTGGCTC  
GATCCTAAACATCT-----G--AAAT-----ATTA-GACATTTACCTTGGCTC  
CAGGCCAAGGTATTTTGTG-AGGTAAATGCGACTTATTATAATAGTTGGCAGAACCT  
CAGGCCAAGGTATTTTGTG-AGGTAAATGCGACTTATTATAATAGTTGGCAGAACCT  
CAGGCCAAGGTATTTTAAAG-AGGTAAAGGCTGACTATTATCATAGTTGGCAAACCT  
CAGGCCAAGGTATTTTAAAG-AGGTAAAGGCTGATTATTACAATAGTTGGCAGAACCT  
CTGGCCAAGGTATTTATT-----ACTAATGTGACCGACTCAGCTGTTAGTTATAATTA

CcoV  
FcoV  
TGE  
PRCoV  
HCoVOC43  
PEDV  
SARSUrba

TGGTGTGGTATTATTAGAAAACTAACAGCACACTACTTAGTGGCTTATATT-ACACAT  
TGGTGTGGTATTATTAGACGAACCTAACAGTACGCTACTTAGTGGCTTATATT-ACACAT  
TGGTGTGGTATTATTAGACAACTAACAGGACGCTACTTAGTGGCTTATATT-ACACAT  
TGGTGTGGTATTATTAGACAACTAACAGGACGATACTTAGTGGCTTATATT-ACACAT  
TGGTGTGGGTATTATTGCGCTTAGCAATGACACCTTTCTAATGGAATTACGT-ACACAT  
AGGTGAGGGTATTATTACCCTTACAAATTCTAGCATTTTGGCAGGTGTTTATT-ATACAT  
TTTTGGGGGTGTAAGTG-TAATTACACCTGGAACAAATGCTTCATCTGAAGTT-GCTGTT

SARSTor2 TTTTGGGGGTGTAAGTG-TAATTACACCTGGAACAAATGCTTCATCTGAAGTT-GCTGTT  
BcoV TTTATATGATTCTAATGGTAATCTCTATGGTTTTAGAGACTACTTAACAAACA-GAACTT  
HEV TCTTTATGATTCTAGTGGTAATCTCTATGGCTTTAGAGATTATTTATCAAATA-GAACTT  
MHV CTTATATGATGTTAATGGCAACTTAATCGGATTTCCGATTTTGTGCTAATA-AGAGTT  
RtCoV CTTATATGATGTTAATGGTAACCTTAAATGGTTCCGTGACATTGTTACCAATA-AGACTT  
IBV TCTAGCAGACGCAGGT-----TTGGCTATTTTAGATACATCTGGTCCATAGACATCT

CcoV CACTATCAGGTGATTTGTTAGGTTTTAAAAATGTTAGTGATGGTGTCTACTCTGTAA  
FcoV CACTATCAGGTGATTTGTTAGGCTTTAAAAATGTTAGTGATGGTGTCTACTCTGTGA  
TGE CACTATCAGGTGATTTGTTAGGTTTTAAAAATGTTAGTGATGGTGTCTACTCTGTAA  
PRCoV CACTATCTGGTGATTTGTTAGGTTTTACAAATGTTAGTGATGGTGTCTACTCTGTAA  
HCoVOC43 CAACTTCAGGTAACTTCTGGGTTTTAAAGATGTTACTAAGGGCACCATCTACTCTATCA  
PEDV CTGATTCTGGACAGTTGTTAGCCTTTAAGAATGTCAGTAGTGGTGTCTTATTCTGTCA  
SARSurba CTATATCAAGATGTTA--ACTGCACTGATGTTTCTACAGCAATTCTGCAGATCAACTCA  
SARSTor2 CTATATCAAGATGTTA--ACTGCACTGATGTTTCTACAGCAATTCTGCAGATCAACTCA  
BcoV TTATGATTGCTAGTTGCTATAGCGGTCGTGTTTCAGCGGCTTTCATGCTAACTCTTCGG  
HEV TTCTTATTGCTAGTGTCTATAGTGGGAGGTTTCAGCAGTTTTCATGCTAACTCATCTG  
MHV ATACTATTGCAAGTTGCTATAGTGGGCGGCTCTCGGCTGCATATCATCAAGATGCACCAG  
RtCoV ATTTATTAAGAAGTTGCTATAGTGGGCGGCTTCGGCTGCATATCATCAAGATGCACCTG  
IBV TTGTTGTACAAGGTGAATATGGTCTTAATTATTATAAGGTTAACCTTGCGAAGATGTCA

CcoV CGCCATGTGATGTAAGTGCAAGCTGCTGT-TATTGATGGTGCCATAGTTGGAGCTATG  
FcoV CGCCATGTGATGTAAGCGCACAAAGCGGCTGT-TATTGATGGTGCCATAGTTGGAGCTATG  
TGE CGCCATGTGATGTAAGCGCACAAAGCAGCTGT-TATTGATGGTACCATAGTTGGGGCTATC  
PRCoV CGCCATGTGATGTTAGCGCACAAAGCAGCTAT-TATTGATGGTACCATAGTTGGGGCTATC  
HCoVOC43 CTCCTTGTAAACCCACCAGATCAGCTTGTGTTTATCAGCAA-GCTGTTGTTGGTGCTATG  
PEDV CGCCATGTTCTTTTTTCAGAGCAGGCTGC-ATATGTTAATGATGATATAGTGGGTGTTATT  
SARSurba CACCA-GCTT-----GGCGCATATATTCTACTGGAACAATG-TATT  
SARSTor2 CACCA-GCTT-----GGCGCATATATTCTACTGGAACAATG-TATT  
BcoV AACCA-GCATTGCTATTTGGAATATTAATGCAATTACGTTTTTAATAATACTC-TTTC  
HEV AACCA-GCTTTGATGTTTCGTAATCTTAAATGCAGCCACGTTTTTAATAATACCA-TTTT  
MHV AACCA-GCGCTACTATATCGCAATTTAAATGTGACTATGTCTTTAACAACAACA-TATC  
RtCoV AACCA-GCGCTACTATATCGCAATTTAAATGTGATTATGTGTTTAATAACAACA-TATC  
IBV -ACCAGCAGTTTGTAGTTTCTGGTGGTAAATTAGTAGGTATTCTTACTTCACGTAATGAG

CcoV ACTTCCATTAAATAGTGAAGTGTAGGT--CTAACTCATTGGACAACAACACCTAATTTTT  
FcoV ACTTCCATTAAACAGTGAAGTGTAGGT--CTAACACATTGGACAACGACACCTAATTTTT  
TGE ACTTCCATTAAACAGTGAAGTGTAGGT--CTAACACATTGGACAACAACACCTAATTTTT  
PRCoV ACTTCCATTAAACAGTGAATGTTAGGT--CTAACACATTGGACAACAACACCTAATTTTT  
HCoVOC43 TTGCTGAAAATT-----TTACTAGTT--ACGGC---TTTTCTAATGTTGTAGAAGTGGC  
PEDV TCT-----AGTT-----TGCTTAAGT--CCACT---TTTAAACAATACTAGGGAGTTGGC  
SARSurba CC-----AGACTCAAGCAGGCTGTCTTAT-AGGAGCTG  
SARSTor2 CC-----AGACTCAAGCAGGCTGTCTTAT-AGGAGCTG  
BcoV ACGACAGCTGCAACCTATTAACCTATTTGATAGTTATCTTGGTTGTGTTGT-CAATGCTG  
HEV AAGACAAATACAGCTTGTAACTATTTGATAGTTACCTTGGTTGTGTTGT-TAATGCTT  
MHV CCGTGAGGAGACACCACTTAACTATTTGATAGTTATCTTGGTTGTGTTGT-TAATGCTG  
RtCoV CCGTGAGGAGACACCACTTAACTATTTGATAGTTATTTGGGTTGTGTTAT-TAATGCTG  
IBV AC-----TGGTTCTCAGCTTCTT-GAGAACCAGTTTTACATCAAATCACTAATGG

CcoV ATTACTACTCATATATAATTATACAAATGTGATGAATCGTGGCAGGCAATTGA---TA  
FcoV ATTACTACTCTATATATAATTACACAAAGTGAGAGGACTCGTGGCACTGCAATTGACAGTA  
TGE ATTACTACTCTATATATAATTACACAAATGATAGGACTCGTGGCACTGCAATTGACAGTA  
PRCoV ATTACTACTCTATATATAATTACACAAATGATAAGACTCGTGGCACTCCAATTGGCAGTA  
HCoVOC43 GAAATTTTTCTATGCGT-----CCAATGGCAC-----TTATAATTGC-----  
PEDV TGGTTTCTTCTACCATT-----CTAATGACGG-----CTCCAATTGT-----  
SARSurba AGCAT-----GTCGACACTT---CTTATGAGTGGCAGATTCTATTGGAGCTGGCATT  
SARSTor2 AGCAT-----GTCGACACTT---CTTATGAGTGGCAGATTCTATTGGAGCTGGCATT  
BcoV ATAATAGTACTTCTAGTGTTG---TTCAAACATGTGATCTCACAGTAGGTAGTGTTACT  
HEV ATAATAATACAGCTAGTGCTG---TAAGTACTTGTGATTTAACCGTTGGTAGCGGCTATT



|          |                                                               |
|----------|---------------------------------------------------------------|
| MHV      | ACAACTCAACTGAAGAAGCTG---TTGACGCGTGTGATTGCGTATGGGTAGTGGGCTTT   |
| RtCoV    | ATAACTCAACTGAGCAGTCTG---TTGACGCGTGTGATTGCGTATGGGTAGTGGGCTTT   |
| IBV      | AACACGTCGTTTTAGACGTTTCTATTACTGAAATG-----TTGCAAATTGCCCTT       |
|          |                                                               |
| CcoV     | ATGATATTGATTGTGAACCTATCATAACATATTCTAATATAGGTGTTTGTAAAAATGGAG  |
| FcoV     | ACGATGTTGATTGTGAACCTGTCTAACCTATTCTAATATAGGTGTTTGTAAAAATGGTG   |
| TGE      | ATGATGTTGATTGTGAACCTGTCTAACCTATTCTAATATAGGTGTTTGTAAAAATGGTG   |
| PRCoV    | ATGACGTTGATTGTGAACCTGTCTAACCTATTCTAATATAGGTGTTTGTAAAAATGGTG   |
| HCoVOC43 | ---ACA-----GACGCTGTTTAACTTATTCTAGTTTTGGCGTTTGTGCAGATGGTT      |
| PEDV     | ---ACA-----GAGCCTGTGTGGTGTATAGTAACATAGGTGTTTGTAAATCTGGCA      |
| SARSUrba | GTGCTAGTTACCATACAGTTTCTTTATTACGTAG-----TACTAGCCAAAAATCTA      |
| SARSTor2 | GTGCTAGTTACCATACAGTTTCTTTATTACGTAG-----TACTAGCCAAAAATCTA      |
| BcoV     | GTGTGGATTACTCTACAAAAGACGAAGTCGTAGAGCGATTACCACTGGTTATCGGTTTA   |
| HEV      | GTGTTGATTATGTTACAGCACTTAGATCACGTAGATCTTTTACTACAGGTTATCGCTTAA  |
| MHV      | GTGTCAACTATTCAACGCTCTCACCCTGCGCAGCTCTGTGAGCAGGGTTATAAATTAA    |
| RtCoV    | GTGTCAACTATTCAATCGCTCACCCTGCGCAGGTCTGTGAGTACGGGTTATAAATTAA    |
| IBV      | ATGTTAGTTATGGTAAGTTTGTATAAAACCTGATGGCT----CAATTGCCACAATAGTA   |
|          |                                                               |
| CcoV     | CTTTGGTTTTTATT--AACGTCACACATTCTG-ATGGAGACGTTCAACCAATTAGCACCG  |
| FcoV     | CTTTGGTTTTTATT--AACGTCACACATTCTG-ACGGAGACGTGCAACCAATTAGCACTG  |
| TGE      | CTTTGGTTTTTATT--AACGTCACACATTCTG-ATGGAGACGTGCAACCAATTAGCACTG  |
| PRCoV    | CTTTGGTTTTTATT--AACGTCACACATTCTG-ATGGAGACGTGCAACCAATTAGCACTG  |
| HCoVOC43 | CTATAATTGCTGTTCAACACGTAATGTTTCATATGATAGTGTTCAGCTATCGTCACAG    |
| PEDV     | GTATTGGCTATGTTCCATCTCAGTATGGCC--AAGTCAAGATTGCACCCACGGTTACTG   |
| SARSUrba | -----TTGTGGCTTATACTATGTCTTTAGGTGCTGATAGTTC--AATTGCTTACTCTAA   |
| SARSTor2 | -----TTGTGGCTTATACTATGTCTTTAGGTGCTGATAGTTC--AATTGCTTACTCTAA   |
| BcoV     | CTAATTTTGAGCCATTTACTGTTAATTCAAGTAATGATAGTTTAGAACCTGTAGGTGGTT  |
| HEV      | CTAATTTTGAGCCATTTGCGCTAATTTGGTAATGATAGTATAGAACCTGTTGGTGGTT    |
| MHV      | CTACTTTTGAGCCATTTACAGTCCGCTTGTCAATGATAGTGTGAGTCTGTTGATGGGT    |
| RtCoV    | CTACTTTTGAGCCATTTACAGTCAGCATTGTCAATGATAGTGTGAGTCTGTTGGTGGAT   |
| IBV      | -----CCAAAACAATTGGAACAGTTTGTGGCACCTTT--ATTTAATGTTACTG         |
|          |                                                               |
| CcoV     | ---GTAATGTCACGATACCCACAAATTTTACTATATCTGTGCAAGTCGAATATATTCAGG  |
| FcoV     | ---GTAATGTCACGATACCTACAAATTTTACTATATCTGTGCAAGTTGAATACATGCAGG  |
| TGE      | ---GTAATGTCACGATACCTACAAATTTTACTATATCTGTGCAAGTCGAATATATTCAGG  |
| PRCoV    | ---GTAACGTCACGATACCTACTAATTTTACTATATCCGTGCAAGTCGAATACATTCAGG  |
| HCoVOC43 | ---CTAATTTGTCTATACCTTCCAATTGGACCACTTCGGTCCAGGTTGAGTATTTACAAA  |
| PEDV     | ---GGAATATTAGTATTCCCAACCACTTTAGTATGAGTATTAGAACAGAATATTTACAGC  |
| SARSUrba | TA-ACACCATTTGCTATACCTACTAATTTTCAATTAGCATTACTACAGAAGTAATGCCTG  |
| SARSTor2 | TA-ACACCATTTGCTATACCTACTAATTTTCAATTAGCATTACTACAGAAGTAATGCCTG  |
| BcoV     | TGTATGAAATTCAAATACCTTCAGAGTTTACTATAGGTAATATGGAGGAGTTTATTCAAA  |
| HEV      | TGTATGAAATACAGATACCTTCAGAGTTTACCATTGGTAATTTAGAAGAGTTCATTCAAA  |
| MHV      | TATATGAGCTGCAAAATACCAACCACTTTACTATAGCTAGCCATCAGGAGTTCGTTCAAA  |
| RtCoV    | TATATGAGATGCAAAATACCTACTAATTTTACTATAGCTAGCCATCAGGAGTTCATTCAAA |
| IBV      | ---AAAATGTGCTCATACCTAACAGTTTCAACTTAAGTGTACAGATGAGTACATACAAA   |
|          |                                                               |
| CcoV     | TTTACACTACACAGTTTCAATAGACTGTGCAAGATACGTTTGCAATGGTAACCCAAGAT   |
| FcoV     | TTTACACTACACAGTATCAATAGATTGTGCAAGATACGTTTGTAATGGTAACCCCTAGAT  |
| TGE      | TTTACACTACACAGTGTCAATAGACTGTTCAAGATATGTTTGAATGGTAACCCCTAGGT   |
| PRCoV    | TTTACACTACACAGTGTCAATAGACTGTTCAAGATATGTTTGAATGGTAACCCCTAGGT   |
| HCoVOC43 | TTTCAAGTACACCTATCGTAGTTGATTGCTCCACTTATGTTTGCAATGGTAATGTGCGCT  |
| PEDV     | TTTACAACACGCTGTTAGTGTGATTGTGCTACATATGTTTGAATGGTAACCTCTCGTT    |
| SARSUrba | TTTCTATGGCTAAAACCTCCGTAGATTGTAATATGTACATCTGCGGAGATTCTACTGAAT  |
| SARSTor2 | TTTCTATGGCTAAAACCTCCGTAGATTGTAATATGTACATCTGCGGAGATTCTACTGAAT  |
| BcoV     | CAAGCTCTCCTAAAGTTACTATTGATTGTTCTGCTTTTGTCTGTGGTGATTATGCAGCAT  |
| HEV      | CGAGATCCCTAAAGTTACTATAGACTGTGCTACATTTGTTTGTGGTGACTATGCAGCAT   |
| MHV      | CGAGGTCTCCAAAGGTTACTATAGACTGTGCTGCATTTGTCTGTGGTGCCACACAGCAT   |
| RtCoV    | CGAGGTCTCCAAAGGTTACTATAGATTGTGCTGCATTTGTCTGTGGTGATTATACAGCGT  |
| IBV      | CGCGTATGGATAAGGTCCAAATTAATTGCTGTCAGTATGTTTGTGGCAGTTCTCTGGATT  |

CcoV GCAATAAGTTATTAACACAATACGTTTCTGCATGTCAAACCTATTGAGCAAGCGCTTGCAA  
 FcoV GTAACAAATTGTTAACACAATATGTGTCTGCATGTCAAACCTATTGAACAAGCACTTGCAA  
 TGE GTAACAAATTGTTAACACAATACGTTTCTGCATGTCAAACCTATTGAGCAAGCACTTGCAA  
 PRCov GTAACAACTGTTAACACAATACGTTTCTGCATGTCAAACCTATTGAGCAAGCACTTGCAA  
 HCoVOC43 GTGTTGAATTGCTTAAGCAGTATACCTTCTGCTTGTAACCTATTGAAGACGCCTTAAGAA  
 PEDV GTAAACAATTACTCACCAGTACACTGCAGCATGTAAGACCATAGAGTCAGCATTACAAC  
 SARSUrba GTGCTAATTTGCTTCTCCAATATGGTAGCTTTTGACACAACCTAAATCGTGCCTCTCAG  
 SARSTor2 GTGCTAATTTGCTTCTCCAATATGGTAGCTTTTGACACAACCTAAATCGTGCCTCTCAG  
 BcoV GTAAATCACAGTTGGTTGAATATGGTAGCTTCTGTGACAATATTAATGCTATACTCACAG  
 HEV GTAGACAACAGTTAGCTGAGTATGGTAGTTTTGTGAGAACATTAATGCTATACTCACAG  
 MHV GCCGTCAGCAGTTGGTTGAGTACGGCTCATTCTGTGATAATATTAATGCCATTCTGGCG  
 RtCoV GTAGACAACAGTTGGTTGATTATGGCTCTTTTGTGATAATATTAATGCCATTCTGGCG  
 IBV GTAGAAAGTTGTTCAACAATATGGGCTGTTTGCACACAATATTGTCTGTAGTAAATA  
 \* \* \* \* \*

CcoV TGGGTGCCAG---ACTTGAAAACATGGAGATTGATTCCATGTTATTGTTTTCGAAAAATG  
 FcoV TGGGTGCCAG---ACTTGAAAACATGGAGTTGATTCCATGTTGTTGTTCTCGAAAAATG  
 TGE TGGGTGCCAG---ACTTGAAAACATGGAGTTGATTCCATGTTGTTGTTTCTGAAAAATG  
 PRCov TGGGTGCCAG---ACTTGAAAACATGGAAGTTGATTCCATGTTATTGTTTCTGAAAAATG  
 HCoVOC43 ATAGCGCCAG---GCTGGAGTCTGCAGATGTTAGTGAGATGCTCATTCTTGACAAGAAAG  
 PEDV TCAGCGCTAG---GCTTGAGTCTGTTGAAGTTAACTCTATGCTTACCATTCTGAAAGAGG  
 SARSUrba GTATTG----CTGCTGAACAGGATCGCAACACACGTGAAGTGTTCGCTCAAGTCAAAACA  
 SARSTor2 GTATTG----CTGCTGAACAGGATCGCAACACACGTGAAGTGTTCGCTCAAGTCAAAACA  
 BcoV AAGTAAATGAACCTACTTGACACTACACAGTTGCAAGT-AGCTAATAGTTTAAATGAATGTT  
 HEV AAGTAAATGAACCTACTTGACACTACACAGTTGCAAGT-AGCTAATAGTTTAAATGAATGGA  
 MHV AGGTAAATAACCTCATAGATACTATGCAACTTCAAGT-TGCAAGTGCTTTAATCCAAGGT  
 RtCoV AGGTGAATAACCTCATAGATACTATGCAATTACAAGT-TGCTAGTGCTCTGATCCAAGGT  
 IBV GTGTTGGTCA---AAAAGAAGATATGGAACCTTTGAATTTCTATTCTTACTAAACCGG  
 \*

CcoV CCCTTA-AATTGGCATCTGTTGAAGCATTCAATAGTACGGAATTTAGACCCCTATTTAT  
 FcoV CCCTTA-AATTGGCATCTGTTGAGGCGTTCAATAGTACAGAAATTTAGATCCTATTATAC  
 TGE CCCTTA-AATTGGCATCTGTTGAAGCATTCAATAGTTCAGAACTTTAGACCCCTATTTAC  
 PRCov CCCTTA-AATTGGCTTCTGTGGAAGCATTCAATAGTTCAGAACTTTAGATCCTATTATAC  
 HCoVOC43 CGTTTACACTT-GCTAATGTTAGT-----AGTTTT---GGTGACTACAACCTTAGC---  
 PEDV C-TTTACAGTTAGCTACCATCAGTTCGTTAATGGT---GATGGATATAACTTTACT---  
 SARSUrba AATGTACAAAACCCCACTTTGAAA-----TATTTTGGTGGTTTAAATT--  
 SARSTor2 AATGTACAAAACCCCACTTTGAAA-----TATTTTGGTGGTTTAAATT--  
 BcoV GTCACCTCTTAGCACTAAGCTTAAAGATGGCGTTAATTTCAATGTAGACGACATCAATT--  
 HEV GTCACCCCTTAGTACCAGATTAAGGATGGCATTAAATTTCAATGTTGACGATATCAACT--  
 MHV GTCACGTTAAGCTCACGCTTATCGGATGGCATTGGTGGTCAAATAGATGATATTAATT--  
 RtCoV GTCACGCTAAGTTTACGCTTGGCAGATGGCATCTCAGGTGAGATTGATGATATTAATT--  
 IBV CTGGTTTAAATACACAGTTCTTAG-----TAATGTTAGCACTGGTGGTGAATTAATA--  
 \*

CcoV AAAGAATGGCCTAACATTGGTGGTTCTTGGCTAGGAGGTTTAAAGATATATTGCCATCT  
 FcoV AAAGAATGGCCTAGCATAGGTGGTTCTTGGCTAGGAGGTCTAAAGATATACTACCGTCC  
 TGE AAAGAATGGCCTAATATAGGTGGTTCTTGGCTAGGAGGTCTAAATACATACTTCCGTCC  
 PRCov AAAGAATGGCCTAATATAGGTGGCTTTTGGCTAGGAGGTCTAAATACATACTTCCGTCC  
 HCoVOC43 ----AGCGTCATA----CCTAGCTTG-----CCACA  
 PEDV ----AATGTGCTG----GGTGCTTCCGTGTACGA-----TCCTGCA  
 SARSUrba ----TTTCACAAATATTACCTGACCCT-----CTAAAGCCAA--  
 SARSTor2 ----TTTCACAAATATTACCTGACCCT-----CTAAAGCCAA--  
 BcoV ----TTTCCCTGTATTAGGTTGTTTAGGAAGCGC-----TTGTAATAAAGTT  
 HEV ----TCTCCCTGTATTAGGTTGTTTAGGAAGCGA-----ATGTAATAGAGCT  
 MHV ----TTAGTCTCTGCTTGGTTGTTTAGGTTCTGA-----CTGTGGCGAAGTT  
 RtCoV ----TTAGTCTCTTCTAGGTTGCCTTGGCTCAGA-----TTGTAGCGAAGGC  
 IBV ----TTTCTCTTCTGTTAACAAATCCT-----AGTAGT

CcoV CATAATAGCAAACGTAAAGTACCGCTCGGCTATAGAAGACTTGCTTTTGTATAAGGTTGTA

FcoV CATAATAGCAAACGTAAGTATGGTCTGCTATAGAAGATTGCTTTTTGATAAAGTTGTA  
TGE CATAATAGCAAACGTAAGTATCGTTAGCTATAGAGGACTTGCTTTTTGATAAAGTTGTA  
PRCoV GATAATAGCAAACGTAAGTATCGTTAGCTATAGAGGACTTGCTTTTTCTAAGGTTGTA  
HCoVOC43 AGTGGTAGTAGAGTGGCTGGTCCGAGTGCCATAGAAGACATACTTTTTAGCAAACCTGTT  
PEDV AGTGGCAGGGTGGTACAAAAAGGTCTGTTATTGAAGACTTGCTTTTTAATAAAGTGGTT  
SARSUrba -CTAAGA-----GGTCTTTTATTGAGGACTTGCTCTTTAATAAAGGTGACA  
SARSTor2 -CTAAGA-----GGTCTTTTATTGAGGACTTGCTCTTTAATAAAGGTGACA  
BcoV TCCAGCA-----G----ATCTGCTATAGAGGATTACTTTTTCTAAAGTAAAG  
HEV TCCACTA-----G----ATCTGCTATAGAGGATTACTTTTTGATAAAGTAAAA  
MHV ACCATGGCAGCTCAAACCGGACGATCTGCTATAGAGGATGTATTATTTGACAAAGTCAAA  
RtCoV ACCAAGGCAGCGCAA---GGGCGATCTGCTATAGAGGATGTATTATTTGATAAAGTCAAA  
IBV CGTAGAA-----AGCGTTCTCTTATTGAAGACCTTCTATTTACAAGCGTTGAA

\*\*\* \*\*

CcoV ACATCTGGCTTAGGTACAGTTGACGAAGATTACAAACGTTCTGCGAGTGGTTATGACA--  
FcoV ACATCTGGTTTAGGTACAGTTGATGAAGATTATAAACGTTGTACTGGTGGTTACGACA--  
TGE ACATCTGGTTTAGGTACAGTTGATGAAGATTATAAACGTTGTACAGTGGTTATGACA--  
PRCoV ACATCTGGTTTAGGTACAGTTGATGAAGATTACAAACGTTGTACAGTGGTTATGACA--  
HCoVOC43 ACTTCTGACTTGGCACTGTGGACGCACTACAAAAAGTGCACTAAGGGTCTTTTCCA--  
PEDV ACTAATGGCCTTGGTACTGTTGATGAAGACTATAAGCGCTGTTCTAATGGTGGCTCTG--  
SARSUrba CTGCTGATGCTGGCTTCATGAA---GCAATATGGCGAATGCCTAGGTGATATTATG--  
SARSTor2 CTGCTGATGCTGGCTTCATGAA---GCAATATGGCGAATGCCTAGGTGATATTATG--  
BcoV TTATCTGATGCTGGCTTCGTTGA---GGCTTATAATAATTGTACTGGAGGTGCCGAAA--  
HEV TTGCTGATGCTGGCTTCGTTGA---GGCTTATAATAATTGTACTGGAGGTGCCGAAA--  
MHV CTCTCTGATGTTGGCTTTGTGCA---AGCATATAACAATTGCACTGGAGGCCAAGAAG--  
RtCoV CTCTCTGATGTTGGCTTTGTGCA---ATCATATAATAATTGCACTGGAGGTCAAGAAG--  
IBV TCTGTTGGACTACCAACAATGA---CGCATATAAAAATTGCACTGCAGGACCTTTAGGC

\*\* \* \*\*

CcoV ----TAGCTGACTTAGTGTGTGCACGATATTACAATGGCATCATGGTGCTACCTGGTGTA  
FcoV ----TAGCAGACTTGGTGTGTGCTCAATATTACAATGGCATCATGGTTCTACCAGGTGTA  
TGE ----TAGCTGACTTAGTATGTGCTCAATACTATAATGGCATCATGGTGCTACCTGGTGTA  
PRCoV ----TAGCTGACTTAGTATGTGCTCAATACTATAATGGCATTATGGTGCTACCTGGTGTA  
HCoVOC43 ----TTGCTGACTTGGCTTGTGCTCAATATTATAATGGCATTATGGTTTGGCTGGCGTC  
PEDV ----TGGCTGATCTAGTCTGTGCGCAGTATTACTCTGGTGCTAGTGGTACCTGGCGTT  
SARSUrba ----CTAGAGATCTCATTGTGCGCAGAAGTTCAATGGACTTACAGTGTGCCACCTCTG  
SARSTor2 ----CTAGAGATCTCATTGTGCGCAGAAGTTCAATGGACTTACAGTGTGCCACCTCTG  
BcoV ----TTAGGGACCTCATTGTGTGCAAGTTATAATGGTATCAAAGTGTGCTCCACTG  
HEV ----TTAGGGATCTCATTGTGTGCAAGTTATAATGGTATCAAAGTGTGCTCCACTG  
MHV ----TTAGAGACCTACTTTGTGTGCAATCTTTAATGGCATCAAAGTGCTACCGCTGTG  
RtCoV ----TTAGAGACCTACTTTGTGTGCAATCTTTAATGGCATTAAAGTGCTACCGCTGTA  
IBV TTTTAAAGGACCTTGGTGTGCTCGTGAATATAATGGTTTGGTGTGCTTCCCTCTATC

\*\* \* \*\*\*\* \* \* \*\* \* \*\*

CcoV GCTAATGATGACAAGATGACTATGTACACTGCATCTCTTACAGGTGGTATAACATTAGGT  
FcoV GCTAATGCTGACAAGATGACTATGTACACAGCATCACTTGCAGGTGGTATAACATTAGGT  
TGE GCTAATGCTGACAAAATGACTATGTACACAGCATCCCTTGCAGGTGGTATAACATTAGGT  
PRCoV GCTAATGCTGACAAAATGACTATGTACACAGCATCCCTCGCAGGTGGTATAACATTAGGT  
HCoVOC43 GCTGATGCTGAACGAATGGCCATGTATACAGGTTCTTTAATTGGTGGAATTGCTTTAGGA  
PEDV GTTGACGCTGAGAAGCTTCAATGTACAGTGCCTCTCATAGGTGGTATGGCGCTAGGA  
SARSUrba CTCAGTGTGATATGATTGCTGCCTACACTGCTGCTCTAGTTAGTGGTACTGCCACTGCT  
SARSTor2 CTCAGTGTGATATGATTGCTGCCTACACTGCTGCTCTAGTTAGTGGTACTGCCACTGCT  
BcoV CTCTCAGTAAATCAGATCAGTGGATACACTTGGCTGCCACCTCTGCTAGTCTGTTTCCCT  
HEV TTATCTGAAAATCAGATCAGTGGCTACACTTGGCAGCCACCGCTGCTAGCTTATCCCT  
MHV TTGTCTGAGAATCAAATTTCTGGTTATACAGCGGGAGCTACTGTATCTGCTATGTTCCCT  
RtCoV TTATCCGAGAGTCAAATCTCTGGTTATACAGCGGGAGCTACTGCATCTGCTATGTTCCCT  
IBV ATAACAGCAGAAATGCAAGCTTTGTATACTAGTTCTCTAGTAGCTTCTATGGCTTTTGGT

\* \*\*

CcoV GCACTTAGTGGTGGCGCAGTGGC-----TATACCTTTTGCAGTAGCAGTTCAGGCT  
FcoV GCACTTGGTGGTGGCGCCGTGGC-----TATACCTTTTGCAGTAGCAGTACAGGCT  
TGE GCACTTGGTGGAGGCGCCGTGGC-----TATACCTTTTGCAGTAGCAGTTCAGGCT  
PRCoV GCACTTGGTGGAGGCGCCGTGGC-----TATACCTTTTGCAGTAGCAGTTCAGGCT

HCovOC43 GGTCTAACATCAG---CCGTTTC-----AATACCATTTCATTAGCAATTCAGGCA  
 PEDV GGTATAACTGCTG---CAGCGGC-----ATTGCCTTTTAGCTATGCTGTTCAAGCG  
 SARSUrba GGATGGACATTGGGTGCTGGCGCTGCTCTTCAAATACCTTTTGCTATGCAAATGGCATAT  
 SARSTor2 GGATGGACATTGGGTGCTGGCGCTGCTCTTCAAATACCTTTTGCTATGCAAATGGCATAT  
 BcoV CCTTTGTGACGAGCAGTAGGTG-----TACCATTTTATTTAAATGTTTCAGTAT  
 HEV CCTTGGACAGCTGCAGCAGGTG-----TACCATTTTATTTAAATGTTTCAGTAT  
 MHV --ATGGTCTGCAGCTGCAGGTG-----TGCCATTTTCTTTAAGTGTTCATAT  
 RtCoV CCATGGTCTGCAGCTGCAGGTG-----TGCCATTTGCTTTAAGTGTTCATAT  
 IBV GGTATTACTGCAG---CTGGTGC-----TATACCTTTTGCCACACAACCTGCAGGCT  
 \* \* \* \* \*

CcoV AGACTTAATTATGTTGCTCTACAACTGATGTATTGAACAAAAACCAACAATCTTGGCT  
 FcoV AGACTTAATTATGTTGCTCTACAACTGATGTATTGAATAAAAAACCAACAGATCTGGCT  
 TGE AGACTTAATTATGTTGCTCTACAACTGATGTATTGAACAAAAACCAACAGATTCTGGCT  
 PRCov AGACTTAATTATGTTGCTCTACAACTGATGTATTGAACAAAAACCAACAGATCTGGCT  
 HCovOC43 CGTTTAAATTATGTTGCTCTACAACTGATGTATTGAACAAAAACCAACAGATCTGGCT  
 PEDV AGACTCAATTATCTTGGCTTTACAGACGGATGTTCTACAGCGGAACCAAGCAATTGCTTGCT  
 SARSUrba AGGTTCAATGGCATTGGAGTTACCCAAAATGTTCTCTATGAGAACCAAAAAACAATCGCC  
 SARSTor2 AGGTTCAATGGCATTGGAGTTACCCAAAATGTTCTCTATGAGAACCAAAAAACAATCGCC  
 BcoV CGTATTAATGGGATTGGGTGTTACCATGGATGTGTTAAGTCAAAATCAAAAGCTTATTGCT  
 HEV CGTATAAATGGGCTTGGCGTCACTATGGATGTGCTAAGTCAAAACCAAAAGCTTATTGCT  
 MHV AGAATTAATGGTCTTGGTGTCACTATGAATGTTCTTAGTGAAAATCAGAAAATGATAGCA  
 RtCoV AGAATTAATGGTCTTGGTGTCACTATGAATGTTCTTAGTGAAAACCAAAAATGATAGCT  
 IBV AGAATTAATCACTTGGGTATTACCCAGTCACTTTTGTGGAAGAATCAAGAAAAAATTGCT  
 \* \* \* \* \*

CcoV AATGCTTTCAATCAAGCTATTGGTAACATTACACAGGCATTTGGTAAGGTTAATGACGCT  
 FcoV AATGCTTTCAATCAAGCTATTGGTAACATTACACAGGCATTTGGTAAGGTTAATGATGCT  
 TGE AGTGCTTTCAATCAAGCTATTGGTAACATTACACAGTCATTTGGTAAGGTTAATGATGCT  
 PRCov AGTGCTTTTAAATCAAGCTATTGGTAACATTACACAGTCATTTGGTAAGGTTAATGATGCT  
 HCovOC43 GCATCTTTTAAACAAAGCAATGACCAACATAGTAGATGCCTTTACTGGTGTAAATGATGCT  
 PEDV GAGTCTTTTAACTCTGCTATTGGTAAATATAACTTCAGCCTTTGAGAGTGTTAAAGAGGCT  
 SARSUrba AACCAATTTAACAAGGCGATTAGTCAAAT-----  
 SARSTor2 AACCAATTTAACAAGGCGATTAGTCAAAT-----  
 BcoV AATGCATTTAACAATGCTCTTGATGCTAT-----  
 HEV AGTGCATTTAACAATGCTCTTGATGCTAT-----  
 MHV AGTGCATTTAACAACGCGATAGGTGCTAT-----  
 RtCoV AGTTCATTTAACAACGCGATAGGTGCTAT-----  
 IBV GCTTCCTTTAATAAGGCCATTGGTCATAT-----  
 \* \* \* \* \*

CcoV ATACATCAAACATCAAAAGGTCTTGCTACTGTTGCTAAAGCATTGGCAAAGGTGCAAGAT  
 FcoV ATACATCAAACATCAAAAGGTCTTGCCACTGTTGCTAAAGCGTTGGCAAAGGTGCAAGAT  
 TGE ATACATCAAACATCAGAGGCTTGCTACTGTTGCTAAAGCATTGGCAAAGGTGCAAGAT  
 PRCov ATACATCAAACATCAGAGGCTTGCTACTGTTGCTAAAGCATTGGCAAAGGTGCAAGAT  
 HCovOC43 ATTACACAACTTCAAGCCCTACAAACAGTTGCTACTGCACCTAACAAGATCCAGGAT  
 PEDV ATTAGTCAAACCTTCAAGGGTTTGAACACTGTGGCTCATGCGCTTACTAAGGTTCAAGAG  
 SARSUrba -----TCAAG-----AATCACTTACAACAACATCAACTGCATTGGGCAAGCTGCAAGAC  
 SARSTor2 -----TCAAG-----AATCACTTACAACAACATCAACTGCATTGGGCAAGCTGCAAGAC  
 BcoV -----TCAGG-----AAGGGTTTGATGCTACCAATTCTGCTTTAGTTAAATTCAGGCT  
 HEV -----CCAGG-----AAGGGTTCGACGCAACCAATTCTGCTTTAGTTAAATTCAGGCT  
 MHV -----ACAGG-----AAGGGTTTGCTGCAACCAATTCTGCTTTAGCAAATAATTCAGTTC  
 RtCoV -----ACAGG-----AAGGGTTCGATGCAACCAATTCTGCTTTAGCGAAAATTCAGTCC  
 IBV -----GCAGG-----AAGGTTTTAGAAAGTACATCTCTAGCATTACAACAATTCAGAT  
 \* \* \* \* \*

CcoV GTTGTTAACACGCAAGGTCAAGCTTTAAGCCACCTAACAGTACAATTGCAAAACAATTTT  
 FcoV GTTGTTAACACACAAGGGCAAGCTTTAAGTCACCTTACAGTACAATTGCAAAATAATTTT  
 TGE GTTGTTAACACACAAGGGCAAGCTTTAAGCCACCTAACAGTACAATTGCAAAATAATTTT  
 PRCov GTTGTTAACACACAAGGTCAAGCTTTAAGACACCTAACAGTACAATTGCAAAATAATTTT  
 HCovOC43 GTTGTTAATCAACAAGGCAACTCATTGAACCAATTAACTTCTCAGTTGAGGCAGAATTTT  
 PEDV GTTGTTAATTCGAGGGTTTCAAGCTTTGAACCACTTACCGTACAGCTGCAACACAATTC  
 SARSUrba GTTGTTAACCAGAATGCTCAAGCATTAAACACACTTGTTAAACAACCTTAGCTCTAATTTT

|          |                                                                |
|----------|----------------------------------------------------------------|
| SARSTor2 | GTTGTTAACCAGAATGCTCAAGCATTAAACACACTTGTAAACAACCTTAGCTCTAATTTT   |
| BcoV     | GTTGTTAATGCAAATGCTGAAGCTCTTAATAACTTATTGCAACAACCTCTAATAGATTT    |
| HEV      | GTTGTTAATGCAAATGCTGAAGCACTTAATAACTTATTGCAGCAACTCTAACAGATTT     |
| MHV      | GTTGTCAATGCAAATGCGGAAGCACTCAATAATTTATTAAACCAGCTTTCCAATAGGTTT   |
| RtCoV    | GTTGTCAACGCAAATGCAGAAGCACTCAATAACCTTTTGAATCAGCTTTCCAATAGGTTT   |
| IBV      | GTTGTTAGTAAACAGAGTGCTATTCTTACTGAGACTATGGCATCACTTAATAAAAATTTT   |
|          | *****                                                          |
| CcoV     | CAAGCCATTAGCAGTTCTATTAGTGACATTTATAACAGGCTTGATGAATTGAGTGCTGAT   |
| FcoV     | CAAGCCATTAGTAGTTCTATTAGTGATATTTATAACAGGCTTGACGAACCTGAGTGCTGAT  |
| TGE      | CAAGCCATTAGTAGTTCTATTAGTGACATTTATAATAGGCTTGACGAATTGAGTGCTGAT   |
| PRCoV    | CAAGCCATTAGTAGTTCTATTAGTGACATTTATAATAGGCTTGATGAATTGAGTGCTGAT   |
| HCoVOC43 | CAAGCTATCTCTAGCTCTATTAGGCTATCTATGACAGACTTGACACTATTGAGGCTGAT    |
| PEDV     | CAAGCCATTTCTAGTTCTATTAGTGACATTTATTCGCGACTGGACATTCTTCAGCCGAT    |
| SARSURba | GGTGCAATTTCAAGTGCTAAATGATATCCTTTCGCGACTTGATAAAGTCGAGGCGGAG     |
| SARSTor2 | GGTGCAATTTCAAGTGCTAAATGATATCCTTTCGCGACTTGATAAAGTCGAGGCGGAG     |
| BcoV     | GGTGCTATAAGTTCTTTTACAAGAAATTTCTATCTAGACTGGATGCTCTTGAAGCGCAA    |
| HEV      | GGTGCCATAAGTGCTCTTTTACAAGAAATTTTATCCAGGCTCGATGCTCTTGAAGCTAAA   |
| MHV      | GGTGCAATTAGTGCTCTTTTACAAGAAATTTCTATCTCGCCTAGATGCTCTTGAAGCGCAG  |
| RtCoV    | GGTGCAATTAGTGCTCTTTTACAAGAAATTTCTATCTCGCCTCGATGCTCTTGAAGCTCAG  |
| IBV      | GGTGCTATTCTCTGTGATTCAAGAAATCTACCAGCAATTTGACGCCATACAAGCAAAAT    |
|          | ** ** *                                                        |
| CcoV     | GCACAAGTTGACAGGCTGATTACAGGACGACTTACAGCACTTAATGCATTTGTGTCTCAG   |
| FcoV     | GCACAAGTTGATAGGCTGATTACAGGTAGACTTACAGCACTTAATGCATTTGTGTCTCAG   |
| TGE      | GCACAAGTTGACAGGCTGATCAGGAAGACTTACAGCACTTAATGCATTTGTGTCTCAG     |
| PRCoV    | GCACAAGTCGACAGGCTGATCAGGAAGACTTACAGCACTTAATGCATTTGTGTCTCAG     |
| HCoVOC43 | CAACAAGTAGATAGGCTGATTACTGGTAGATTGGCTGCTTTGAATGTATTGCTTTCTCAT   |
| PEDV     | GTTCAGGTTGATCGTCTCATCACC GG CAGATTATCAGCACTTAATGCTTTTGTGCCCCAA |
| SARSURba | GTACAAATTGACAGGTTAATTACAGGCAGACTTCAAAGCCTTCAAACCTATGTAACACAA   |
| SARSTor2 | GTACAAATTGACAGGTTAATTACAGGCAGACTTCAAAGCCTTCAAACCTATGTAACACAA   |
| BcoV     | GCTCAGATAGACAGACTTATTAATGGGCGTCTTACCGCTCTTAATGTTTATGTTTCTCAA   |
| HEV      | GCTCAGATAGACAGACTTATCAATGGGCGTCTCACC GCTCTTAATGCTTATGTTTCTCAG  |
| MHV      | GCTCAGATAGACCGTCTTATTAATGGCAGATTAACTGCACTTAATGCATATGTCTCTAAG   |
| RtCoV    | GCTCAGATAGACCGTCTTATTAATGGCAGATTAACTGCACTTAATGCATATGTCTCTAAG   |
| IBV      | GCTCAAGTGGATCGTCTTATAACTGGTAGATTGTCATCACTTTCTGTTTTAGCATCTGCT   |
|          | ** * * * *                                                     |
| CcoV     | ACTTTAACCAGACAAGCAGAGGTTAGGGCTAGTAGACAACCTTGCTAAAGACAAGGTTAAT  |
| FcoV     | ACTCTAACCAGACAAGCAGAGGTTAGGGCTAGTAGACAACCTTGCCAAAGACAAGGTTAAT  |
| TGE      | ACTCTAACCAGACAAGCGGAGGTTAGGGCTAGTAGACAACCTTGCCAAAGACAAGGTTAAT  |
| PRCoV    | ACTCTAACCAGACAAGCCGAGGTTAGGGCTAGTAGACAACCTTGCTAAAGACAAGGTTAAT  |
| HCoVOC43 | ACATTGACTAAGTACACTGAAGTTCGTGCTTCCAGACAGCTTGACACAACAAAAGTGAAT   |
| PEDV     | ACCCTCACTAAGTATACTGAGGTTTACGGCTAGCAGGAAGCTAGCACAGCAAAAGGTTAAT  |
| SARSURba | CAACTAATCAGGGCTGCTGAAATCAGGGCTTCTGCTAATCTTGCTGCTACTAAAATGTCT   |
| SARSTor2 | CAACTAATCAGGGCTGCTGAAATCAGGGCTTCTGCTAATCTTGCTGCTACTAAAATGTCT   |
| BcoV     | CAGCTTAGTGATTCTACACTAGTAAAATTTAGTGACAGACAAGCTATGGAGAAGGTTAAT   |
| HEV      | CAGCTTAGTGATTCTACACTAGTAAAATTTAGTGACAGACAAGCTATGAGAAAGTAAAT    |
| MHV      | CAGCTGAGTGACATGACCCCTGTTAAGGTGAGTGAGCAGCCAGGCTATAGAGAAAGTTAAT  |
| RtCoV    | CAGCTGAGCGACATGACCCCTATTAAGGTGAGTGCTGCCAGGCTATAGAGAAAGTTAAT    |
| IBV      | AAGCAGGCGGAGTATATTAGAGTGTCACAACAGCGTGAGTTAGCTACTCAGAAAATTAAT   |
|          | * ** *                                                         |
| CcoV     | GAATGCGTTAGGTCTCAATCCCAGAGATTTGGATTCTGTGGTA--ATGGTACACATTTG    |
| FcoV     | GAATGTGTTAGGTCTCAGTCTCAGAGATTCGGATTCTGTGGTA--ATGGTACACATTTG    |
| TGE      | GAATGCGTTAGGTCTCAGTCTCAGAGATTCGGATTCTGTGGTA--ATGGTACACATTTG    |
| PRCoV    | GAATGCGTTAGGTCTCAGTCTCAGAGATTCGGATTCTGTGGTA--ATGGTACACATTTG    |
| HCoVOC43 | GAGTGTGTCAAATCCCAGTCTAAGCGTTATGGCTTCTGTGGAA--ATGGCACTCACATT    |
| PEDV     | GAGTGCGTCAAATCGCAATCTCAGCGTTACGGTTTTTGTGGTGGTGATGGCGAGCACATT   |
| SARSURba | GAGTGTGTTCTTGGACAATCAAAAAGAGTTGACTTTTGTGGAA--AGGGCTACCACCTT    |
| SARSTor2 | GAGTGTGTTCTTGGACAATCAAAAAGAGTTGACTTTTGTGGAA--AGGGCTACCACCTT    |
| BcoV     | GAATGTGTCAAAGCCAATCATCTAGGATAAATTTTGTGGTA--ATGGTAATCATATT      |
| HEV      | GAATGTGTTAAAAGCCAATCATCTAGGATAAATTTCTGTGGTA--ATGGTAATCATATT    |

MHV GAGTGTGTTAAAAGCCAATCATCTAGGATAAAATTTCTGTGGCA---ATGGCAATCATATA  
RtCoV GAGTGTGTTAAAAGCCAATCACCTAGGATAAAATTTCTGTGGCA---ATGGCAATCATATA  
IBV GAGTGTGTTAAGTCACAGTCTATTAGGTACTCCTTTTGTGGTA---ATGGACGACATGTT  
\* \* \* \* \*

CcCoV TTTTCACTTGCAAATGCGGCACCAAATGGCATGATTTTCTTTCACACAGTGCTATTACCA  
FcoV TTTTCACTAGCAAATGCAGCACCAAATGGCATGATTTTCTTTCATACAGTACTATTACCA  
TGE TTTTCACTCGCAAATGCAGCACCAAATGGCATGATTTTCTTTCACACAGTGCTATTACCA  
PRCoV TTTTCACTCGCAAATGCAGCACCAAATGGCATGATCTTCTTTCACACAGTGCTATTACCA  
HCoVOC43 TTCTCAATTGTTAATGCTGCTCCTGAGGGGCTTGTCTTCTCCACACTGTCTTGTGCGG  
PEDV TTCTCTCTGGTACAGGCCGCACCTCAGGGCCTGCTGTTCTTACATACAGTACTTGTACCG  
SARSUrba ATGTCCTTCCACAAGCAGCCCCGCGATGGTGTGTCTTCTACATGTACGTATGTGCCA  
SARSTor2 ATGTCCTTCCACAAGCAGCCCCGCGATGGTGTGTCTTCTACATGTACGTATGTGCCA  
BcoV ATATCATTAGTGCAGAAATGCTCCATATGGTTTGTATTTTATCCACTTTAGCTATGTCCCT  
HEV ATATCATTAGTACAGAAATGCTCCATATGGTTTGTATTTTATCCACTTTAGCTATGTCCCT  
MHV TTGTCTATTAGTCCAGAAATGCGCCTTATGGTTTATATTTTATTCAATTCAGCTATGTGCCT  
RtCoV TTGTCTATTAGTCCAGAAATGCGCCTTACGGTTTATATTTTATTCAATTCAGCTATGTGCCT  
IBV CTAACCATACCGCAAATGCACCTAATGGTATAGTGTATACACTTTTCTTATACTCCA  
\* \* \* \* \*

CcCoV ACAGCTTATGAAACTGTGACGGCCTGGTCAGGTATTTGTGCGT---CAGATGGCAGTCGC  
FcoV ACAGCTTATGAAACTGTAAACAGCTTGGTCAGGTATTTGTGCTT---CAGATGGCGATCGC  
TGE ACGGCTTATGAAACTGTGACTGCTTGGCCAGGTATTTGTGCTT---CAGATGGTGATCGC  
PRCoV ACGGCGTATGAAACTGTGACTGCTTGGTCAGGTATTTGTGCTT---TAGATGTTGATCGC  
HCoVOC43 ACACAATATAAGGATGTTGAAGCGTGGTCTGGGTTGTGCGTTG---ATGGTACAACGGT  
PEDV GGTGATTTTGTAAATGTTCTTGCCATCGCTGGCTTATGCGTTA---ATGGTGAAATTGGC  
SARSUrba TCCCAGGAGAGGAACCTTACCACAGCGCCAGCAATTTGTCATG---AAGGCAAAGCATAC  
SARSTor2 TCCCAGGAGAGGAACCTTACCACAGCGCCAGCAATTTGTCATG---AAGGCAAAGCATAC  
BcoV ACTAAGTATGTCACTGCCAAGGTTAGTCCCGGTCTGTGCATTG---CTGGTGATAGAGGT  
HEV ACCAAGTATGTTACAGCAAAGGTTAGTCTGGGTTTGTGCATTG---CTGGCGATATAGGA  
MHV ACTTCCTTTACAACGGCAAATGTGAGTCTTGGGCTATGCATT---CTGGTGATAGAGGA  
RtCoV ACTTCCTTTACAACGGTAAATGTGAGTCTTGGACTATGCATT---CTGGTGATAGAGGA  
IBV GATAGTTTGTAAATGTTACTGCAATAGTGGGTTTTTGTGTAAAGCCAGCTAATGCTAGT  
\* \* \* \* \*

CcCoV ACTTTTGACTTGTTGTTGAGGATGTCCAGCTGACGC-TATTTGCGAA-----TTTAGAT  
FcoV ACTTTGCGACTTGTCGTTAAAGATGTGCAGTTGACGT-TGTTTCGTAA-----TCTAGAT  
TGE ACTTTTGACTTGTCGTTAAAGATGTCCAGTTGACTT-TGTTTCGTAA-----TCTAGAT  
PRCoV ACTTTTGACTTGTCGTTAAAGATGTCCAGTTGACTT-TATTTGCTAA-----TCTAGAT  
HCoVOC43 TATGTGTTGCGACAACCTAATCTTGCTCT--TTACAAAGAAGGCA-----ATTATT  
PEDV TTGACTCTACGTGAGCCTGGCTTAGTCTTGTGTTACGCATGAACCTTCAACTTATATCGG  
SARSUrba TTCCCT-----CGTGAAGGTGTTTTTGTGTTAATG-----GCACTT  
SARSTor2 TTCCCT-----CGTGAAGGTGTTTTTGTGTTAATG-----GCACTT  
BcoV ATAGCC-----CCTAAGAGTGTTATTTTGTGTTAATGTAA-----ATAATA  
HEV ATATCG-----CCTAAGAGTGTTATTTTATTAATGTAA-----ATAATT  
MHV TTAGCA-----CCTAAGCTGGATATTTTGTTCAGATG-----ATGGAG  
RtCoV TTAGCA-----CCTAAGCTGGATATTTTGTTCAGATC-----ATGGAG  
IBV CAGTATGCAATAGTGCCCGCTAATGGTAGGGTATTTTATACAA-----GTTAAT  
\* \* \* \* \*

CcCoV GAAAAATTTTATTTGACGCCCAGAACTATGTATCAGCCCAGAGTTGCAACTAGTTCGTGAT  
FcoV GACAAGTTCTATTTGACCCCCAGAACTATGTATCAGCCTAGAGTTGCAACTAGTTCGTGAT  
TGE GACAAGTTCTATTTGACCCCCAGAACTATGTATCAGCCTAGAGTTGCAACTAGTTCGTGAT  
PRCoV GACAAGTTCTATTTGACACCCAGAACTATGTATCAGCCTAGAGTTGGCAACTAGTTCGTGAT  
HCoVOC43 ATAGAAT-----CACATCTCGCATATGTTTGAACCACGTATTCTTACCATGGCAGAT  
PEDV ACGGAATATTTGTTTCATCGCGACGTATGTTTGAACCTAGAAAACCTACCGTTAGTGAT  
SARSUrba CTTGGTTTAT----TACACAGAGGAACCTTCTTTCTCCACAAATAATTACTACAGACAAT  
SARSTor2 CTTGGTTTAT----TACACAGAGGAACCTTCTTTCTCCACAAATAATTACTACAGACAAT  
BcoV CTTGGATGTT----CACTGGTAGTGTTATTACTACCCTGAACCCATAACTGGAATAAT  
HEV CTTGGATGTT----CACTGGTAGTAGCTATTACTACCCTGAACCTATAACCCAAAATAAT  
MHV AGTGGAAGTT----CACAGGTAGTAATTATTATTACCCTGAACCCATTACAGATAAAAAT  
RtCoV AATGGAAGTT----CACAGGTAGCAATTATTACTACCCTGAATCCATTACAGATAAAAAC  
IBV GGTAGTTACTACATCACTGCACGAGATATGTATATGCCAAGAGCTATTACTGCAGGAGAT

CcoV TTTGTTCAAATAGAAGGCTGTGATGTGTTGTTGTTAATGGAACGTAAATTGAATTGCCT  
 FcoV TTTGTTCAAATTGAAGGGTGTGATGTGTTGTTGTTCAACGCGACTGTAATTGATTGCCT  
 TGE TTTGTTCAAATTGAAGGGTGTGATGTGTTGTTGTTAATGCAACTGTAAGTGATTGCCT  
 PRCoV TTTGTTCAAATTGAAGGGTGTGATGTGTTGTTGTTAATACAACGTAAAGTGATTGCCT  
 HCoVOC43 TTTGTTCAAATTGAAAATTGCAATGTACATTGTTAATCTCTCGCTCTGAGTTGCAA  
 PEDV TTTGTTCAAATTGAGAGTTGTGTGGTCACCTATGTCAATCTGACTAGCGACCAGCTACCA  
 SARSUrba ACATTTGTCTCAGGAAATTGTGATGTGTTATTGGCATCATTAAACAACACAGTTTATGAT  
 SARSTor2 ACATTTGTCTCAGGAAATTGTGATGTGTTATTGGCATCATTAAACAACACAGTTTATGAT  
 BcoV GTTGTTGTTATGAGTACCTGTGCTGTTAACTATACTAAAGCGCCGGATGTAATGCTGAAC  
 HEV GTTGTTGATGAGTACCTGTGCTGTTAATTATACTAAAGCACCGGATCTAATGCTGAAC  
 MHV AGTGTCTGATGAGTAGTTGCGCAGCAAACTACACAAAGGCACCTGAAGTTTTCTTGAAC  
 RtCoV AGTGTCTGATGAGTAGTTGCGCAGTAACTACACAAAGGCACCTGAAGTTTTCTTGAAC  
 IBV GTAGTTACGCTTACTTCTTGTCAAGCAAATTATGTAAGTGAAATAAGACCGTCATTACT

\* \*\* \*

CcoV AGTATCATA---CCTGACTATATCGATATTAATCAAACGTTCAGGACATATTAGAAAAT  
 FcoV AGTATTATA---CCTGACTATATTGACATTAATCAAACGTTCAGGACATATTAGAAAAT  
 TGE AGTATTATA---CCTGATTATATTGATATTAATCAGACTGTTCAAGACATATTAGAAAAT  
 PRCoV AGTATTATA---CCTGATTATATTGATATTAATCAGACTGTTCAAGACATATTAGAAAAT  
 HCoVOC43 ACCATTGTG---CCAGAGTATATTGATGTTAATAAGACGCT--GCAAGAATTAAAGTTACA  
 PEDV GATGTAATC---CCAGATTACATCGATGTTAACAACAACTGATGAGATTTTAGCTTCT  
 SARSUrba CCTCTGCAA---CCTGAGCTCGACTCATTCAAAGAAGAGCTGGACAAGTACTTCAAAAAT  
 SARSTor2 CCTCTGCAA---CCTGAGCTGACTCATTCAAAGAAGAGCTGGACAAGTACTTCAAAAAT  
 BcoV ATTTCAACA---CCCAACCTCCATGATTTTAAGGAAGAGTTGGATCAATGGTTTAAAAAC  
 HEV ACATCGACA---CCCAACCTTCTGACTTCAAGGAAGAATTGTATCAATGGTTTAAAAAC  
 MHV ACTTCAATA---CCTAATCTACCCGACTTTAAGGAGGAGTTAGATAAATGGTTTAAAAAT  
 RtCoV ACTTCAATA---ACTAATCTACCCGACTTTAAGGAGGAGTTAGATAAATGGTTTAAAGAAT  
 IBV ACATTCTGATGACATGATGATTTTATTTAATGACGAATTGTCAAAATGGTGAATGAT

\* \*\* \*

CcoV TTCAGACCAAATTGGACTGTACCCGAGTTGCCACTTGACATTTTTCATGCAACCTACTTA  
 FcoV TACAGACCAAATTGGACTGTACCTGAATTTACACTTGATATTTTCAACGCAACCTATTTA  
 TGE TTTAGACCAAATTGGACTGTACCTGAGTTGACATTTGACATTTTAAACGCAACCTATTTA  
 PRCoV TTTAGACCAAATTGGACTGTACCTGAGCTGACATTGGACGTTTAAACGCAACCTATTTA  
 HCoVOC43 AATTG-CCAAATTACACTGTTCCAGACCTAGTTGTGCAACAGTACAACCAGACTATTTTG  
 PEDV --CTG-CCCAATAGAAGTGTCCAGTCTTCCCTAGATGTTTTTAATGCCACTTATCTT  
 SARSUrba CATACATCACCAGATGTTGATCT-TGGCGACATTTCAGGCA--TTAACGCTTCTGTGCTC  
 SARSTor2 CATACATCACCAGATGTTGATCT-TGGCGACATTTCAGGCA--TTAACGCTTCTGTGCTC  
 BcoV CAAACATCAGTGGCACCAGATTTGTCACTTGATTATA-----TAAATGTTACATTCTTG  
 HEV CAATCTTCAGTGGCACCAGATTTGTCACTTGATTATA-----TAAATGTTACGTTCTTG  
 MHV CAGACGTCTATTGCGCTGATTTATCTCTGATTTCGAGAAATTAAAGCTTACCCTCTG  
 RtCoV CAGACGTCTATTGTGCTGATTTATCTTTCGATATCGGGAAATTAAATGTTACATTCTT  
 IBV -ACTAAGCATGAGCTACCAGACTTTGAC--AAATCAATTA--CACAGTACCTATACTT

\* \*

CcoV AACCTGACTGGTGAAATTAATGACTTAGAATTTAGGTGAGAAAAGTTACATAACACCACA  
 FcoV AATCTGACTGGTGAAATTGATGACTTAGAGTTTAGGTGAGAAAAGCTACATAACACTACA  
 TGE AACCTGACTGGTGAAATTGATGACTTAGAATTTAGGTGAGAAAAGCTACATAACACCCT  
 PRCoV AACCTGACTGGTGAAATTGATGACTTAGAGTTTAGGTGAGAAAAGCTACATAACACTACT  
 HCoVOC43 AATTTGACCAAGTGAATTAGCACCCTTGAATAAATCTGCGGAGCTTAATTACACTGTT  
 PEDV AATCTTACTGGTGAAATTGAGATCTAGAGCAGCGTTGAGAGTCTCTCCGTAATACTACA  
 SARSUrba AACATTCAAAAAGAAATTGACCGCTCAATGAGG-----  
 SARSTor2 AACATTCAAAAAGAAATTGACCGCTCAATGAGG-----  
 BcoV GACCTACAAGATGAAATGAATAGGTTACAGGAGG-----  
 HEV GACCTACAAGATGAAATGAATAGGTTACAGGAGG-----  
 MHV GACCTGACTGATGAGATGAACAGGATTACAGGAGG-----  
 RtCoV GACCTGTCTATGAGATGAACAGGATTACAGGAGG-----  
 IBV GACATTGATAGTGAATTTGATCGTATTCAAGGCG-----

\* \* \*\* \*

CcoV GTAGAACTTGCTATTCTCATTGATAATATTAATAACACATTAGTCAATCTTGAATGGCTC

|          |                                                                |
|----------|----------------------------------------------------------------|
| FcCoV    | GTAGAACTTGCCATTCTCATTGATAACATTAATAATACATTAGTCAATCTTGAATGGCTC   |
| TGE      | GTAGAACTTGCCATTCTCATTGACAACATTAACAATACATTAGTCAATCTTGAATGGCTC   |
| PRCoV    | GTAGAACTTGCCATTCTCATTGACAACATTAACAATACAGTAGTCAATCTTGAATGGCTT   |
| HCoVOC43 | CAAAAATTGCAAACTCTGATTGACAACATAAATAGCACATTAGTCGACTTAAAGTGGCTC   |
| PEDV     | GAAGAGCTCCGAAGTCTCATTAAACAACATCAACAACACACTTGTGACCTTGAGTGGCTC   |
| SARSUrba | -----TCGCTAAAAATTTAAATGAATCACTCATTGACCTTCAAGAATTG              |
| SARSTor2 | -----TCGCTAAAAATTTAAATGAATCACTCATTGACCTTCAAGAATTG              |
| BCoV     | -----CAATAAAGTTTTAAATCAGAGCTACATCAATCTCAAGGACATT               |
| HEV      | -----CTATAAAGTTTTAAATCAGAGCTACATCAATCTCAAGGACATT               |
| MHV      | -----CAATTAAGAAGTTAAATGAGAGTTACATCAACCTCAAGGACGTT              |
| RtCoV    | -----CAATTAAGAATTTAAATGAGAGTTACATCAACCTCAAGGAAATT              |
| IBV      | -----TTATACAGGGTCTTAATGACTCTCTAATAGACCTTGAAAACTT               |
|          | * * *                                                          |
| CcCoV    | AACAGAATTGAACTTATGTAAATGGCCTTGGTATGTTGGCTACTAATTGGATTAGTA      |
| FcCoV    | AATAGAATTGAACTTATGTAAATGGCCTTGGTATGTTGGCTACTGATAGGTTTAGTA      |
| TGE      | AATAGAATTGAACTTATGTAAATGGCCTTGGTATGTTGGCTACTAATAGGCTTAGTA      |
| PRCoV    | AATAGAATTGAACTTATGTAAATGGCCTTGGTATGTTGGCTACTAATAGGCTTAGTA      |
| HCoVOC43 | AACCGGGTTGAGACTTACATCAAGTGGCCGTGGTGGGTGTGGTGTGTCATTTAGTGGTG    |
| PEDV     | AACCGAGTTGAGACATACATCAAGTGGCCGTGGTGGGTGTGGTGTGTCATTTAGTGGTG    |
| SARSUrba | GGAAAAATGAGCAATATATTAAATGGCCTTGGTATGTTGGCTCGGCTTCA---TTGCT     |
| SARSTor2 | GGAAAAATGAGCAATATATTAAATGGCCTTGGTATGTTGGCTCGGCTTCA---TTGCT     |
| BCoV     | GGTACATATGAGTATTATGTAAATGGCCTTGGTATGTTGGCTTTAATTGGCTTTGCT      |
| HEV      | GGTACATATGAGTATTATGTAAATGGCCTTGGTATGTTGGCTTTAATTGGCTTTGCT      |
| MHV      | GGCACATATGAAATGTATGTAAATGGCCTTGGTATGTTGGCTTTAATTGGATAGCT       |
| RtCoV    | GGCACATATGAGATGTATGTAAATGGCCTTGGTATGTTGGCTGCTAATTGGATAGCT      |
| IBV      | TCAATACTCAAACTTATATTAAAGTGGCCTTGGTATGTTGGTTAGCCATAGCTTTTGCC    |
|          | * * * * *                                                      |
| CcCoV    | GTAATATTCTGCATACCATATTGCTATTTTGTGTTGTAGTACTGGTGTGTTGGATGT      |
| FcCoV    | GTAATATTCTGCATACCATATTGCTATTTTGTGTTGTAGTACTGGTGTGTTGGATGC      |
| TGE      | GTAATATTCTGCATACCATATTGCTATTTTGTGTTGTAGTACTGGTGTGTTGGATGC      |
| PRCoV    | GTAATATTCTGCATACCATATTGCTATTTTGTGTTGTAGTACTGGTGTGTTGGATGC      |
| HCoVOC43 | CTCATCTTTGTGGTGAGTATGTTGCTATTATGTTGTTGTTCTACTGGTGTGTTGGCTTC    |
| PEDV     | CTCATCTTTGTGGTGAGTATGTTGCTATTATGTTGTTGTTCTACTGGTGTGTTGGCTTC    |
| SARSUrba | GGACTAATTGCCATCGTCATGGTTACAATCTTGCTTTGTTGCATGACTAGTTGTTGCAGT   |
| SARSTor2 | GGACTAATTGCCATCGTCATGGTTACAATCTTGCTTTGTTGCATGACTAGTTGTTGCAGT   |
| BCoV     | GGTGTAGCTATGCTTGTGTTTACTATTCTTCATATGCTGTTGTACAGGATGTGGGACTAGT  |
| HEV      | GGTGTAGCTATGCTTGTGTTTACTATTCTTCATATGCTGCTGTACAGGATGTGGGACTAGT  |
| MHV      | GGTGTAGCTGTTTGTGTTGTTTATTTTTCATATGTTGCTGCACGGGTGTGGCTCATGT     |
| RtCoV    | GGTGTAGCTGTTTGTGTTGTTTATTTTATATGTTGCTGCACAGGTGTGGCTCTTGT       |
| IBV      | ACTATTATCTTCATCTTAATACTAGGATGGGTTTCTTCATGACTGGTGTGTTGGTTGT     |
|          | * * *                                                          |
| CcCoV    | ATCGGGTGTGTTAGGAAGCTGTTGTCACTTCCATAT-GTAGTAGAGGCCA---ATTGAAAG  |
| FcCoV    | ATAGGTTGTTTAGGAAGTGTGTTGCTACTCTATAT-GTAGTAGAAGACA---ATTGAAAA   |
| TGE      | ATAGGTTGTTTAGGAAGTGTGTTGCTACTCTATAT-GTAGTAGAAGACA---ATTGAAAA   |
| PRCoV    | ATAGGTTGTTTAGGAAGTGTGTTGCTACTCTATAT-TCAGTAGAAGACA---ATTGAAAA   |
| HCoVOC43 | TTTAGTTGTTTGCATCTTCTATTAGAGGTTGTT-GTGAATCAACTAA---ACTTCCTTA    |
| PEDV     | TGCGGTTGCTGCGGTGCTTGTGTTTTCAGGTTGTT-GTAGGGGTCCCTAG---ACTTCAACC |
| SARSUrba | TGCCTCAAGGGTGCATGCTCTTGTGGTCTTGCT-GCAAGTTTGATGA---GGATGACTC    |
| SARSTor2 | TGCCTCAAGGGTGCATGCTCTTGTGGTCTTGCT-GCAAGTTTGATGA---GGATGACTC    |
| BCoV     | TGTTTTAAGAT---ATG---TGGTGGTTGTTGTG-ATGATTATACTGG---ACACCAGG-   |
| HEV      | TGTTTTAAGAA---ATG---TGGCGGTTGTTGTG-ATGATTATACTGG---ACACCAGG-   |
| MHV      | TGTTTCAAGAA---GTG---TGGAAATTGTTGTG-ATGAGTGTGGAGG---ACACCAGGA   |
| RtCoV    | TGTTTTAAGAA---ATG---TGGAAATTGTTGTG-ATGAGTATGGAGG---ACGTCAGGC   |
| IBV      | TGTTGTGGATGC-TTGGCATTATGCCTCTAATGAGTAAGTGTGGTAAGAAATCTTCTTA    |
|          | *                                                              |
| CcCoV    | TTATGAACCTATTGAAAAAGTTCATGTTCACTGA-----                        |
| FcCoV    | TTATGAACCAATTGAAAAAGTGCATGTCCACTAA-----                        |
| TGE      | TTACGAACCAATTGAAAAAGTGCACGTCCATTAA-----                        |
| PRCoV    | TTATGAACCTATTGAAAAAGTGCACGTCCATTAA-----                        |



|          |                                                              |
|----------|--------------------------------------------------------------|
| HCoVOC43 | TTACGACG---TTGAAAAGATCCACATACAGTAA-----                      |
| PEDV     | TTACGAAGCTTTTGAAAAGGTCCACGTGCAGTGA-----                      |
| SARSUrba | TGAGCCAGTTCTCAAGGGTGTCAAATTACATTACACATAA-----                |
| SARSTor2 | TGAGCCAGTTCTCAAGGGTGTCAAATTACATTACACATAA-----                |
| BcoV     | -AGT-TAGTAAT-TAAAA-----CATCACATGACGACTAA-----                |
| HEV      | -AGT-TTGTAAT-CAAAA-----CTTCACATGACGATTAA-----                |
| MHV      | CAGTATTGTGATACATAATATTTCTCTCATGAGGATTGA-----                 |
| RtCoV    | AGGTATTGTGATACATAATATTTCTCTCATGAGGATTGA-----                 |
| IBV      | TTACACGACTTTTGATAACGATGTGGTAACTGAACAATACAGACCTAAAAAGTCTGTTTG |

\* \*

|          |   |
|----------|---|
| CcoV     | - |
| FcoV     | - |
| TGE      | - |
| PRCoV    | - |
| HCoVOC43 | - |
| PEDV     | - |
| SARSUrba | - |
| SARSTor2 | - |
| BcoV     | - |
| HEV      | - |
| MHV      | - |
| RtCoV    | - |
| IBV      | A |

**Figure 4: List of Molecular Designs for S Gene**

LK249 5'-FAM-CCCACGCCAGAAGGTAGATCACGAACTACACGTGGG-3'-Dubcyl

LK249.N 5'-FAM-GCCCCACGCCAGAAGGTAGATCACGAACTACACGTGGGC-3'-  
Dubcyl

LK250

5'-CTCTATGTTTATAAGGGCTATCAACCTATAGATGTAGTTCGTGATCTA  
CCTTCTGGTTTTAACACTTTGAAACCTATTTTAAAGTTGCCTCTTGG -3'

LK251 5'-CTCTATGTTTATAAGGGCTATCAACC-3'

LK251-T7 5'-TAATACGACTCACTATAGGCTCTATGTTTATAAGGGCTATCAACC-3'

LK252 5'-CCAAGAGGCAACTTAAAAATAGGTTTC- 3'

LK252-RT 5'- AGGCTGTAAGAACCAAGAGGCAACTTAAAAATAGGTTTC- 3'

S-RT 5'-AGGCTGTAAGAA-3'

**Figure 5:** CLUSTAL W (1.81) multiple DNA sequence alignment of coronavirus E genes from strains isolated from different species

|          |                                                            |
|----------|------------------------------------------------------------|
| SARS-Urb | -----                                                      |
| SARS-Tor | -----                                                      |
| HCoOC43  | -----                                                      |
| PEDV     | -----                                                      |
| TGE      | -----                                                      |
| PRCoV    | -----                                                      |
| CcoV     | -----                                                      |
| FcoV     | -----                                                      |
| MHV      | -----                                                      |
| RtCoV    | -----                                                      |
| BcoV     | -----                                                      |
| IBV      | ATGAATTATTGAATAAGTCGCTAGAGGAGAATGGAAGTTTTCTAACAGCGCTTACATA |

|          |                                                               |
|----------|---------------------------------------------------------------|
| SARS-Urb | -----ATGTA                                                    |
| SARS-Tor | -----ATGTA                                                    |
| HCoOC43  | -----ATGTTCC                                                  |
| PEDV     | -----ATGCTACA                                                 |
| TGE      | ATGACGTTTCCTAGGGCATTGACTGTCATAGATGACAA-TGGAATGGTCATTAAACATCAT |
| PRCoV    | ATGACGTTTCCTAGGGCATTGACTGTCATAGATGACAA-CGGAATGGTCATTAGCATCAT  |
| CcoV     | ATGACGTTCCCTCGGGCATTGACTGTCATAGATGACAA-TGGAATGGTCATTAGTATCAT  |
| FcoV     | ATGACGTTCCCTAGGGCATTGACTGTCATAGATGACAA-TGGAATGGTCATTAGTATCAT  |
| MHV      | -----ATGTTTAATTTATTCCCTACAGATACAGTATGGTATGTGGGGCAG-ATTAT      |
| RtCoV    | -----ATGTTTAATTTATTCCCTATAGACACAGTATGGTATGTGGGGCAG-ATTAT      |
| BcoV     | ---ATGTTTATGGCTGATGCTTATTTTGCAGACACTGTGTGGTATGTGGGGCAA-ATAAT  |
| IBV      | ATTGTAGGATTTTACACTTTATCTTCTAGGTA--GAGCACTTCAAGCATTGTACAGG     |

|          |                                                              |
|----------|--------------------------------------------------------------|
| SARS-Urb | ACTTCTTTTTCTTGCTTTTCGTTGGTATT-----CTTGCTAGTCACACTAGCCATCCTTA |
| SARS-Tor | ACTTCTTTTTCTTGCTTTTCGTTGGTATT-----CTTGCTAGTCACACTAGCCATCCTTA |
| HCoOC43  | ACTCTGGTGTGTGGTGCTTATAGTGAT-----ACTACTAGTGTGTATTACAATAATTA   |
| PEDV     | ACTTTGGCTTTTCGTA                                             |
| TGE      | TTTCTGGTTCTGTTGATAATTATATT-----GATATTACTTTCAATAGCATTGCTAA    |
| PRCoV    | TTTTTGGTTCTGTTGATAATTATATT-----GATATTACTTTCAATAGCATTGCTAA    |
| CcoV     | TTTCTGGTTCTGTTGATAATTATATT-----GATATTATTTTCAATAGCATTGCTAA    |
| FcoV     | CTTCTGGCTCCTGTTGATAATTATATT-----GATATTGTTTTCAATAGCATTGCTAA   |
| MHV      | TTTTATAGTCGCAGTGTGTTTGTATGGT-----CACCATAATAGTGGTTGCCTTCCTTG  |
| RtCoV    | TTTTATAGTCGCAGTGTGTTTGTATGGT-----CACCATAATAGTGGTTGCCTTCCTTG  |
| BcoV     | TTTTATAGTTGCCATTGTGTTTATGGT-----TATAATAGTTGTAGTGGCATTTTTGG   |
| IBV      | CTGCTGATGCTTGTGTTTATTTTGGTATACATGGGTAGTAATCCAGGAGCTAAGGGTA   |

|          |                                                               |
|----------|---------------------------------------------------------------|
| SARS-Urb | CTGCGCTTCGATT---GTGTGCGTACTGCTGCAATATTGTTAACGTGAGTTTAGTAAAC   |
| SARS-Tor | CTGCGCTTCGATT---GTGTGCGTACTGCTGCAATATTGTTAACGTGAGTTTAGTAAAC   |
| HCoOC43  | AACTAATTAAGCT---TTGTTTCACTTGCCATATGTTTGTAAATAGAACAGTTTATGGCC  |
| PEDV     | AATTGGTTAATCT---GTGCTTCACTTGTCAACGGTTGTGTAATAGCGCAGTTTATACAC  |
| TGE      | ATATAATTAAGCT---ATGCATGGTGTGTGCAATTTAGGAAGGACAGTTATTATTGTTC   |
| PRCoV    | ATATAATTAAGCT---ATGCATGGTGTGTGCAATTTAGGAAGGACAGTTATTATTGTTC   |
| CcoV     | ATATAATTAAGCT---ATGCATGGTGTGTGCAATTTAGGAAGGACAGTTATTATTGTTC   |
| FcoV     | ATGTTATTAAATT---GTGCATGGTATGTTGCAATTTAGGAAGGACAGTTATTATTGTTC  |
| MHV      | CGTCTATCAA                                                    |
| RtCoV    | CGTCTATCAA                                                    |
| BcoV     | CAACTTTTAAATT---GTGTATTCAACTTTGCGGTTGTGTAATACTTTGTTGCTGTCTC   |
| IBV      | CAGCCTTTGTATACAAGTATACATATGGTAGAAAACCTTAACAATCCGGAATTAGAAGCAG |

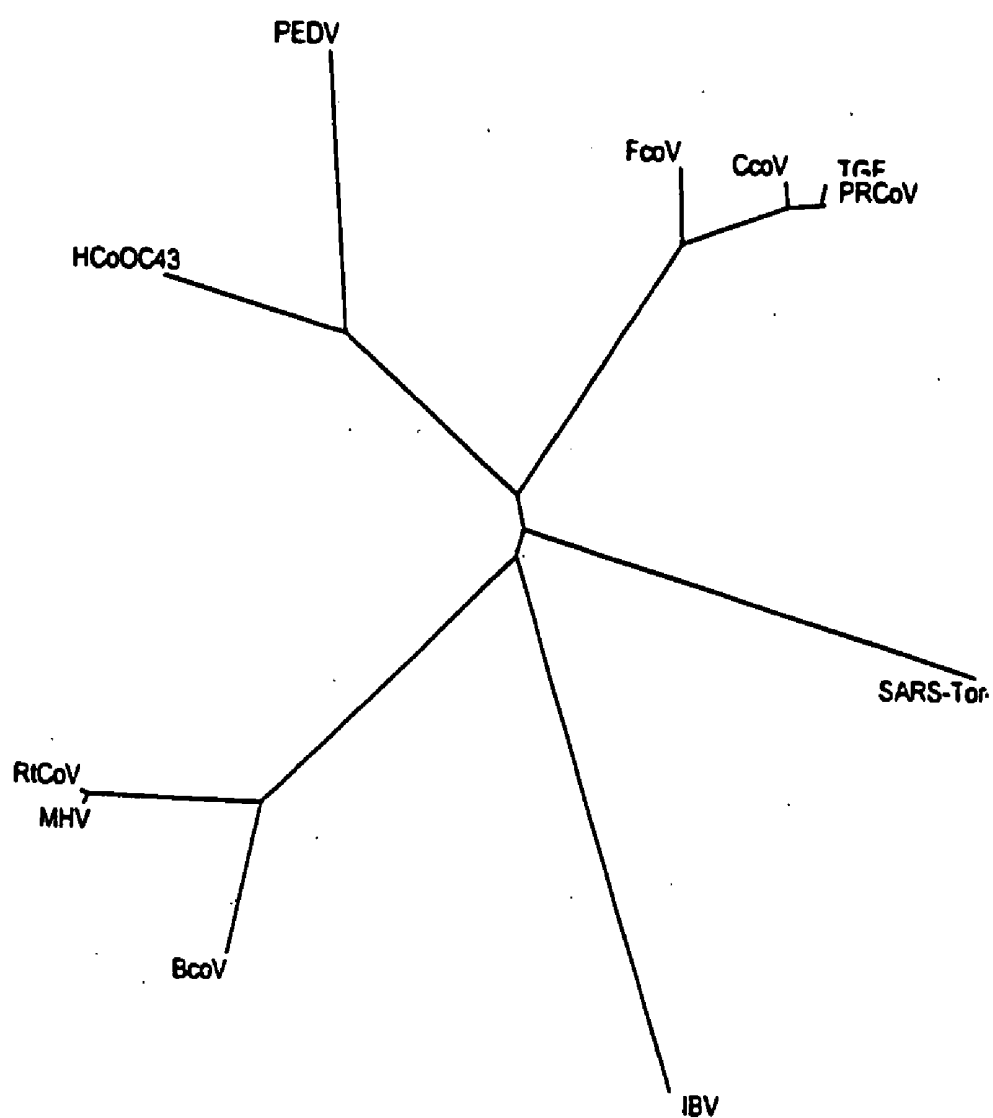
  

|          |                                                             |
|----------|-------------------------------------------------------------|
| SARS-Urb | CAACGGTTTACGTCTAC--TCGCGTG--TTAAAAATCTGAACTCTTCTGAAGGA----- |
| SARS-Tor | CAACGGTTTACGTCTAC--TCGCGTG--TTAAAAATCTGAACTCTTCTGAAGGA----- |

|         |                                                               |
|---------|---------------------------------------------------------------|
| HCoOC43 | CCATTAAAAATGTGTA---CCACATT--TACCAATCATATATGCACATAGACCC-----T  |
| PEDV    | CTATAGGGCGCCTGTA---TAGAGTT--TATAAGTCTTACATGCGAATTGACCC-----C  |
| TGE     | CAGCGCAACATGCTTA---CGATGCC--TATAAGAATTTTATGCGAATTAAAGCAT--AC  |
| PRCoV   | CAGTGCAACATGCTTA---CGATGCC--TATAAGAATTTTATGCGAATTAAAGCAT--AC  |
| CcoV    | CAGCTCGACATGCCTA---TGATGCC--TATAAGAATTTTATGCGAATTAAAGCAT--AC  |
| FcoV    | CTGCACGCCATGCATA---TGATGCC--TATAAGACCTTTATGCAAACCAAGGCAT--AT  |
| MHV     | CTTCTATTTGTGTGTATAATAGGAGT--AAGCAGCTTTATAAGTATTATAATGAAGAAGT  |
| RtCoV   | CTTCTATTTATGTGTATAATAGGAGT--AAGCAGCTTTATAAGTATTATAATGAAGAAGT  |
| BcoV    | CTTCTATTTATGTGTTTAATAGAGGT--AGGCAGTTTATGAGTTTTACAACGAT---GT   |
| IBV     | TTATTGTTAACGAGTTTCCTAAGAACGGTTGGAATAATAAAAAATCCAGCAAATTTTCAAG |

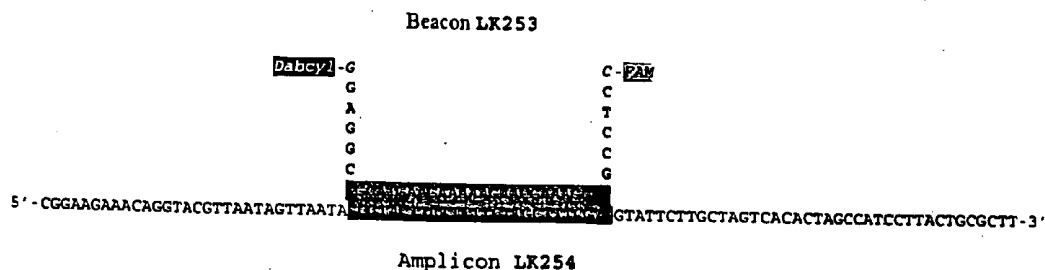
|          |                                                  |
|----------|--------------------------------------------------|
| SARS-Urb | GTTCCCTGATCTTCTGGTCTAA-----                      |
| SARS-Tox | GTTCCCTGATCTTCTGGTCTAA-----                      |
| HCoOC43  | TTCCCTAAACGAGTTATTGATTTCTAA-----                 |
| PEDV     | CTCCCAGTACTGTTATTGACGTATAA-----                  |
| TGE      | AACCCCGATGGAGCACTCCTTGCTTGA-----                 |
| PRCoV    | AACCCTGATGGAGCACTCCTTGTTTGA-----                 |
| CcoV     | AACCCTGATGAAGCACTCCTTGTTTGA-----                 |
| FcoV     | AATCCCGACGAAGCATTTTTGGTTTGA-----                 |
| MHV      | GAGACCGCCCCGTTAGAGGTGGATGATATAATAATCCAAACATTATGA |
| RtCoV    | GAGACCGCCCCGTTAGAGGTGGATGATATAATAATCCAAACATTATGA |
| BcoV     | AAAACCACCAGTTCTTGATGTGGATGACGTT-TAG-----         |
| IBV      | ATGCCCAACGAGACAAATGTACTCTTGA-----                |

**Figure 6:** Phylogenetic Analysis of *E* Gene



**Figure 7: Molecular Designs for SARS-Associated E Gene**

**NOTE:** LK253 is a TET-molecular beacon, which recognizes the *E* gene of coronavirus (SARS Tor2 and SARS urbani human pathogenic strains). It will be used in a real-time PCR diagnostic for the identification of SARS-associated coronavirus RNA/DNA.



**LK253**

|                                       |                                                            |
|---------------------------------------|------------------------------------------------------------|
| E. Target recognition sequence:       | 26 nucleotides (11 G/C)                                    |
| F. Length of the arms:                | 6 nucleotides (5 G/C)                                      |
| G. Melting temperature of the beacon: | dG = -2.29 dH = -67.2 dS = -200.8 T <sub>m</sub> = 61.5 °C |
| H. Melting temperature of target:     | °C                                                         |

**LK255** 5'-CGGAAGAAACAGGTACGTTAATAG-3'

Length: 24 nucleotides (10 G/C)  
T<sub>m</sub>: °C  
Position: (see alignment below)

**LK256** 5'-AAGCGCAGTAAGGATGGCTA-3'

Length: 20 nucleotides (10 G/C)  
T<sub>m</sub>: °C  
Position: (see alignment below)

**E-RT** 5'-TATTGCAGCAGTAC-3'

Length: 14 nucleotides (10 G/C)  
T<sub>m</sub>: 47 °C  
Position: (see alignment below)

5'CGGAAGAAACAGGTACGTTAATAGTTAATAGCGTACTTCTTTTTCTTGCTTTCGT  
GGTATTCTTGTAGTCACACTAGCCATCCTTACTGCGCTT-3'

|          |                                                               |
|----------|---------------------------------------------------------------|
| kk       |                                                               |
| SARS-Urb | -----                                                         |
| SARS-Tor | -----                                                         |
| HCoOC43  | -----                                                         |
| PEDV     | -----                                                         |
| TGE      | -----                                                         |
| PRCoV    | -----                                                         |
| CcoV     | -----                                                         |
| FcoV     | -----                                                         |
| MHV      | -----                                                         |
| RtCoV    | -----                                                         |
| BcoV     | -----                                                         |
| IBV      | ATGAATTTATTGAATAAGTCGCTAGAGGAGAAATCGAAGTTTTCTAACAGCGCTTTACATA |

SARS-Urb -----ATGTACTCATTGTTTCGGAAGAAACAGGTACGTTAATAGTTAATAAGT  
SARS-Tor -----ATGTACTCATTGTTTCGGAAGAAACAGGTACGTTAATAGTTAATAAGT  
HCoV43 -----ATGTTCTTAAGCTAGTGGATGATCA-TGCTTTGGTGTGAATGTAC  
PEDV -----ATGCTACAATTAGTGAATGATAA-TGGTCTAGTAGTTAATGTTA  
TGE ATGACGTTTCCTAGGGCATTGACTGT CATAGATGACAA-TGGAATGGTCATTAACATTA  
PRCoV ATGACGTTTCCTAGGGCATTGACTGT CATAGATGACAA-CGGAATGGTCATTAGCATTA  
Cov ATGACGTTCCCTCGGGCATTGACTGT CATAGATGACAA-TGGAATGGTCATTAGTATTA  
Fov ATGACGTTCCCTAGGGCATTACTATCATAGATGACCA-TGGCATGGTGTGTAGCGTTT  
MHV -----ATGTTTAATTTATTCCTTACAGATACAGTATGGTATGTGGGGCAG-ATTA  
RtCoV -----ATGTTTAATTTATTCCTTATAGACACAGTATGGTACGTGGGGCAG-ATTA  
Bov ---ATGTTTATGGCTAGTCTTATTTTCAGACACTGTGTGGTATGTGGGGCAA-ATAA  
IBV ATTGTAGGATTTTATGACCATTTATCTCTTAGGTA--GAGCACTTCAGCATTTGTGATCAAG

LK255 5'-CGGAAGAAACAGGTACGTTAATAG -3'  
 ~~~~~

Genome	Accession	Position	Sequence
SARS-Urb	U01731	10000	GTATT-----CTTGCTAGTCACACTAGCCATCCTTA
SARS-Tor	U01731	10000	GTATT-----CTTGCTAGTCACACTAGCCATCCTTA
HCoVOC43	U01731	10000	CTGG GTG G TGC TA AGTGAT-----ACTACTAGTGTGTATTACAATAATTA
PEDV	U01731	10000	TGGC TT C TAC CT TTTCCCT-----GCTTATTATAAGCATTACCTTCGTCC
TGE	U01731	10000	CTGG C C GTTGA AA TATATT-----GATATTACTTTCAATAGCATTGCTAA
PRCoV	U01731	10000	TGG C C GTTGA AA TATATT-----GATATTACTTTCAATAGCATTGCTAA
CcCoV	U01731	10000	CTGG C C GTTGA AA TATATT-----GATATTACTTTCAATAGCATTGCTAA
FCoV	U01731	10000	CTGGC C C GTTGA AA TATATT-----GATATTGTTTTCAATAGCATTGCTAA
MHV	U01731	10000	TA AG CGCA TG GTT ATGGT-----CACCATAATAGTGGTTGCCTTCCTTG
RtCoV	U01731	10000	TA AG CGCA TG GTT ATGGT-----CACCATAATAGTGGTTGCCTTCCTTG
BcCoV	U01731	10000	TA AG TGCCATT GTT ATGGT-----TATAATAGTTGTAGTGCCATTTTGG
IBV	U01731	10000	CTGCTGA GCT GTTG- TA TTTGGTATACATGGGTAGTAA TTCAGGAGCTTAAGGGT

LK253 BEACON LK256 3'-ATCGGTAGGAAT
 #####

SARS-Urb CTGCGCTTCGATT--GTGTGCGTACTGCTGCAATATTGTTAACGTGAGTTTAGTAAAC
SARS-Tor CTGCGCTTCGATT--GTGTGCGTACTGCTGCAATATTGTTAACGTGAGTTTAGTAAAC

HCoOC43	AACTAATTAAGCT---TTGTTTCACTTGCCATATGTTTTGTAATAGAACAGTTTATGGCC
PEDV	AATTGGTTAATCT---GTGCTTCACTTGTCACCGGTTGTGTAATAGCGCAGTTTATACAC
TGE	ATATAATTAAGCT---ATGCATGGTGTGTTGCAATTTAGGAAGGACAGTTATTATTGTTT
PRCoV	ATATAATTAAGCT---ATGCATGGTGTGTTGCAATTTAGGAAGGACAGTTATTATTGTTT
CcoV	ATATAATTAAGCT---ATGCATGGTGTGTTGCAATTTAGGAAGGACAGTTATTATTGTTT
FcoV	ATGTTATTAAATT---GTGCATGGTGTGTTGCAATTTGGGTAAGACTATTATAGTACTAC
MHV	CGTCTATCAAAC---TTGTATTCAAACTTTGCGGTTTGTGTAATACTTTGTTGCTGTCTC
RtCoV	CGTCTATTAAC---GTGTATTCAAACTTTGCGGTTTGTGTAATACTTTGTTGCTGTCTC
BcoV	CAACTTTTAAATT---GTGTATTCAAACTTTGCGGTTTGTGTAATACTTTGTTGCTGTCTC
IBV	CAGCCTTTGTATACAAGTATACATATGGTAGAAAACCTTAACAATCCGGAATTAGAAGCAG

* * *

GACGCGAA-5' 3'-CATGACGACGTTAT-5' E-RT

<<<<<<<<<<

SARS-Urb	CAACGGTTTACGTCTAC--TCGCGTG--TTAAAAATCTGAACTCTTCTGAAGGA-----
SARS-Tor	CAACGGTTTACGTCTAC--TCGCGTG--TTAAAAATCTGAACTCTTCTGAAGGA-----
HCoOC43	CCATTAAAAATGTGTA---CCACATT--TACCAATCATATATGCACATAGACCC-----T
PEDV	CTATAGGGCGCCTGTA---TAGAGTT--TATAAGTCTTACATGCGAATTGACCC-----C
TGE	CAGCGCAACATGCTTA---CGATGCC--TATAAGAATTTTATGCGAATTAAAGCAT--AC
PRCoV	CAGTGCAACATGCTTA---CGATGCC--TATAAGAATTTTATGCGAATTAAAGCAT--AC
CcoV	CAGCTCGACATGCCTA---TGATGCC--TATAAGAATTTTATGCAAACCAAGGCAT--AT
FcoV	CTGCACGCCATGCATA---TGATGCC--TATAAGACCTTTATGCAAACCAAGGCAT--AT
MHV	CTTCTATTTGTGTGTATAATAGGAGT--AAGCAGCTTTATAAGTATTATAATGAAGAAGT
RtCoV	CTTCTATTTATGTGTATAATAGGAGT--AAGCAGCTTTATAAGTATTATAATGAAGAAGT
BcoV	CTTCTATTTATGTGTTTAAATAGAGGT--AGGCAGTTTTATGAGTTTTACAACGAT---GT
IBV	TTATTGTTAACGAGTTTCCTAAGAACGGTTGGAATAATAAAAAATCCAGCAAATTTTCAAG

* * *

SARS-Urb	GTTCTGATCTTCTGGTCTAA-----
SARS-Tor	GTTCTGATCTTCTGGTCTAA-----
HCoOC43	TTCCCTAAACGAGTTATTGATTCTAA-----
PEDV	CTCCCCAGTACTGTTATTGACGTATAA-----
TGE	AACCCCGATGGAGCACTCCTTGCTTGA-----
PRCoV	AACCTTGATGGAGCACTCCTTGTTTGA-----
CcoV	AACCTTGATGAAGCACTCCTTGTTTGA-----
FcoV	AATCCCGACGAAGCATTTTTGTTTGA-----
MHV	GAGACCGCCCCCGTTAGAGGTGGATGATATAATAATCCAAACATTATGA
RtCoV	GAGACCGCCCCCGTTAGAGGTGGATGATATAATAATCCAAACATTATGA
BcoV	AAAACCACCAAGTTCTTGATGTGGATGACGTT-TAG-----
IBV	ATGCCCAACGAGACAAATTGTACTCTTGA-----

*

Figure 8: Molecular Designs for SARS-Associated E Gene

LK253 5'-FAM-CCTCCGCACGAAAGCAAGAAAAAGAAGTACGCCGGAGG-3'-
Dubcyl

LK253.N 5'-FAM-GCCTCCGCACGAAAGCAAGAAAAAGAAGTACGCCGGAGGC-3'-
Dubcyl

LK254 5'-CGGAAGAAACAGGTACGTTAATAGTTAATAGCGTACTTCTTTTC
TTGCTTTCGTGGTATTCTTGCTAGTCACACTAGCCATCCTTACTGCGCTT
-3'

LK255 5'- CGGAAGAAACAGGTACGTTAATAG -3'

LK255-T7 5'-TAATACGACTCACTATAGGCGGAAGAAACAGGTACGTTAATAG -3'

LK256 5'- AAGCGCAGTAAGGATGGCTA - 3'

LK256-RT 5'- TATTGCAGCAGTACAAGCGCAGTAAGGATGGCTA - 3'

E-RT 5' -TATTGCAGCAGTAC-3'

Figure 9: DNA Sequence Alignment of Coronavirus *M* Genes Isolated from different Species

TGE	-----
PRCoV	-----
CcCoV	-----
FCoV	-----
HCoVOC43	ATGCATATGATGCCTATAAGACCTTTATGCAAACCAAGGCATATAATCCCGACGAAGCAT
PEDV	-----
BCoV	-----
HEV	-----
MHV	-----
RtCoV	-----
SARS-Urb	-----
SARS-Tor	-----
IBV	-----

TGE	-----ATGAAGATTTTGTTAATATTAGCGTGTGTGATTGCA
PRCoV	-----ATGAAGATTTTGTGATATTAGCGTGTGCGATTGCA
CcCoV	-----ATGAAGAAAAATTTGTTTTTACTAGCGTGTGCAATTGCA
FCoV	TTTTGGTTTGAACATAACAAAATGAAGTACATTTTGCTAATACTCGCGTGCATAATTGCA
HCoVOC43	-----
PEDV	-----
BCoV	-----
HEV	-----
MHV	-----
RtCoV	-----
SARS-Urb	-----
SARS-Tor	-----
IBV	-----

TGE	TGCGCATGTGGAGAACGCTATTGTGCTATGAAATCCGATACAGATTGTGCATGTCGCAAT
PRCoV	TGCACATGTGGAGAACGCTATTGTGCTATGAAAGACGATACAGGTTGTGCATGTCGCAAT
CcCoV	TGCGTCTATGGAGAACGCTATTGTGCCATGA---CTGAAAGTTCTACGTCATGTCGTAAT
FCoV	TGCGTTTATGGTGAACGCTACTGTGCCATGCAA---GACAGTGGCTTGCAGTGTATTAAT
HCoVOC43	-----
PEDV	-----
BCoV	-----
HEV	-----ATGAGTAGTG
MHV	-----ATGAGTAGTC
RtCoV	-----ATGACTAGTA
SARS-Urb	-----ATGAGTAGTA
SARS-Tor	-----
IBV	-----

TGE	AGTACAGCGTCTGATTGTGAGTCA--TGCTTCAACGGAGGCGATCTTATTTGGCATCTTG
PRCoV	GGCACGGCGTCTGATTGTGAGTCA--TGCTTCAACAGAGGCGATCTTATTTGGCTTCTTG
CcCoV	AGCACGGCTGGCAACTGTGCTTCA--TGCTTCGAAACAGGTGATCTTATTTGGCATCTTG
FCoV	GGCACAAATTCAAGATGTCAAACC--TGCTTTGAACGTGGTGATCTTATTTGGCATCTTG
HCoVOC43	-----ATGTCAAATG---ACAATTGTACGGGTGACATTGTCAACCATTTGA
PEDV	-----ATGTCTAACGGTTCTATTCGGTTGATGAGGTGATTGAACACCTTA
BCoV	TAAC---ACACCAGCACCAGTTTACACCTGGACTGCTGATGAAGCTATTAAATTCCTAA
HEV	CAACT---ACACCAGTACCAGTTATTAGCTGGACTGCTGATGAAGCTATTAAATTCCTAA
MHV	CCACTCAGGCTCCACAGCCTGTTTATCAGTGGACGGCTGATGAGGCAATTCGATTCCCTTA
RtCoV	CCACTCCAGCCCCCAGACTGTCTATCAATGGACGGCCGATGTGGCAGTTCGATTCCCTTA
SARS-Urb	--TTGCTTATCATGGCAGACAACGGTACTATTACCGTTGAGGAGCTTAAACAACCTCCTGG
SARS-Tor	--TTGCTTATCATGGCAGACAACGGTACTATTACCGTTGAGGAGCTTAAACAACCTCCTGG

-----ATGCCCAACGAGACAAATTGTACTCTTGACTTTGAACAGTCAGTTCAGCTTTTTTA

CAAACTGGAACCTTCAGCTGGTCTATAATATTGATCGTTTTTATAACTGTGCTACAATATG
 CAAACTGGAACCTTCAGCTGGTCTATAATATTGATCATTTTTTATTACTGTGCTACAATATG
 CAAACTGGAACCTTCAGCTGGTCTGTAATATTGATCATTTTTTATAACAGTGTTACAATATG
 CTAACTGGAACCTTCAGCTGGTCTGTAATATTGATTGTTTTTATAACAGTGTTACAATATG
 AGAATTTGGAATTTTGGTTGGAATGTTATTCTAACCATATTCAATTGTTATTCTTCAGTTTG
 GAAACTGGAATTTTCACATGGAATATCATACTGACGATACTACTTGTAGTGCTTCAGTATG
 AGGAATGGAACCTTTCTTTGGGTATTATACTACTTTTTATTACAATCATATTGCAATTTG
 AGGAATGGAATTTTCTTTGGGTATAATAGTACTCTTTTATCAACATCATACTTCAATTTG
 AGGAATGGAATTTCTCTCTCGGCATTATACTACTCTTTTGGTTACTATCATACTACAGTTTCG
 AGGAATGGAACCTTCTGTGGGCATTATACTACTCTTTATTACTATCATACTACAGTTTCG
 AACAAATGGAACCTAGTAATAGGTTTCCTATTCTAGCCTGGATTATGTTACTACAATTTG
 AACAAATGGAACCTAGTAATAGGTTTCCTATTCTAGCCTGGATTATGTTACTACAATTTG
 AAGAGTATAATTTATTATAACTGCATTTCTGTGTTCTTAAACATAATACTTCAGTATG

GAAGACCTCAATTAGCTGGTTCGTGTATGGCATTAAATGCTTATAATGTGGCTATTAT
GAAGACCTCAATTAGCTGGTTCGTGTATGGCATTAAATGCTTATAATGTGGCTATTAT
GAAGACCTCAATTTAGCTGGTTCGTGTGTGGCATTAAATGCTTATTATGTGGCTGTAT
GCAGACCACAATTTAGCTGGCTCGTTTATGGCATTAAATGCTGATCATGTGGCTATTAT
GACACTATAAACTCCAGATTGTTTTATGGTTTTGAAGATGCTTGTACTGTGGCTTCTTT
GCCATTACAAGTACTCTGTGTTCTTGTATGGTGTCAAGATGCCTATTCTATGGATACTTT
GATATACAAGTCGCAGTATGTTGTTTATGTTTAAAGATGATCATTTTGTGGCTTATGT
GATATACAAGTCGCAGTATGTTTGTATGTTTAAAGATGCTTATCTGTGGCTCATGT
GTTACACGAGCCGTAGCATGTTTGTATGTTGTGAAAATGATACTTTGTGGCTTATGT
GTTACACGAGCCGTAGCATGTTTATATATGTTGTGAAAATGATAATCTTGTGGTTAATGT
CCTATTCTAATCGGAACAGGTTTTGTACATAATAAAGCTTGTTCCTCTGGCTCTTGT
CCTATTCTAATCGGAACAGGTTTTGTACATAATAAAGCTTGTTCCTCTGGCTCTTGT
GCTATGCAACAAGAAGTAAGGTTATTATACACTGAAAATGATAGTGTATGGTGCTTTT

GGCCCGTTGTTTTGGCTCTTACGATTTTTAATGCATACTCGGAATACCAAGTGTCAGAT
GGCCGATTGTTTTGGCTCTTACGATTTTTAATGCATACTCGGAATACCAAGTGTCAGGT
GGCCCATTTGTTTTAGCTCTTACGATTTTTAATGCATACTCGGAATACCGAGTTCCAGT
GGCCTATTGTTCTAGCGCTTACGATTTTTAATGCATACTCTGAGTACCAAGTTTCAGAT
GGCCACTCGTACTTGCTTTGTCAATCTTTGACAC--CTGGGCTAATTGGGATTCTAATT
GGCCTCTTGTTGTTGGCACTGTCACTTTTGACGCATGGGCTAGCTTCCAGGT--CAACT
GGCCCCTTACTATCACTTAACTATTTTCAAT-----TGCGTGTAT--GCGTTGAATA
GGCCTCTTACTATCAATTTTAACTATCTTCAAC-----TGCGTATAC--GCGTTGAATA
GGCCACTAACTATTGTTTTGTGATTTTTAAAC-----TGCGTCTAT--GCGCTAAATA
GGCCACTGACTATTGTTTTGTGATTTTTAAT-----TGCGTGTAT--GCGCTAAATA
GGCCAGTAACACTTGCTTGTTTTGTGCTTGCTG-----CTGTCTACAGAAT---TAATT
GGCCAGTAACACTTGCTTGTTTTGTGCTTGCTG-----CTGTCTACAGAAT---TAATT
GGCCCCCTTAAACTTTGCAGTAGGTGTAAATTTCA-----TGTACATACC--CACCAAACA
**** *

ATGTAATGTTCCGGCTTTAGTATTGCAGGTGCAATTGTTACATTTGTACTCTGGATTATGT
ATGTAATGTTCCGGCTTTAGTATTGCAGGTGCAATTGTTACATTTGTACTCTGGATTATGT
ATGTAATGTTCCGGCTTTAGTGTTGCAGGTGCAACTGTTACATTTAATACTTTGGATTATGT
ATGTAATGTTCCGGCTTTAGTGTTGCAGGTGCAGTTGTAACGTTTGCACTTTGGATGATGT
GGGCCTTTGTTGCATTTAGCTTTTTTATGGCCGATCAACACTCGTTATGTGGGTGATGT
GGGTCTTTTTTCGCTTTCAGCATCCTTATGGCTTGCACTACTCTTATGCTGTGGATAATGT
ATGTGTATCTTGGCTTTTCTATAGTTTTCACTATAGTGGCCATTATCATGTGGATTGTGT
ATGTGTACCTTGGCTTCTCTATAGTTTTACTATAGTGGCCATTATTATGTGGGTGTTTT
ATGTGTATCTTGGATTTTCTATAGTGTTTACTATAGTGTCCATTATAATGTGGATTATGT
ATGTGTATCTTGGATTCTCTATAGTGTTTACTATAGTGTCCATTGTAATGTGGATTATGT
GGGTGACTGGCGGGATTGCGATTGCAATGGCTTGATTGTAGGCTTGATGTGGCTTAGCT
GGGTGACTGGCGGGATTGCGATTGCAATGGCTTGATTGTAGGCTTGATGTGGCTTAGCT
CAGGAGGTCTTGTCGACGGATAATACTTACAGTGTGTTGCGTGTCTGTCTTTTGTAGGTT

TGE
PRCoV
CcoV
FCoV
HCoVOC43
PEDV
BCoV
HEV
MHV
RtCoV
SARS-Urb
SARS-Tor
IBV

ATTTTGTAAGATCCATTAGTTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCAACCCTG
ATTTTGTAAGATCCATTAGTTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCAACCCTG
ATTTTGTTAGATCCATTAGTTATACAGAAGGACTAAGTCTTGGTGGTCTTTCAACCCTG
ATTTTGTTAGATCTGTTAGCTATATAGAAGAACCATAATCATGGTGGTCTTTTAATCCTG
ACTTCGCAAACAGTTTCAGACTTTTCCGACGTGCTCGAATCTTTTGGGCATGGAATCCTG
ATTTTGTTCAATAGCATTGCGTTGTGGCGCAGGACACATTCTTGGTGGTCTTTCAATCCTG
ATTTTGTTGAATAGTATCAGGTTGTTTATTAGAACTGGAAGTTGGTGGAGTTTCAACCCAG
ATTTTGTTGAATAGTATCAGGTTGTTTATTAGAACTGGAAGTTGGTGGAGTTTCAACCCAG
ATTTTGTTAATAGCATCAGGTTGTTTATCAGGACTGGCAGCTGGTGGAGCTTCAACCCCG
ATTTTGTTAATAGCATCAGGTTGTTTATCAGGACTGGTGGAGCTTCAACCCCG
ACTTCGTTGCTTCTTCAGGCTGTTTGTCTCGTACCCGCTCAATGTGGTCAATCAACCCAG
ACTTCGTTGCTTCTTCAGGCTGTTTGTCTCGTACCCGCTCAATGTGGTCAATCAACCCAG
ATTGGATCCAGAGTATTAGACTCTTTAAGCGGTGTAGGTCTGGTGGTCAATTAATCCAG
* * * * *

TGE
PRCoV
CcoV
FCoV
HCoVOC43
PEDV
BCoV
HEV
MHV
RtCoV
SARS-Urb
SARS-Tor
IBV

AAACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCTCTCGAAG
AAACTAACGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCTCTCGAAG
AAACTAGCGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCTCTCGAAG
AGACTAATGCAATTCTTTGTTAATGCATTGGGTAGAAGTTATGTGCTTCTCTTAGATG
AGGTTAATGCAATCACTGTCACAACCGTGTGGGACAGACATACTATCAACCCATTCAAC
AAACTGACGCGCTTCTCACTACTTCTGTGATGGGCGGACAGGTCGCAATCCAGTGCTTG
AAACAAACAACCTTGATGTGTATAGATATGAAGGGAAGGATGTATGTTAGGCCGATAATTG
AAACAAACAACCTTGATGTGTATAGATATGAAGGGAAGGATGTATGTTAGGCCGATTATTG
AAACAAACAACCTAATGTGTATAGATATGAAGGGAAGGATGTATGTTAGGCCATTATAG
AAACAAACAACCTAATGTGTATAGATGTGAAGGGAAGGATGTATGTTAGGCCATTATTG
AAACAAACATTCTTCTCAATGTGCTTCTCCGGGGGACAATTGTGACCAGACCGCTCATGG
AAACAAACATTCTTCTCAATGTGCTTCTCCGGGGGACAATTGTGACCAGACCGCTCATGG
AATCTAATGCCGTAGGTTCAATACTCCTAATAATGGTCAACAATGTAATTTTGCTATAG
* * * * *

TGE
PRCoV
CcoV
FCoV
HCoVOC43
PEDV
BCoV
HEV
MHV
RtCoV
SARS-Urb
SARS-Tor
IBV

GTGTG---CCAACTGGTGTCACTCTAACTTTGCTTTTCAAGGAATTGTACGCTGAAGGGT
GTGTG---CCAACTGGTGTCACTCTAACTTTGCTTTTCAAGGAATTGTACGCTGAAGGGT
GTGTG---CCAACTGGTGTCACTCTAACTTTGCTTTTCAAGGAATTGTGTGCTGAAGGGT
GTACT---CCTACAGGTGTTACCTTACTCTACTTTTCAAGGAATCTATATGCTGAAGGGT
AAGCT---CCAACAGGCAATTACTGTGACCTTGTGAGCGGCGTGCTTTACGTTGACGGAC
GAGCA---CCAACGGTGTGAACGCTTAACACTCCTTAGTGGTACATTGTTAGAGGGCT
AGGAC---TACCATACCTTACGGTCACAATAATACGTGGTCACTTTTACATGCAAGGTA
AGGAC---TACCACACCCTTACTGCCACAATAATACGTGGCCACCTCTACATCCAAGGTA
AGGAT---TACCATACCTAACAGCCACTATCATTCTGGTCACTCTATATGCAAGGTG
AAGAT---TACCATACCTAACAGCCACAATAATGACGTGGCCACCTTTATATGCAAGGTG
AAAGT---GAACTTGTCAATTGGTGTGCTGATCATTCTGGTCACTTGCGAATGGCCGGAC
AAAGT---GAACTTGTCAATTGGTGTGCTGATCATTCTGGTCACTTGCGAATGGCCGGAC
AGAGTGTGCCAATGGTGCTTTCTCCAATTATAAAGAATGGTGTCTTTATTGTGAGGGT
* * * * *

TGE
PRCoV
CcoV
FCoV
HCoVOC43
PEDV
BCoV
HEV
MHV
RtCoV
SARS-Urb
SARS-Tor
IBV

TCAAAATTGCAGGTGGTATGAACATCGACAATTTACCAAATACGTAATGGTTGCATTAC
TCAAAATTGCAGGTGGTATGACCATCGACAATTTGCCAAATACGTAATGGTTGCATTAC
TCAAAATTGCAGGTGGTATGAACATCGACAATTTACCAAATATGTAATGGTTGCATTAC
TCAAAATTGGCTGGTGGTTAAACCATCGAGCATTGCTTAAATACGTCATGATTGCTACAC
ATAGATTGGCTTCAAGGTGTTCAAGGTTCATAACCTACCTGAATACATGACAGTTGCCGTGC
ATAAGGTTGCTACTGGCGTACAGGTAAGTCAATTACCTAATTTCTGTCACAGTCCGCAAGG
TAAACTAGGTACTGGCTATTCTTTGTGAGATTTGCCAGCTTATGTGACTGTTGCTAAGG
TAAACTAGGTACTGGCTATTCTTTGTGAGATTTGCCGTGCTTATGTGACCGTTGCTAAGG
TTAAGCTAGGCACTGGCTTCTTTGTGCTGATTTGCCGTGCTTATGTTACAGTTGCTAAGG
TTAAGCTAGGCACTGGCTTCTTTGTGCTGATTTGCCGTGCTTATGTTACAGTTGCTAAGG
ACCCCTAGGGCGCTGTG---ACATTAAGGACCTGCCAAAAGAGATCACTGTGGCTACAT
ACTCCCTAGGGCGCTGTG---ACATTAAGGACCTGCCAAAAGAGATCACTGTGGCTACAT
AGTGGCTTGTCAAGTGTG---AACCAGACCACTTGCCTAAAGATATATTTGTTGTACAC
* * * * *

TGE	CTAGCAGGACTATTGTCTACACAC--TTGTTGGCAAGAAGTTGAAAGCAAGTAGTGCGAC
PRCoV	CCAGCAGGACTATTGTTTACACAC--TTGTTGGCAAGAAGTTGAAAGCAAGTAGTGCGAC
CcCoV	CTGTCAGAACCATAGTCTACACAC--TTGTTGGCAAGAAATTGAAAGCAAGTAGTGCAAC
FCoV	CTAGTAGAACCATCGTTTATACAT--TAGTTGGAAAACAATTAAAAGCAACTACTGCCAC
HCoVOC43	CGAGCACTACTATAATTTATAGTA--GAGTCGGAAGGTCCGTAAATTCACAAAATAGCAC
PEDV	CCACTACAACAATTGTCTACGGAC--GTGTTGGTCGTTCACTCAATGCTTCATCTGGCAC
BCoV	T--CTCACACCTGCTCACGTATAA--GCGT-GGTTTTCTTGACAAGATAGGCGATACTAG
HEV	T--TACACACCTGTGCACATATAA--GCGT-GGTTTTCTTGATAGGATAGGCGATACTAG
MHV	T--GTCTCACCTTTGCACCTATAA--GCGC-GCATTCTTAGACAAGGTAGACGGTGTTAG
RtCoV	T--GTGCGACCTTTGCACCTATAA--GCGC-GCATTCTTAGACAAGGTGACGGTGTTAG
SARS-Urb	C---ACGAACGCTTTCTTATTACA--AATTAGGAGCGTCGCAGCGTGTAGGCACTGATTC
SARS-Tor	C---ACGAACGCTTTCTTATTACA--AATTAGGAGCGTCGCAGCGTGTAGGCACTGATTC
IBV	CGGATAGACGTAATATCTACCGTATGGTGCAGAAATATACTGGTGACCAAAGCGGAAATA

TGE	TGGATGGGCTTACTATGTAAAATCTAAAGCTGGTGATTACTCAACAGAGG---CAAGAAC
PRCoV	TGGATGGGCTTACTATGTAAAATCTAAAGCTGGTGATTACTCAACAGAGG---CAAGAAC
CcCoV	AGGATGGGCTTACTATGTAAAGTCTAAAGCTGGTGATTACTCAACAGAGT---CACGAAC
FCoV	AGGATGGGCTTACTACGTAAAATCTAAAGCTGGTGATTACTCAACAGAG---CACGTAC
HCoVOC43	AGGCTGGGTTTTCTACGTACGAGTAAACACGGTGATTTTTCTGCAGTGAGCTCTCCCAT
PEDV	TGGTTGGGCTTTCTATGTCCGGTCAAACACGGCGACTATTCACTGTGAGTAATCCGAG
BCoV	TGGTTTTGCTGTTTATGTTAAGTCCAAAGTCGGTAATTACCGACTGCCATCAACCCATAA
HEV	TGGTTTTGCTGTTTATGTTAAGTCCAAAGTCGGTAATTACCGACTGCCCTCAAATAAACCC
MHV	CGGTTTTGCTGTTTATGTTAAGTCCAAAGTCGGTAATTACCGACTGCCCTCAAATAAACCC
RtCoV	CGGTTTTGCTGTTTATGTTAAGTCCAAAGTCGGTAATTACCGACTGCCCTCAAATAAACCC
SARS-Urb	AGGTTTTGCTGCATACAACCGCTACCGTATTGGAAACTATAAATTAAATACAGACCACGC
SARS-Tor	AGGTTTTGCTGCATACAACCGCTACCGTATTGGAAACTATAAATTAAATACAGACCACGC
IBV	AGAAAAGGTTTGCTACGTTTG-TCTATGCAAAGCAGTCAGTAGATACTGGCGAGCTAGAA

TGE	TGATAATTTGAGTGAGCAAGAAAAATTATTACATATGGTATAA
PRCoV	TGATAATTTGAGTGAGCAAGAAAAATTATTACATATGGTATAA
CcCoV	TGATAATTTGAGTGAGCATGAAAAATTATTACATATGGTATAA
FCoV	TGACAATTTGAGTGAACATGAAAAATTATTACATATGGTGTA
HCoVOC43	GAGCAACATGACAGAAAAACGAAGATTGCTTCATTTTTCTAA
PEDV	TGCGGTTCTCACAGATAGTGAGAAAGTGCTTCATTTAGTCTAA
BCoV	GGGTTCTGGCATGGACACCGCATTGTTGAGAAATAATATCTAA
HEV	GGGCTCAGGCATGGACACCGCATTGTTGAGAAATAATATCTAA
MHV	GAGT---GGCATGGACACCGCATTGTTGAGAATCTAA-----
RtCoV	GAGT---GGCGCGACACCGCATTGTTGAGAATCTAA-----
SARS-Urb	CGGTAGCAACGACAATATTGCTTTGCTAGTACAGTAA-----
SARS-Tor	CGGTAGCAACGACAATATTGCTTTGCTAGTACAGTAA-----
IBV	AGTGTAGCAACAGGAGGAAGTAGTCTTTACACATAA-----

Figure 10: Phylogenetic Analysis of *M* Gene

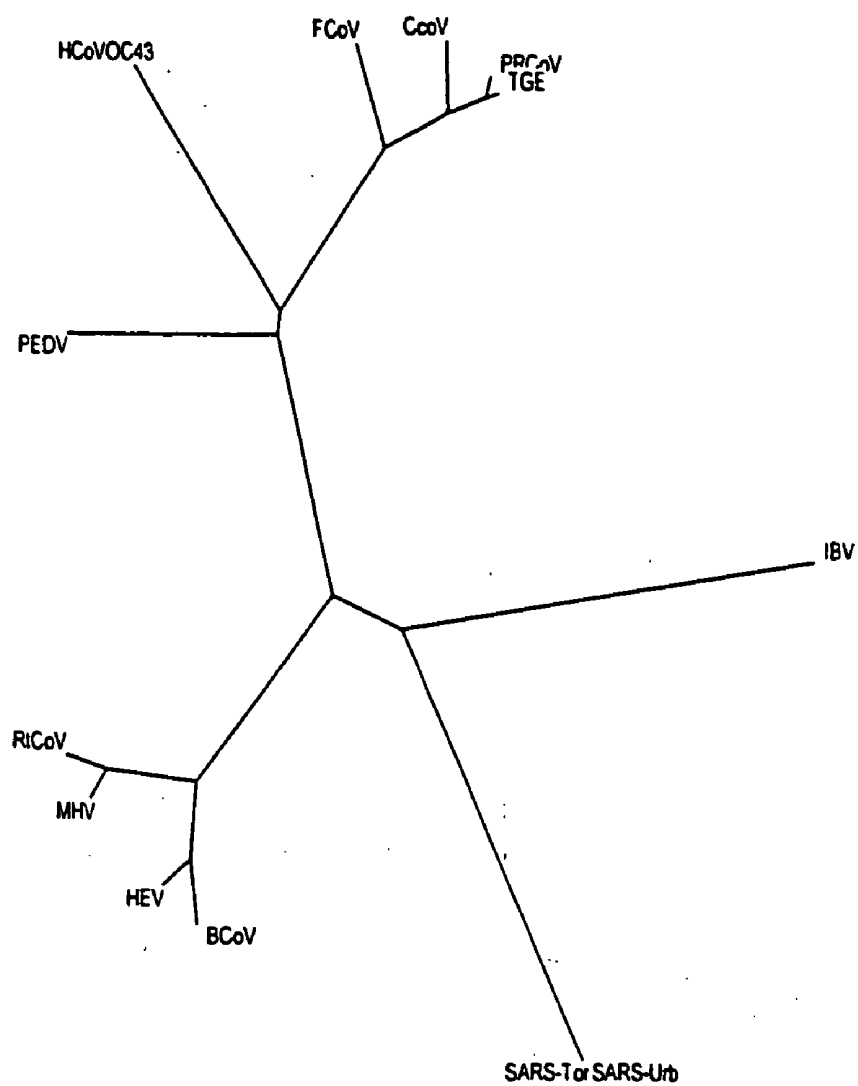
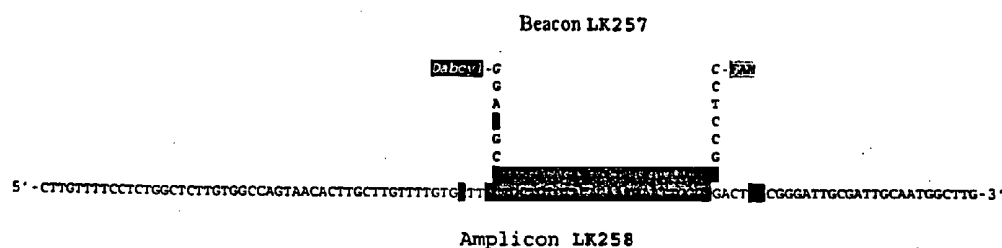


Figure 11: Molecular Designs for SARS-Associated *M* Gene

NOTE: LK257 is a TET-molecular beacon, which recognizes the *M* gene of coronavirus (SARS Tor2 and SARS urbani human pathogenic strains). It will be used in a real-time PCR diagnostic for the identification of SARS-associated coronavirus RNA/DNA.



LK257

- | | |
|---------------------------------------|--|
| I. Target recognition sequence: | 26 nucleotides (11 G/C) + (3 nts arms G/C) |
| J. Length of the arms: | 6 nucleotides (5 G/C) |
| K. Melting temperature of the beacon: | dG = -1.52 dH = -46.6 dS = -139.6 Tm = 60.7 °C |
| L. Melting temperature of target: | °C (including 3 nts from the arms) |

LK259 5'-CTTGTTTTCCTCTGGCTCTTG-3'

Length: 21 nucleotides (10 G/C)

Tm: °C

Position: (see alignment below)

LK260 5'-CAAGCCATTGCAATCGCAATC-3'

Length: 21 nucleotides (10 G/C)

Tm: °C

Position: (see alignment below)

M-RT 5'-AAGCAACGAAGTAG-3'

Length: 14 nucleotides (6 G/C)

Tm: 47 °C

Position: (see alignment below)

LK258 Amplicon (107 nucleotides)

5'-

CTTGTTTTCTCTGGCTCTTGTGGCCAGTAACACTTGCTTGTTTTGTGCTTGCTGCTG
TCTACAGAAATTAATTGGGTGACTGGCGGGATTGCGATTGCAATGGCTTG -3'

**DNA sequence alignment of complete
M genes from corona virus strains**

TGE	-----
PRCoV	-----
CcoV	-----
FCoV	ATGCATATGATGCCTATAAGACCTTTATGCAAACCAAGGCATATAATCCCGACGAAGCAT
HCoVOC43	-----
PEDV	-----
BCoV	-----
HEV	-----
MHV	-----
RtCoV	-----
SARS-Urb	-----
SARS-Tor	-----
IBV	-----

TGE	-----ATGAAGATTTTGTTAATATTAGCGTGTGTGATTGCA
PRCoV	-----ATGAAGATTTTGTTGATATTAGCGTGTGCGATTGCA
CcoV	-----ATGAAGAAAATTTGTTTTTACTAGCGTGTGCAATTGCA
FCoV	TTTTGGTTTGAACATAAACAAATGAAGTACATTTTGCTAATACTCGCGTGCATAATTGCA
HCoVOC43	-----
PEDV	-----
BCoV	-----
HEV	-----
MHV	-----
RtCoV	-----
SARS-Urb	-----
SARS-Tor	-----
IBV	-----

TGE	TGCGCATGTGGAGAACGCTATTGTGCTATGAAATCCGATACAGATTTGTCATGTCGCAAT
PRCoV	TGCACATGTGGAGAACGCTATTGTGCTATGAAAGACGATACAGGTTTGTGTCATGTCGCAAT
CcoV	TGCGTCTATGGAGAACGCTATTGTGCCATGA---CTGAAAGTTCTACGTCATGTCGTAAT
FCoV	TGCGTTTATGGTGAACGCTACTGTGCCATGCAA---GACAGTGGCTTGCAAGTGTATTAAT
HCoVOC43	-----
PEDV	-----
BCoV	-----ATGAGTAGTG
HEV	-----ATGAGTAGTC
MHV	-----ATGACTAGTA
RtCoV	-----ATGAGTAGTA
SARS-Urb	-----
SARS-Tor	-----
IBV	-----

TGE	AGTACAGCGTCTGATTGTGAGTCA--TGCTTCAACGAGGCGATCTTATTTGGCATCTTG
PRCoV	GGCACGGCGTCTGATTGTGAGTCA--TGCTTCAACAGAGGCGATCTTATTTGGCTTCTTG

TGE	GAAGACCTCAATTAGCTGGTTCGTGTATGGCATTAAAATGCTTATAATGTGGCTATTAT
PRCoV	GAAGACCTCAATTAGCTGGTTCGTGTATGGCATTAAAATGCTTATAATGTGGCTATTAT
CcCoV	GAAGACCTCAATTTAGCTGGTTCGTGTGTGGCATTAAAATGCTTATTATGTGGCTGTTAT
FCoV	GCAGACCACAATTTAGCTGGCTCGTTTATGGCATTAAAATGCTGATCATGTGGCTATTAT
HCoVOC43	GACACTATAAATACTCCAGATTGTTTTATGGTTTGAAGATGCTTGTACTGTGGCTTCTTT
PEDV	GCCATTACAAGTACTCTGTGTTCTTGATGGTGTCAAGATGGCTATTCTATGGGATACTTT
BCoV	GATATACAAGTCGCAGTATGTTTGTTATGTTATTAAGATGATCACTTTGTGGCTTATGT
HEV	GATATACAAGTCGCAGTATGTTTGTTATGTTATTAAGATGGTTATTCTGTGGCTCATGT
MHV	GTTACACGAGCCGTAGCATGTTTGTTTATGTTGTGAAAATGATACTTTTGTTGGCTTATGT
RtCoV	GTTACACGAGCCGTAGCATGTTTATATATGTTGTGAAAATGATAATCTTGTTGGTTAATGT
SARS-Urb	CCTATTCTAATCGGAACAGGTTTTTGTTACATAATAAAGCTTGTTTTCTCTGGCTCTTGT
SARS-Tor	CCTATTCTAATCGGAACAGGTTTTTGTTACATAATAAAGCTTGTTTTCTCTGGCTCTTGT
IBV	GCTATGCAACAAGAAGTAAAGTTTATTATACACTGAAAATGATGCTGTTTATGCTGGCTTTT

[illegible]

LK258 BEACON

TGE	AT	AAATGTTTCGGCTTTAGTATTGCAGGTGCAATTGTTACATTTGTA	CTGGATTATGT
PRCoV	AT	AAATGTTTCGGCTTTAGTATTGCAGGTGCAATTGTTACATTTGTA	CTGGATTATGT
CcCoV	AT	AAATGTTTCGGCTTTAGTATTGCAGGTGCAACTGTTACATTTATA	CTGGATTATGT
FCoV	AT	AAATGTTTCGGCTTTAGTATTGCAGGTGCAAGTTGTAACGTTTGC	CTGGATTATGT
HCoVOC43	AT	AAATGTTTCGGCTTTAGTATTGCAGGTGCAAGTTGTAACGTTTGC	CTGGATTATGT
PEDV	AT	AAATGTTTCGGCTTTAGTATTGCAGGTGCAAGTTGTAACGTTTGC	CTGGATTATGT
BCoV	ATG	CTTTTTCGCTTTTCTATAGTATTTTCTATAGTATAGTGGCCATT	TATCATGTGGATTGTGT
HEV	ATG	CTTTTTCGCTTTTCTATAGTATTTTCTATAGTATAGTGGCCATT	TATCATGTGGATTGTGT
MHV	ATG	CTTTTTCGCTTTTCTATAGTATTTTCTATAGTATAGTGGCCATT	TATCATGTGGATTGTGT
RtCoV	ATG	CTTTTTCGCTTTTCTATAGTATTTTCTATAGTATAGTGGCCATT	TATCATGTGGATTGTGT
SARS-Urb	ATG	CTTTTTCGCTTTTCTATAGTATTTTCTATAGTATAGTGGCCATT	TATCATGTGGATTGTGT
SARS-Tor	ATG	CTTTTTCGCTTTTCTATAGTATTTTCTATAGTATAGTGGCCATT	TATCATGTGGATTGTGT
IBV	CA	GAGGTCTTGTGCGCAGCGATAATACTTACAGTGTGTCGTCGTCTG	CTTTTGTAGGTT

3' - CTAACGCTAACGTTACCGAAC - 5' LK260 3' - GA

TGE	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
PRCoV	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
CcCoV	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
FCoV	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
HCoVOC43	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
PEDV	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
BCoV	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
HEV	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
MHV	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
RtCoV	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
SARS-Urb	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
SARS-Tor	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG
IBV	ATTTTGTAGATCCATTAGTGTACAGAAGGACTAAGTCTTGGTGGTCTTTCA	ACCCTG

TGE	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
PRCoV	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
CcCoV	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
FCoV	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
HCoVOC43	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
PEDV	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
BCoV	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
HEV	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
MHV	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
RtCoV	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
SARS-Urb	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
SARS-Tor	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG
IBV	AACTAAAGCAATTCTTTGCGTTAGTGCATTAGGAAGAAGCTATGTGCTTCT	CGAAG

TGE	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
PRCoV	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
CcCoV	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
FCoV	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
HCoVOC43	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
PEDV	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
BCoV	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
HEV	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
MHV	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
RtCoV	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
SARS-Urb	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
SARS-Tor	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT
IBV	GTGTG --- CCAACTGGTGTCACTCTA	CTTGTCTTTCAGGGAATTTGTACGCTGAAGGGT

TGE	TCAAAATTGCAGGTGGTATGAACATCGACAATTTACCAAATACGTAATGGTTGCATTAC
-----	---

PRCoV	TCAAAATTGCAGGTGGTATGACCATCGACAATTTGCCAAAATACGTAATGGTTGCATTAC
CcoV	TCAAAATTGCAGGTGGTATGAACATCGACAATTTACCAAAATATGTAATGGTTGCATTAC
FCoV	TCAAAATGGCTGGTGGTTTAAACATCGAGCATTTGCCTAAATACGTCATGATTGCTACAC
HCoVOC43	ATAGATTGGCTTCAGGTGTTACAGTTTCATAACCTACCTGAATACATGACAGTTGCCGTGC
PEDV	ATAAGGTTGCTACTGGCGTACAGGTAAGTCAATTACCTAATTTTCGTACAGTCGCCAAGG
BCoV	TAAACTAGGTACTGGCTATTCTTTGTCTAGATTGGCAGCTTATGTGACTGTTGCTAAGG
HEV	TAAACTAGGTACTGGCTATTCTTTGTCTAGATTGGCCTGCTTATGTGACCGTTGCTAAGG
MHV	TTAAGCTAGGCACTGGCTTCTCTTTGTCTGATTGGCCTGCTTATGTTACAGTTGCTAAGG
RtCoV	TTAAGCTAGGCACTGGCTTCTCTTTGTCTGATTGGCCCGCTTATGTTACAGTTGCTAAGG
SARS-Urb	ACCCCTAGGGCGCTGTG--ACATTAAGGACCTGCCAAAAGAGATCACTGTGGCTACAT
SARS-Tor	ACTCCCTAGGGCGCTGTG--ACATTAAGGACCTGCCAAAAGAGATCACTGTGGCTACAT
IBV	AGTGGCTTGCTAAGTGTG--AACCAGACCCTTGCCCTAAAGATATATTTGTTGTACAC

* * * * *

TGE	CTAGCAGGACTATTGTCTACACAC--TTGTTGGCAAGAAGTTGAAAGCAAGTAGTGCGAC
PRCoV	CCAGCAGGACTATTGTTTACACAC--TTGTTGGCAAGAAGTTGAAAGCAAGTAGTGCGAC
CcoV	CTGTCAGAACCATAGTCTACACAC--TTGTTGGCAAGAAATTGAAAGCAAGTAGTGCAAC
FCoV	CTAGTAGAACCATCGTTTATACAT--TAGTTGGAAAACAATTAAAAGCAACTACTGCCAC
HCoVOC43	CGAGCACTACTATAATTATAGTA--GAGTCGGAAGGTCGTAATTCACAAAATAGCAC
PEDV	CCACTACAACAATTGTCTACGGAC--GTGTTGGTCGTTCACTCAATGCTTCATCTGGCAC
BCoV	T--CTCACACCTGCTCACGTATAA--GCGT--GGTTTTCTTGACAAGATAGGCGATACTAG
HEV	T--TACACACCTGTGCACATATAA--GCGT--GGTTTTCTTGATAGGATAGGCGATACTAG
MHV	T--GTCTCACCTTTGCACCTATAA--GCGC--GCATTCTTAGACAAGGTAGACGGTGTTAG
RtCoV	T--GTGCGACCTTTGCACCTATAA--GCGC--GCATTTTGTAGACAAGGTGACGGTGTTAG
SARS-Urb	C--ACGAACGCTTTCTTATTACA--AATTAGGAGCGTCGCAGCGGTAGGCACTGATTTC
SARS-Tor	C--ACGAACGCTTTCTTATTACA--AATTAGGAGCGTCGCAGCGGTAGGCACTGATTTC
IBV	CGGATAGACGTAATATCTACCGTATGGTGCAGAAATATACTGGTGACCAAAGCGGAAATA

*

TGE	TGGATGGGCTTACTATGTAAAATCTAAAGCTGGTGATTACTCAACAGAGG---CAAGAAC
PRCoV	TGGATGGGCTTACTATGTAAAATCTAAAGCTGGTGATTACTCAACAGAGG---CAAGAAC
CcoV	AGGATGGGCTTACTATGTAAAGTCTAAAGCTGGTGATTACTCAACAGAGG---CACGAAC
FCoV	AGGATGGGCTTACTACGTAAATCTAAAGCTGGTGATTACTCAACAGAGG---CACGTAC
HCoVOC43	AGGCTGGGTTTTCTACGTACGAGTAAACACCGGTGATTTTCTGCAGTGAGCTCTCCCAT
PEDV	TGGTTGGGCTTTCTATGTCCGGTCAAAACACGGCGACTATTTCAGCTGTGAGTAATCCGAG
BCoV	TGGTTTTGCTGTTTATGTTAAGTCCAAAGTCGGTAATTACCGACTGCCATCAACCCAAAA
HEV	TGGTTTTGCTGTTTATGTTAAGTCCAAAGTCGGTAATTATCGATTGCCTTCAACCCATAA
MHV	CGGTTTTGCTGTTTATGTTAAGTCCAAAGTCGGTAATTACCGACTGCCCTCAATAAACC
RtCoV	CGGTTTTGCTGTTTATGTTAAGTCCAAAGTCGGTAATTACCGACTGCCCTCAATAAACC
SARS-Urb	AGGTTTTGCTGCATACAACCGCTACCGTATTGGAAACTATAAATTAAATACAGACCACGC
SARS-Tor	AGGTTTTGCTGCATACAACCGCTACCGTATTGGAAACTATAAATTAAATACAGACCACGC
IBV	AGAAAAGGTTTGCTACGTTTG-TCTATGCAAAGCAGTCAGTAGATACTGGCGAGCTAGAA

* * * * *

TGE	TGATAATTTGAGTGAGCAAGAAAAATTATTACATATGGTATAA
PRCoV	TGATAATTTGAGTGAGCAAGAAAAATTATTACATATGGTATAA
CcoV	TGATAATTTGAGTGAGCATGAAAAATTATTACATATGGTATAA
FCoV	TGACAATTTGAGTGAACATGAAAAATTATTACATATGGTGTAA
HCoVOC43	GAGCAACATGACAGAAAACGAAAGATTGCTTCATTTTTCTAA
PEDV	TGCGGTTCTCACAGATAGTGAGAAAGTGCTTCATTTAGTCTAA
BCoV	GGGTTCTGGCATGGACACCGCATTGTTGAGAAATAATATCTAA
HEV	GGGCTCAGGCATGGACACCGCATTGTTGAGAAATAATATCTAA
MHV	GAGT---GGCATGGACACCGCATTGTTGAGAAATCTAA-----
RtCoV	GAGT---GGCGCGACACCGCATTGTTGAGAAATCTAA-----
SARS-Urb	CGGTAGCAACGACAATATTGCTTTGCTAGTACAGTAA-----
SARS-Tor	CGGTAGCAACGACAATATTGCTTTGCTAGTACAGTAA-----
IBV	AGTGTAGCAACAGGAGGAAGTAGTCTTTACACATAA-----

* *

Figure 12: List of Molecular Designs for *M* Gene

LK257 5'-FAM-CCTCCGACCCAATTAATTCTGTAGACAGCAGCCGGAGG-3'-
Dubcyl

LK257.N 5'-FAM-GCCTCCGACCCAATTAATTCTGTAGACAGCAGCCGGAGGC-3'-
Dubcyl

LK258

5'-CTTGTTTTCTCTGGCTCTTGTTGGCCAGTAACACTTGCTTGTTTTGTGCT
TGCTGCTGTCTACAGAATTAATTGGGTGACTGGCGGGATTGCGATTGCA
AT
GGCTTG-3'

LK259 5'- CTTGTTTTCTCTGGCTCTTG -3'

5'- TAATACGACTCACTATAGGCTTGTTTTCTCTGGCTCTTG -3'

LK260 5'- CAAGCCATTGCAATCGCAATC- 3'

LK260-RT 5'- AAGCAACGAAGTAGCAAGCCATTGCAATCGCAATC- 3'

M-RT 5'-AAGCAACGAAGTAG -3'

Figure 13: DNA Sequence Alignment of Coronavirus N Genes isolated from different Species

TGE	-----
PRCoV	-----
CcoV	-----
FCoV	-----
SARS-Urb	-----ATGTCTGATAATGGACCCCAATCAAACCAACGTAGT
SARS-Tor	-----ATGTCTGATAATGGACCCCAATCAAACCAACGTAGT
BcoV	ATGTCTTTTACTCCTGG-TAAGCAAT--CCAGTAGTAGAGCGTCCTTTGGAAATCGTTCT
HEV	ATGTCTTTTACTCCTGG-CAAGCAGT--CCAGCAGTAGAGCGTCCTCTGGAAATCGTTCT
MHV	ATGTCTTTTGTTCCTGGGCAAGAAAATGCCGGTAGCAGAAGCTCCTCTGGAAACCGCGCT
RtCoV	ATGTCTTTTGTTCCTGGGCAAGAAAACGCCGGTAGCAGAAGCTCCTCTGGAAACCGCGCT
HCoVOC43	-----
PEDV	-----
IBV	-----

TGE	-----ATGGCCAA-CCAGGGACAA-----
PRCoV	-----ATGGCCAA-CCAGGGACAA-----
CcoV	-----ATGGCCCTC-TCAGGGACAA-----
FCoV	-----ATGGCCAC-ACAGGGACAA-----
SARS-Urb	GCCCCCGCATTACATTTGGTGGACCCACAGATTCAACTGA--CAATAAC-----
SARS-Tor	GCCCCCGCATTACATTTGGTGGACCCACAGATTCAACTGA--CAATAAC-----
BcoV	GGTAATGGCAT--CCTTAAGTGGGCGGATCAGTCCGACCAATCTAGAAATGT-----
HEV	GGTAATGGCAT--CCTTAAGTGGGCGGATCAGTCCGACCAATCTAGAAATGT-----
MHV	GGTAATGGCAT--CCTCAAGAAGACCACTTGGGCTGACCAAAACCGAGCG-----
RtCoV	GGTAATGGAAT--CCTCAAGAAGACCACTTGGGCTGACCAAAACCGAGCGCGGACAAAATA
HCoVOC43	-----
PEDV	-----
IBV	-----ATGGCAAGCGGTAAAGCAGC-----

TGE	-CGTGTCAAGTTGGGGAGATGAATCTACCAAAACACGTGGTCTG-TCCAATTC---CCGTG
PRCoV	-CGTGTCAAGTTGGGGAGATGAATCCACCAAAATACGTGGTCTG-TCCAATTC---CCGTG
CcoV	-CGTGTCAAGTTGGGGAGATGAATCCACCAAGAGACGCGGTCTG-TCTAATTC---TCGTG
FCoV	-CGCGTCAACTGGGGAGATGAACCTTCCAAAAGACGTGGTCTG-TCTAATTC---TCGTG
SARS-Urb	-CAGAATGGAGGACGCAATGGGGCAAGGCCAAAACAGCGCCGA-CCCCAAGG---TTTA
SARS-Tor	-CAGAATGGAGGACGCAATGGGGCAAGGCCAAAACAGCGCCGA-CCCCAAGG---TTTA
BcoV	-TCAAACAGGGGTAGAAGAGCTCAACCCAAGCAAAGTCTGCTAC-TTCTCAGCTACCATCA
HEV	-TCAAACAGGGGTAGAAGAGCTCAATCCAAGCAAAGTCTGCTAC-TTCTCAGCAACCATCA
MHV	-TGGAAATAGAGGCAGAAGGAATCAGCCCAAGCAGACTGCAAC-TACTCAGC--CCAATG
RtCoV	ATGGAAATAGAGGCAGAAGGAATCAGCCCAAGCAGACTGCAAC-TACTCAGC--CCAATA
HCoVOC43	-----ATGGCTACAGTCAAATGGGCTGATGCATCTGAACCACAACGTG
PEDV	-----ATGGCTTCTGTCTCAGCTTTTCAGG
IBV	-TGGAAAAACAGACGCCCCAGCGCCAGTCATTAACTAGGAGGACCAAAACCACTAAAG

TGE	GTCGGAAGAATAATAACATACC-TCTTTTATTCTTCAACCCCATACCCCTCCAACAAGGT
PRCoV	GTCGGAAGATTAATAACATACC-TCTTTTATTCTTCAACCCCATACCCCTCCAACAAGGT
CcoV	GCCGGAAGAATAATGATATACC-TCTTTTATTCTTCAACCCCATACCCCTCGAGCAAGGA
FCoV	GTCGGAAGAATAATGATATACC-TTTGTCTATTCTACAACCCCATACCCCTCGAACAAGGA
SARS-Urb	CCCAATAATACTGCG-----TCTTGGTTTCAAGCTCTCACTCAGCATGGCAAGG--
SARS-Tor	CCCAATAATACTGCG-----TCTTGGTTTCAAGCTCTCACTCAGCATGGCAAGG--
BcoV	GGAGGGAATGTTGTACCTACTATTCTTGGTTCTCTGGAATTACTCAGTTTCAAAAAGGA
HEV	GGAGGGAATGTTGTACCTACTATTCTTGGTTCTCTGGAATTACTCAGTTTCAAAAAGGA
MHV	CC-GGGAGTGTGGTTCCCCATTACTCTTGGTTTTCGGGCATCACCAGTTTCAAAAAGGA
RtCoV	CC-GGGAGTGTGGTTCCCCATTACTCTTGGTTTTCGGGCATCACCAGTTTCAAAAAGGA
HCoVOC43	GTCTGTCAGGGTAGAA--TACC-TTATTCTCTTATAGCCCTTTGCTTGTGATAGTG--

PEDV ATCGTGGCCGCAACGGGTGCCATTA-TCTCTCTATGCCCCCTCTTAGGGTTACTAATGAC
IBV TCGGTTCTTCTGGAAATGCA- - - TCTTGGTTTCAAGCAATAAAGCCAAGAAGTTAAAT

TGE TCAAAATTTTGGAACTTATGTCCGAGAGACTTGTACCCAAAGGAATAGGTAACAGGGAT
PRCoV GCAAAATTTTGGAACTCATGTCCGAGAGATTTGTACCCAAAGGAATAGGTAATAGGGAT
CcoV TCAAAGTTTGGGACTTATGTCCGAGAGACTTGTACCCAAAGGAATAGGTAATAAGGAT
FCoV TCTAAATTTTGGAAATTTATGTCCGAGAGACCTTGTTCCTCCAAAGGAATAGGTAATAAGGAT
SARS-Urb -AGGAACTTAGATTCCCTCGAGGCCAGGGCGTTCCAATCAACACCAATAGTGGTCCAGAT
SARS-Tor -AGGAACTTAGATTCCCTCGAGGCCAGGGCGTTCCAATCAACACCAATAGTGGTCCAGAT
BcoV AAGGAGTTTGAATTTGCAGAGGGACAGGTGTGCCTATTGCACCAGGAGTCCCATCTACT
HEV AAGGAGTTTGAATTTGCAGAGGGACAGGTGTGCCTATTGCACCAGGAGTCCCATCTACT
MHV AAGGAGTTCCAGTTTGCACAAGGACAGGGAGTGCCTATTGCCAGTGGAAATCCCGCTTCA
RtCoV AAAGAGTTCCAGTTTGCAGGTGGACAGGAGTGCCTATTGCCAATGGAATCCACCTTCT
HCoVOC43 -AACAACTTGGAAAGGTGATACCTCGTAATTTGGTACCCATCAACAAGAAAGCAAAAAT
PEDV AAGCCCCCTTTCTAAGGTACTTGCACAACCGCTGTACCCACTAACAAAGGGGAATAAGGAC
IBV ACACCTCCGCCCAAGTTTGAAGGTAGCGGTGTTCTTGATAACGAAAACATTAAGCCAAGC

TGE CAACAGATTGGTTATTGGAATAGACAAACTCG- - - - - CTATCGCATGGTGAAGGGCCAA
PRCoV CAACAGATTGGTTATTGGAATAGACAAACTCG- - - - - CTATCGCATGGTGAAGGGCCAA
CcoV CAACAAATTGGTTATTGGAACAGGCCAAACCG- - - - - TTATCGCATGGTGAAGGGTCGA
FCoV CAACAAATTGGTTATTGGAATAGACAGATTCTG- - - - - TTATCGTATTGTAAAAGGCCAG
SARS-Urb GACCAAATTGGCTACTACCGAAGAGCTACCCGACGAGTTCGTGGT- - - GGTGACGGCAAA
SARS-Tor GACCAAATTGGCTACTACCGAAGAGCTACCCGACGAGTTCGTGGT- - - GGTGACGGCAAA
BcoV GAAGCTAAGGGGTACTGGTACAGACACAACAGACGTTCTTTTAAACAGCCGATGGCAAC
HEV GAAGCTAAGGGGTACTGGTACAGACACAACAGACGTTCTTTTAAACAGCCGACGGCAAT
MHV GAGCAAAAGGGATATTGGTATAGACACAACCGACGTTCTTTTAAACACCTGATGGCCAG
RtCoV GAGCAAAAGGGATATTGGTATAGACACAACCGTCTTTTAAACACCTGATGGCCAG
HCoVOC43 AAGCTTATAGGCTATTGGAATGTTCAAAAACG- - - - - TTTGAGAACTAGAAAGGGCAAA
PEDV CAGCAAATTGGGTACTGGAATGAGCAAATTCG- - - - - CTGGCGCATGCGCGGTGGTGAG
IBV CAGCAACATGGTACTGGAGACGCCAAGCCAG- - - - - GTTTAAGCCAGGCAAGGTGGA

TGE CGTAAAGAGCTTCTGAAAGGTGGTTCTTCTACTACTTAGGTACTGGACCTCATGCAGAT
PRCoV CGTAAAGAGCTTCTGAAAGGTGGTTCTTTTACTACTTAGGCACTGGACCTCATGCAGAT
CcoV CGTAAAAATCTTCTGAAAGGTGGTTCTTCTACTATTAGGAACCTGGACCTCATGCTGAT
FCoV CGTAAGGAACCTCGCTGAGAGGTGGTTCTTTTACTTCTTAGGTACAGGACCTCATGCTGAT
SARS-Urb ATGAAAGAGCTCAGCCCCAGATGGTACTTCTATTACCTAGGAACCTGGCCAGAAGCTTCA
SARS-Tor ATGAAAGAGCTCAGCCCCAGATGGTACTTCTATTACCTAGGAACCTGGCCAGAAGCTTCA
BcoV CAGCGTCAACTGCTGCCACGATGGTATTTTACTATCTTGAACAGGACCGCATGCCAAA
HEV CAGCGTCAACTGCTGCCACGATGGTACTTTTACTACCTGGGAACAGGACCGCATGCCAAA
MHV CACAAGCAGCTACTGCCCAGATGGTATTTTACTATCTTGAACAGGGCCCCATGCTGGC
RtCoV CAGAAGCAACTACTCCCCAGATGGTATTTTACTATCTTGGGACGGGCCCCATGCTGGA
HCoVOC43 CGGGTGGATTTGTCAACCAAGCTGCATTTTATTATCTTGGCACAGGACCCGATAAAGAT
PEDV CGAATTGAACAACTTCCAATTGGCATTCTTACTACCTCGGAACAGGACCTCACGGCGAC
IBV AGAAAACAGTCCAGATGCTTGGTACTTTTACTATACTGGAACAGGACCTGCCGCTGAC

TGE GCCAAATTTAAAGATAAATTAGATGGAGTTGTCTGGGTTGCCAAGGATGGTGCCATGAAC
PRCoV GCCAAATTTAAAGATAAATTAGATGGAGTTGTCTGGGTTGCCAAGGATGGTGCCATGAAC
CcoV GCCAAATTTAAAGCAAAAATTAGATGGAGTTGTCTGGGTTGCTAGGGGAGATTCCATGACT
FCoV GCTAAATTTAAAGACAAGATTGATGGAGTCTTCTGGGTTGCAAGGGATGGTGCCATGAAC
SARS-Urb CTTCCCTACGGCGCTAACAAAGAAGGCATCGTATGGGTTGCAACTGAGGGAGCCTTGAAT
SARS-Tor CTTCCCTACGGCGCTAACAAAGAAGGCATCGTATGGGTTGCAACTGAGGGAGCCTTGAAT
BcoV GACCAGTATGGCACCAGATTTGACGGAGTCTTCTGGGTCGCTAGTAACAGGCTGATGTC
HEV GACCAGTACGGCACCAGATTTGACGGAGTCTTCTGGGTCGCTAGTAACAGGCTGATATT
MHV GCAGAGTATGGCAGCATATCGAAGGAGTTGTCTGGGTCGCAAGCCAACAGGCCGACACT
RtCoV GCCAGTTTTCGAGACAGCATTGAGGGAGTCTTCTGGGTTGCAAAATAGTCAGGCCGATACC
HCoVOC43 GCAAAATTTAGAGAGCGTGTGAAGGTGTCTGCTGGGTTGCTGTTGATGGTGCTAAAACT
PEDV CTCCGTTATAGGACTCGTACTGAGGGTGTCTTCTGGGTTGCTAAAGAAGGCCAAAGACT
IBV CTGAACCTGGGGTGATACTCAAGATGGTATAGTGTGGGTTGCTGCTAAGGGTGTGATACT

TGE AAACCAACCACGC---TTGGTAGTCGTGGTGCTAATA---ATGAATCCAAAGCTTTGAAA
PRCoV AAACCAACCACGC---TTGGTAGTCGTGGTGCTAATA---ATGAATCCAAAGCTTTGAAA
CcoV AAGCCAACAATC---TTGGTACTCGTGGCACTAATA---ATGAATCAAAGGCTTTGAAA
FCoV AAGCCCAACACGC---TTGGCACTCGTGGGAACCAATA---ACGAATCCAAACCACTGAGA
SARS-Urb ACACCCAAAGACCACATTGGCACC CGCAATCCTAATAACAATGCTGCCACCGTGCTACAA
SARS-Tor ACACCCAAAGACCACATTGGCACC CGCAATCCTAATAACAATGCTGCCACCGTGCTACAA
BcoV AATACCCCGGCTGACATTCTCGATCGGGACCCAAGTAGCGATGAGGCTATTCCGACTAGG
HEV AATACCCCGGCTGACATTGTCTGATCGGGATCCAAGTAGCGATGAGGCTATTCCGACTAGG
MHV AAGACCACTGCCGATGTTGTTGAAAGGGACCCAAGCAGTCATGAGGCTATTCTACTAGG
RtCoV AACACCTCTGCTGACATTGTTGAAAGGGACCCAAGTAGCCAATGAGGCTATTCTACTAGG
HCoVOC43 GAACCTACAGGTTA---CGGTGTTAGGCGCAAGAATT---CAGAACAGAGATACCACA
PEDV GAACCCACTAATT---TGGGTGTCAGAAAGGCGTCTG---AAAAGCCAATCATTCCAAA
IBV AAATCTAGATCCAATCAGGGTACAAGAGATCTGATAA-GTTTGACCAATACCCACTACG

TTCG---ATGGTAAAGTGCCAGGCGAA---TTTCAACTTGAAGTTAATCAATCAAGAGAC
PRCoV TTCG---ATGGTAAAGTGCCAGGCGAA---TTTCAACTTGAAGTTAACCAGTCTAGGGAC
CcoV TTCG---ATGTCAAAGTACCATCAGAA---TTTCACCTTGAAGTGAACCAATTAAGGGAC
FCoV TTTG---ATGGTAAGATACCGCCACAG---TTTCAGCTTGAAGTGAACCGTTCTAGGAAC
SARS-Urb CTTCTCAAGGAACAACATTGCCAAAGGCTTCTACGCAGAGGGAAGCAGAGGCGGCAGT
SARS-Tor CTTCTCAAGGAACAACATTGCCAAAGGCTTCTACGCAGAGGGAAGCAGAGGCGGCAGT
BcoV TTTCCGCTTGGCAGGCTACTCCCTCAGGGTACTATATTGAAGG---CTCAGGAAGGTCT
HEV TTTCCGCTTGGCAGGCTACTCCCTCAGGGTACTATATTGAAGG---CTCAGGAAGGTCT
MHV TTTGCGCCCGGCACGGTATTGCCTCAGGGCTTTTATGTAGAAGG---CTCGGGAAGGTCT
RtCoV TTTGCGCCCGGTACGGTATTGCCTCAGGGTCTTCTATGTTGAAGG---CTCGGGAAGGTCT
HCoVOC43 CTTCTCAAGGAACAACATTGCCAAAGGCTTCTACGCAGAGGGAAGCAGAGGCGGCAGT
PEDV ATTC---TCTCAACAGCTCCCAAGTGTGTA---GTTGAGATTGTTGAACCTAACACCTCTCT
IBV ATTC---TCGGATGGCGGACCTGATGTAATTTCCGTTGGGACTTCATTCCTCTGAACC

TGE AATTCAAGGTCACGCTCTCAATCTAGATCTC-----GGTCTAGAAATAGATCTCAATCT
PRCoV AACTCAAGGTCACGCTCTCAATCTAGATCTC-----GGTCTAGAAACAGATCTCAATCT
CcoV AATTCAAGGTCAGGTCCTCAATCTAGATCTC-----AGTCCAGAAATAGGTCCTCAATCT
FCoV AATTCAAGGTCAGGTCCTCAATCTAGATCTC-----TTTCAAGAAACAGATCTCAATCT
SARS-Urb CAAGCCTCTTCTCGCTCTCTCATCAGTAGTCGCGTAATTCAAGAAATCAACTCCTGGC
SARS-Tor CAAGCCTCTTCTCGCTCTCTCATCAGTAGTCGCGTAATTCAAGAAATCAACTCCTGGC
BcoV GCTCCTAATTCAGATCTACTTCGCGTGCAACCAATAGAGCCCTAGTGCAGGATCGCGT
HEV GCTCCTAATTCAGATCTACTTCGCGTGCAACCAATAGAGCCCTAGTGCAGGATCGCGT
MHV GCACCTGCTAGTCGATCTGGTTCGCGGTAC-----AATCCCGTGGGCCAAATAATCGC
RtCoV GCACCTGCTAGTCGATCTGGTTCGCGGTAC-----AATCCCGTGGGCCAAATAATCGC
HCoVOC43 CCTTCCCGGTCTCAGTCGAGGTCGAGAGTCGCGGTCTGGTGAATCCAAACCTCAATCT
PEDV GCTTCAGGTGCAAAATTCGCGTAGCAGGAGTCGTGGCAATGGCAACAATAGGTCTAGATCT
IBV GTGGTAGGAGTGGAAGATCAACAGCAGCTTCATCA-GCAGCAGCTAGTAGAGCACCATCA

TGE AGAGGCAGGCAACAATTCAATAACAAGAAGGAT-----GACAGTGTAGAACAAGCTGT
PRCoV AGAGGTAGGCAACAATCCAATAACAAGAAGGAT-----GACAGTGTAGAACAAGCTGT
CcoV AGAGGAAGGCAACTATCCAATAATAAGAAGGAT-----GACAATGTTGAACAAGCTGT
FCoV AGAGGAAGACACCAATCCAATAAACCAGAA---T-----AATAATGTTGAGGATACAAT
SARS-Urb AGCAGTAGGGGAAATTCTCTGCTCGAATGGCT-----AGCGGAGGTGGTGAAACTGC
SARS-Tor AGCAGTAGGGGAAATTCTCTGCTCGAATGGCT-----AGCGGAGGTGGTGAAACTGC
BcoV AG---TAGAGCCAATTCTGGCAACAGAACCCCT-----ACCTCTGGTGAACACCTGA
HEV AG---TAGAGCCAATTCTGGCAATAGAACCTCT-----ACCCCTGGTGAACACCTGA
MHV GC---TAGAAGCAGTTCCAACCAGCGCCAGCCT-----GCCTCTGCTGTAACACCTGA
RtCoV GC---TAGAAGCAGTTCCAACCAGCGCCAGCCT-----GCCTCTACTGTAAACCTGA
HCoVOC43 CGGAATCTCTCAAGTGACAGAAACATAACAGTCAG---GATGACATCATGAAGGCAGT
PEDV CCAAGTAACAACAGAGGCAATAACCAAGTCCCGTGGTAATTCACAGAATCGTGGAATAAC
IBV CG-----TGAAGGTTCCGCTGGTCTGAGAAGT-----GATTCTGGAGATGACCTTAT

TGE T---CTTGCCGCACTT-----AAAAGTTAGGTGTTGACACAGAAAAACAACAGCA-ACG

PRCoV	T---CTTGCCGCACTT-----AAAAAGTTAGGTGTTTACACAGAAAAACAACAGCA-ACG
CcoV	T---CTTGCTGCATC-----AAAAAGTTAGGTGTTGACACAGAAAAACAA---CA-AAG
FCoV	T---GTAGCCGTGCTT-----GAAAAATTAGGTGTT---ACTGACAAACAA-----AG
SARS-Urb	C---CTCGC-G--CTA-----TTGCTGCTAGAC-AGATTGAACCAGCTTGAGAGCA-AAG
SARS-Tor	C---CTCGC-G--CTA-----TTGCTGCTAGAC-AGATTGAACCAGCTTGAGAGCA-AAG
BcoV	T---ATGGCTG--ATC-----AAATTGCTAGTC-TTGTCTGGCAAACTTG-GCA-AGG
HEV	C---ATGGCTG--ATC-----AAATTGCTAGTC-TTGTCTGGCAAACTTG-GCA-AGG
MHV	C---ATGGCCG--AAG-----AAATTGCTGCTC-TTGTCTGGCTAAGCTTG-GTA-AAG
RtCoV	T---ATGGCCG--AAG-----AAATTGCTGCTC-TTGTCTGGCTAATCTAG-GCA-AAG
HCoVOC43	T---GCTGCGGCTCTT-----AAATCTTTAGGTTTTGACAAGCCTCAGGAAAAAGATAAA
PEDV	CAGGGTCGTGGAGCTTCTCAGAACAGAGGAGCAATAATAATAACAATAACAAGTCTCGT
IBV	TGCTCGTGCAGCAAAG-----ATAATCCAGGATCAGCAGAAAAAGGGCTCTCGCA--TT

TGE	CTCTCGTTCTAAATCTAAAG--AACGTAGTAACTCTAAGAC-AAGA-----GATACT
PRCoV	CTCTCGTTCTAAATCTAAAG--AACGTAGTAACTCTAAAC-AAGA-----GATACT
CcoV	ATCTCGTTCCAAATCTAAGG--AACGTAGCAGCTCTAAGAC-AAGA-----GATACT
FCoV	GTCACGTTCTAAACCTAGAG--AACGTAGTGATTCCAAACC-TAGG-----GACACA
SARS-Urb	TTTCTGGTAAAGGCCAACAA-CAACAAGGCCAACTGTCACTAAGA-----AATCTG
SARS-Tor	TTTCTGGTAAAGGCCAACAA-CAACAAGGCCAACTGTCACTAAGA-----AATCTG
BcoV	ATGCCACTAAGCCACAGCAAGTAACTAAGC-AGACTGCCA--AAGA-----AATCAG
HEV	ATGCCACTAAGCCCTCAGCAAGTAACTAAGC-AGACTGCCA--AAGA-----GGTCAG
MHV	ATGCCGGCCAGCCCAAGCAGGTAACCTAAGC-AAAGCGCCA--AAGA-----AGTCAG
RtCoV	ATGCCGGACAGCCTAAGCAAGTAACTAAGC-AAAGTGCCA--AAGA-----AGTCAG
HCoVOC43	AAGTCAGCGAAAACGGGTAC--TCCTAAGCCTTCTCGTAATCAGAGT----CCTGCTTCT
PEDV	AACCAGTCCAATAACAGGAACCAAGTCAAAATGACCGTGGTGGTGAACATCACGCGATGAT
IBV	ACCAAGGCAAAGGCAGATGA--AATGGCTCATCGCCGGTATTGCAAG----CGCACTATC

TGE	ACACCTAAGAATGAAAACAAACACACCTGGA---AGAGAACTGCAGGTAAA---GGTG--
PRCoV	ACGCCTAAGAATGAAAACAAACACACCTGGA---AGAGAACTGCAGGTAAA---GGTG--
CcoV	ACACCTAAGAATGAAAACAAACACACCTGGA---AGAGAACTGCAGGTAAA---GGTG--
FCoV	ACACCTAAGAATGCCAACAAACACACCTGGA---AGAAACTGCAGGCAAG---GGAG--
SARS-Urb	CTGCTGAGGCATCTAAA-AAGCCTCGCCAAA---AACGTACTGCCACAAAAC--AGTACA
SARS-Tor	CTGCTGAGGCATCTAAA-AAGCCTCGCCAAA---AACGTACTGCCACAAAAC--AGTACA
BcoV	--ACAGAAAATTTTGAATAAGCCCCGCCAGA---AGAGGAGCCCCAATAAAC--AATGCA
HEV	--ACAGAAAATCTTGAATAAGCCCCGCCAGA---AGAGGAGCCCCAATAAAC--AATGCA
MHV	--GCAGAAAATTTTAACTAAGCCTCGTCAAA---AGAGGACTCCAAACAAGC--AGTGCC
RtCoV	--GCAGAAAATTTTAAATAAGCCTCGCCAAA---AGAGGACTCCAAACAAGC--AGTGCC
HCoVOC43	TCTCAAATCTCTGCCAAGAGTCTTGCTCGTTCTCAGAGTTCTGAAACAAAAG--AACAAA
PEDV	CTGGTGGCTGCTGTCAAGGATGCACTTAAATCTTTGGGTATTGGAGAAAATCCTGACAGG
IBV	CCACCTAATTATAGGGTTGATCAAGTGTTTGGTCCCCGTACTAAAGGTAAGG--AGGGGA

TGE	---ATGTGACA---AGATTTTATGGAGCTAGAAGCAGTT--CAGCC-----AAT-TTT
PRCoV	---ATGTGACA---AGATTTTATGGAGCTAGAAGCAGTT--CAGCC-----AAT-TTT
CcoV	---ATGTGACA---AAATTTTATGGAGCTAGAAGTAGTT--CAGCC-----AAT-TTT
FCoV	---ATGTGACA---ACTTTCTATGGTGCTAGAAGTAGTT--CAGCT-----AAC-TTT
SARS-Urb	A-CGTCACTCA---AGCATTTGGGAGACGTGGTCCAGAA-CAAAACCAAGGAAAT-TTC
SARS-Tor	A-CGTCACTCA---AGCATTTGGGAGACGTGGTCCAGAA-CAAAACCAAGGAAAT-TTC
BcoV	C-TGTTCAAGCA---GTGTTTTGGGAAGAGAGGCCCAAT--CAGA-----AT-TTT
HEV	C-TGTTCAAGCA---GTGTTTTGGGAAGAGAGGCCCAAT--CAGA-----AT-TTT
MHV	C-AGTGCAGCA---GTGTTTTGGGAAGAGAGGCCCAAT--CAGA-----AC-TTT
RtCoV	C-AGTGCAGCA---GTGTTTTGGGAAGAGAGGCCCAAT--CAGA-----AT-TTT
HCoVOC43	AGCATGAAATGC---AAAAGCCACGGTGGAAAAGACAGCC--TAATGATGATGTGACATCT
PEDV	CATAAGCAACAGCAGAAAGCCTAAGCAGGAAAAGTCTGACAAACAGCGGCAAAAATACACCT
IBV	A--TTTTGGTG-----ATGACAAGATGAATGAGGAAGGTATTAAGGATG---GGCGTGT

TGE GGTGACACTGACCTCGTTGCCAAT----GGGAGCAGTGCCAAGCATTACCCACAACCTGGC
 PRCoV GGTGACAGTGACCTCGTTGCCAAT----GGGAGCAGTGCCAAGCATTACCCACAATTGGC
 CCoV GGTGACAGCGATCTTGTGGCCAAT----GGGAACGGTGCCAAGCATTACCCACAACCTGGC
 FCoV GGTGATAGTGATCTCGTTGCCAAT----GGTAACGCTGCCAAATGCTACCCCTCAGATAGC
 SARS-Urb GGGGACCAAGACCTAATCAGACAA---GGAAGTATTACAAACATTGGCCGCAAATTGC
 SARS-Tor GGGGACCAAGACCTAATCAGACAA---GGAAGTATTACAAACATTGGCCGCAAATTGC
 BCoV GGTGGTGGAGAAATGTTAAACCTT---GGAAGTATTGACCCACAGTTCCCATTCCTTGC
 HEV GGTGGTGGAGAAATGTTAAACCTT---GGAAGTATTGACCCACAGTTCCCATTCCTTGC
 MHV GGAGGCTCTGAAATGTTAAACCTT---GGAAGTATTGATCCGCAGTTCCCATTCCTTGC
 RtCoV GGAGGCCCTGAAATGTTAAACCTT---GGAAGTATTGATCCACAGTTCCCATTCCTTGC
 HCoVOC43 AATGTCACACAATGTTTGGCCCC---AGAGACCTTGAC---CACAACTTTGGAAGTGC
 PEDV AAGAAGAACAATCCAGGGCCACTTCGAAGGAACGTGACCTCAAAGACATCCAGAGTGG
 IBV TACAGCAATGCTCAACCTAGTCCCT---AGCAGCCATGCT-----TGCTTTTTTGAAGT

TGE TGAATGTGTT-CCATCTGTGTC--TAGCATT---CT--GTTTGGAA-GCTATTGGACTT
 PRCoV TGAATGTGTT-CCATCTGTGTC--TAGCATT---TT--GTTTGGAA-GCTATTGGACTT
 CCoV TGAATGTGTT-CCATCTGTATC--TAGCATT---CT--GTTTGGAA-GCCATTGGACTG
 FCoV TGAATGTGTT-CCATCAGTGTC--TAGCATA---AT--CTTTGGCA-GTCAATGGTCTG
 SARS-Urb ACAATTTGCT-CCAAGTGCCTC--TGCA-----TT--CTTTGGAATGTCAC--GCATT
 SARS-Tor ACAATTTGCT-CCAAGTGCCTC--TGCA-----TT--CTTTGGAATGTCAC--GCATT
 BCoV AGAAGTGCCT-CCACAGCTGG--TGCGTTT---TT--CTTTGGATCAAGATTAGAGTT
 HEV AGAAGTGCCT-CCACAGCTGG--TGCGTTT---TT--CTTTGGATCAAGATTAGAGTT
 MHV AGAGTTGGCT-CCAACACCTAG--TGCCTTC---TT--CTTTGGATCTAAATTAGAATT
 RtCoV AGAGTTGGCT-CCAACACCTAG--TGCCTTC---TT--CTTTGGATCTAAATTAGAATT
 HCoVOC43 AGGTGTTGTGGCCAATGGTGT--AAAGCTAAAGGCT--ATCCACAATTTGCTGAGCTTG
 PEDV AGGAGAATTC-CCAAGGGCGAAATAGCGTAGCAGCTTGCTTCGACCCAGAGGGGGCTT
 IBV AGAGTGACACCCAACTTCAAC--TAGATGG--GCTTCACTTGAGATTTGAATTTACTAC

TGE CAAAGGAA--GATGGCG---ACCAGATAGAAGTCAC---GTTACACACAAATACC--
 PRCoV CAAAGGAA--GATGGCG---ACCAGATAGAAGTCAC---GTTACACACAAATACC--
 CCoV CTAAGGAA--GATGGTG---ACCAGATTGAAGTCAC---ATTACACACAAATACC--
 FCoV CTGAAGAA--GCTGGTG---ATCAAGTGAAAGTCAC---GCTCACTCACACCTACT--
 SARS-Urb GGCA-----TGGAAGTCAC---ACCTTCGGGAACATG---
 SARS-Tor GGCA-----TGGAAGTCAC---ACCTTCGGGAACATG---
 BCoV GGCCAAAG--TGCAGAA---TTTGTCTGGGAATCTTGACGAGCCCCAGAAGGATGTTTA
 HEV GGCCAAAG--TGCAGAA---TTTGTCTGGGAATCTTGACGAGCCCCAGAAGGATGTTTA
 MHV GGTCAAAA-----AGAA---CT--CTGGTGGTGCTGATGAACCCACCAAGATGTTTA
 RtCoV GGTCAAAA-----AGAA---TT--CTGGTGGCGTTGATGAACCCACCAAGATGTTTA
 HCoVOC43 TGCCGTCA--ACAGCTGCTATGCTGTTTGTAGTAC--ATTGTTTCCAAGAGTCAGGCA
 PEDV CAAAACTTTGGAGATGCGGAATTTGTCGAAAAAGGTGTTGATGCGTCAGGCTATGCTCA
 IBV TGTGGTCCCATGTGATGACCCGAGTTTGATAATTATGTGAAAATTTGTGATCAGTGT--

TGE --ACT-TGCCAAAGGATGA--TCCTA--AGACTGGACAATTCCTTCAGCAGATTAATGCC
 PRCoV --ACT-TGCCAAAGGATGA--TCCTA--AACTGAACAATTCCTTCAGCAGATTAATGCC
 CCoV --ACT-TGCCAAAGGATGA--TCCTA--AGACTGGACAATTCCTTCAGCAGATTAATGCC
 FCoV --ACC-TGCCAAAGGATGA--TGCCA--AACTAGTCAATTCCTAGAACAGATTGACGCT
 SARS-Urb ---GC-TGACTTATCATGG--AGCCATTAAATTGGATGACAAAGATCCACAATTCAAAGA
 SARS-Tor ---GC-TGACTTATCATGG--AGCCATTAAATTGGATGACAAAGATCCACAATTCAAAGA
 BCoV TGAAT-TGCGCTATAATGG--TGCAATTAGATTTGACAGTACACTTTTCAGGTTTTGAGAC
 HEV TGAAT-TGCGCTATAATGG--CGCGATTAGATTTGACAGCAGTCTCAGGTTTTGAAAC
 MHV TGAAT-TGCAGTATTCAGG--TGCAATTAGATTTGATAGTACTCTACCCGGTTTTGAGAC
 RtCoV TGAGC-TGCAATATTCAGG--TGCAAGTCAATTTGATAGTACTCTACCTGGTTTTGAGAC
 HCoVOC43 AACTGTGGTCTTGACTTT--CACTACTAGAGT-GACTGTGCCCAAAGACCATCCACACT
 PEDV GATCGCCAGTTTAGCACCAATGTTGAGCATTGCTCTTTGGTGGTAAATGTGGCTGTTTCG
 IBV -GTCGATGGTGTAGGAACGCGTCCAA---AAGATGACGA-ACCAAACCAAAGTCACGCT

TGE TATGCTCG--TCCATCAGAAGTGGCAAAAGAA--CAGAGA-AAAAGA-----AAATCTCG
 PRCoV TATGCTAG--CCATCAGAATTGGCAAAAGAA--CAGAGA-AAAAGA-----AAGTCTCG
 CCoV TACGCCCG--TCCATCAGAGGTGGCTAAAGAA--CAGAGA-CAACGC-----AAAGCTCG

FCoV	TACAAGCG--ACCTTCTGAAGTGGCTAAGGAT--CAGAGG-CAAAGA-----AGATCCCG
SARS-Urb	CAACGTCA--TACTGCTGAACAAGCACATTGA--CGCATA-CAAAAC-----ATTCCCAC
SARS-Tor	CAACGTCA--TACTGCTGAACAAGCACATTGA--CGCATA-CAAAAC-----ATTCCCAC
BcoV	CATAATGA--AGGTGTTGAATGAGAATTTGAA--TGCATATCAACAA-----CA---AGA
HEV	CATTATGA--AGGTGCTTAACCAGAATTTGAA--TGCCTATCAACAT-----CAGGAAGA
MHV	TATCATGA--AAGTGTGACTGAGAATTTGAA--TGCCTACCAGGAC-----CAAGCTGG
RtCoV	TATCATGA--AAGTGTGACTGAGAATTTGAA--TGCCTACCAGAAT-----CAAGCTGG
HCoVOC43	TG-GGTAA--GTTTCTTGAGGAGTTAAATGCATTCACTAGAGAAATG-----CAACAACA
PEDV	TGAGCTAGCGGACTCTTACGAGATTACATACAACTATAAAATGACTGTGCCAAAGTCAGA
IBV	CAAGTTCAAGACCTGCTACAAGAGGAAATTCT--CCAGCGCCAAGACAACAGCGCCCAAA

TGE	TTCTAAATCTGCAGAAAGGTCAGAGCAAGATGTGGTACCTGATGCATTAATAGAA-AATT
PRCoV	TTCTAAATCTGCAGAAAGGTCAGAGCAAGAGGTGGTACCTGATTCAATTAATAGAA-AACT
CcoV	TTCTAAATCTGTAGAAAGGGTAGCAAGAGGTGTACCTGATGCATTAACAGAA-AATT
FCoV	TTCTAAGTCTGCTGATAAG--AAGCCTGAGGAGTTGTCTGTAACCTCTGTGGAG-GCAT
SARS-Urb	CAACAGAGCCTAAAAAGGACAAAAAGAAAAAGACTGATGAAGCTCAGCCTTTGCC-GCAG
SARS-Tor	CAACAGAGCCTAAAAAGGACAAAAAGAAAAAGACTGATGAAGCTCAGCCTTTGCC-GCAG
BcoV	TGGTATGATGAATATGAGTCCAAAACCAAGCGTCAGCGTGGTCAGAAG-----AATG
HEV	TGGGATGATGAATATTAGTCTCTAAACCAAGCGGACGCGTGGTCAGAAG-----AATG
MHV	TAGTGTAGATCTAGTGAGCCCAAGCCTCCAAGAAGAGGTCGTAGACAGGCTCAA-GAAA
RtCoV	TGGTGCAGATGTAGTGAGCCCAAGCCTCCAAGAAGAGGTCGTAGACAGGCTCAA-GAAA
HCoVOC43	TCCTCTTCTTAACCTTAGTGACTAGAAATTCAACCCATCTCAAACCTCACCTGCA-ACTG
PEDV	TCCAAATGTTGAGCTTCTTGTTCACAGGTGGATGCATTTAAACTGGGAATGCAAACT
IBV	GAAGGAGAAAAAGCTAAAGAAGCAGGATGATGAAGCAGATAAAGCATTGACCTCAGATGA

TGE	ATACAGATGTGTTTGAT-GACACACAGGT-TGAGATAATTGATGAGGTA-ACGAACTAA-
PRCoV	ATACAGATGTGTTTGAT-GACACACAGGT-TGAGATGATTGACGAGGTA-ACGAACTAA-
CcoV	ACACAGATGTGTTTGAT-GACACACAGGT-TGAGATTATTGATGAGGTA-ACGAACTAA-
FCoV	ACACAGATGTGTTTGAT-GACACACAGGT-TGAGATGATTGATGAGGTT-ACGAACTAA-
SARS-Urb	AGACAAAAGAAGCAGCCCACTGTGACTCT-TCTT---CCTGCGGCTGAC-ATG-GATGAT
SARS-Tor	AGACAAAAGAAGCAGCCCACTGTGACTCT-TCTT---CCTGCGGCTGAC-ATG-GATGAT
BcoV	GACAAGGAGAAAATGAT-AATATAAGTGT-TGCAGCGCCTAAAAGCCGT-GTGCAGCAAA
HEV	GACAAGTGAAGTAGAT-AATGTAAGTGT-TGCAGCGCCTAAAAGCCGT-GTGCAGCAAA
MHV	AGAAAGATGAAGTAGAT-AATGTAAGCGT-TGCAAAGCCCAAAAGCTTG-GTGCAGCGAA
RtCoV	AGAAAGAGAATTAGAT-AGTATAAGCGT-TGCAAAGCCCAAAAGTGCC-GTGCAGCGAA
HCoVOC43	CTGAACCAGTGCGTGAT-GAAGTTTCTAT-TGAAA---CTGACATAATTG-ATGAAGTAA
PEDV	CCAGAGAAAGAAGGAAAAGAACAAGCGTGAAACCAAGCTGCAGCAGCATGAAGAGGC
IBV	GGAGAGGAACAATGCACAGCTGGAATTTTATGATGAGCCCAAGGTAATTAAGTGGGGGA

TGE	-----
PRCoV	-----
CcoV	-----
FCoV	-----
SARS-Urb	TTCTCCAGACAACTTCAAAATCCATGAGTGGAGCTTCTGCTGATTCAACTCAGGCATAA
SARS-Tor	TTCTCCAGACAACTTCAAAATCCATGAGTGGAGCTTCTGCTGATTCAACTCAGGCATAA
BcoV	ATAAGAGTAGAGAGTTGACTGCAGAGGACATCAGC--CTTCTTAAGAAGAT---GGATGA
HEV	ATAAGAGTAGAGAGTTGACAGCAGAGGACATCAGC--CTTCTTAAGAAGAT---GGATGA
MHV	ATGTAAGTAGAGAATTAAACCCCGAGGATCGTAGC--CTGCTGGCTCAGATCCTAGACGA
RtCoV	ATGTAAGCAGAGAATTAAACCCCGAGGATAGAAGC--CTGTTGGCGCAGATCCTAGATGA
HCoVOC43	CTAA-----
PEDV	CATCTACGATGATGTGGGTGCGCCATCTGATGTGACCCATGCCAATCTGGAATGGGACAC
IBV	TGCAGCTCTAGGAGAGAATGAACCTTTGA-----

TGE	-----
PRCoV	-----
CcoV	-----
FCoV	-----
SARS-Urb	-----

SARS-Tor	-----
BcoV	--GCCCTATACTGAA-----GACACCTCAGAAATATAA-----
HEV	--GCCCTATACTGAA-----GATACCTCAGAAATATAA-----
MHV	TGGCGTTGTGCCAGATGGGTTGGAAGATGACTCTAATGTGTAA-----
RtCoV	TGGCGTTGTGCCTGATGGGTT---AGATGACTCTAATGTGTAA-----
HCoVOC43	-----
PEDV	AGCTGTTGATGGTGGTGATACGGCCGTTGAAATTATCAACGAGATCTTCGATACAGGAAA
IBV	-----

TGE	----
PRCoV	----
CcoV	----
FCoV	----
SARS-Urb	----
SARS-Tor	----
BcoV	----
HEV	----
MHV	----
RtCoV	----
HCoVOC43	----
PEDV	TTAA
IBV	----

Figure 14: Phylogenetic Analysis of *N* Gene

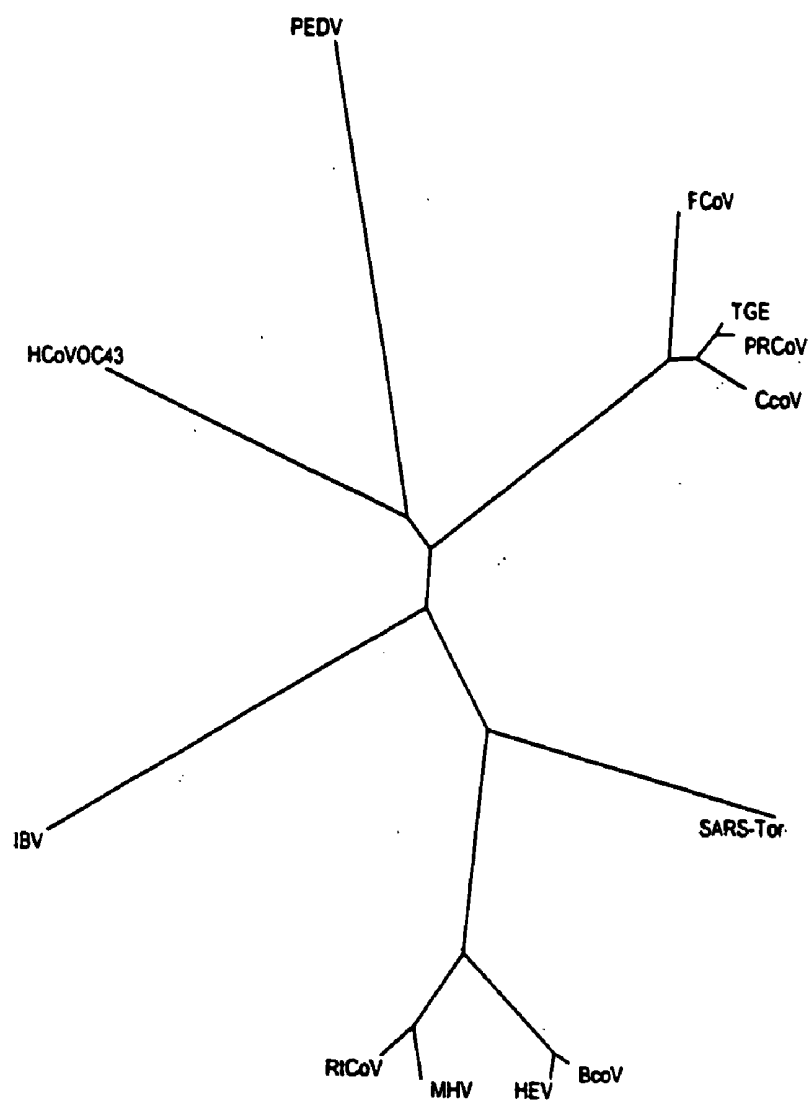
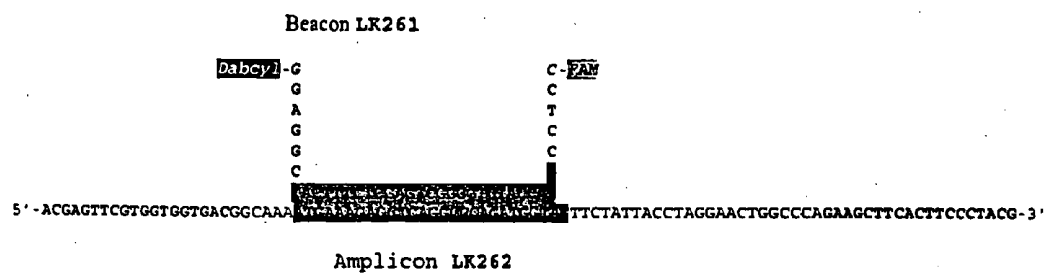


Figure 15: Molecular Designs for SARS-Associated N Gene

NOTE: LK261 is a TET-molecular beacon, which recognizes the *N* gene of coronavirus (SARS Tor2 and SARS urbani human pathogenic strains). It will be used in a real-time PCR diagnostic for the identification of SARS-associated coronavirus RNA/DNA.



LK261

M. Target recognition sequence:	26 nucleotides (11 G/C) + (1 G/C arm)
N. Length of the arms:	6 nucleotides (5 G/C)
O. Melting temperature of the beacon:	dG = -1.64 dH = -48.7 dS = -145.8 Tm = 61.0 °C
P. Melting temperature of target:	°C (including 1 nucleotide from the arms)

LK263 5'-ACGAGTTCGTGGTGGTGAC-3'

Length: 19 nucleotides (11 G/C)

Tm: °C

Position: (see alignment below)

LK264 5'-CGTAGGGAAGTGAAGCTTC-3'

Length: 19 nucleotides (10 G/C)

Tm: °C

Position: (see alignment below)

N-RT 5'-GCCITCTTTGTTAG-3'

Length: 14 nucleotides (6 G/C)

Tm: 47 °C

Position: (see alignment below)

LK262 Amplicon (95 nucleotides)

5'-

ACGAGTTCGTGGTGGTGACGGCAAATGAAAGAGCTCAGCCCCAGATGGTAC
TTCTATTACCTAGGAACTGGCCCCAGAAGCTTCACTTCCCTACG-3'

**DNA sequence alignment of complete
N genes from corona virus strains**

TGE	-----
PRCoV	-----
CcCoV	-----
FCoV	-----
SARS-Urb	-----ATGTCTGATAATGGACCCCAATCAAACCAACGTAGT
SARS-Tor	-----ATGTCTGATAATGGACCCCAATCAAACCAACGTAGT
BcCoV	ATGTCTTTTACTCCTGG-TAAGCAAT--CCAGTAGTAGAGCGTCCTTTGGAAATCGTTCT
HEV	ATGTCTTTCACTCCTGG-CAAGCAGT--CCAGCAGTAGAGCGTCCTCTGGAAATCGTTCT
MbV	ATGTCTTTTGTTCCTGGGCAAGAAAATGCCGCTAGCAGAAGCTCCTCTGGAAACCGCGCT
RtCoV	ATGTCTTTTGTTCCTGGGCAAGAAAATGCCGCTAGCAGAAGCTCCTCTGGAAACCGCGCT
HCoVOC43	-----
PEDV	-----

IBV

TGE
PRCoV
CcoV
FCoV
SARS-Urb
SARS-Tor
BcoV
HEV
MHV
RtCoV
HCoVOC43
PEDV
IBV
-----ATGGCCAA-CCAGGGACAA-----
-----ATGGCCAA-CCAGGGACAA-----
-----ATGGCCTC-TCAGGGACAA-----
-----ATGGCCAC-ACAGGGACAA-----
GCCCCCGCATTACATTGGTGGACCCACAGATTCAACTGA--CAATAAC-----
GCCCCCGCATTACATTGGTGGACCCACAGATTCAACTGA--CAATAAC-----
GGTAATGGCAT--CCTTAAGTGGGCGGATCAGTCCGACCAATCTAGAAATGT-----
GGTAATGGCAT--CCTTAAGTGGGCGGATCAGTCCGACCAATCTAGAAATGT-----
GGTAATGGCAT--CCTCAAGAAGACCACTTGGGCTGACCAAACCGAGCG-----
GGTAATGGAAT--CCTCAAGAAGACCACTTGGGCTGACCAAACCGAGCGCGGACAAAATA-----

-----ATGGCAAGCGGTAAAGCAGC-----

TGE
PRCoV
CcoV
FCoV
SARS-Urb
SARS-Tor
BcoV
HEV
MHV
RtCoV
HCoVOC43
PEDV
IBV
-CGTGTCAAGTTGGGGAGATGAATCTACCAAAACACGTGGTTCGT-TCCAATTC---CCGTG
-CGTGTCAAGTTGGGGAGATGAATCCACCAAAATACGTGGTTCGT-TCCAATTC---CCGTG
-CGTGTCAAGTTGGGGAGATGAATCCACCAAGAGACGCGGTTCGT-TCTAATTC---TCGTG
-CGCGTCAACTGGGGAGATGAACCTTCCAAAGAGCGTGGTTCGT-TCTAATTC---TCGTG
-CAGAAATGGAGGACGCAATGGGGCAAGGCCAAAACAGCGCCGA-CCCCAAGG---TTTA
-CAGAAATGGAGGACGCAATGGGGCAAGGCCAAAACAGCGCCGA-CCCCAAGG---TTTA
-TCAAACCAAGGGGTAGAAGAGCTCAACCCAAGCAAACCTGCTAC-TTCTCAGCTACCATCA
-TCAAACCAAGGGGTAGAAGAGCTCAATCCAAGCAAACCTGCTAC-TTCTCAGCAACCATCA
-TGGAAATAGAGGCAGAAGGAACCATCCCAAGCAGACTGCAAC-TACTCAGC--CCAATG
ATGGAAATAGAGGCAGAAGGAATCAGCCCAAGCAGACTGCAAC-TACTCAGC--CCAATA
-----ATGGCTACAGTCAATGGGCTGATGCATCTGAACCACAACGTG
-----ATGGCTTCTGTCAAGTTTCAGG
-TGGAAAAACAGACGCCCCAGCGCCAGTCATTAAACTAGGAGGACCAAAACCACTAAAG

TGE
PRCoV
CcoV
FCoV
SARS-Urb
SARS-Tor
BcoV
HEV
MHV
RtCoV
HCoVOC43
PEDV
IBV
GTCCGAAGAATAATAACATACC-TCTTTCATTCTTCAACCCCATACCCCTCCAACAAGGT
GTCCGAAGAATAATAACATACC-TCTTTCATTCTTCAACCCCATACCCCTCCAGCAAGGT
GTCCGAAGAATAATGATATACC-TCTTTCATTCTTCAACCCCATACCCCTCGAGCAAGGA
GTCCGAAGAATAATGATATACC-TTGTCTATTCTACAACCCCATACCCCTCGAACAAGGA
CCCAATAATACTGCG-----TCTTGGTTCAAGCTCTCACTCAGCATGGCAAGG--
CCCAATAATACTGCG-----TCTTGGTTCAAGCTCTCACTCAGCATGGCAAGG--
GGAGGGAATGTTGTACCCTACTATTCTTGGTTCTCTGGAATTACTCAGTTTCAAAAAGGA
GGAGGGAATGTTGTACCCTACTATTCTTGGTTCTCTGGAATTACTCAGTTTCAAAAAGGA
CC-GGGAGTGTGGTTCCCACTACTCTTGGTTTTCGGGCATACCCAGTTTCAAAAAGGA
CC-GGGAGTGTGGTTCCCACTACTCTTGGTTTTCGGGCATACCCAGTTTCAAAAAGGA
GTCTGTCAGGGTAGAA---TACC-TTATCTCTTTATAGCCCTTTGCTTGTGATAGTG--
ATCGTGGCCGCAACGGGTGCCATTA-TCTCTCTATGCCCTCTTAGGGTTACTAATGAC
TCGGTTCTTCTGGAATGCA---TCTTGGTTTCAAGCAATAAAGCCAAGAAGTTAAAT

TGE
PRCoV
CcoV
FCoV
SARS-Urb
SARS-Tor
BcoV
HEV
MHV
RtCoV
HCoVOC43
PEDV
IBV
TCAAAATTTTGGAACTTATGTCCGAGAGACTTTGTACCCAAAGGAATAGGTAACAGGGAT
GCAAAATTTTGGAACTCATGTCCGAGAGATTTGTACCCAAAGGAATAGGTAATAGGGAT
TCAAAGTTTGGGACTTATGTCCGAGAGACTTTGTACCCAAAGGAATAGGTAATAAGGAT
TCTAAATTTTGGAAATTTATGTCCGAGAGACTTTGTACCCAAAGGAATAGGTAATAAGGAT
-AGGAACTTAGATTCCCTCGAGGCCAGGGCGTTCCAATCAACACCAATAGTGGTCCAGAT
-AGGAACTTAGATTCCCTCGAGGCCAGGGCGTTCCAATCAACACCAATAGTGGTCCAGAT
AAGGAGTTTGAATTTGCAGAGGGACAAGGTGTGCCTATTGCACCAGGAGTCCCAGCTACT
AAGGAGTTTGAATTTGCAGAGGGACAAGGTGTGCCTATTGCACCAGGAGTCCCAGCTACT
AAGGAGTTTCCAGTTTGCACAAGGACAGGGAGTGCCTATTGCCAGTGGAAATCCCGCTTCA
AAAGAGTTTCCAGTTTGCAGGTGGACAAGGAGTGCCTATTGCCAATGGAATCCACCTTCT
-AACAACTTGAAGGTGATACCTCGTAATTTGGTACCCATCAACAAGAAAGACAAAAT
AAGCCCTTTCTAAGGTACTTTGCAACAACGCTGTACCCACTAACAAGGGGAATAAGGAC
ACACCTCCGCCCAAGTTTGAAGGTAGCGGTGTTCTGATAACGAAAACATTAAGCCAAGC

TGE	CAACAGATTGGTTATTGGAATAGACAAACTCG-----CTATCGCATGGTGAAGGGCCAA
PRCoV	CAACAGATTGGTTATTGGAATAGACAAACTCG-----CTATCGCATGGTGAAGGGCCAA
CcCoV	CAACAAATTGGTTATTGGAACAGGCAAAACCG-----TTATCGCATGGTGAAGGGTCGA
FCoV	CAACAAATTGGTTATTGGAATAGACAGATTCTG-----TTATCGTATTGTAAAAGGCCAG
SARS-Urb	GACCAAATTGGCTACTACCGAAGAGCTACCCGACGAGTTCGTGGT---GGTGACGGCAAA
SARS-Tor	GACCAAATTGGCTACTACCGAAGAGCTACCCGACGAGTTCGTGGT---GGTGACGGCAAA
BcoV	GAAGCTAAGGGGTACTGGTACAGACACAACAGACGTTCTTTTAAAACAGCCGATGGCAAC
HEV	GAAGCTAAGGGGTACTGGTACAGACACAACAGACGTTCTTTTAAAACAGCCGACGGCAAT
MHV	GAGCAAAAGGGATATTGGTATAGACACAACCGACGTTCTTTTAAAACACCTGATGGCCAG
RtCoV	GAGCAAAAGGGATATTGGTATAGACACAACCGTCGTCTTTTAAAACACCTGATGGCCAG
HCoVOC43	AAGCTTATAGGCTATTGGAATGTTCAAAAACG-----TTTCAGAACTAGAAAGGGCAAA
PEDV	CAGCAAATTGGGTACTGGAATGAGCAAATTCG-----CTGGCGCATGCGCCGTGGTGAG
IBV	CAGCAACATGGTACTGGAGACGCCAAGCCAG-----GTTTAAGCCAGGCAAAGGTGGA

LK263 5'-ACGAGTTCGTGGT---GGTGAC-3'

TGE	CGT	TCCTGAA	TTCTTCTACTACTTAGGTACTGGACCTCATGCAGAT
PRCoV	CGT	TCCTGAA	TTCTTTTACTACTTAGGCACTGGACCTCATGCAGAT
CcCoV	CGT	TCCTGAA	TTCTTCTACTATTTAGGAACTGGACCTCATGCTGAT
FCoV	CGT	GCTGAG	TTCTTTTACTTCTTAGGTACAGGACCTCATGCTGAT
SARS-Urb	CTTCTATTACCTAGGA	CTGCTTCTATTACCTAGGA	CTGCTTCTATTACCTAGGA
SARS-Tor	CTTCTATTACCTAGGA	CTGCTTCTATTACCTAGGA	CTGCTTCTATTACCTAGGA
BcoV	CA	CGTCA	TTTTTACTATCTTGGAACAGGACCGCATGCCAAA
HEV	CA	CGTCA	TTTTTACTACCTGGGAACAGGACCGCATGCCAAA
MHV	CAC	GC	TTTTTACTATCTTGGAACAGGGCCCCATGCTGGC
RtCoV	CAC	GC	TTTTTACTATCTTGGGACGGGCCCCCATGCTGGA
HCoVOC43	CG	GTG	TTTTTATTATCTTGGCACAGGACCCATAAAGAT
PEDV	CGA	TT	TTTCTACTACCTCGGAACAGGACCTCACGGCGAC
IBV	GAG	CCAG	CTTTTACTATACTGGAACAGGACCTGCCGCTGAC

LK261 BEACON

LK264 3'-CTTCGAAGT

TGE	GCCAAATTTAAAGATAAATTAGATGGAGTTGTCTGGGTTGCCAAGGATGGTGCCATGAAC
PRCoV	GCCAAATTTAAAGATAAATTAGATGGAGTTGTCTGGGTTGCCAAGGATGGTGCCATGAAC
CcCoV	GCCAAATTTAAAGCAAAATTAGATGGAGTTGTCTGGGTTGCTAGGGGAGATTCCATGACT
FCoV	GCTAAATTCAAAGACAAGATTGATGGAGTCTTCTGGGTTGCAAGGGATGGTGCCATGAAC
SARS-Urb	CTTCCCTACGGCGCTAACAAAGAAGGCATCGTATGGGTTGCAACTGAGGGAGCCTTGAAT
SARS-Tor	CTTCCCTACGGCGCTAACAAAGAAGGCATCGTATGGGTTGCAACTGAGGGAGCCTTGAAT
BcoV	GACCAGTATGGCACCAGATATTGACGGAGTCTTCTGGGTCGCTAGTAACCAAGGCTGATGTC
HEV	GACCAGTACGGCACCAGATATTGACGGAGTCTTCTGGGTCGCTAGTAACCAAGGCTGATATT
MHV	GCAGAGTATGGCGACGATATCGAAGGAGTTGTCTGGGTCGCAAGCCAACAGGCCGACACT
RtCoV	GCCAGTTTCGGAGACAGCATTGAGGGAGTCTTCTGGGTTGCAAAATAGTCAGGCCGATACC
HCoVOC43	GCAAAATTTAGAGAGCGTGTGAAAGGTGTCTGCTGGGTTGCTGTTGATGGTGCTAAAAC
PEDV	CTCCGTTATAGGACTCGTACTGAGGGTGTCTTCTGGGTTGCTAAAGAAGGCGCAAGACT
IBV	CTGAAGTGGGGTGATACTCAAGATGATAGTGTGGGTTGCTGCTAAGGGTGCTGATACT

GAAGGGATGC-5'

3'-GATTGTTTCTTCCG-5' N-RT

TGE	AAACCAACCACGC---TTGGTAGTCGTGGTGCTAATA---ATGAATCCAAAGCTTTGAAA
PRCoV	AAACCAACCACGC---TTGGTAGTCGTGGTGCTAATA---ATGAATCCAAAGCTTTGAAA
CcCoV	AAGCCAACAACCTC---TTGGTACTCGTGGCACTAATA---ATGAATCAAAGGCTTTGAAA
FCoV	AAGCCCACAACGC---TTGGCACTCGTGGAAACCAATA---ACGAATCCAAACCACTGAGA
SARS-Urb	ACACCCAAAGACCACATTGGCACCCGCAATCCTAATAACAATGCTGCCACCGTGCTACAA
SARS-Tor	ACACCCAAAGACCACATTGGCACCCGCAATCCTAATAACAATGCTGCCACCGTGCTACAA
BcoV	AATACCCCGGCTGACATTCTCGATCGGGACCCAAGTAGCGATGAGGCTATTCCGACTAGG
HEV	AATACCCCGGCTGACATTCTCGATCGGGATCCAAGTAGCGATGAGGCTATTCCGACTAGG
MHV	AAGACCACTGCCGATGTTGTTGAAAGGGACCCAAGTAGCATGAGGCTATTCTACTAGG
RtCoV	AACACCTCTGCTGACATTGTTGAAAGGGACCCAAGTAGCATGAGGCTATTCTACTAGG
HCoVOC43	GAACCTACAGGTTA---CGGTGTTAGGCGCAAGAATT---CAGAACCAGAGATACCACA
PEDV	GAACCCACTAATT---TGGGTGTGAGAAAGGCGTCTG---AAAAGCCAATCATTCACAA

IBV AAATCTAGATCCAATCAGGGTACAAGAGATCCTGATAA-GTTTGACCAATACCCACTACG
* * *

TGE TTCG---ATGGTAAAGTGCCAGGCGAA---TTTCAACTTGAAGTTAATCAATCAAGAGAC
PRCoV TTCG---ATGGTAAAGTGCCAGGCGAA---TTTCAACTTGAAGTTAACCAGTCTAGGGAC
CcoV TTCG---ATGTCAAAGTACCATCAGAA---TTTCACTTGAAGTGAACCAATTAAGGGAC
FCoV TTTG---ATGGTAAGATACCGCCACAG---TTTCAGCTTGAAGTGAACCGTTCTAGGAAC
SARS-Urb CTTCCTCAAGGAACAACATTGCCAAAAGGCTTCTACGCAGAGGGAAGCAGAGGCGGCAGT
SARS-Tor CTTCCTCAAGGAACAACATTGCCAAAAGGCTTCTACGCAGAGGGAAGCAGAGGCGGCAGT
BcoV TTTCCGCTGGCAGCGTACTCCCTCAGGGTACTATATTGAAGG---CTCAGGAAGGTCT
HEV TTTCCGCTGGCAGCGTACTCCCTCAGGGTACTATATTGAAGG---CTCAGGAAGGTCT
MHV TTTGCGCCCGGCACGGTATTGCTCAGGGCTTTTATGTAGAAGG---CTCGGAAGGTCT
RtCoV TTTGCGCCCGGTACGGTATTGCTCAGGGTTTCTATGTTGAAGG---CTCGGAAGGTCT
HCoV43 CTTC--AATCAAAAGCTCCCAAATGGTGTTACTGTTGTTGAAGAACCTGACTCCCGTGCT
PEDV ATTC--TCTCAACAGCTCCCAAGTGTA---GTTGAGATTGTTGAACCTAACACACCTCCT
IBV ATTC---TCGGATGGCGACCTGATGGTAATTTCCGTTGGGACTTCATTCCCTGAACC
*

TGE AATTCAAGGTCACGCTCTCAATCTAGATCTC-----GGTCTAGAAATAGATCTCAATCT
PRCoV AACTCAAGGTCACGCTCTCAATCTAGATCTC-----GGTCTAGAAACAGATCTCAATCT
CcoV AATTCAAGGTCAGGTCTCAATCTAGATCTC-----AGTCCAGAAATAGGTCTCAATCT
FCoV AATTCAAGGTCGTGTTCTCAGTCTAGATCTG-----TTTCAAGAAACAGATCTCAATCT
SARS-Urb CAAGCCTCTTCTCGCTCCTCATCAGTAGTCGCGGTAATTCAAGAAATTCAACTCTCTGGC
SARS-Tor CAAGCCTCTTCTCGCTCCTCATCAGTAGTCGCGGTAATTCAAGAAATTCAACTCTCTGGC
BcoV GCTCCTAATTCAGATCTACTTCACGCGCATCCAGTAGAGCCTCTAGTGCAGGATCGCGT
HEV GCTCCTAATTCAGATCTACTTCGCGTCACCCCAATAGAGCCCTAGTGCAGGATCGCGT
MHV GCACCTGCTAGTCGATCTGGTTTCGCGGTCAC-----AATCCCGTGGGCCAAATAATCGC
RtCoV GCACCTGCTAGTCGATCTGGTTTCGCGGTCAC-----AATCCCGTGGGCCAAATAATCGC
HCoV43 CCTTCCCGTCTCAGTCGAGGTCGAGAGTCGCGGTCGTGGTGAATCAAACCTCAATCT
PEDV GCTTCACGTGCAAATTTCGCTAGCAGGAGTCGTGGCAATGGCAACAATAGGTCTAGATCT
IBV GTGGTAGGAGTGGAAGATCAACAGCAGCTTCATCA-GCAGCAGCTAGTAGAGCACCATCA

TGE AGAGGCAGGCAACAATTCAATAACAAGAAGGAT-----GACAGTGTAGAACAAGCTGT
PRCoV AGAGGTAGGCAACAATCCAATAACAAGAAGGAT-----GACAGTGTAGAACAAGCTGT
CcoV AGAGGAAGGCAACTATCCAATAATAAGAAGGAT-----GACAATGTTGAACAAGCTGT
FCoV AGAGGAAGACACCATTCCAATAACCAGAA---T-----AATAATGTTGAGGATACAAT
SARS-Urb AGCAGTAGGGGAAATTCTCCTGCTCGAATGGCT-----AGCGGAGGTGGTGAAACTGC
SARS-Tor AGCAGTAGGGGAAATTCTCCTGCTCGAATGGCT-----AGCGGAGGTGGTGAAACTGC
BcoV AG---TAGAGCCAATTCTGGCAACAGAACCCCT-----ACCTCTGGTGTAAACACTGA
HEV AG---TAGAGCCAATTCTGGCAATAGAACCTCT-----ACCCCTGGTGTAAACACTGA
MHV GC---TAGAAGCAGTTCCAACCAGCGCCAGCCT-----GCCTCTGCTGTAAAACCTGA
RtCoV GC---TAGAAGCAGTTCCAACCAGCGCCAGCCT-----GCCTCTACTGTAAAACCTGA
HCoV43 CGGAATCCTTCAAGTGACAGAAACCATAACAGTCAG---GATGACATCATGAAGGCAGT
PEDV CCAAGTAACAACAGAGGCAATAACAGTCCCGTGGTAATTCACAGAATCGTGGAATAAC
IBV CG-----TGAAGGTTTCGCTGGTTCGTAGAAGT-----GATTCTGGAGATGACCTTAT
*

TGE T---CTTGCCGCACTT-----AAAAAGTTAGGTGTTGACACAGAAAAACAACAGCA-ACG
PRCoV T---CTTGCCGCACTT-----AAAAAGTTAGGTGTTTACACAGAAAAACAACAGCA-ACG
CcoV T---CTTGCTGCACTC-----AAAAAGTTAGGTGTTGACACAGAAAAACAA---CA-AAG
FCoV T---GTAGCCGTGCTT-----GAAAAATTAGGTGTT---ACTGACAAACAA-----AG
SARS-Urb C---CTCGC-G-CTA-----TTGCTGCTAGAC-AGATTGAACCAGCTTGAGAGCA-AAG
SARS-Tor C---CTCGC-G-CTA-----TTGCTGCTAGAC-AGATTGAACCAGCTTGAGAGCA-AAG
BcoV T---ATGGCTG--ATC-----AAATTGCTAGTC-TTGTTCTGGCAAAACTTG-GCA-AGG
HEV C---ATGGCTG--ATC-----AAATTGCTAGTC-TTGTTCTGGCAAAACTTG-GCA-AGG
MHV C---ATGGCCG--AAG-----AAATTGCTGCTC-TTGTTTTGGCTAAGCTTG-GTA-AAG
RtCoV T---ATGGCCG--AAG-----AAATTGCTGCTC-TTGTTTTGGCTAATCTAG-GCA-AAG
HCoV43 T---GCTGCGCTCTT-----AAATCTTAGGTTTGAACAAGCCTCAGGAAAAAGATAAA
PEDV CAGGGTCGTGGAGCTTCTCAGAACAGAGGAGGCAATAATAATAACAATAACAAGTCTCGT
IBV TGCTCGTGAGCAAAG-----ATAATCCAGGATCAGCAGAAAAAGGGCTCTCGCA--TT
* *

TGE	CTCTCGTTCTAAATCTAAAG--AACGTAGTAACTCTAAGAC-AAGA-----GATACT
PRCoV	CTCTCGTTCTAAATCTAAAG--AACGTAGTAACTCTAAAC-AAGA-----GATACT
CcCoV	ATCTCGTTCCAAATCTAAGG--AACGTAGCAGCTCTAAGAC-AAGA-----GATACT
FCoV	GTCACGTTCTAAACCTAGAG--AACGTAGTGATTCCAAACC-TAGG-----GACACA
SARS-Urb	TTTCTGGTAAAGGCCAACAA-CAACAAGGCCAACTGTCACTAAGA-----AATCTG
SARS-Tor	TTTCTGGTAAAGGCCAACAA-CAACAAGGCCAACTGTCACTAAGA-----AATCTG
BcCoV	ATGCCACTAAGCCACAGCAAGTAAGTAAAGC-AGACTGCCA--AAGA-----AATCAG
HEV	ATGCCACTAAGCCCTCAGCAAGTAAAGTAAAGC-AGACTGCCA--AAGA-----GGTCAG
MHV	ATGCCGGCCAGCCCAAGCAGGTAAGTAAAGC-AAAGCGCCA--AAGA-----AGTCAG
RtCoV	ATGCCGGACAGCCTAAGCAAGTAAAGTAAAGC-AAAGTGCCA--AAGA-----AGTCAG
HCoVOC43	AAGTCAGCGAAAACGGGTAC--TCCTAAGCCTTCTCGTAATCAGAGT---CCTGCTTCT
PEDV	AACCAAGTCCAATAACAGGAACCAAGTCAAATGACCGTGGTGGTGAACATCAGCGGATGAT
IBV	ACCAAGGCCAAAGGCAGATGA--AATGGCTCATCGCCGGTATTGCAAG---CGCACTATC

TGE	ACACCTAAGAATGAAAAACAAACACACCTGGA---AGAGAACTGCAGGTAAA---GGTG--
PRCoV	ACGCCTAAGAATGAAAAACAAACACACCTGGA---AGAGAACTGCAGGTAAA---GGTG--
CcCoV	ACACCTAAGAATGAAAAACAAACACACCTGGA---AGAGAACTGCAGGTAAA---GGTG--
FCoV	ACACCTAAGAATGCCAACAAACACACCTGGA---AGAAAACCTGCAGGCAAG---GGAG--
SARS-Urb	CTGCTGAGGCATCTAAA-AAGCCTCGCCAAA---AACGTACTGCCACAAAAC--AGTACA
SARS-Tor	CTGCTGAGGCATCTAAA-AAGCCTCGCCAAA---AACGTACTGCCACAAAAC--AGTACA
BcCoV	--ACAGAAAATTTTGAATAAGCCCCGCCAGA---AGAGGAGCCCCCAATAAAC--AATGCA
HEV	--ACAGAAAATCTTGAATAAGCCCCGCCAGA---AGAGGAGCCCCCAACAAAC--AATGCA
MHV	--GCAGAAAATTTTAACTAAGCCTCGTCAAA---AGAGGACTCCAAACAAGC--AGTGCC
RtCoV	--GCAGAAAATTTTAAATAAGCCTCGCCAAA---AGAGGACTCCAAACAAGC--AGTGCC
HCoVOC43	TCTCAAACCTTCTGCCAAGAGTCTTGCTCGTTCTCAGAGTTCTGAAACAAAAG--AACAAA
PEDV	CTGGTGGCTGCTGTCAAGGATGCACCTAAATCTTTGGGTATTGGAGAAAATCCTGACAGG
IBV	CCACCTAATTATAGGGTTGATCAAGTGTGTTGGTCCCCGCTACTAAAGGTAAGG--AGGGGA

**

TGE	---ATGTGACA---AGATTTTATGGAGCTAGAAGCAGTT--CAGCC-----AAT-TTT
PRCoV	---ATGTGACA---AGATTTTATGGAGCTAGAAGCAGCT--CAGCC-----AAT-TTT
CcCoV	---ATGTGACA---AAATTTTATGGAGCTAGAAGTAGTT--CAGCC-----AAT-TTT
FCoV	---ATGTGACA---ACTTTCTATGGTGCTAGAAGTAGTT--CAGCT-----AAC-TTT
SARS-Urb	A-CGTCACCTCA---AGCATTGGGAGACGTGGTCCAGAA--CAAACCCAAGGAAAT-TTC
SARS-Tor	A-CGTCACCTCA---AGCATTGGGAGACGTGGTCCAGAA--CAAACCCAAGGAAAT-TTC
BcCoV	C-TGTTTCAGCA---GTGTTTTGGGAAGAGAGGCCCAAT--CAGA-----AT-TTT
HEV	C-TGTTTCAGCA---GTGTTTTGGGAAGAGAGGCCCAAT--CAGA-----AT-TTT
MHV	C-AGTGACAGCA---GTGTTTTGGGAAGAGAGGCCCAAT--CAGA-----AC-TTT
RtCoV	C-AGTGACAGCA---GTGTTTTGGGAAGAGAGGCCCAAT--CAGA-----AT-TTT
HCoVOC43	AGCATGAAATGC---AAAAGCCACGGTGGAAAAGACAGCC--TAATGATGATGTGACATCT
PEDV	CATAAGCAACAGCAGAAGCCTAAGCAGGAAAAGTCTGACAAACAGCGGCAAAAATACACCT
IBV	A--TTTTGGTG-----ATGACAAGATGAATGAGGAAGGTATTAAGGATG---GGCGTGT

*

TGE	GGTGACACTGACCTCGTTGCCAAT---GGGAGCAGTGCCAAGCATTACCCACAACCTGGC
PRCoV	GGTGACAGTGACCTCGTTGCCAAT---GGGAGCAGTGCCAAGCATTACCCACAATTGGC
CcCoV	GGTGACAGCGATCTTGTGCCAAT---GGGAACGGTGCCAAGCATTACCCACAACCTGGC
FCoV	GGTGATAGTGATCTCGTTGCCAAT---GGTAACGCTGCCAAATGCTACCCCTCAGATAGC
SARS-Urb	GGGGACCAAGACCTAATCAGACAA---GGAAGTGAATACAAACATTGGCCGCAAAATTGC
SARS-Tor	GGGGACCAAGACCTAATCAGACAA---GGAAGTGAATACAAACATTGGCCGCAAAATTGC
BcCoV	GGTGGTGGAGAAATGTTAAACTT---GGAAGTGAATGACCCACAGTTCCCCATTCTTGC
HEV	GGTGGTGGAGAAATGTTAAACTT---GGAAGTGAATGACCCACAGTTCCCCATTCTTGC
MHV	GGAGGCTCTGAAATGTTAAACTT---GGAAGTGAATGATCCGAGTTCCCCATTCTTGC
RtCoV	GGAGGCCCTGAAATGTTAAACTT---GGAAGTGAATGATCCACAGTTCCCCATTCTTGC
HCoVOC43	AATGTCACACAATGTTTGGCCCC---AGAGACCTTGAC---CACAACTTTGGAAGTGC
PEDV	AAGAAGAACAATCCAGGGCCACTTCGAAGGAACGTGACCTCAAAGACATCCCAGAGTGG
IBV	TACAGCAATGCTCAACCTAGTCCCT---AGCAGCCATGCT-----TGCTTTTTGGAAGT

*

*

TGE	TGAATGTGTT-CCATCTGTGTC--TAGCATT----CT--GTTTGGAA-GCTATTGGACTT
-----	--

PRCoV TGAATGTGTT-CCATCTGTGTC--TAGCATT----TT--GTTTGGAA-GCTATTGGACTT
CcoV TGAATGTGTT-CCATCTGTATC--TAGCATT----CT--GTTTGGAA-GCCATTGGACTG
FCoV TGAATGTGTT-CCATCAGTGC--TAGCATA----AT--CTTTGGCA-GTCAATGGTCTG
SARS-Urb ACAATTTGCT-CCAAGTGCCTC--TGCA-----TT--CTTTGGAATGTCAC--GCATT
SARS-Tor ACAATTTGCT-CCAAGTGCCTC--TGCA-----TT--CTTTGGAATGTCAC--GCATT
BcoV AGAACTCGCA-CCCACAGCTGG--TGCCTTT----TT--CTTTGGATCAAGATTAGAGTT
HEV AGAACTCGCA-CCCACAGCTGG--TGCCTTT----TT--CTTTGGATCAAGATTAGAGTT
MHV AGAGTTGGCT-CCAACACCTAG--TGCCTTC----TT--CTTTGGATCTAAATTAGAATT
RtCoV AGAGTTGGCT-CCAACACCTAG--TGCCTTC----TT--CTTTGGATCTAAATTAGAATT
HCoVOC43 AGGTGTTGTGGCCAATGGTGT--AAAGCTAAAGGCT--ATCCACAATTGTGCTGAGCTTG
PEDV AGGAGAAATC-CCAAGGGCGAAAATAGCGTAGCAGCTTGCTTCGGACCCAGAGGGGGCTT
IBV AGAGTGACACCCAACTTCAAC--TAGATGG--GCTTCACTTGAGATTGAATTACTAC

TGE CAAAGGAA--GATGGCG----ACCAGATAGAAGTCAC----GTTACACACAAATACC--
PRCoV CAAAGGAA--GATGGCG----ACCAGATAGAAGTCAC----GTTACACACAAATACC--
CcoV CTAAGGAA--GATGGTG----ACCAGATTGAAGTCAC----ATTACACACAAATACC--
FCoV CTGAAGAA--GCTGGTG----ATCAAGTGAAAGTCAC----GCTCACTCACACCTACT--
SARS-Urb GGCA-----TGGAAAGTCAC----ACCTTCGGGAACATG---
SARS-Tor GGCA-----TGGAAAGTCAC----ACCTTCGGGAACATG---
BcoV GGCCAAAG--TGCAGAA----TTTGTCTGGGAATCTTGACGAGCCCCAGAAGGATGTTTA
HEV GGCCAAAG--TGCAGAA----TTTGTCTGGGAATCTTGACGAGCCCCAGAAGGATGTTTA
MHV GGTCAAAA----AGAA----CT--CTGGTGGTGCTGATGAACCCACCAAGATGTTTA
RtCoV GGTCAAAA----AGAA----TT--CTGGTGGCGTTGATGAACCCACCAAGATGTTTA
HCoVOC43 TGCCGTCA--ACAGCTGCTATGCTGTTTGATAGTCAC-ATTGTTTCCAAAGAGTCAGGCA
PEDV CAAAAA--CTTTGGAGATGCGGAATTTGTGCAAAAAGGTGTTGATGCGTCAGGCTATGCTCA
IBV TGTGTTCCATGTGATGACCCGAGTTTGATAATTATGTGAAAATTTGTGATCAGTGT--

TGE --ACT-TGCCAAAGGATGA--TCCTA--AGACTGGACAATTCCTTCAGCAGATTAATGCC
PRCoV --ACT-TGCCAAAGGATGA--TCCTA--AAACTGAACAATTCCTTCAGCAGATTAATGCC
CcoV --ACT-TGCCAAAGGATGA--TCCTA--AGACTGGACAATTCCTTCAGCAGATTAATGCA
FCoV --ACC-TGCCAAAGGATGA--TGCCA--AAACTAGTCAATTCCTAGAACAGATTGACGCT
SARS-Urb ---GC-TGACTTATCATGG--AGCCATTAAATTGGATGACAAAGATCCCAATTCAAAGA
SARS-Tor ---GC-TGACTTATCATGG--AGCCATTAAATTGGATGACAAAGATCCCAATTCAAAGA
BcoV TGAAT-TGCGCTATAATGG--TGCAATTAGATTGACAGTACACTTTTCAGGTTTTGAGAC
HEV TGAAT-TGCGCTATAATGG--CGCGATTAGATTGACAGCAGTCTCAGGTTTTGAAAC
MHV TGAAT-TGCAGTATTGAG--TGCAATTAGATTGATAGTACTCTACCCGGTTTTGAGAC
RtCoV TGAGC-TGCAATATTGAG--TGCAATTAGATTGATAGTACTCTACCCGGTTTTGAGAC
HCoVOC43 ACAGTGTGGTCTTGACTTT--CACTACTAGAGT-GACTGTGCCCCAAGACCATCCCACT
PEDV GATCGCCAGTTTAGCACCAAATGTTGACGATTTGCTCTTTGGTGGTAATGTGGCTGTTG
IBV -GTCGATGGTGTAGGAACGCGTCCAA--AAGATGACGA-ACCAAACCAAGTCACGCT

TGE TATGCTCG--TCCATCAGAAGTGGCAAAAGAA--CAGAGA-AAAAGA-----AAATCTCG
PRCoV TATGCTAG--CCCATCAGAATTGGCAAAAGAA--CAGAGA-AAAAGA-----AAGTCTCG
CcoV TACGCCCC--TCCATCAGAGGTGGCTAAAGAA--CAGAGA-CAACGC-----AAAGCTCG
FCoV TACAAGCG--ACCTTCTGAAGTGGCTAAGGAT--CAGAGG-CAAAGA-----AGATCCCG
SARS-Urb CAACGTCA--TACTGCTGAACAAGCACATTGA--CGCATA-CAAAAC-----ATTCCCAC
SARS-Tor CAACGTCA--TACTGCTGAACAAGCACATTGA--CGCATA-CAAAAC-----ATTCCCAC
BcoV CATAATGA--AGGTGTTGAATGAGAATTGAA--TGCATATCAACAA-----CA--AGA
HEV CATTATGA--AGGTGCTTAACCAGAATTGAA--TGCCTATCAACAT-----CAGGAAGA
MHV TATCATGA--AAGTGTGACTGAGAATTGAA--TGCCTACCAGGAC-----CAAGCTGG
RtCoV TATCATGA--AAGTGTGACTGAGAATTGAA--TGCCTACCAGAAT-----CAAGCTGG
HCoVOC43 TG-GGTAA--GTTTCTTGAGGAGTTAAATGCATTCACTAGAGAAATG-----CAACAACA
PEDV TGAGCTAGCGGACTCTTACGAGATTACATACAATAAATGACTGTGCCAAAGTCAGA
IBV CAAGTTCAAGACCTGCTACAAGAGGAAATTCT--CCAGCGCCAAGACAACAGCGCCCAA

TGE TTCTAAATCTGCAGAAAGGTGAGCAAGATGTGGTACCTGATGCATTAAATAGAA-AATT
PRCoV TTCTAAATCTGCAGAAAGGTGAGCAAGAGGTGGTACCTGATTCATTAAATAGAA-AACT
CcoV TTCTAAATCTGTAGAAAGGTGAGCAAGAGGTGTACCTGATGCATTAAACAGAA-AATT

FCoV	TTCTAAGTCTGCTGATAAG---AAGCCTGAGGAGTTGTCTGTAACCTCTTGTGGAG-GCAT
SARS-Urb	CAACAGAGCCTAAAAAGGACAAAAAGAAAAAGACTGATGAAGCTCAGCCTTTGCC-GCAG
SARS-Tor	CAACAGAGCCTAAAAAGGACAAAAAGAAAAAGACTGATGAAGCTCAGCCTTTGCC-GCAG
BcoV	TGGTATGATGAATATGAGTCCAAAACACAGCGTCAGCGTGGTCAGAAG-----AATG
HEV	TGGGATGATGAATATTAGTCCTAAACCACAGCGGCAGCGTGGTCAGAAG-----AATG
MHV	TAGTGTAGATCTAGTGAGCCCAAAGCCTCCAAGAAGAGGTCGTAGACAGGCTCAA-GAAA
RtCoV	TGGTGCAGATGTAGTGAGCCCAAAGCCCCAAAGAAAGAGAGGGACGAAACAAACG-GCTC
HCoVOC43	TCCTCTTCTTAACCTAGTGCACTAGAAATTCAACCCATCTCAAACCTTCACTGCA-ACTG
PEDV	TCCAAATGTTGAGCTTCTTGTTCACAGGTGGATGCATTTAAAACTGGGAATGCAAACT
IBV	GAAGGAGAAAAAGCTAAAGAAGCAGGATGATGAAGCAGATAAAGCATTGACCTCAGATGA

TGE	ATACAGATGTGTTTGAT-GACACACAGGT-TGAGATAATTGATGAGGTA-ACGAACTAA-
PRCoV	ATACAGATGTGTTTGAT-GACACACAGGT-TGAGATGATTGACGAGGTA-ACGAACTAA-
CcoV	ACACAGATGTGTTTGAT-GACACACAGGT-TGAGATTATTGATGAGGTA-ACGAACTAA-
FCoV	ACACAGATGTGTTTGAT-GACACACAGGT-TGAGATGATTGATGAGGTT-ACGAACTAA-
SARS-Urb	AGACAAAAGAAGCAGCCCACTGTGACTCT-TCTT---CCTGCGGCTGAC-ATG-GATGAT
SARS-Tor	AGACAAAAGAAGCAGCCCACTGTGACTCT-TCTT---CCTGCGGCTGAC-ATG-GATGAT
BcoV	GACAAGGAGAAAATGAT-AATATAAGTGT-TGCAGCGCCTAAAAGCCGT-GTGCAGCAAA
HEV	GACAAGTAGAAAATGAT-AATGTAAGTGT-TGCAGCGCCTAAAAGCCGT-GTGCAGCAAA
MHV	AGAAAGATGAAGTAGAT-AATGTAAGCGT-TGCAAAGCCCCAAAGCTTG-GTGCAGCGAA
RtCoV	AGAAAGAAGAATTAGAT-AGTATAAGCGT-TGCAAAGCCCCAAAGTGCC-GTGCAGCGAA
HCoVOC43	CTGAACCAAGTGCCTGAT-GAAGTTTCTAT-TGAAA--CTGACATAATTG-ATGAAGTAAA
PEDV	CCAGAGAAAGAAGGAAAAGAAGCAAGCGTGAAACCACGCTGCAGCAGCATGAAGAGGC
IBV	GGAGAGGAACAATGCACAGCTGGAATTTTATGATGAGCCCAAGGTAATTAACCTGGGGGA

TGE	-----
PRCoV	-----
CcoV	-----
FCoV	-----
SARS-Urb	TTCTCCAGACAACCTTCAAATTCATGAGTGGAGCTTCTGCTGATTCAACTCAGGCATAA
SARS-Tor	TTCTCCAGACAACCTTCAAATTCATGAGTGGAGCTTCTGCTGATTCAACTCAGGCATAA
BcoV	ATAAGAGTAGAGAGTTGACTGCAGAGGACATCAGC--CTTCTTAAGAAGAT---GGATGA
HEV	ATAAGAGTAGAGAGTTGACAGCAGAGGACATCAGC--CTTCTTAAGAAGAT---GGATGA
MHV	ATGTAAGTAGAGAATTAACCCCGAGGATCGTAGC--CTGCTGGCTCAGATCCTAGACGA
RtCoV	ATGTAAGCAGAGAATTAACCCCGAGGATAGAAGC--CTGTTGGCGCAGATCCTAGATGA
HCoVOC43	CTAA-----
PEDV	CATCTACGATGATGTGGGTGCGCCATCTGATGTGACCCATGCCAATCTGGAATGGGACAC
IBV	TGCAGCTCTAGGAGAGAATGAACCTTGA-----

TGE	-----
PRCoV	-----
CcoV	-----
FCoV	-----
SARS-Urb	-----
SARS-Tor	-----
BcoV	--GCCCTATACTGAA-----GACACCTCAGAAATATAA-----
HEV	--GCCCTATACTGAA-----GATACCTCAGAAATATAA-----
MHV	TGGCGTTGTGCCAGATGGGTTGGAAGATGACTCTAATGTGTAA-----
RtCoV	TGGCGTTGTGCCTGATGGGTT--AGATGACTCTAATGTGTAA-----
HCoVOC43	-----
PEDV	AGCTGTTGATGGTGGTGATACGGCCGTTGAAATTATCAACGAGATCTTCGATACAGGAAA
IBV	-----

TGE	----
PRCoV	----
CcoV	----
FCoV	----
SARS-Urb	----
SARS-Tor	----

BcOV

- - - -

HEV

- - - -

MHV

- - - -

RtCoV

- - - -

HCoVOC43

- - - -

PEDV

TTAA

IBV

- - - -

,

Figure 16: List of Molecular Designs for N Gene

LK261 5'-FAM-CCTCCGTACCATCTGGGGCTGAGCTCTTTCATCGGAGG-3'-
Dubcyl

LK261.N 5'-FAM-GCCTCCGTACCATCTGGGGCTGAGCTCTTTCATCGGAGGC-3'-
Dubcyl

LK262

5'-ACGAGTTCGTGGTGGTGACGGCAAAATGAAAGAGCTCAGCCCCAGAT
GGTACTTCTATTACCTAGGAACTGGCCCAGAAGCTTCACTTCCCTACG-3'

LK263 5'- ACGAGTTCGTGGTGGTGAC -3'

LK263-T7 5'-TAATACGACTCACTATAGGACGAGTTCGTGGTGGTGAC -3'

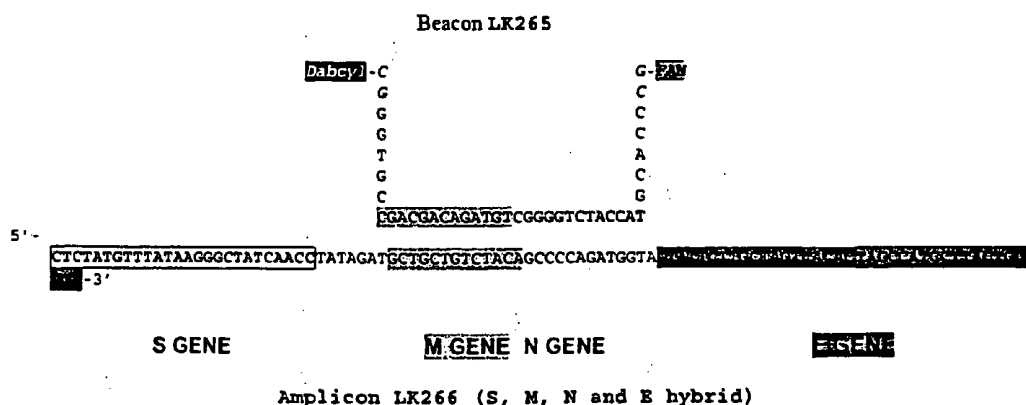
LK264 5'- CGTAGGGAAGTGAAGCTTC- 3'

LK264-RT 5'- GCCTTCTTTGTTAGCGTAGGGAAGTGAAGCTTC- 3'

N-RT 5' -GCCTTCTTTGTTAG-3'

Figure 17: Molecular Designs for Internal Positive Control (IPC)

NOTE: LK265 is a TET-molecular beacon, which recognizes an artificial target (scrambled amplicon from S, E M and N genes of coronavirus (SARS-associated coronavirus Tor2 and SARS strains). It will be used as an internal positive control (IPC) in a real-time PCR diagnostic for the identification of SARS-associated coronavirus RNA/DNA.



LK249

Q. Target recognition sequence:	24 nucleotides (11 G/C)
R. Length of the arms:	6 nucleotides (5 G/C)
S. Melting temperature of the beacon:	dG = -2.37 dH = -46.3 dS = -135.9 Tm = 67.7 °C
T. Melting temperature of target:	°C

LK251 5'-CTCTATGTTTATAAGGGCTATCAACC-3'

Length: 26 nucleotides (10 G/C)
Tm: °C
Position: (see alignment below)

LK256 5'-AAGCGCAGTAAGGATGGCTA-3'

Length: 20 nucleotides (10 G/C)
Tm: °C
Position: (see alignment below)

LK266 Amplicon (98 nucleotides)

5'-

CTCTATGTTTATAAGGGCTATCAACCTATAGATGCTGCTGTCTACAGCCCCAGA
TGGTAGTATTCTTGCTAGTCACACTAGCCATCCTTACTGCGCTT-3'

Figure 18: List of Molecular Designs for IPC

LK265 5'-FAM-GCCCACGTACCATCTGGGGCTGTAGACAGCAGCCGTGGGC-3'-
Dubcyl

LK266

5'-CTCTATGTTTATAAGGGCTATCAACCTATAGATGCTGCTGTCTACAGC
CCCAGATGGTAGTATTCTTGCTAGTCACACTAGCCATCCTTACTGCGCTT
-3'

LK251 5'-CTCTATGTTTATAAGGGCTATCAACC-3'

LK251-T7 5'-TAATACGACTCACTATAGGCTCTATGTTTATAAGGGCTATCAACC-3'

LK256 5'- AAGCGCAGTAAGGATGGCTA - 3'

LK256-RT 5'- TATTGCAGCAGTACAAAGCGCAGTAAGGATGGCTA - 3'

E-RT 5' -TATTGCAGCAGTAC-3'

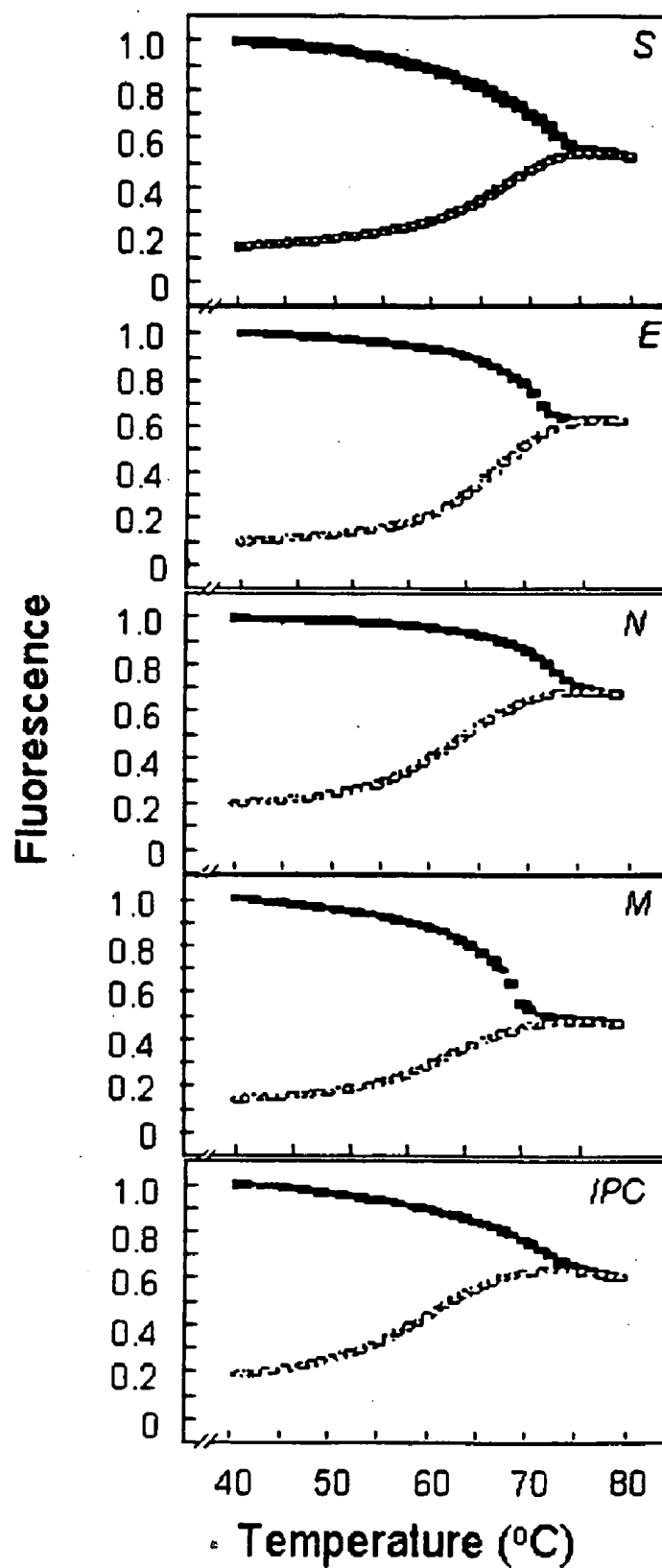
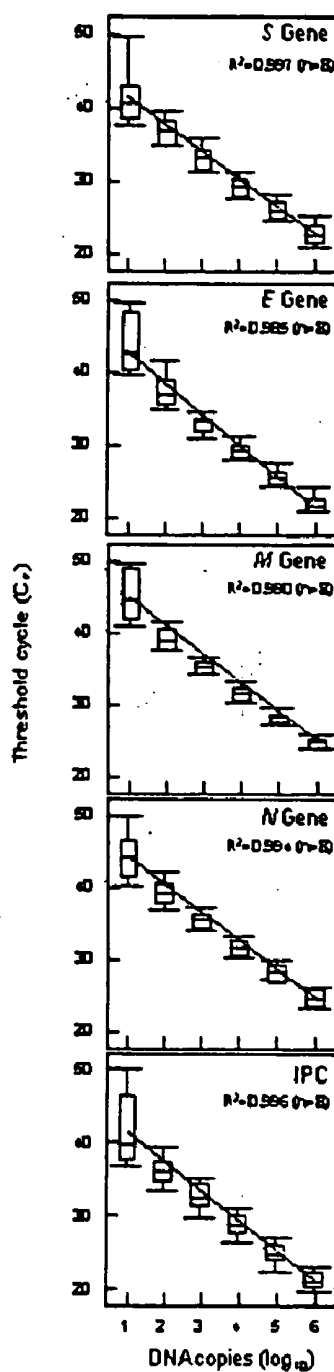
Figure 19: Molecular Beacon Melting Curves

Figure 20: Uniplex Real-time PCR Amplifications (Serial Dilutions-Dynamic Range)



MULTI-ALLELIC MOLECULAR DETECTION OF SARS-ASSOCIATED CORONAVIRUS

[0001] This Patent Application is a Non-Provisional Patent Application based on Provisional Patent Application Ser. No. 60/496,995 (Attorney Docket 42392-191812) filed Aug. 22, 2003, and Provisional Application Ser. No. 60/576,314 (Attorney Docket 42392-203685) filed on Jun. 3, 2004, the contents of which are incorporated herein by reference in their entirety.

BACKGROUND OF THE INVENTION

[0002] 1. Field of Invention

[0003] This invention is directed to methods for the detection and/or quantitation of the SARS virus, reagents and test kits containing the same for use in the method.

[0004] 2. Background of the Invention

[0005] Severe acute respiratory syndrome (SARS) is one of the most recent emerging infectious diseases. The cause of SARS has been identified as a new coronavirus—a virus within the family Coronaviridae—designated as the “SARS coronavirus” (SARS-CoV) [1, 2] by the World Health Organization, following assessment of causation according to Koch’s postulates, including monkey inoculation [3]. The coronaviruses are enveloped positive single-stranded RNA viruses with genomes approximately 30 kb in length—the largest of any of the RNA viruses—that replicate in the cytoplasm of host cells without going through DNA intermediates. Coronaviruses have been reported to cause common colds in humans, and to cause respiratory, enteric, and neurological diseases, as well as hepatitis, in animals. Human coronaviruses are usually difficult to culture in vitro, whereas most animal coronaviruses and SARS-CoV can easily be cultured in Vero E6 cells [4]. There are three groups of coronaviruses: Groups 1 and 2 encompass mammalian viruses, whereas Group 3 encompasses avian viruses. Within each group, the coronaviruses are classified into distinct species according to host range, antigenic relationships, and genomic organization. Human coronaviruses (HCoV) were previously reported to belong in Group 1 (HCoV-229E) and Group 2 (HCoV-OC43), and are responsible for mild respiratory illnesses.

[0006] Recently, two independent groups, one at the British Columbia Cancer Agency (BCCA) in Canada [5] (Tor2 isolate), and the other at the Centers for Disease Control and Prevention (CDCP) in the United States [6] (Urbani isolate), were first to obtain full genomic sequences of SARS-CoV. Phylogenetic analyses, based on the genome sequences, revealed that both isolates were distantly related to previously characterized coronaviruses, including the two previously isolated nonpathogenic human coronaviruses strains, HCoV-OC43 and HCoV-229E. The genome of the Tor2 CoV isolate is 29,751 nucleotides long, and the genome of the Urbani CoV isolate is 29,727 nucleotides long, and their sequences differ at only 24 nucleotide positions. The genomic organization of both isolates is characteristic of coronaviruses having the following typical gene order: 5'-replicase (rep), spike (S), envelope (E), membrane (M), and nucleocapsid (N). The SARS-CoV rep gene, which is approximately 20,000 nucleotides long, is predicted to encode two polypeptides (ORF1a and ORF1b) that undergo proteolytic processing, resulting in several nonstructural

proteins. There are four genes downstream of rep that encode the structural proteins S, E, M, and N.

[0007] The genome of SARS-CoV has several distinct genomic characteristics that distinguish it from other coronavirus isolates and that could be of biological significance. The gene encoding hemagglutinin-esterase, which is present between ORF1a and S in Group 2 coronaviruses (and in some Group 3 coronaviruses) is absent, and so is the short anchor of the S protein. Furthermore, the short anchor of the S protein, the specific number and location of the small ORFs, and the presence of only one copy of PLP PR provide a combination of genetic features that readily distinguish SARS-CoV isolates from previously described coronaviruses [5, 6]. There are several publications that describe reverse-transcriptase polymerase chain reaction assays (RT-PCR assays) for the detection of SARS-CoV.

[0008] Perris et al. [2] developed an RT-PCR assay that identifies the virus from nasopharyngeal aspiration samples obtained from patients infected with SARS-CoV. Total RNA from clinical samples is reverse transcribed in the presence of random hexamers, and the resulting cDNA is amplified with primers 5'-TACACACCTCAGCGTTG-3' and 5'-CAC-GAACGTGACGAAT-3'. To determine the genetic sequence of an unknown RNA virus, they perform a random RT-PCR assay. Total RNA from virus-infected and virus-uninfected fetal rhesus kidney cells were isolated, reverse transcribed with primer 5'-GCCGGAGCTCTGCAGAAT-TCNNNNNN-3', and the resulting cDNA was amplified with primer 5'-GCCGGAGCTCTGCAGAATTC-3'.

[0009] Ksiazek et al. [1] developed a reverse transcription and real-time PCR assay to identify SARS-CoV. Oligonucleotide primers used for amplification and sequencing of the SARS-related coronavirus were designed from alignments in open reading frame 1b of the coronavirus polymerase gene sequences. They used the primer pair IN-2 (+) 5'-GGGTGTTGGACTATCCTAAGTGTGA-3' and IN-4 (-) 5'-TAACACACAACICCATC ATCA-3', which was previously designed to hybridize to conserved regions of open reading frame 1b (ORF1b), in order to achieve broad reactivity with the coronavirus/genus. These primers were used to amplify DNA from SARS isolates, and the amplicon sequences obtained were used to design SARS-specific primers Cor-p-F2 (+) 5'-CTAACATGCTTAGGATAATGG-3', Cor-p-F3 (+) 5'-GCCTCTCTTGTCTGCTCGC-3', and Cor-p-R1 (-) 5'-CAGGTAAGCG TAAACTCATC-3', which were used in turn to test patient specimens. Drosten et al. [4] used a PCR-based random-amplification procedure to genetically characterize a 300-nucleotide-long SARS-CoV genomic segment. On the basis of the sequence that was obtained, conventional and real-time PCR assays for specific detection of SARS-CoV ORF1b were established. Poon et al. [7] developed an RT-real-time-PCR assay. Total RNA isolated from stool specimens from SARS-CoV-infected individuals is reverse transcribed with random hexamers and the resulting cDNA is amplified with primers coro3 5'-TACACACCTCAGCGTTG-3' and coro4 5'-CAC-GAACGTGACGAAT-3', which recognize a region of the viral polymerase gene. It is important to note that these authors acknowledged in their publication that the primers that they use in their assay can cross-react with the non-pathogenic human coronavirus strain HCoV-OC43.

[0010] SARS-specific PCR primers and diagnostic procedures were developed in several World Health Organization

network laboratories for the amplification of a region of the open reading frame 1b (ORF1b) of the SARS-CoV polymerase gene sequence [8]. These primers are currently being assessed to determine their relative performance and sensitivity with different specimens obtained at different times over the course of illness. Lipkin and Briese have announced they develop a PCR-based SARS diagnostic that detects a SARS-CoV gene that is present in multiple copies, but no further information is available in the literature.

[0011] Problems with the prior art that the current invention is designed to solve. The main problems with current molecular diagnostic assays are: a) failure to consider the intrinsically polymorphic nature of coronaviruses, including the current SARS-CoV strains originated from the Tor2 and Urbani isolates—the ability of the virus to mutate and recombine during the period of time it is within the infected individual, and during horizontal transmission; and b) failure to account for the possibility of continuous and/or multiple introduction of non non-genetically identical SARS-CoV strains into the human population.

[0012] A characteristic of RNA viruses is their high rate of genetic mutation, which leads to evolution of new viral strains, and is a well-established mechanism by which viruses escape the immune system. Coronaviruses, including SARS-CoV, are quite sloppy when it comes to replicating their genetic material, producing one error for every 10,000 nucleotides that they copy, which is roughly the same error rate as occurs during the replication of the human immunodeficiency virus, HIV-1. Coronavirus RNA polymerase sometimes jumps between multiple copies of the viral genome that are present in an infected cell. Therefore, each new genome is actually copied from several templates, reducing the chance that any given mutation will become well established in the viral population. Moreover, if one of these jumps is imprecise, a whole chunk of genome can get skipped, resulting in the deletion of part of an important gene. The consequences can be dramatic, particularly if the change affects the protein spikes that enable the virus to bind to the surface of the host's cells. For example, in 1984 a new respiratory sickness appeared on European pig farms. It turned out to be a deletion mutant of a coronavirus that previously had infected piglets' stomachs [9]. It possessed an altered spike protein that enabled the virus to infect a different cell type. Although the new disease was not generally lethal, it has since spread worldwide, and it has complicated the diagnosis of the gut disease. Another example is the recent introduction of SARS-CoV into the human population. It is likely that a genetic deletion may have helped the SARS virus to make the transition from its animal reservoir to humans. Genetics analyses of the viral strains found in animals for sale in Southern Chinese markets indicated that these SARS virus strains lack 29 nucleotides in the gene encoding a protein of unknown function, and the protein product of this gene is attached to the inside of the virus' coat protein. Furthermore, in a recent publication, full genome sequences of 14 isolates from SARS-CoV-infected patients in Singapore, Toronto, China, and Hong Kong were compared, and 14 mutations were revealed [10]. In one respect, this finding may be viewed as indicating that the SARS virus fails to mutate; however, this virus has so far encountered little resistance from its new human hosts, and there has, therefore, been little selective pressure to cause new mutants to be retained. SARS-CoV will probably not remain as stable as it has been so far. Our immune systems

could force changes, similar to the changes that frequently occur in flu viruses. In summary, we deemed it prudent to develop a new SARS-CoV diagnostic assay that accounts for the genetically polymorphic nature of coronaviruses, including SARS-CoV.

SUMMARY OF THE INVENTION

[0013] The present invention includes a molecular-beacon-based multi-allelic RT-real-time-PCR assay for the detection of and discrimination between SARS-associated and other coronavirus isolates in clinical samples. The main elements of the assay design are: a) mismatch-tolerant molecular beacons; b) four sets of PCR primers for four different viral genes, and four different molecular beacons (each labeled with the same fluorophore, and each specific for a different SARS-CoV gene); c) an exogenous RNA standard that is added to the sample that can be reverse-transcribed and amplified by one of the primer sets; and d) a fifth molecular beacon that is labeled with a different fluorophore that is specific for the exogenous RNA standard. The assay further includes RNA isolation from clinical samples (blood, tissue, sputum, nasopharyngeal aspiration samples, and others), reverse transcription, PCR amplification and simultaneous automated amplicon detection in a spectrofluorometric thermal cycler that measures the fluorescence intensity of each color during the annealing phase of each thermal cycle.

[0014] Multiple target sequences within the SARS-CoV S, E, M and N genes (Urbani and Tor2 strains) were identified. The S, M, and E genes encode structural proteins that are present on the outside of the virus, whereas the N gene encodes a structural protein that is required for viral RNA packaging inside the virion. The principle underlying the selection of four target sequences that uniquely identify SARS-CoV (rather than only one target sequence) is that the use of four different targets enhances the likelihood that the fundamental genetic drift of the virus will not lead to a false negative result—that is, one has better chance of hitting a moving target with a shotgun than with a rifle. Thus, by detecting four different target alleles in the same assay tube, and by using a single-fluorophore detection system, the design of the assay significantly minimizes the likelihood of missing the presence of the SARS-CoV in a clinical sample due to the continuous viral evolution of the viral sequence. Moreover, by simultaneously detecting four different target sequences in the same assay tube, the intrinsic sensitivity of the assay is enhanced.

[0015] In order to identify the best target sequences within each viral gene that discriminate the SARS-Urbani and SARS-Tor2 strains from other nonpathogenic human and animal coronavirus strains, we used DNA alignments and phylogenetic analysis of available coronavirus gene sequences deposited in GenBank. DNA sequences of SARS-CoV genes were compared with those from reference viruses representing each species in the three known groups of coronaviruses [group 1 (G1): human coronavirus 229E (HCoV-229E), af304460; porcine epidemic diarrhea virus (PEDV), af353511; transmissible gastroenteritis virus (TGEV), aj271965; canine coronavirus (CCoV), d13096; feline coronavirus (FCoV), ay204704; porcine respiratory coronavirus (PRCoV), z24675;—Group 2 (G2): bovine coronavirus (BCoV), af220295; murine hepatitis virus (MHV), af201929; human coronavirus OC43 (HCoV-

OC43), m76373; porcine hemagglutinating encephalomyelitis virus (HEV), ay078417; rat coronavirus (RtCoV), af207551; and—Group 3 (G3): infectious bronchitis virus (IBV), m95169]. Sequence alignments were performed by CLUSTALW, which is a multiple sequence alignment tool that is commonly used in the bioinformatics community. It produces global multiple sequence alignments through three major phases: a) pairwise alignment, b) guide-tree construction, and c) multiple alignment. The guide tree generated by CLUSTALW is an estimate of relationships between sequences that are much like those shown by phylogenetic trees.

[0016] The criteria for selecting SARS-CoV gene-specific PCR primers were based on: a) the identification of genomic regions in SARS-CoV that, as a result of an examination of the sequence alignments, showed the highest genetic distance between SARS-CoV and other coronavirus strains; b) selection of primer sequences for amplification of the SARS-CoV targets that form primer-target hybrids whose theoretical melting temperature maximizes the ability of the primer to bind to the target even if nucleotide substitutions are present (mismatch tolerance), and yet enable all of the primers to hybridize to their targets at the same temperature in a multiplex assay (T_m approximately 60° C.); and c) selection of primer sequences that enable the amplicons containing each of the four target sequences to be approximately the same (relatively short) length (approximately 100 nucleotides long).

[0017] The criteria for selecting the molecular beacon probe sequences, and their arm sequences, were based on: a) the identification of approximately 30-nucleotide-long regions in SARS-CoV (within the amplicons to be generated) that, as a result of an examination of the sequence alignments, showed the highest genetic distance between SARS-CoV and other coronavirus strains (with special emphasis on probe target sequences that encompass gaps or deletions in the SARS-CoV sequence compared to the sequence of other coronaviruses); b) selection of probe sequences that form probe-target hybrids whose theoretical melting temperature maximizes the ability of the probe to bind to the target sequence even if nucleotide substitutions are present (mismatch tolerance), and yet enable all of the probes to hybridize to their targets at the same temperature in a multiplex assay (T_m approximately 63° C.); and c) selection of arm sequences that provide the same degree of stability for the stem hybrids of all of the molecular beacon probes (stem T_m of approximately 70° C.).

[0018] The assays described herein can be performed in either a heterogeneous or homogeneous format. The reagents needed for performance of the assay can be supplied in a kit format. The kit contains the detectants necessary for measuring two or more of the coronavirus genes S, E, M and N. It is recommended that the kit also contain an internal standard IPC. The reagents including the detectants can be separately packaged in individual containers. The kits may also contain a substrate including reaction tubes for performing an assay for a given sample. The kit may also contain additional reagents for performing amplification reactions including PCR and also for sample pretreatment including those reagent necessary to release and/or purify the coronavirus.

[0019] When there is a need to perform two or more different assays on the same sample, most of the time in a

single vessel and at about the same time, a multiplex format can be utilized. Such formats are known in the art. Multiplex assays are typically used to determine simultaneously the presence or concentration of more than one molecule in the sample being analyzed, or alternatively, several characteristics of a single molecule.

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] FIG. 1 shows the DNA Sequence Alignment of Coronavirus S Genes isolated from different species.

[0021] FIG. 2 shows the Phylogenetic Analysis of S Gene.

[0022] FIG. 3 shows molecular designs for SARS-Associated S Gene.

[0023] FIG. 4 lists Molecular Designs for S Gene.

[0024] FIG. 5 shows the DNA Sequence Alignment of Coronavirus E Genes isolated from different Species.

[0025] FIG. 6 shows the phylogenetic analysis of E Gene.

[0026] FIG. 7 shows molecular designs for SARS-Associated E Gene.

[0027] FIG. 8 shows molecular designs for SARS-Associated E Gene

[0028] FIG. 9 shows the DNA Sequence Alignment of Coronavirus M Genes isolate from different species.

[0029] FIG. 10 shows the phylogenetic analysis of M Gene

[0030] FIG. 11 shows the molecular designs for SARS-Associated M Gene.

[0031] FIG. 12 lists molecular designs for M Gene.

[0032] FIG. 13 shows the DNA Sequence Alignment of Coronavirus N Genes isolate from different species.

[0033] FIG. 14 shows the phylogenetic analysis of N Gene.

[0034] FIG. 15 shows the molecular designs for SARS-Associated N Gene.

[0035] FIG. 16 list molecular designs for N Gene.

[0036] FIG. 17 shows molecular designs for Internal Positive Control (IPC).

[0037] FIG. 18 lists molecular designs for IPC.

[0038] FIG. 19 shows Molecular Beacon Melting Curves.

[0039] FIG. 20 shows Uniplex Real-time PCR Amplifications (Serial Dilutions-Dynamic Range).

DETAIL DESCRIPTION OF THE INVENTION

[0040] The general steps for the assay involve the performance of the following steps:

[0041] Step 1. An RNA standard that can be reverse-transcribed and amplified by one of the primer sets is added to each sample prior to isolation of RNA from the sample. RNA is then extracted from each clinical sample (nasopharyngeal aspirations, stool samples, or whole blood, obtained from patients suspected of being infected with SARS-CoV).

RNA is then purified, using a QIAamp Viral RNA Kit (Qiagen, Inc., Valencia, Calif.), according to the manufacturer's instructions.

[0042] Step 2. The isolated RNA obtained from each clinical sample is then reverse transcribed with four target-specific primers (S Gene, S-RT 5'-AGGCTGTAAGAA-3'; E-Gene, E-RT 5'-TATTGCAGCAGTAC-3'; M Gene, M-RT 5'-AAGCAACGAAGTAG-3'; N Gene, N-RT 5'-GCCTTCTTTGTTAG-3'; Internal Positive Control, E-RT 5'-TATTGCAGCAGTAC-3'). Reverse transcription with SARS-CoV viral RNA from patient samples is performed by adding 20 μ L viral RNA to a mixture of 0.125 μ M of (each) gene-specific primer and incubating at 80° C. for 5 minutes to denature secondary structures. The tubes are then immediately placed on ice for at least 2 minutes. Reverse transcription reactions consist of PCR buffer II (Applied Biosystems), 3 mM MgCl₂, 0.5 mM (each) dNTP, 10 mM dithiothreitol, 20 Units ribonuclease inhibitor (Roche Molecular Biochemicals, Indianapolis, Ind.) and 80 Units SuperScript II Ribonuclease H-reverse transcriptase (GibcoBRL) in a final volume of 40 μ L. The reactions are then incubated at 42° C. for 50 minutes, followed by inactivation at 70° C. for 15 minutes.

[0043] Step 3. Real-time PCR amplification of SARS-CoV cDNA is performed using four primer pairs and five molecular beacons in the same reaction, one primer pair for each viral gene (amplification of the internal positive control is enabled by one of the primer pairs that was designed to enable the amplification of one of the for the viral gene targets). Each PCR reaction consists of 20 μ L of cDNA products, 1 $\times$ PCR buffer II (Applied Biosystems), 3.5 mM MgCl₂, 0.5 mM (each) dNTP, 0.4 μ M of each primer, and 2.5 Units of AmpliTaq Gold DNA polymerase (Applied Biosystems) in a final volume of 50 μ L. Fifty cycles of amplification (94° C. for 15 seconds, 53° C. for 30 seconds, and 72° C. for 30 seconds) are performed in a 7700 Prism spectrofluorometric thermal cycler (Applied Biosystems). For quantitative measurements, duplicates of six-fold serial dilutions (10⁶ to 10 copies) of RNA standards are used as quantitative controls along with the samples being tested for a given experimental run. Viral RNA copy number for each clinical sample is calculated by interpolation of the experimentally determined threshold cycle for the test specimen onto a standard regression curve obtained from the control RNA standards (the logarithm of the number of genomic copies present in the clinical sample is inversely proportional to the observed threshold cycle).

[0044] Explanation of how the invention solves the problems of the prior art. The main problem with the prior art is its failure to consider the intrinsically polymorphic nature of coronaviruses and to account for the possibility of continuous and/or multiple introductions of non non-genetically identical SARS-CoV strains into the human population. The present invention solves these problems by using multiple genetic sequences as targets (the S, E, M, and N genes). The primary principle of using four different genetic targets to identify SARS-CoV is to evade the fundamental genetic drift of the virus. Thus, by using four molecular beacons, each specific for a different amplified SARS-CoV target, and each labeled with same colored fluorophore, the likelihood of not detecting SARS-CoV due to continuous evolutionary changes in the virus is minimized. Furthermore, the assay design includes the presence of an internal positive control

RNA, the reverse transcription and PCR amplification of which generates a signal in a different color, thus assuring that if there is an unexpected problem with RNA isolation, reverse transcription, or target amplification, the absence of the control signal will indicate that a problem occurred.

[0045] Summary of the features of other SARS nucleic acid assays and description of the differences between those assays and the current invention. As outlined in the previous sections, there are five SARS nucleic acid assays: an RT-PCR assay published by Perris et al. [2], an RT-real-time-PCR assay published by Ksiazek et al. [1], a similar RT-real-time-PCR assay published by Drosten et al. [4], another RT-real-time-PCR assay published by Poon et al. [7], and a PCR-based SARS diagnostic assay developed by Lipkin and Briese—no publication is available describing this assay. All of the published assays use RNA extracted from clinical samples. In addition, all of the published assays initiate reverse transcription of SARS-CoV RNA with random primers, and all of the published assays generate cDNA with primers previously designed to enable the amplification of conserved regions of open reading frame 1b (ORF1b), in order to achieve broad reactivity with the coronavirus genus. The present invention differs from these inventions in many different ways. The present assay uses four different targets instead of one and it has an internal positive RNA control (artificial RNA molecule) that can be reverse-transcribed and amplified with primers designed for the viral genes (it possesses a unique target recognition sequence for detection by a unique molecular beacon). This RNA molecule serves as a control for RNA isolation, reverse transcription, and PCR amplification. The present uses real-time PCR for nucleic acid amplification and molecular beacons for real-time detection. The present employs a dual-color detection scheme, a yellow signal (tetrachlorofluorescein) for all four SARS-CoV targets and a green signal (fluorescein) indicating that the internal positive control has been isolated, reverse transcribed, and PCR amplified.

[0046] Another important aspect of our invention, which is not an aspect of the published assays, is the construction of four viral RNA targets that contain gene-specific reverse transcription sequences built in to their 3' ends. Collectively, these molecules serve as SARS-specific positive controls. All of the present designs are thermodynamically compatible to work together in a five-amplicon multiplex assay.

[0047] Also multiplex polymerase chain reaction (mPCR) are envisioned. It is a procedure for simultaneously performing PCR on greater than two different sequences. A mPCR reaction comprises: treating said extracted DNA to form single stranded complementary strands, adding a plurality of labelled paired oligonucleotide primers, each paired primer specific for a different short tandem repeat sequence, one primer of each pair substantially complementary to a part of the sequence in the sense strand and the other primer of each pair substantially complementary to a different part of the same sequence in the complementary antisense strand, annealing the plurality of paired primers to their complementary sequences, simultaneously extending said plurality of annealed primers from the 3' terminus of each primer to synthesize an extension product complementary to the strands annealed to each primer, said extension products, after separation from their complement, serving as templates for the synthesis of an extension product for the other primer of each pair, separating said extension products from said

templates to produce single stranded molecules, amplifying said single stranded molecules by repeating at least once said annealing, extending and separating steps.

[0048] Lower stringent conditions are routinely used to accommodate the capture of multiple target sequences that contain variations in their nucleic acid sequences. The stringency is reduced by either powering the temperature of hybridization and wash or by modification of the buffer. When the stringent conditions are reduced and the target nucleic acid sequence is very similar to nucleic acid sequences of another genus specificity of the capture probe for the target genus can be lost.

[0049] When multiple capture probes are used and are selected to compatible to variations in the target nucleic acid sequences, the specificity under high stringent conditions can be regained. The blending of multiple probes permits a single positive response for the presence of a group of target organisms.

[0050] In a multiplex assay, numerous conditions of interest are simultaneously examined. Multiplex analysis relies on the ability to sort sample components or the data associated therewith, during or after the assay is completed.

EXAMPLES

Example 1

Design of SARS-CoV-Specific Molecular Beacons and Primers for Reverse Transcription and for PCR

[0051] Purpose: The overall rationale in the design of molecular beacons and oligonucleotides for our SARS assay is to construct mismatch-tolerant molecular beacons that are thermodynamically compatible to work in a five-amplicon multiplex assay.

[0052] Design: The molecular beacons were designed so that they are able to hybridize to their targets at the annealing temperature of the PCR, while unbound molecular beacons remain in the closed conformation. These basic aspects were achieved by using coronavirus gene-specific multiple alignments and thermodynamic considerations to select the target sequences, the identity and length of the PCR primers, the identity and length of the probe sequences (target recognition sequences), and the length of the arm sequences.

[0053] Materials: In order to theoretically calculate the melting temperatures of the PCR primers and the probe-target hybrids, was used the Oligo Toolkit that is available on the internet. The melting temperatures and secondary structure predictions of the molecular beacons were calculated by using the DNA folding program developed by Michael Zuker that is available on the internet.

[0054] Results: The theoretical melting temperatures of the PCR primers was about 60° C.; the T_m of the reverse transcription primers was 47° C.; the T_m of the probe-target hybrid was about 63° C.; and the T_m of the stem hybrids of the molecular beacons was about 70° C.

[0055] Conclusion: The mismatch-tolerant molecular beacons that are thermodynamically compatible are designed to work in a final five-amplicon multiplex SARS-CoV assay.

[0056] See the following Figures: The molecular designs for the S gene target of the SARS-CoV assay are described

in detail in FIGS. 14; for the E gene target see FIGS. 5-8; for the M gene target, see FIGS. 9-12; for the N gene target, see FIGS. 13-16; and for the Internal Positive Control (IPC), see FIGS. 17 and 18.

Example 2

Experimental Characterization of the Molecular Beacons and the Molecular Beacon-Target Complexes

[0057] Purpose: The overall rationale of these experiments is to evaluate the thermodynamic properties of the constructed molecular beacons prior to carrying out real-time PCR experiments.

[0058] Design: For each molecular beacon, we have determined two melting curves—one for beacon alone, and one for the beacon-target complex—by using the ABI Prism 7700 spectrofluorometric thermal cycler.

[0059] Materials: For each molecular beacon, melting curves were obtained by preparing two tubes containing 50 μ L of 200 nM molecular beacon dissolved in 3.5 mM $MgCl_2$ and 10 mM Tris-HCl, pH 8.0, and by adding a complementary oligonucleotide target to one of the tubes at a final concentration of 400 nM.

[0060] The fluorescence of each solution was determined as a function of temperature, using a thermal cycler with the capacity to monitor fluorescence. Temperature was decreased linearly with time from 80° C. to 10° C. in 1° C. steps; with each holding period lasting one minute, and fluorescence intensity was measured during each hold.

[0061] Results: The theoretical melting temperature of the PCR primers was 60° C. $\pm$ 2° C.; the theoretical T_m of the reverse transcription primers was 47 $\pm$ 2° C.; the theoretical T_m of the probe target-hybrids was about 63 $\pm$ 3° C.; and the theoretical T_m of the stem hybrid of the molecular beacons was 70 $\pm$ 2° C.

[0062] Conclusion: The designed mismatch-tolerant molecular beacons was determined to correctly recognize their DNA targets, and to be thermodynamically compatible to work together in a five-amplicon multiplex SARS-CoV assay.

[0063] Figures: The melting curves of the molecular beacons and the molecular beacon-target hybrids are shown in FIG. 19.

Example 3

Uniplex SARS-CoV Viral and IPC PCR Amplifications Using SYBR Green to Detect the Amplicons

[0064] Purpose: The overall rationale of these experiments is to evaluate the PCR primers and PCR conditions.

[0065] Design: For each SARS-CoV gene-specific and IPC amplification, a synthetic target DNA was used. PCR reactions were performed using a spectrofluorometric thermal cycler (Cepheid).

[0066] Materials: The PCR protocols are shown in the following exhibits:

[0067] for S Gene:

[0068] (A) SYBR Green-Based Detection of S Gene Amplicon (LK250) of SARS-Associated CoV

Mixture	Per reaction
dH ₂ O	15 μ l
10X PCR Buffer (10X)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK251 (10 pmole/ μ l)	0.5 μ l
LK252 (10 pmole/ μ l)	0.5 μ l
Sybr Green DNA (25X)	1.0 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0069] Smart Cyclor (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1		
Target Temperature (° C.):	95	120 sec

[0070]

Primary Amplification Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

[0071] (B) Molecular-Beacon-Based Detection of S Gene Amplicon (LK250) of SARS-Associated CoV

Mixture	Per reaction
dH ₂ O	15.75 μ l
10X PCR Buffer (10X)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK251 (10 pmole/ μ l)	0.5 μ l
LK252 (10 pmole/ μ l)	0.5 μ l
LK249 Beacon (10 pmole/ μ l)	0.25 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0072] Smart Cyclor (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1		
Target Temperature (° C.):	95	120 sec

[0073]

Primary Amplification Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

[0074] (C) SYBR Green-Based Detection of S Gene Amplicon (T7- and RT-Amplicon)

Mixture	Per reaction
dH ₂ O	15 μ l
10X PCR Buffer (10X)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK251-T7 (10 pmole/ μ l)	0.5 μ l
LK252-RT (10 pmole/ μ l)	0.5 μ l
Sybr Green DNA (25X)	1.0 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0075] Smart Cyclor (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1		
Target Temperature (° C.):	95	120 sec

[0076]

Primary Amplification Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

[0077] (A) SYBR Green-Based Detection of E Gene Amplicon (LK254) of SARS-Associated CoV

Mixture	Per reaction
dH ₂ O	15 μ l
10X PCR Buffer (10X)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK255 (10 pmole/ μ l)	0.5 μ l
LK256 (10 pmole/ μ l)	0.5 μ l
Sybr Green DNA (25X)	1.0 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0078] Smart Cycler (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1			
Target Temperature (° C.):	95	120 sec	

[0079]

Primary Amplification Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

[0080] (B) Molecular-Beacon-Based Detection of E Gene Amplicon (LK254) of SARS-Associated CoV

Mixture	Per reaction
dH ₂ O	15.75 μ l
10X PCR Buffer (10X)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK255 (10 pmole/ μ l)	0.5 μ l
LK256 (10 pmole/ μ l)	0.5 μ l
LK253 Beacon (10 pmole/ μ l)	0.25 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0081] Smart Cycler (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1			
Target Temperature (° C.):	95	120 sec	

[0082]

Primary Amplification Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

[0083] (C) SYBR Green-Based Detection of E Gene Amplicon (T7- and RT-Amplicon)

Mixture	Per reaction
dH ₂ O	15 μ l
10X PCR Buffer (10X)	2.5 μ l

-continued

Mixture	Per reaction
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK255-T7 (10 pmole/ μ l)	0.5 μ l
LK256-RT (10 pmole/ μ l)	0.5 μ l
Sybr Green DNA (25X)	1.0 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0084] Smart Cycler (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1			
Target Temperature (° C.):	95	120 sec	

[0085]

Primary Amplification Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

for the M Gene

[0086] (A) SYBR Green-Based Detection of M Gene Amplicon (LK258) of SARS-Associated CoV

Mixture	Per reaction
dH ₂ O	15 μ l
10X PCR Buffer (10X)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK259 (10 pmole/ μ l)	0.5 μ l
LK260 (10 pmole/ μ l)	0.5 μ l
Sybr Green DNA (25X)	1.0 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0087] Smart Cycler (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1			
Target Temperature (° C.):	95	120 sec	

[0088]

Primary Amplification Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

[0089] (B) Molecular-Beacon-Based Detection of M Gene Amplicon (LK258) of SARS-Associated CoV

Mixture	Per reaction
dH ₂ O	15.75 μ l
10 $\times$ PCR Buffer (10 $\times$)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK259 (10 pmole/ μ l)	0.5 μ l
LK260 (10 pmole/ μ l)	0.5 μ l
LK257 Beacon (10 pmole/ μ l)	0.25 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0090] Smart Cyclor (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1			
Target Temperature (° C.):	95	120 sec	

[0091]

Primary Amplification Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

[0092] (C) SYBR Green-Based Detection of M Gene Amplicon (T7- and RT-Amplicon)

Mixture	Per reaction
dH ₂ O	15 μ l
10 $\times$ PCR Buffer (10 $\times$)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK259-T7 (10 pmole/ μ l)	0.5 μ l
LK260-RT (10 pmole/ μ l)	0.5 μ l
Sybr Green DNA (25 $\times$)	1.0 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0093] Smart Cyclor (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1			
Target Temperature (° C.):	95	120 sec	

[0094]

Primary Amplification Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

[0095] (A) SYBR Green-Based Detection of N Gene Amplicon (LK262) of SARS-Associated CoV

Mixture	Per reaction
dH ₂ O	15 μ l
10 $\times$ PCR Buffer (10 $\times$)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK263 (10 pmole/ μ l)	0.5 μ l
LK264 (10 pmole/ μ l)	0.5 μ l
Sybr Green DNA (25 $\times$)	1.0 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0096] Smart Cyclor (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1			
Target Temperature (° C.):	95	120 sec	

[0097]

Primary Amplification Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

[0098] (B) Molecular-Beacon-Based Detection of N Gene Amplicon (LK262) of SARS-Associated CoV

Mixture	Per reaction
dH ₂ O	15.75 μ l
10X PCR Buffer (10X)	2.5 μ l

-continued

Mixture	Per reaction
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK263 (10 pmole/ μ l)	0.5 μ l
LK264 (10 pmole/ μ l)	0.5 μ l
LK261 Beacon (10 pmole/ μ l)	0.25 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0099] Smart Cycler (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1		
Target Temperature (° C.):	95	120 sec

[0100]

Primary Amplification Cycles: 35		
Denaturation:	95° C.	15 sec
Annealing:	53° C.	15 sec Spectra ON
Extension:	72° C.	15 sec

[0101] (C) SYBR Green-Based Detection of N Gene Amplicon (T7- and RT-Amplicon)

Mixture	Per reaction
dH ₂ O	15 μ l
10X PCR Buffer (10X)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK263-T7 (10 pmole/ μ l)	0.5 μ l
LK264-RT (10 pmole/ μ l)	0.5 μ l
Sybr Green DNA (25X)	1.0 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0102] Smart Cycler (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1		
Target Temperature (° C.):	95	120 sec

[0103]

Primary Amplification Cycles: 35		
Denaturation:	95° C.	15 sec
Annealing:	53° C.	15 sec Spectra ON
Extension:	72° C.	15 sec

and for Internal Positive Control (IPC)

[0104] (A) SYBR Green-Based Detection of Internal Positive Control (LK266)

Mixture	Per reaction
dH ₂ O	15 μ l
10X PCR Buffer (10X)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK251 (10 pmole/ μ l)	0.5 μ l
LK256 (10 pmole/ μ l)	0.5 μ l
Sybr Green DNA (25X)	1.0 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0105] Smart Cycler (Cepheid)

DNA Denaturation & Enzyme Activation Cycles: 1		
Target Temperature (° C.):	95	120 sec

[0106]

Primary Amplification Cycles: 35		
Denaturation:	95° C.	15 sec
Annealing:	53° C.	15 sec Spectra ON
Extension:	72° C.	15 sec

[0107] (B) Molecular-Beacon-Based Detection of Internal Positive Control (LK266)

Mixture	Per reaction
dH ₂ O	15.75 μ l
10X PCR Buffer (10X)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK251 (10 pmole/ μ l)	0.5 μ l
LK256 (10 pmole/ μ l)	0.5 μ l
LK265 Beacon (10 pmole/ μ l)	0.25 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0108] Smart Cycler (Cepheid)

DNA Denaturation & Enzyme Activation		
Cycles: 1		
Target Temperature (° C.):	95	120 sec

[0109]

Primary Amplification			
Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

[0110] (C) SYBR Green-Based Detection of Internal Positive Control (T7- and RT-Amplicon)

Mixture	Per reaction
dH ₂ O	15 μ l
10x PCR Buffer (10x)	2.5 μ l
MgCl ₂ (25 mM)	4.0 μ l
Plat Taq DNA Pol (5 U μ l ⁻¹)	0.3 μ l
dNTP (25 mM)	0.3 μ l
LK251-T7 (10 pmole/ μ l)	0.5 μ l
LK256-RT (10 pmole/ μ l)	0.5 μ l
Sybr Green DNA (25X)	1.0 μ l
Target DNA	1.0 μ l
TOTAL	25.0 μ l

[0111] Smart Cycler (Cepheid)

DNA Denaturation & Enzyme Activation		
Cycles: 1		
Target Temperature (° C.):	95	120 sec

[0112]

Primary Amplification			
Cycles: 35			
Denaturation:	95° C.	15 sec	Spectra ON
Annealing:	53° C.	15 sec	
Extension:	72° C.	15 sec	

[0113] Results: Real-time PCR amplification curves were consistent with the presence or absence of target DNA and the amplicons that were synthesized in the PCR reactions had the correct lengths.

[0114] Conclusion: The synthesized primers work well under uniform PCR conditions.

Example 4

Uniplex SARS-CoV Viral and IPC PCR
Amplifications Using Gene-Specific Molecular
Beacons

[0115] Purpose: The overall rationale of these experiments is to evaluate the molecular beacons, using the uniform PCR condition established in the tests with the PCR primers.

[0116] Design: For each SARS-CoV gene-specific and IPC amplification, a synthetic target DNA and molecular beacon are used. PCR reactions were performed using the spectrofluorometric thermal cycler (Cepheid). For each assay, utilized target dilutions are performed to establish the linearity and the dynamic range of the molecular beacon-based real-time PCR assays.

[0117] Materials: The PCR protocols are shown above in Example 3 for the S Gene, E gene, M Gene, N Gene, and the Internal Positive Control (IPC).

[0118] Results: Real-time PCR amplification curves were consistent with the presence or absence of target DNA.

[0119] Conclusion: The SARS-CoV-specific and IPC-specific molecular beacons work well in under uniform PCR conditions. See **FIG. 20** (Exhibit 25).

Example 5

Uniplex SARS-CoV Viral and IPC PCR
Amplifications Using Bacteriophage T7 RNA
Polymerase and Reverse Transcriptase Target PCR
Primers

[0120] Purpose: The overall rationale of these experiments is for each of the five amplicons (SARS-CoV S, E, M, and N genes and IPC) to produce dsDNA molecules that contain a bacteriophage T7 promoter target recognition sequence at their 5' ends and the gene-specific reverse transcriptase primer-binding site at their 3' ends. The synthesized amplicons are used for in vitro RNA production. The synthesized RNA molecules have the specific reverse transcriptase primer-binding site at their 3' ends.

[0121] Design: For each SARS-CoV gene-specific and IPC amplification, a synthetic target DNA and bacteriophage T7-RT-PCR primers are used. PCR reactions were performed using the spectrofluorometric thermal cycler (Cepheid), using SYBR green to detect the amplicons.

[0122] Materials: The PCR protocols are shown in Example 3.

[0123] Results: Real-time PCR amplification curves are consistent with the presence or absence of target DNA and the amplicons synthesized in the PCR reactions had the correct lengths.

[0124] Conclusion: SARS-CoV-specific bacteriophage T7-RT amplicons were generated for use as templates for in vitro RNA transcription, in order to produce the target RNAs that will be used to qualify the PCR assays. See **FIG. 20**.

Example 6

In Vitro RNA Transcription of SARS-CoV and
IPC-Specific RNA Molecules

[0125] Purpose: The overall rationale for these experiments is to produce RNA molecules containing the specific reverse transection primer-binding site at their 3' ends.

[0126] Design: For each SARS-CoV gene-specific and IPC amplification, a T7-RT-PCR dsDNA amplicon (generated from Experiment 5) is used.

[0127] Materials: RNA transcripts corresponding to the four SARS-CoV-specific and IPC alleles were prepared by in vitro transcription of PCR products that contain the T7 RNA polymerase promoter site, by using a MEGAscript T7 kit (Ambion, Houston, Tex.).

[0128] Results: RNA molecules had the correct lengths, based on 8% polyacrylamide gel electrophoretic analysis of the product strands.

[0129] Conclusion: SARS-CoV-specific T7-RT amplicons were generated to be used for in vitro RNA transcription.

Example 7

Uniplex SARS-CoV-Specific and IPC-Specific RNA Reverse Transcription and Molecular Beacon-Based Real-Time PCR

[0130] Purpose: The overall rationale of these experiments is to test whether the RNA molecules containing the specific reverse transcription primer-binding site at their 3' ends can be reverse transcribed and the generated cDNA can be amplified and detected by real-time PCR.

[0131] Design: For each SARS-CoV gene-specific and IPC amplification, a T7-RT-PCR dsDNA amplicon (generated from Experiment 5) is used.

[0132] Materials: Reverse transcription with viral and IPC RNA was performed by adding 20 μ L of SARS-CoV-specific and IPC-specific RNA to 0.125 μ M of SARS-CoV-specific and IPC-specific primers and incubated at 80° C. for 5 minutes. The PCR-tubes were then immediately placed on ice for at least 2 minutes. the reverse transcriptase reactions contained PCR buffer II (Applied Biosystems), 3 mM MgCl₂, 0.5 mM of each dNTP (GibcoBRL), 10 mM dithiothreitol, 20 Units ribonuclease inhibitor (Roche Molecular Biochemicals) and 80 Units SuperScript II RNase H-reverse transcriptase (GibcoBRL) in a final volume of 40 μ L. The reactions were incubated at 42° C. for 50 minutes, followed by inactivation at 70° C. for 15 minutes. Real-time PCR of cDNA, using 10 μ L cDNA, 1 $\times$ PCR buffer, 3.5 mM MgCl₂, 0.5 mM of each dNTP, 0.4 μ M of each molecular beacon, 0.4 μ M of each PCR primer, and 2.5 Units AmpliTaq Gold DNA polymerase in a final volume of 50 μ L. 35 cycles of amplification (94° C. for 15 sec, 53° C for 30 sec, and 72° C. for 30 sec) were performed in a 7700 Prism spectrofluorometric thermal cycler (Applied Biosystems).

[0133] Results: SARS-CoV-specific and IPC-specific RNA molecules can be reverse transcribed, and the generated cDNA can be amplified and detected by SARS-CoV-specific and IPC-specific molecular-beacons in real-time PCR assays.

[0134] Conclusion: SARS-CoV-specific RNA molecules can be used as controls in the final assay.

Example 8

Multiplex SARS-CoV-Specific and IPC-Specific RNA Reverse Transcription and Molecular Beacon-Based Real-Time PCR

[0135] Purpose: The overall rationale of this experiment is to multiplex the uniplex SARS-CoV-specific and IPC-specific RT-PCR reactions in a multiplex RT-PCR reaction.

[0136] Design: All five RT-PCR reactions are incorporated into one.

[0137] Materials: Identical to Experiment 7, with the exception that all five RT primers, four sets of PCR primers, and five molecular beacons are used in a single RT-PCR reaction

[0138] Results: SARS-CoV-specific and IPC-specific RNA molecules can be reverse transcribed and generate cDNA, and can then be amplified and detected by SARS-CoV-specific and IPC-specific molecular beacons in a real-time PCR assay.

[0139] Conclusion: SARS-CoV-specific RNA molecules can be used as controls in a multiplex assay.

Example 9

Evaluate the Complete SARS-CoV Assay Using Clinical Samples

[0140] Purpose: The overall rationale of these experiments is to evaluate the SARS-CoV assay using real samples (isolated SARS-CoV from cultures, primary patient isolates from saliva, and whole blood and stool specimens).

[0141] Design: Identical to Experiment 8.

[0142] Materials: Identical to Experiment 8.

[0143] Results: SARS-CoV assay detects SARS-CoV and discriminates between SARS-CoV and other non-pathogenic coronaviruses.

[0144] Conclusion: SARS-CoV assay detects SARS RNA extracted from cultured SARS strains and primary isolates.

Example 10

Clinical Evaluation

[0145] 64 samples collected from 23 individuals who were clinically diagnosed to have SARS based on CDC, WHO and Health Canada case definitions.

[0146] The sample types included: bronchial lavage and sputum (pre-mortem samples) as well as lung, liver, small and large bowel, and spleen tissue (post mortem). 65 samples from 15 patients served as controls. 26 were bone marrow samples sent for routing pathogen screening. 39 were post mortem organ samples from 10 patients who died during the outbreak but whose deaths were attributed to other causes including congestive heart failure, cerebrovascular accidents, atherosclerotic heart disease, chronic obstructive pulmonary disease, invasive Group A streptococcal infection, amiodorone pulmonary toxicity, and pulmonary fibrosis.

[0147] All samples were blind assayed by using the developed assay (using all four genes: S, E, M, N) and the specificity was 100%.

[0148] 1. Ksiazek, T. G., et al., A novel coronavirus associated with severe acute respiratory syndrome. N Engl J Med, 2003. 348(20): p. 1953-66.

[0149] 2. Peiris, J. S., et al., Coronavirus as a possible cause of severe acute respiratory syndrome. Lancet, 2003. 361(9366): p. 1319-25.

- [0150] 3. Munch, R., Robert Koch. *Microbes Infect*, 2003. 5(1): p. 69-74.
- [0151] 4. Drosten, C., et al., Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med*, 2003.348(20): p. 1967-76.
- [0152] 5. Marra, M. A., et al., The Genome sequence of the SARS-associated coronavirus. *Science*, 2003. 300(5624): p. 1399-404.
- [0153] 6. Rota, P. A., et al., Characterization of a novel coronavirus associated with severe acute respiratory syndrome. *Science*, 2003. 300(5624): p. 1394-9.
- [0154] 7. Poon, L. L., et al., Rapid diagnosis of a coronavirus associated with severe acute respiratory syndrome (SARS). *Clin Chem*, 2003. 49(6 Pt 1): p. 953-5.
- [0155] 8. Organization, W. H., <http://www.who.int/csr/sars/primers/en/>.
- [0156] 9. Pensaert, M., P. Callebaut, and J. Vergote, Isolation of a porcine respiratory, non-enteric coronavirus related to transmissible gastroenteritis. *Vet Q*, 1986. 8(3): p. 257-61.
- [0157] 10. Ruan, Y. J., et al., Comparative full-length genome sequence analysis of 14 SARS coronavirus isolates and common mutations associated with putative origins of infection. *Lancet*, 2003. 361(9371): p. 1779-85.
- [0158] The content of each of the document identified above and cited in the specification documents is expressly incorporated herein by reference.

 SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 94

<210> SEQ ID NO 1

<211> LENGTH: 4356

<212> TYPE: DNA

<213> ORGANISM: Canine coronavirus

<400> SEQUENCE: 1

```

atgattgtgc ttacattgtg ccttttcttg tttttgtaca gtagtgtgag ctgtacatca      60
aacaatgact gtgtacaagt taatgtgaca caactgcctg gcaatgaaaa tattatcaaa      120
gattttctat ttcagaactt taaagaagaa ggaagttagg ttgtttggtg ttattacccc      180
acagaggtgt ggtataactg ttccacaact caacaaacta ccgcttataa gtatttttagt      240
aatatacatg cattttatgt tgatatggaa gccatggaga atagtactgg caatgcacgt      300
ggtaaacctt tactagtaca tgttcatggg aatcctgtta gtatcattgt ttacatatca      360
gcttatagag atgatgtgca atttaggccc cttttaagc atgggtttatt gtgtataact      420
aaaaatgaca ccgttgacta taatagcttt acaattaacc aatggcgaga catatgtttg      480
ggtgacgaca gaaaaatacc attctctgta gtaccacag ataatggtag gaaattatgt      540
ggtcttgagt ggaatgatga ctatgttaca gcctatatta gtgatgagtc tcaccgtttg      600
aatatcaata ataattgggt taacaatgtt acaactcctat actcacgtac aagcaccgcc      660
acgtggcaac acagtgtctg atatgtttat caaggtgttt caaattttac ttattacaag      720
ttaaataaaa ccgtggtgct aaaaagctat gaattgtgtg aagattatga atactgcact      780
ggctatgcaa ccaatgtgtt tgctccgaca tcaggtgggt atatacctga tggattcagt      840
tttaacaatt ggtttatgct tacaaacagc tccacttttg ttagtggcag atttgaaca      900
aatcaaccgc tgctagttaa ttgcttggg ccagtgccca gttttggcgt cgcagcacia      960
gaattttgtt ttgaagggtg tcagtttagc caatgtaacg gtgtttcttt aaataataca      1020
gtagatgtta ttagatttaa ccttaatttc actacagatg tacaatctgg catgggtgct      1080
acagtatgtt cactgaatac aacaggcggg gtcattcttg agatttcttg ttataatgac      1140
acagtgagtg agtcgagttt ctacagttat ggtgaaattc cattcggcgt aactgatgga      1200
ccacgttact gttatgtact ctacaatggc acagctctta agtatttagg aacattacca      1260
cctagtgtca aggaaattgc tattagtaag tggggacatt tttatattaa tggttacaat      1320

```

-continued

ttcttttagca	cgttttcctat	tgattgtata	gcttttaatt	taaccactgg	tgctagtggga	1380
gcatttttggga	caattgctta	tacgtcgtac	acagaagcat	tagtacaagt	tgaaaacaca	1440
gctattaaaa	aggtgacgta	ttgtaacagt	cacattaata	acatcaaatg	ttctcaactt	1500
actgctaatt	tgcaaaatgg	tttttaccct	gttgcttcaa	gtgaagttgg	tcttgtcaat	1560
aagagtgttg	tgttactacc	tagtttctat	tcacatacca	gtgttaatat	aactattgat	1620
cttggtatga	agcgtagtgt	tacggtcacc	atagcctcac	cattaagtaa	catcacacta	1680
ccaatgcagg	ataataacat	agacgtgtac	tgtattcgtt	ctaaccaatt	ctcagtttat	1740
gttcattcca	cttgcaaaaag	ttcttttatgg	gataacaatt	ttaattcagc	atgtaccgac	1800
gttttttagacg	ccacagctgt	tataaaaact	ggtacttgto	ctttctcatt	tgataaattg	1860
aataattact	taacttttaa	caagttctgt	ttgtcgttga	atcccggttg	tgccaactgt	1920
aagtttagatg	ttgccgcccg	tacaagaacc	aatgagcagg	tttttggaag	tttatatgta	1980
atatatgaag	aaggagacaa	catagtgggt	gtaccgtctg	ataatagtgg	tttgacgat	2040
ttgtcagtgt	tgcaacttaga	ctctgttaca	gattacaata	tatatggtag	aactggtgtt	2100
ggattattta	gaaaaactaa	cagcacacta	cttagtggct	tatattacac	atcactatca	2160
ggtgatttgt	taggttttaa	aaatgttagt	gatgggttg	tctactctgt	aacgccatgt	2220
gatgtaagtg	cacaagctgc	tgttattgat	ggtgccatag	ttggagctat	gacttccatt	2280
aatagtgaac	tgtaggtct	aactcattgg	acaacaacac	ctaattttta	ttactactcc	2340
atatataatt	atacaaatgt	gatgaatcgt	ggcacggcaa	ttgataatga	tattgattgt	2400
gaacctatca	taacatatct	taatataggt	gtttgtaaaa	atggagcttt	ggtttttatt	2460
aacgtcacac	attctgatgg	agacgttcaa	ccaattagca	cggtaatgt	cacgataccc	2520
acaaatttta	ctatatctgt	gcaagtcgaa	tatattcagg	tttacctac	accagtttca	2580
atagactgtg	caagatacgt	ttgcaatggt	aaccaagat	gcaataagtt	attaacacaa	2640
tacgtttctg	catgtcaaac	tattgagcaa	gcgcttgcaa	tggttgccag	acttgaaaac	2700
atggagattg	attccatgtt	atttgtttcg	gaaaatgccc	ttaaattggc	atctgttgaa	2760
gcattcaata	gtacggaaaa	tttagaccct	atttataaag	aatggcctaa	cattggtggt	2820
tcttggctag	gaggttttaa	agatatattg	ccatctcata	atagcaaacg	taagtaccgc	2880
tcggctatag	aagacttgct	ttttgataag	gttgtaacat	ctggcttagg	tacagttgac	2940
gaagattaca	aacgttctgc	aggtggttat	gacatagctg	acttagtggt	tgacagatat	3000
tacaatggca	tcattggtgt	acctggtgta	gctaattgat	acaagatgac	tatgtacact	3060
gcactcttta	caggtggtat	aacattaggt	gcacttagtg	gtggcgcagt	ggctatacct	3120
tttgacgtag	cagttcaggc	tagacttaat	tatgttgcto	tacaaactga	tgtattgaac	3180
aaaaaccaac	aaatcttggc	taatgctttc	aatcaagcta	ttggttaacat	tacacaggca	3240
tttggttaag	ttaatgacgc	tatacatcaa	acatcaaaag	gtcttgctac	gtttgctaaa	3300
gcattggcaa	aggtgcaaga	gttggttaac	acgcaaggtc	aagctttaag	ccacctaaca	3360
gtacaattgc	aaaacaattt	tcaagccatt	agcagttcta	ttagtgacat	ttataacagg	3420
cttgatgaat	tgagtgtctg	tgacacaagt	gacaggtgta	ttacaggacg	acttacagca	3480
cttaatgcat	ttgtgtctca	gactttaacc	agacaagcag	aggttagggc	tagtagacaa	3540
cttgctaaag	acaagggttaa	tgaatgcgtt	aggtctcaat	cccagagatt	tggattctgt	3600

-continued

```

ggtaatggta cacatttggt ttcacttgca aatgcggcac caaatggcat gattttcttt 3660
cacacagtgc tattaccaac agcttatgaa actgtgacgg cctggtcagg tatttgtgcg 3720
tcagatggca gtcgcacttt tggacttggt gttgaggatg tccagctgac gctatttcgc 3780
aatttagatg aaaaatttta ttgacgccc agaactatgt atcagcccag agttgcaact 3840
agttctgatt ttgttcaaag agaaggctgt gatgtgttgt ttgttaatgg aactgtaatt 3900
gaattgccta gtatcatacc tgactatata gatattaatc aaactgttca ggacatatta 3960
gaaaatttca gaccaaattg gactgtaccc gagttgccac ttgacatttt tcatgcaacc 4020
tacttaaacc tgactggtga aattaatgac ttagaattta ggtcagaaaa gttacataac 4080
accacagtag aacttgctat tctcattgat aatattaata acacattagt caatcttgaa 4140
tggctcaaca gaattgaaac ttatgtaaaa tggccttggt atgtttggct actaattgga 4200
ttagtagtaa tattctgcat acccatattg ctattttggt gttgtagtac tggttgttgt 4260
ggatgtatcg ggtgtttagg aagctgttgt cattccatat gtagtagagg ccaatttgaa 4320
agttatgaac ctattgaaa agttcatggt cactga 4356

```

```

<210> SEQ ID NO 2
<211> LENGTH: 4359
<212> TYPE: DNA
<213> ORGANISM: Feline coronavirus

```

```

<400> SEQUENCE: 2

```

```

atgattgtgc tcgtaacttg cctcttggtt ttatgttcat accacacagt tttagtaca 60
acaaataatg aatgcataca agttaacgta acacaattgg ctggcaatga aaaccttatc 120
agagattttc tgtttagtaa ctttaaagaa gaaggaagtg tagttgttgg tggttattac 180
cctacagagg tgtgttaca ctgctctaga acagctcgaa ctactgcctt tcagtatttt 240
aataatatac atgcctttta ttttgttatg gaagccatgg aaaatagcac tggtaatgca 300
cgtggtaaac cattattatt tcatgtgcat ggtgagcctg ttagtggtat tatatcggct 360
tatagggatg atgtgcaaa aaggccctt ttaaaccatg ggtagtggtg cataactaaa 420
aatcgccata ttaactatga acaattcacc tccaaccagt ggaattccac atgtacgggt 480
gctgacagaa aaattccttt ctctgtcata cccacggaca atggaacaaa aatctatggt 540
cttgagtgga atgatgactt tgttacagct tatattagtg gtcgttctta tcacttgaa 600
atcaatacta attggtttta caatgtcaca cttttgtatt cacgctcaag cactgctacc 660
tgggaatata gtgctgcata tgcttaccaa ggtgtttcta acttcactta ttacaagtta 720
aataacacca atgggtctaa aacctatgaa ttatgtgaag attatgaaca ttgcaactggc 780
tatgctacca atgtatttgc tccgacatca ggtggttaca tacctgatgg atttagtttt 840
aacaattggt tcttgcttac aaatagtcc acttttggtta gtggcagggt tgaacaaaat 900
caaccattat tgattaattg cttgtggcca gtgccagtt ttggtgtagc agcacaagaa 960
ttttgttttg aaggtgcaca gtttagccaa tgtaatggtg tgtctttaaa taacacagtg 1020
gatgttatta gattcaacct taatttcact gcagatgtac aatctggtat ggtgtctaca 1080
gtattttcac tgaatacaac aggtgggtgc attcttgaaa tttcatgtta tagtgacaca 1140
gtgagtgagt ctagttctta cagttatggt gaaatcccg tggcataaac tgacggacca 1200
cgatactggt atgtacttta caatggcaca gctcttaaat atttaggaac attaccaccc 1260

```

-continued

agtgtaaagg aaattgctat tagtaagtgg ggccattttt atattaatgg ttacaatttc	1320
tttagcacat ttcttattgg ttgtatatct tttaatTTaa ccaactggtgt tagtgagct	1380
ttttggacaa ttgcttacac atcgtatact gaagcattag tacaagttga aaacacagct	1440
attaaaaatg tgacgtattg taacagtcac attaataaca ttaaatgttc tcaacttact	1500
gctaatttga ataattgatt ttatcctggt gcttcaagtg aagtaggttt cgtaataaag	1560
agtgttggtg tattacctag ctttttcaca tacaccgctg tcaatataac cattgatctt	1620
ggtatgaagc ttatggttta tggTcaacc atagcctcga cactaagtaa catcacacta	1680
ccaatgcagg ataacaatac tgatgtgtac tgtattcgtt ctaaccaatt ctCagtttat	1740
gttcattcca cttgcaaaaag ttctttatgg gacaatattt ttaatcaaga ctgcacggat	1800
gttttagagg ctacagctgt tataaaaact ggtacttgtc ctttctcatt tgataaattg	1860
aacaattact tgacttttaa caagtTctgt ttgtcgttga gtcctgttgg tgctaattgc	1920
aagtttgatg ttgtcgcacg tacaagaacc aatgagcagg ttgttagaag tctatatgta	1980
atatatgaag aaggagacaa catagtgggt gtaccgtctg ataatagcgg tctgcacgat	2040
ttgtctgtgc tacacctaga ctctgttaca gattacaata tatatggtag aactgggtgt	2100
ggtattatta gacgaactaa cagtacgcta cttagtggct tatattacac atcactatca	2160
ggtgatttgt taggctttaa aaatgttagt gatggtgtca tttattctgt gacgccatgt	2220
gatgtaagcg cacaagcggc tgTtattgat ggtgccatag ttggagctat gacttccatt	2280
aacagtgaac tgTtaggtct aacacattgg acaacgacac ctaattttta ttactactct	2340
atatataatt acacaagtga gaggactcgt ggcactgcaa ttgacagtaa cgatgttgat	2400
tgtgaacctg tcataaccta ttctaataa ggtgtttgta aaaatggTgc tttggTTTT	2460
attaacgtca cacattctga cggagacgtg caaccaatta gcactggtaa tgcacgata	2520
cctacaaatt ttactatatc tgtgcaagtt gaatacatgc aggtttacac tacaccagta	2580
tcaatagatt gtgcaagata cgTttgtaat ggtaacccta gatgtaacaa attgttaaca	2640
caatatgtgt ctgcatgtca aactattgaa caagcacttg caatgggtgc cagacttgaa	2700
aacatggagg ttgattccat gttgtttgTc tcggaaaatg cccttaaatt ggcatctgtt	2760
gaggcgttca atagtacaga aaatttagat cctatttaca aagaatggcc tagcataggt	2820
ggttcttggc taggaggtct aaaagatata ctaccgtccc ataatagcaa acgtaagtat	2880
ggttctgcta tagaagattt gctttttgat aaagttgtaa catctggTtt aggtacagtt	2940
gatgaagatt ataaacgttg tactggTggt tacgacatag cagacttggT gtgtgctcaa	3000
tattacaatg gcatcatggt tctaccaggt gtagctaatt ctgacaagat gactatgtac	3060
acagcatcac ttgcaggtgg tataacatta ggtgcacttg gtggtggcgc cgtggctata	3120
ccttttgCag tagcagtaca ggctagactt aattatgttg ctctacaaac tgatgtattg	3180
aataaaaacc aacagatcct ggctaagtct ttcaatcaag ctattggtaa cattacacag	3240
gcttttgGta aggttaatga tgctatacat caaacatcac aaggtcttgc cactgttgct	3300
aaagcgttgg caaaagtgca agatgttgTc aacacacaag ggcaagcttt aagtcacctt	3360
acagtacaat tgcaaaataa ttttcaagcc attagtagtt ctattagtga tatttataac	3420
aggcttgacg aactgagtgc tgatgcacaa gttgataggc tgattacagg tagacttaca	3480
gcacttaatg catttgtgTc tcagactcta accagacaag cagagggttag ggctagtaga	3540

-continued

```

caacttgcca aagacaaggt taatgaatgt gttaggtctc agtctcagag attcggattc 3600
tgtggtaaatg gtacacattt gttttcacta gcaaatgcag caccaaatgg catgattttc 3660
tttcatacag tactattacc aacagcttat gaaactgtaa cagcttggtc aggtattttgt 3720
gcttcagatg gcgatcgcac ttctggactt gtcgttaaag atgtgcagtt gacgttggtt 3780
cgtaatctag atgacaagtt ctatttgacc ccagaaacta tgtatcagcc tagagtggca 3840
actagttctg attttgttca aattgaaggg tgtgatgtgt tgtttgtcaa cgcgactgta 3900
attgatttgc ctagtattat acctgactat attgacatta atcaaactgt tcaagacata 3960
ttagaaaatt acagacaaaa ctggactgta cctgaattta cacttgatat tttcaacgca 4020
acctatttaa atctgactgg tgaaattgat gacttagagt ttaggtcaga aaagctacat 4080
aacactacag tagaacttgc cattctcatt gataacatta ataatacatt agtcaatctt 4140
gaatggctca atagaattga aacttatgta aaatggcctt ggtatgtgtg gctactgata 4200
ggtttagtag tagtattttg cataccatta ctgctatttt gctgttttag cacaggttgt 4260
tgtggatgca taggttgttt aggaagtgtt tgcactcta tatgtagtag aagacaattt 4320
gaaaattatg aaccaattga aaaagtgcac gtccactaa 4359

```

<210> SEQ ID NO 3

<211> LENGTH: 4344

<212> TYPE: DNA

<213> ORGANISM: Transmissible gastroenteritis virus

<400> SEQUENCE: 3

```

atgaaaaaac tatttgtggt ttgggtcgta atgccattga tttatggaga caattttcct 60
tgttctaaat tgactaatag aactataggc aaccagtgga atctcattga aaccttcctt 120
ctaaactata gtagtaggtt accaccta atcagatgtg tgtaggtgta ttattttcct 180
actgtacaac ctgggtttta ttgcattcgc aatgatagta atgaccttta tgttacctg 240
gaaaaatctta aagcattgta ttgggattat gctacagaaa atatcacttg gaatcacaga 300
caacggttta acgtagtcgt taatggatac ccatactcca tcacagttac aacaaccgc 360
aattttaatt ctgctgaagg tgctattata tgcatTTgta agggctcacc acctactacc 420
accacagaat ctagtttgac ttgcaattgg ggtagttagt gcagggttaa ccataagttc 480
cctatatgtc cttctaatto agaggcaaat tgtggttaata tgctgtatgg cctacaatgg 540
tttgcagatg aggttgttgc ttattttacat ggtgctagtt accgtattag ttttgaaaat 600
caatggctcg gcactgtcac atttggtgat atgctgtcga caacattaga agtctgtggc 660
acgctttag acctttgggt gttaaatcct gtttatgatg tcagttatta tagggttaat 720
aataaaaatg gtactaccgt agtttccaat tgcactgac aatgtgctag ttatgtggct 780
aatgttttta ctacacagcc aggaggtttt ataccatcag attttagttt taataattgg 840
ttccttctaa ctaatagctc cacgttggtt agtggtaaat tagttacaa acagccgtta 900
ttagttaatt gcttatggcc agtccctagc ttgaagaag cagcttctac attttgtttt 960
gaggggtctg gctttgatca atgtaatggt gctgttttaa ataatactgt agacgtcatt 1020
aggttcaacc ttaattttac tacaatgta caatcaggt aggggtccac agtggtttca 1080
ttgaacacaa cgggtgggtg cactcttgaa atttcatgtt atacagttag tgactcgagc 1140
tttttcagtt acgggtgaaat tccgttcggc gtaactgatg gaccacggt ctgttacgta 1200

```

-continued

cactataatg gcacagctct taagtattta ggaacattac cacctagtgt caaggagatt	1260
gctattagta agtggggcca tttttatatt aatggttaca atttcttttag cacatttcct	1320
attgattgta tatcttttaa ttgaccact ggtgatagtg acgttttctg gacaatagct	1380
tacacatcgt acactgaagc attagtacaa gttgaaaaca cagctattac aaaggtagcg	1440
tattgtaata gtcacgttaa taacattaaa tgctctcaaa ttactgctaa ttgaataat	1500
ggattttatc ctgtttcttc aagtgaagtt ggtcttgta ataagagtgt tgtgttacta	1560
cctagctttt acacacatac cattgttaac ataactattg gtcttggtat gaagcgtagt	1620
ggttatggtc aacctatagc ctcaacatta agtaacatca cactaccaat gcaggatcac	1680
aacaccgatg tgtactgtat tcgttctgac caattttcag tttatgttca ttctacttgc	1740
aaaagtgcct tatgggacaa tatttttaag cgaaactgca cggacgtttt agatgccaca	1800
gctgttataa aaactggtac ttgtcctttc tcatttgata aattgaacaa ttacttaact	1860
tttaacaagt tctgtttgtc gttgagtcct gttggtgcta attgtaagtt tgatgtagct	1920
gcccgtacaa gaaccaatga gcagggtgtt agaagtttgt atgtaataata tgaagaagga	1980
gacaacatag tgggtgtacc gtctgataat agtgggtgac acgatttgta agtgctacac	2040
ctagattcct gcacagatta caatatatat ggtagaactg gtgttggtat tattagacaa	2100
actaacagga cgtacttagg tggcttatat tacacatcac tatcagggtga ttgttaggt	2160
tttaaaaatg ttagtgatgg tgctcatctac tctgtaacgc catgtgatgt aagcgacaaa	2220
gcagctgtta ttgatggtac catagttggg gctatcactt ccattaacag tgaactgtta	2280
ggtctaacac attggacaac aacacctaat ttttattact actctatata taattacaca	2340
aatgatagga ctggtggcac tgcaattgac agtaatgatg ttgattgtga acctgtcata	2400
acctattcta acataggtgt ttgtaaaaat ggtgcttttg tttttattaa cgtcacacat	2460
tctgatggag acgtgcaacc aattagcact ggtaatgtca cgatacctac aaactttacc	2520
atatccgtgc aagtcgaata tattcaggtt tacactacac cagtgtcaat agactgttca	2580
agatatgttt gtaatggtaa cctaggtgt aacaaattgt taacacaata cgtttctgca	2640
tgtcaaaacta ttgagcaagc acttgcaatg ggtgccagac ttgaaaacat ggaggttgat	2700
tccatgttgt ttgtttctga aaatgccctt aaattggcat ctgttgaagc attcaatagt	2760
tcagaaaact tagacctat ttacaaagaa tggcctaata taggtggttc ttggctagaa	2820
ggtctaaaat acatacttcc gtcccataat agcaaacgta agtatcgttc agctatagag	2880
gacttgcttt ttgataaggt tgtaacatct ggtttaggtta cagttgatga agattataaa	2940
cgttgtagag gtggttatga catagctgac ttagtatgtg ctcaatacta taatggcatc	3000
atggtgtcac ctggtgtggc taatgctgac aaaatgacta tgtacacagc atcccttgca	3060
ggtggtataa cattaggtgc acttggtgga ggcgcgtgg ctataccttt tgcagtagca	3120
gttcaggcta gacttaatta tgttgctota caaactgatg tattgaacaa aaaccagcag	3180
attctggcta gtgctttcaa tcaagctatt ggtaacatta cacagtcatt tggtaaggtt	3240
aatgatgcta tacatcaaac atcacgaggt cttgctactg ttgctaaagc attggcaaaa	3300
gtgcaagatg ttgtcaacat acaagggcaa gctttaagcc acctaacagt acaattgcaa	3360
aataatttcc aagccattag tagttctatt agtgacattt ataataggct tgacgaattg	3420
agtgctgatg cacaagttga caggctgac acaggaagac ttacagcact taatgcattt	3480

-continued

```

gtgtctcaga ctctaaccag acaagcggag gttagggcta gtagacaact tgccaaagac 3540
aagggttaatg aatgcgttag gtctcagtct cagagattcg gattctgtgg taatggtaca 3600
catttgtttt cactcgcaaa tgcagcacca aatggcatga ttttctttca cacagtgcta 3660
ttaccaacgg cttatgaaac tgtgactgct tggccaggta tttgtgcttc agatggtgat 3720
cgcacttttg gacttgtcgt taaagatgtc cagttgactt tgtttcgtaa tctagatgac 3780
aagttctatt tgacccccag aactatgtat cagcctagag ttgcaactag ttctgacttt 3840
gttcaaattg aaggggtgca tgtgctgttt gttaatgcaa ctgtaagtga ttgcctagt 3900
attatacctg attataattga tattaatcag actgttcaag acatattaga aaattttaga 3960
ccaaattgga ctgtacctga gttgacattt gacattttta acgcaacctt tttaaacctg 4020
actggtgaaa ttgatgactt agaatttagg tcagaaaagc tacataacac cactgtagaa 4080
cttgccattc tcattgacaa cattaacaat acattagtca atcttgaatg gctcaataga 4140
attgaaacct atgtaaaatg gccttggat gtgtggctac taataggctt agtagtaata 4200
ttttgcatac cattactgct attttgcgtt ttagtagacg gttgctgtgg atgcataggt 4260
tgttttagaa gttgttgtca ctctatatgt agtagaagac aatttgaaaa ttacgaacca 4320
attgaaaaag tgcacgtcca ttaa 4344

```

<210> SEQ ID NO 4

<211> LENGTH: 3678

<212> TYPE: DNA

<213> ORGANISM: Porcine respiratory coronavirus

<400> SEQUENCE: 4

```

atgaaaaaat tatttgtggt cttggttgta atgccattga tttatggaga caagtttcct 60
acttccgtag tttccaattg cactgatcaa tgtgctagtt atgtggctaa tgtttttact 120
atactaccag gaggttttat accatcagat tttagtttta ataattgggt cctcctaact 180
aatagctcca cgttgggttaa tggtaaatta gttaccaaac agcctctatt agttaattgc 240
ttatggccag tccttagctt tgaagaagta gcttctacat tttgttttga aggtgctgac 300
tttgatcaat gtaatgggtgc tgtttttaa aacactgtag acgtcattag gtttaacctt 360
aattttacta caaatgtaca atcaggtaag ggtgctacag tgttttcatt gaacacaacg 420
ggtggtgtca ctcttgaaat ctcatgttat aatgatacag tgagtgttc gagcttttcc 480
agttacgggtg aaattccgtt cggcgtaact aatggaccac ggtactgtta cgtactctat 540
aatggcacag ctcttaagta tctaggaaca ttaccaccta gtgtcaagga gattgtctatt 600
agtaagtggg gccattttta tattaatggt tacaatttct ttagcacatt tcctattgat 660
tgtatatcct ttaatttgac tactgggtgat agtgacgtct tctggacaat agcttacaca 720
tcgtacactg aagcattagt acaagttgaa aacacagcta ttacaaatgt gacgtattgt 780
aatagttatg ttaataacat taaatgctct caacttactg ctaatttgaa taatggattt 840
tatcctgttt cttcaagtga agttggttct gtcaataaga gtgttgtgtt actacctagc 900
tttctgacac ataccattgt taacataact attggtcttg gtatgaagcg tagtggttat 960
ggtcaaccca tagcctcaac gctaagtaac attacactac caatgcagga taacaacaac 1020
gatgtgtact gtgttcgttc tgaccaattt tcagtttatg ttcattctac ttgcaaaagt 1080
gttttatggg acaatgtttt taagcgaaac tgcacggacg ttttagatgc cacagctgtt 1140

```

-continued

ataaaaactg	gtacttgtcc	tttctcattt	gataaattga	acaattactt	aacttttaac	1200
aagttctgtt	tgctgttgag	tcccggtggg	gctaattgta	agtttgatgt	agctgcccgt	1260
acaagaacca	atgatcaggt	tgtagaagt	ttgtatgtaa	tatatgaaga	aggagacagc	1320
atagttgggt	taccgtctga	caatagtggt	ttgcacgatt	tgtagtgct	acacctagat	1380
tcgtgcacag	attacaatat	atatggtaga	actgggtgtg	gtattattag	acaaactaac	1440
aggacgatac	ttagtggtt	atattacaca	tcactatctg	gtgatttgtt	aggttttaca	1500
aatgttagtg	atgggtttat	ctactctgta	acgccatgtg	atgttagcgc	acaagcagct	1560
attattgatg	gtaccatagt	tggtggctatc	acttcatta	acagtgaatt	gttaggtcta	1620
acacattgga	caacaacacc	taatttttat	tactactcta	tatataatta	cacaaatgat	1680
aagactcgtg	gcactccaat	tggtcagta	gacgttgatt	gtgaacctgt	cataacctat	1740
tctaacatag	gtgtttgtaa	aaatgggtgt	ttggttttta	ttaacgtcac	acattctgat	1800
ggagacgtgc	aaccaattag	cactggtaac	gtcacgatac	ctactaactt	tactatatcc	1860
gtgcaagtcg	aatacattca	ggtttacact	acaccagtgt	caatagactg	ttcaagatat	1920
gtttgtaatg	gcaaccctag	gtgtaacaaa	ctgttaacac	aatacgtttc	tgcatgtcaa	1980
actattgagc	aagcacttgc	aatgggtgcc	agacttgaaa	acatggaagt	tgattccatg	2040
ttattttgtt	ctgaaatgc	ccttaaattg	gcttctgtcg	aagcattcaa	tagttcagaa	2100
actttagatc	ctatttatac	agaatggcct	aatataggtg	gcttttggt	agaaggtcta	2160
aaatacatac	ttccgtccga	taatagcaaa	cgtaagtatc	gttcagctat	agaggacttg	2220
cttttttcta	agggtgtaac	atctgggtta	ggtacagttg	atgaagatta	caaacgttgt	2280
acaggtgggt	atgacatagc	tgacttagta	tgtgctcaat	actataatgg	cattatgggtg	2340
ctacctgggt	tggtcaatgc	tgacaaaatg	actatgtaca	cagcatccct	cgcaggtgggt	2400
ataacattag	gtgcacttgg	tggtggcgcc	gtggctatac	cttttgtagt	agcagttcag	2460
gctagactta	attatgttgc	tctacaaaact	gatgtattga	acaaaaacca	gcagatcctg	2520
gotagtgcct	ttaatcaagc	tattggtaac	attacacagt	catttggtta	ggttaatgat	2580
gctatacatc	aaacatcacg	aggctttaca	actgttgcta	aagcattggc	aaaagtgcaa	2640
gatgttgta	acacacaagg	tcaagcttta	agacacctaa	cagtacaatt	gcaaaataat	2700
ttccaagcca	ttagtagttc	tattagtgc	atttataata	ggcttgatga	attgagtgtc	2760
gatgcacaag	tcgacaggct	gatcacagga	agacttacag	cacttaatgc	atttgtgtct	2820
cagactctaa	ccagacaagc	cgagggttag	gctagtagac	aacttgctaa	agacaagggt	2880
aatgaatgcg	ttaggtctca	gtctcagaga	ttcggcttct	gtggaatgg	tacacatttg	2940
ttttcactcg	caaatgcagc	accaaaggc	atgatcttct	ttcacacagt	gctattacca	3000
acggcgtatg	aaactgtgac	tgcttggta	ggtatttgg	ctttagatgt	tgatcgcaact	3060
tttggaactg	tcgttaaaag	tggtcagttg	actttatttc	gtaactctaga	tgacaagttc	3120
tatttgacac	ccagaactat	gtatcagcct	agagtggcaa	ctagttctga	ttttgttcaa	3180
attgaagggt	gcgatgtgct	gtttgttaat	acaactgtaa	gtgatttgcc	tagtattata	3240
cctgattata	ttgatattaa	tcagactggt	caagacatat	tagaaaattt	tagaccaa	3300
tggactgtac	ctgagctgac	attggacgtt	tttaacgcaa	cctattttaa	cctgactgggt	3360
gaaattgatg	acttagagtt	taggtcagaa	aagctacata	acactactgt	agaacttgcc	3420

-continued

attctcattg acaacattaa caatacagta gtcaatcttg aatggcttaa tagaattgaa	3480
acttatgtaa aatggccttg gtatgtgtgg ctactaatag gcttagtagt aatattttgc	3540
ataccattac tgctattttg ctgtttagt acaggttgct gtggatgcat aggttgttta	3600
ggaagtgtgt gtcactctat attcagtaga agacaatttg aaaattatga acctattgaa	3660
aaagtgcacg tccattaa	3678

<210> SEQ ID NO 5

<211> LENGTH: 3522

<212> TYPE: DNA

<213> ORGANISM: Human coronavirus OC43

<400> SEQUENCE: 5

atgtttgttt tgcttggtgc atatgccttg ttgcatattg ctggttgta aactacaaat	60
gggctgaaca ctagtactc tgcttgcaac ggctgtgttg gttattcaga aaatgtattt	120
gctgttgaga gtggtgggta tataccctcc gactttgcat tcaataattg gttccttcta	180
actaatacct catctgttgt agatgggtgt gtgaggagt ttcagccttt gttgcttaat	240
tgcttatggc ctgtttctgg ctgctgttt actactgggt ttgtctatct taatgggtact	300
gggagagggt attgtaaaagg ttttctctca gatgttttgt ctgatgtcat acgttacaac	360
ctcaattttg aagaaaacct tagacgtgga accattttgt ttaaaacatc ttatgggtgt	420
gttgtgtttt attgtaccaa caacacttta gtttcagggt atgctcacat accatttggt	480
acagtttttg gcaattttta ttgctttgta aatactacta ttggcaatga aactacgtct	540
gcttttggtg gtgcactacc taagacagtt cgtgagtttg ttatttcacg cacaggacat	600
ttttatatta atggctatcg ctatttcact ttaggtaatg tagaagccgt taatttcaat	660
gtcactactg cagaaaccac tgatttttgt actgttgctg tagcttctta tgctgacgtt	720
ttgggttaatg tgcacaaaac ctctattgct aatataattt attgcaactc tgttattaac	780
agactgagat gtgaccagtt gtcctttgat gtaccagatg gtttttattc tacaagccct	840
attcaatccg ttgagctacc tgtgtctatt gtgtcgtac ctgtttatca taaacatacg	900
tttattgtgt tgtacgttga cttcaaacct cagagtggcg gtggcaagtg ctttaactgt	960
tatcctgctg gtgttaatat tacactggcc aattttaatg aaactaaagg gcctttgtgt	1020
gttgacacat cacacttcac taccaaatac gttgctgttt atgccaatgt tggtaggtgg	1080
agtgctagta ttaacacggg aaattgccct tttcttttg gcaaagttaa taactttgtt	1140
aaatttgga gtgtatgttt ttgcctaaag gatatacccg gtggttgccg aatgcctata	1200
gtggctaatt gggcttatag taagtactat actataggct cattgtatgt ttcttgaggt	1260
gatggtgatg gaattactgg cgtccacaaa cctgttgagg gtgttagttc ctttatgaat	1320
gttacattgg acaaatgtac taaatataat atttatgatg tatctggtgt ggggtttatt	1380
cgcgttagca atgacacctt tcttaattga attacgtaca catcaacttc aggtaacctt	1440
ctgggtttta aagatgttac taagggcacc atctactcta tcaactcttg taaccaccca	1500
gatcagcttg ttgtttatca gcaagctgtt gttggtgcta tgtgtctga aaattttact	1560
agttacggct tttctaattg tgtagaactg ccgaaatctt tctatgcgtc caatggcact	1620
tataattgca cagacgtgtt tttaacttat tctagttttg gcgtttgtgc agatgggtct	1680
ataattgctg ttcaaccacg taatgtttca tatgatagt tttcagctat cgtcacagct	1740

-continued

```

aatttgtcta taccttccaa ttggaccact tcggtccagg ttgagtattt acaaattaca 1800
agtacaccta tcgtagttga ttgctccact tatgtttgca atggtaatgt gcgctgtgtt 1860
gaattgctta agcagtatac ttctgcttgt aaaactattg aagacgcctt aagaaatagc 1920
gccaggctgg agtctgcaga tgtagtgag atgctcactt ttgacaagaa agcgtttaca 1980
cttgctaatag ttagtagttt tggtgactac aaccttagca gcgcatacc tagcttgccc 2040
acaagtggta gtagagtggc tggtcgcagt gccatagaag acatactttt tagcaaaactt 2100
gttacttctg gacttggcac tgtggacgca gactacaaaa agtgcactaa ggttctttcc 2160
attgctgact tggcttgtgc tcaatattat aatggcatta tggttttgcc tggcgtcgct 2220
gatgctgaac gaatggccat gtatacaggt tctttaattg gtggaattgc ttaggaggt 2280
ctaacatcag ccgtttcaat accattttca ttagcaattc aggcacgttt aaattatgtt 2340
gcattgcaga ctgatgtttt acaagaaaat cagaaaattc ttgctgcac ttttaacaaa 2400
gcaatgacca acatagtaga tgcttttact ggtgttaatg atgctattac acaaaacttca 2460
caagccctac aaacagtgtc tactgcactt aacaagatcc aggatgttgt taatcaacaa 2520
ggcaactcat tgaaccattt aacttctcag ttgaggcaga attttcaagc tatctctagc 2580
tctattcagg ctatctatga cagacttgac actattcagg ctgatcaaca agtagatagg 2640
ctgattactg gtagattggc tgctttgaat gtattcgttt ctcatacatt gactaagtac 2700
actgaagttc gtgcttccag acagcttgca caacaaaag tgaatgagtg tgtcaaatcc 2760
cagtctaagc gttatggctt ctgtggaaat ggcaactcaca ttttctcaat tgttaatgct 2820
gctcctgagg ggcttgtttt tctccacact gtcttggtgc cgacacaata taaggatgtt 2880
gaagcgtggt ctgggtgttg cggtgatggt acaaacggtt atgtgttgcg acaacctaatt 2940
cttgctcttt acaagaagg caattattat agaatcacat ctgcataat gtttgaacca 3000
cgtattccta ccatggcaga ttttgttcaa attgaaaatt gcaatgtcac atttgttaac 3060
atttctcgct ctgagttgca aaccattgtg ccagagtata ttgatgttaa taagacgctg 3120
caagaattaa gttacaaaat gccaaaattc actgttccag acctagtgtg cgaacagtac 3180
aaccagacta ttttgaattt gaccagtga attagcacc ttgaaaataa atctgcggag 3240
cttaattaca ctgttcaaaa attgcaaact ctgattgaca acataaatag cacattagtc 3300
gacttaaagt ggtcaaccg ggttgagact tacatcaagt ggccgtggtg ggtgtggttg 3360
tgcatttcag tcgtgctcat ctttgtggtg agtatgttgc tattatgttg ttgttctact 3420
ggttgctgtg gcttcttttag ttgttttgca tcttctatta gaggtgttg tgaatcaact 3480
aaacttcctt attacgacgt tgaaaagatc cacatacagt aa 3522

```

<210> SEQ ID NO 6

<211> LENGTH: 4152

<212> TYPE: DNA

<213> ORGANISM: Porcine epidemic diarrhea virus

<400> SEQUENCE: 6

```

atgaggtcct taatttactt ctggttgctc ttaccagtac ttccaacact cagcctacca 60
caagatgtca ctagggtcca gtctactact aacttttagg ggttcttttc aaaatttaat 120
gttcaggcac ctgccgtcgt cgttttgggt ggttacctac ctagtatgaa ctcttctagc 180
tggtagctgt gcacagcat tgaaactgct agtggcgctc atggtatttt tctcagctac 240

```


-continued

atcgattctg gtcagggtt tgagattggc atttcgcaag agccgtttga tcctagtgg	300
taccagcttt atttacataa ggcactaat ggtaacacta atgctattgc acgactgcgc	360
atttgccagt tccccgataa taaaacattg ggcctactg ttaatgatgt tacaacaggt	420
cgtaactgcc tattcaacaa agccattcca gcttatatgc gtgatggaaa agatattgtt	480
gtcggcataa catgggataa tgatcgtgtc actgtttttg ctgacaagat ctatcatttt	540
tatcttaaaa atgattggtc ccgcgttgcg acaagatgtt acaatcgag aagttgtgct	600
atgcaatatg tttatacacc tacctactac atgcttaatg ttactagtgc aggtgaggat	660
ggcatttatt atgaaccctg tacagctaata tgcactgggt acgctgcaa tgtatttgc	720
actgattcca atggccatat accagaaggt tttagtttta ataattgggt tcttttatcc	780
aatgactcca ctttgttgca tggtaaagtg gtttccaacc aaccttggtt ggtcaattgt	840
cttttgcca ttccaaagat ttatggacta ggccaatttt tctcattcaa tcacacgatg	900
gatggcggtt gtaattggagc tgctgtggat cgtgccccag aggctctgag gtttaatat	960
aatgacacct ccgtcattct tgctgaaggc tcaattgtac ttcatactgc tttaggaaca	1020
aatctttctt ttgtttgcag taattcctca gatcctcatt tagccatctt tgccatacct	1080
ctgggtgcta ctgaagtacc ctactattgc tttcttaaag tggatactta caactccact	1140
gtttataaat tcttggtgtt tttacctct actgtcaggg aaattgtcat caccaagtat	1200
ggtgatgtt atgtcaatgg gtttggtctat ttgcatctcg gtttgttga tgctgcaca	1260
attaatttca ctggtcatgg cactgacgat gacgtttcag gtttctggac catagcatcg	1320
actaattttg ttgatgcact catcgaggtt caaggaaact ccattcagcg tattctttat	1380
tgtgatgatc ctgttagcca actcaagtgt tctcagggtg cttttgacct tgacgatgg	1440
ttttacccca tctcttctag aaacctctg agtcacgaac agccaatttc tttgtttact	1500
ttgccatcat ttaatgatca ttcttttgtt aatattactg tctctgcggc ttttggtggt	1560
cttagtagtg ccaatctcgt tgcactgac actactatca atgggtttag ttctttctgt	1620
gttgacacta gacaatttac cattacactg ttttataatg ttacaaacag ttatggttat	1680
gtgtctaaat cacaggatag taattgtcct ttcaccttgc aatctgttaa tgattacctg	1740
tcttttagca aattttgtgt ttcaaccagc cttttggctg gtgctgtac catagatctt	1800
tttggttacc ctgcgttcg tagtggtgtt aagttgacgt ccttttattt tcaattcaca	1860
aaaggtagt tgattactgg cacgcctaaa ccacttgaag gtatcacaga cgtttctttt	1920
atgactctgg atgtgtgtac caagtatact atctatggct ttaaagggtg ggtattatt	1980
acccttaca attctagcat tttggcaggt gtttattata catctgattc tggacagttg	2040
ttagccttta agaatgtcac tagtggtgct gtttattctg tcacgccatg ttctttttca	2100
gagcaggctg catatgttaa tgatgatata gtgggtgtta tttctagttt gtctaactcc	2160
acttttaaca atactaggga gttgctggtt ttcttctacc attctaataa cggtccaat	2220
tgtacagagc ctgtgttggt gtatagtaac atagggtgtt gtaaatctgg cagtattggc	2280
tatgttccat ctgagtatgg ccaagtcaag attgcacca cggttactgg gaatattagt	2340
attcccacca acttttagt tagtattaga acagaatatt tacagcttta caacacgcct	2400
gtagtggtg attgtgtctac atatgtttgt aatggtaact ctggtgttaa acaattactc	2460
accagttaca ctgcagcatg taagaccata gagtcagcat tacaactcag cgctaggctt	2520

-continued

```

gagtcctgttg aagttaactc tatgcttacc atttctgaag aggcctttaca gttagctacc 2580
atcagttcgt ttaatgggtga tggatataac ttactaatg tgctgggtgc tcccggtgac 2640
gatcctgcaa gtggcagggt ggtacaaaaa aggtctgtta ttgaagactt gctttttaat 2700
aaagtgggta ctaatggcct tggactgtt gatgaagact ataagcgtg ttctaattgt 2760
cgctctgttg ctgatctagt ctgtgcgcag tattactctg gtgtcatggt actacctggc 2820
gttgttgacg ctgagaagct tcacatgtac agtgcgtctc tcataggtgg tatggcgcta 2880
ggagggtataa ctgctgcagc ggcattgcct tttagctatg ctgttcaagc gagactcaat 2940
tatcttgctt tacagacgga tgtttctacag cggaaaccagc aattgcttgc tgagtctttt 3000
aactctgcta ttggtaatat aacttcagcc ttgagagtg ttaaagaggc tattagtcaa 3060
actccaagg gtttgaacac tgtggctcat gcgcttacta aggttcaaga ggttgtaaat 3120
tcgcagggtt cagctttgaa ccaacttacc gtacagctgc aacacaactt ccaagccatt 3180
tctagttcta ttgatgacat ttattcccga ctggacatc tttcagccga tgttcagggt 3240
gatcgtctca tcaccggcag attatcagca cttaatgctt ttgttgcca aaccctcact 3300
aagtatactg aggttcaggc tagcaggaaag ctgacacagc aaaagggtta tgagtgcgtc 3360
aaatcgcaat ctacagcgtta cggtttttgt ggtggtgatg gcgagcacat tttctctctg 3420
gtacaggccg cacctcaggg cctgctgttc ttacatacag tacttgtacc ggtgatttt 3480
gtaaatgttc ttgccatgc tggcttatgc gttaatggtg aaattgcctt gactctacgt 3540
gagcctggct tagtcttgtt tacgcctgaa cttcaaaact atactgcgac ggaatatatt 3600
gtttcatcgc gacgtatgtt tgaacctaga aaacctaccg ttagtgattt tgttcaaatt 3660
gagagttgtg tggtcaccta tgtcaatctg actagcgacc agctaccaga tgtaatccca 3720
gattacatcg atgttaacaa aacacttgat gagattttag cttctctgcc caatagaact 3780
ggtccaagtc tccccctaga tgtttttaat gccacttato ttaatcttac tggtgaaatt 3840
gcagatctag agcagcgttc agagtctctc cgtaatacta cagaagagct ccgaagtctc 3900
attaacaaca tcaacaacac acttgttgac cttgagtggc tcaaccgagt tgagacatac 3960
atcaagtggc cgtggtgggt ttggttgatc attgttattg ttctcatctt tgttgtgtca 4020
ttactagtgt tctgctgcat ttccacgggt tgttgtggat gctgcggtg ctgcggtgct 4080
tgtttttcag gttgtgtgag gggctctaga cttcaacctt acgaagcttt tgaaaaggtc 4140
cacgtgcagt ga 4152

```

<210> SEQ ID NO 7

<211> LENGTH: 3768

<212> TYPE: DNA

<213> ORGANISM: SARS coronavirus urbani

<400> SEQUENCE: 7

```

atgtttatct tcttattatt tcttactctc actagtggta gtgacctga ccggtgcacc 60
acttttgatg atgttcaagc tcctaattac actcaacata cttcatctat gaggggggtt 120
tactatcctg atgaaatctt tagatcagac actctttatt taactcagga ttattttctt 180
ccattttatt ctaatgttac agggtttcat actattaato atacgttttg caaccctgtc 240
atacctttta aggatgggtat ttattttgct gccacagaga aatcaaatgt tgtccgtggt 300
tggtgttttg gttctacat gaacaacaag tcacagtcgg tgattattat taacaattct 360

```

-continued

actaatgttg ttatacgagc atgtaacttt gaattgtgtg acaacccttt ctttgctgtt	420
tctaaaccca tgggtacaca gacacatact atgatattcg ataatgcatt taattgcact	480
ttcaggtaca tatctgatgc cttttcgctt gatgtttcag aaaagtcagg taattttaaa	540
cacttacgag agtttggttt taaaaataaa gatgggtttc tctatgttta taagggttat	600
caacctatag atgtagttcg tgatctacct tctggtttta acactttgaa acctattttt	660
aagttgcctc ttggtattaa cattacaaat ttagagcca ttcttacagc cttttcacct	720
gotcaagaca ttgggggac gtcagctgca gcctattttg ttggtatatt aaagccaact	780
acatttatgc tcaagtatga tgaaaatggt acaatcacag atgctgttga ttgttctcaa	840
aatccacttg ctgaactcaa atgctctgtt aagagctttg agattgacaa aggaatttac	900
cagacctcta atttcagggt tgttccctca ggagatgttg tgagattccc taatattaca	960
aacttggtgc cttttggaga ggtttttaat gctactaaat tcccttctgt ctatgcatgg	1020
gagagaaaaa aaatttctaa ttgtgttgcg gattactctg tgctctacaa ctcaacattt	1080
ttttcaacct ttaagtgcga tggcgtttct gccactaagt tgaatgatct ttgcttctcc	1140
aatgtctatg cagattcttt tgtagtcaag ggagatgatg taagacaaat agcgccagga	1200
caaaactggtg ttattgctga ttataattat aaattgccag atgatttcat ggtgtgtgtc	1260
cttgcttga atactaggaa cattgatgct acttcaactg gtaattataa ttataaatat	1320
aggatctta gacatggcaa gcttaggcc tttgagagag acatatctaa tgtgcctttc	1380
tcccctgatg gcaaaccttg caccacacct gctcttaatt gttattggcc attaaatgat	1440
tatggttttt acaccactac tggcattggc taccaacctt acagagtgtg agtactttct	1500
tttgaacttt taaatgcacc ggccacggtt tgtggaccaa aattatccac tgaccttatt	1560
aagaaccagt gtgtcaattt taattttaat ggactcaactg gtactggtgt gttaactcct	1620
tcttcaaaga gatttcaacc atttcaacaa ttggccgtg atgtttctga ttactgat	1680
tccgttcgag atcctaaaac atctgaaata ttagacattt caccttgctc ttttgggggt	1740
gtaagtgtaa ttacacctgg aacaaatgct tcatctgaag ttgctgttct atatcaagat	1800
gttaactgca ctgatgtttc tacagcaatt catgcagatc aactcacacc agcttggcgc	1860
atatattcta ctggaacaa tgtattccag actcaagcag gctgtcttat aggagctgag	1920
catgtcgaca cttcttatga tggcgacatt cctattggag ctggcatttg tgctagtta	1980
catacagttt ctttattacg tagtactagc caaaaatcta ttgtggctta tactatgtct	2040
ttaggtgctg atagttcaat tgcttactct aataacacca ttgctatacc tactaacttt	2100
tcaattagca ttactacaga agtaatgcct gtttctatgg ctaaaacctc cgtagattgt	2160
aatatgtaca tctgcggaga ttctactgaa tgtgctaatt tgcttctcca atatggtagc	2220
ttttgcacac aactaaatcg tgcactctca ggtattgctg ctgaacagga tcgcaacaca	2280
cgtgaagtgt tcgctcaagt caaacaaatg tacaaaacct caactttgaa atattttgt	2340
ggttttaatt ttccacaaat attacctgac cctctaaagc caactaagag gtcttttatt	2400
gaggacttgc tctttaataa ggtgacactc gctgatgctg gcttcattgaa gcaatatggc	2460
gaatgcctag gtgatattaa tgctagagat ctcatattgt cgcagaagtt caatggactt	2520
acagtgttgc cacctctgct cactgatgat atgattgctg cctacactgc tgctctagtt	2580
agtgttactg ccaactgctg atggacattt ggtgctggcg ctgctcttca aatacctttt	2640

-continued

```

gctatgcaaa tggcatatag gttcaatggc attggagtta cccaaaatgt tctctatgag 2700
aaccaaaaac aaatcgccaa ccaatttaac aaggcgatta gtcaaattca agaactactt 2760
acaacaacat caactgcatt gggcaagctg caagacgttg ttaaccagaa tgctcaagca 2820
ttaaacacac ttgttaaaca acttagctct aattttggtg caatttcaag tgtgctaaat 2880
gatatccttt cgcgacttga taaagtcgag gcggaggtag aaattgacag gttaattaca 2940
ggcagacttc aaagccttca aacctatgta acacaacaac taatcagggc tgctgaaatc 3000
agggctcttg ctaatcttgc tgctactaaa atgtctgagt gtgttcttgg acaatcaaaa 3060
agagttgact tttgtgaaa gggctaccac cttatgtcct toccacaagc agccccgcat 3120
ggtgttgtct tcctacatgt caggtatgtg ccatcccagg agaggaactt caccacagcg 3180
ccagcaatth gtcataagag caaagcatac ttccctcgtg aaggtgtttt tgtgtttaat 3240
ggcacttctt ggtttattac acagaggaac ttcttttctc cacaataaat tactacagac 3300
aatacatttg tctcaggaaa ttgtgatgtc gttattggca tcattaacaa cacagtttat 3360
gatcctctgc aacctgagct cgactcattc aaagaagagc tggacaagta cttcaaaaat 3420
catacatcac cagatgttga tcttgccgac atttcaggca ttaacgcttc tgcgtcaaac 3480
attcaaaaag aaattgaccg cctcaatgag gtcgctaaaa atttaaatga atcactcatt 3540
gaccttcaag aattgggaaa atatgagcaa tatattaaat ggccttggtg tgtttggctc 3600
ggcttcattg ctggactaat tgccatcgtc atggttacaa tcttgctttg ttgcatgact 3660
agttgttgca gttgcctcaa ggggtcatgc tcttggtggt cttgctgcaa gtttgatgag 3720
gatgactctg agccagttct caagggtgtc aaattacatt acacataa 3768

```

<210> SEQ ID NO 8

<211> LENGTH: 3768

<212> TYPE: DNA

<213> ORGANISM: SARS coronavirus Tor2

<400> SEQUENCE: 8

```

atgtttatth tcttattatt tottactctc actagtggta gtgacctga ccggtgcacc 60
acttttgatg atgttcaagc tcttaattac actcaacata cttcatctat gagggggggt 120
tactatcctg atgaaattht tagatcagac actctttatt taactcagga tttatttctt 180
ccattttatt ctaatgttac agggtttcat actattaatc atacgttttg caaccctgtc 240
atacctthta aggatgggat ttattttgct gccacagaga aatcaaatgt tgcctgtggt 300
tgggtttttg gttctaccat gaacaacaag tcacagtcgg tgattattat taacaattct 360
actaatgttg ttatacagac atgtaactth gaattgtgtg acaaccctth ctttgctgtt 420
tctaaacca tgggtacaca gacacatact atgatattcg ataatgcatt taattgcact 480
ttcgagtaca tatctgatgc cttttcgctt gatgtttcag aaaagtcagg taattthtaa 540
cacttacgag agtttgtgtt taaaaataaa gatgggtthc totatgttht taagggttat 600
caacctatag atgtagtctg tgatctacct tctggtthta acactttgaa acctattht 660
aagttgcctc ttggtattaa cattacaaat ttagagcca ttcttacagc cttttcacct 720
gctcaagaca tttggggcac gtcagctgca gcctatthtg ttggtattht aaagccaact 780
acatttatgc tcaagtatga tgaaaatggt acaatcacag atgctgttga ttgttctcaa 840
aatccacttg ctgaactcaa atgctctgtt aagagctthg agattgacaa aggaatttht 900

```

-continued

cagacctcta atttcaggg	tgttccctca ggagatgtg	tgagattccc taatattaca	960
aacttgtgtc cttttggaga	ggtttttaaat gctactaaat	tcccttctgt ctatgcatgg	1020
gagagaaaaa aaatttctaa	ttgtgttgct gattactctg	tgctctacaa ctcaacattt	1080
ttttcaacct ttaagtgtca	tggcgtttct gccactaagt	tgaatgatct ttgcttctcc	1140
aatgtctatg cagattcttt	tgtagtcaag ggagatgatg	taagacaaat agcgccagga	1200
caaactgggtg ttattgctga	ttataattat aaattgccag	atgatttcat gggttgtgtc	1260
cttgcttggg atactaggaa	cattgatgct acttcaactg	gtaattataa ttataaatat	1320
aggtatctta gacatggcaa	gcttaggccc ttgagagag	acatatctaa tgtgcctttc	1380
tcccctgatg gcaaaccttg	caccccacct gctcttaatt	gttattggcc attaaatgat	1440
tatgggtttt acaccactac	tggcattggc taccaacctt	acagagttgt agtactttct	1500
tttgaacttt taaatgcacc	ggccacgggt tgtggaccaa	aattatccac tgaccttatt	1560
aagaaccagt gtgtcaattt	taattttaat ggactcactg	gtactggtgt gttaactcct	1620
tcttcaaaga gatttcaacc	atttcaacaa ttggccgtg	atgtttctga ttctactgat	1680
tccgttcgag atcctaaaac	atctgaaata ttagacattt	caccttgccg ttttgggggg	1740
gtaagtgtaa ttacacctgg	aacaaatgct tcatctgaag	ttgctgttct atatcaagat	1800
gttaactgca ctgatgtttc	tacagcaatt catgcagatc	aactcacacc agcttggcgc	1860
atatattcta ctggaacaa	tgtattccag actcaagcag	gctgtcttat aggagctgag	1920
catgtcgaca cttcttatga	gtgcgacatt cctattggag	ctggcatttg tgctagttag	1980
catacagttt ctttattacg	tagtactagc caaaaatcta	tttggtgctta tactatgtct	2040
ttaggtgctg atagttcaat	tgcttactct aataacacca	ttgctatacc tactaacttt	2100
tcaattagca ttactacaga	agtaatgcct gtttctatgg	ctaaaacctc cgtagattgt	2160
aatatgtaca tctgcggaga	ttctactgaa tgtgctaatt	tgttctcca atatggtagc	2220
ttttgcacac aactaaatcg	tgactctca ggtattgctg	ctgaacagga tcgcaacaca	2280
cgtgaagtgt tcgctcaagt	caaacaaatg tacaaaacc	caactttgaa atattttgg	2340
ggttttaatt ttccacaaat	attacctgac cctctaaagc	caactaagag gtcttttatt	2400
gaggacttgc tctttaataa	ggtagacctc gctgatgctg	gcttcataaa gcaatatggc	2460
gaatgcctag gtgatattaa	tgctagagat ctcatgtgtg	cgcagaagtt caatggactt	2520
acagtgttgc cacctctgct	cactgatgat atgattgctg	cctacactgc tgcctagtgt	2580
agtgttactg ccaactgctg	atggacattt ggtgctggcg	ctgctcttca aatacctttt	2640
gctatgcaaa tggcatatag	gttcaatggc attggagtta	cccaaatgt tctctatgag	2700
aaccaaaaac aaatcgccaa	ccaatttaac aaggcgatta	gtcaaattca agaatacatt	2760
acaacaacat caactgcatt	gggcaagctg caagacgttg	ttaaccagaa tgcctcaagca	2820
ttaaacacac ttgttaaaca	acttagctct aattttgggt	caatttcaag tgtgctaaat	2880
gatatccttt cgcgacttga	taaagtcgag gcggaggtag	aaattgacag gttaattaca	2940
ggcagacttc aaagccttca	aacctatgta acacaacaac	taatcagggc tgcctgaaatc	3000
agggtctctg ctaatcttgc	tgctactaaa atgtctgagt	gtgttcttgg acaatcaaaa	3060
agagttgact tttgtgaaa	gggctaccac cttatgtcct	tcccacaagc agccccgcat	3120
ggtgttgtct tcctacatgt	cacgtatgtg ccatcccagg	agaggaaact caccacagcg	3180

-continued

```

ccagcaattt gtcataaagg caaagcatac ttccctcgtg aaggtgtttt tgtgtttaat 3240
ggcacttcctt ggttttattac acagaggaac ttcttttctc cacaataat tactacagac 3300
aatacatttg ttcaggaaa ttgtgatgac gttattggca tcattaacaa cacagtttat 3360
gatcctctgc aacctgagct tgactcattc aaagaagagc tggacaagta cttcaaaaat 3420
catacatcac cagatgttga tcttgccgac atttcaggca ttaacgcttc tgcgtcaac 3480
attcaaaaag aaattgaccg cctcaatgag gtcgctaaaa atttaaatga atcactcatt 3540
gaccttcaag aattgggaaa atatagcaa tatattaaat ggccttggtg tgtttggctc 3600
ggcttcattg ctggactaat tgccatcgtc atgggtacaa tottgctttg ttgcatgact 3660
agttgttgca gttgcctcaa ggggtcatgc tcttggtgtt cttgctgcaa gtttgatgag 3720
gatgactctg agccagtctt caagggtgtc aaattacatt acacataa 3768

```

<210> SEQ ID NO 9

<211> LENGTH: 4092

<212> TYPE: DNA

<213> ORGANISM: Bovine coronavirus

<400> SEQUENCE: 9

```

atgtttttga tacttttaat ttccttacca atggcttttg ctgttatagg agatttaaag 60
tgtactacgg ttccattaa tgatgttgac accggtgctc cctctattag cactgatatt 120
gtcagatgta ctaatggttt aggtacttat tatgttttag atcgtgtgta tttaaatact 180
acgttgttgc ttaatggtta ctacctact tcaggttcta catatcgtaa tatggcactg 240
aagggaaatt tactattgag cagactatgg tttaaaccac cttttcttcc tgattttatt 300
aatggtattt ttgctaaggt caaaaatacc aaggttatta aaaagggtgt aatgtatagt 360
gagtttcctg ctataactat aggtagtact tttgtaaata catcctatag tgtggtagta 420
caaccacata ctaccaattt ggataataaa ttacaaggtc tcttagagat ctctgtttgc 480
cagtatacta tgtcgagta cccacatacg atttgcctc ctaagctggg taataaacgc 540
gtagaactat ggcattggga tacaggtgtt gtttcctgtt tatataagcg taatttcaca 600
tatgatgtga atgctgatta cttgtatttc catTTTTtato aagaagggtg tactttttat 660
gcatatttta cagacactgg tgttggtact aagtttctgt ttaatgttta tttaggcacg 720
gtgctttcac attattatgt cctgcctttg acttgttcta gtgctatgac tttagaatat 780
tgggttacac ctctcacttc taaacaatat ttactagctt tcaatcaaga tgggtttatt 840
tttaatgctg ttgattgtaa gagtgttttt atgagtgaga ttaagtgtaa aacactatct 900
atagcaccat ctactggtgt ttatgaatta aacggttaca ctgttcagcc aattgcagat 960
gtttaccgac gtatacctaa tcttcccgat tgtaatatag aggccttggt taatgataag 1020
tcggtgccct ctccattaaa ttgggaacgt aagacctttt caaattgtaa ttttaatatg 1080
agcagcctga tgtcttttat tcaggcagac tcatttactt gtaataatat tgatgctgct 1140
aagatatatg gtatgtgttt ttccagcata actatagata agtttgctat acccaatggt 1200
aggaaggttg acctacaatt gggcaatttg ggctatttgc agtcttttaa ctatagaatt 1260
gatactactg ctacaagttg tcagttgtat tataatttac ctgctgctaa tgtttctgtt 1320
agcaggttta atccttctac ttggaatagg agatttggtt ttacagaaca atttgTTTT 1380
aagcctcaac ctgtaggtgt ttttactcat catgatgttg tttatgcaca acattgtttt 1440

```

-continued

aaagctccca aaaatttctg tccgtgtaaa ttggatgggt ctttgtgtgt aggtaatggt	1500
cctggtatag atgctgggta taaaaatagt ggtataggca cttgtcctgc aggtactaat	1560
tatttaactt gccataatgc tgcccaatgt gattgtttgt gcactcccg cccattaca	1620
tctaaatcta cagggcctta caagtgcgcc caaactaaat acttagttgg cataggtgag	1680
cactgttcgg gtcttgctat taaaagtgat tattgtggag gtaatccttg tacttgccaa	1740
ccacaagcat ttttgggttg gtctgttgac tctgttttac aaggggatag gtgtaatatt	1800
tttgctaatt ttatttttca tgatgttaat agtggtacta cttgttctac tgatttaca	1860
aatcaaaca cagacataat tcttggtggt tgtgttaatt atgatcttta tggattaca	1920
ggccaaggta tttttgttga ggtaaatgag acttattata atagttggca gaaccttta	1980
tatgattcta atggtaatct ctatggtttt agagactact taacaaacag aacttttatg	2040
attcgtagtt gctatagcgg tcgtgtttca gcggccttcc atgctaactc ttccgaacca	2100
gcattgctat ttcggaatat taaatgcaat tacgttttta ataatactct ttcacgacag	2160
ctgcaaccta ttaactatth tgatagttat cttggttggt ttgtcaatgc tgataatagt	2220
acttctagtg ttgttcaaac atgtgatctc acagtaggta gtggttactg tgtggattac	2280
tctacaaaaa gacgaagtcg tagagcgatt accactgggt atcgggttac taattttgag	2340
ccattttactg ttaattcagt aaatgatagt ttagaacctg taggtgggtt gtatgaaatt	2400
caaatacctt cagagtttac tataggtaat atggaggagt ttattcaaac aagctctcct	2460
aaagttacta ttgattgttc tgcttttgct tgtggtgatt atgcagcatg taaatcacag	2520
ttggttgaat atggtagctt ctgtgacaat attaatgcta tactcacaga agtaaatgaa	2580
ctacttgaca ctacacagtt gcaagtagct aatagtttaa tgaatgggtg cactcttagc	2640
actaagctta aagatggcgt taatttcaat gtagacgaca tcaatttttc ccctgtatta	2700
ggttgttttag gaagcgcttg taataaagtt tccagcagat ctgctataga ggatttactt	2760
ttttctaaag taaagttatc tgatgtcggg ttcgttgagg cttataataa ttgtactgga	2820
gggtccgaaa ttagggacct catttgtgtg caaagttata atggtatcaa agtgttcct	2880
ccactgtctc cagtaaatca gatcagtga tacactttgg ctgccacctc tgctagtctg	2940
tttctcctt tgctcagcgc agtaggtgta ccattttatt taaatgttca gtatcgtatt	3000
aatgggattg gtgttaccat ggatgtgtta agtcaaaatc aaaagcttat tgctaattgca	3060
tttaacaatg ctcttgatgc tattcaggaa gggtttgatg ctaccaattc tgetttagtt	3120
aaaattcaag ctgttggtta tgcaaatgct gaagctctta ataacttatt gcaacaactc	3180
tctaatagat ttggtgctat aagttcttct ttacaagaaa ttctatctag actggatgct	3240
cttgaagcgc aagctcagat agacagactt attaatgggc gtcttaccgc tcttaatgtt	3300
tatgtttctc aacagcttag tgattctaca ctagtataat ttagtgcagc acaagctatg	3360
gagaagggtta atgaatgtgt caaaagccaa tcatctagga taaatttttg tggtaatggt	3420
aatcatatta tatcattagt gcagaatgct ccatatgggt tgtattttat ccactttagc	3480
tatgtcccta ctaagtatgt cactgcgaag gttagtcccg gtctgtgcat tgctggtgat	3540
agaggatag ccctcaagag tgggtatttt gttaatgtaa ataactttg gatgttcact	3600
ggtagtggtt attactacct tgaaccata actggaaata atgttggtgt tatgagtacc	3660
tgtgctgtta actatactaa agcgccggat gtaatgctga acatttcaac acccaacctc	3720

-continued

```

catgatttta aggaagagtt ggatcaatgg tttaaaaacc aaacatcagt ggcaccagat 3780
ttgtcacttg attatataaa tgttacattc ttggacctac aagatgaaat gaatagggtta 3840
caggaggcaa taaaagtttt aaatcagagc tacatcaato tcaaggacat tggtagatat 3900
gagtattatg taaatggcc ttggtatgta tggcttttaa ttggctttgc tgggttagct 3960
atgcttgttt tactattctt catatgctgt tgtacaggat gtgggactag ttgttttaag 4020
atatgtgggtg gttgtgtgta tgattatact ggacaccagg agttagtaat taaaacatca 4080
catgacgact aa 4092

```

<210> SEQ ID NO 10

<211> LENGTH: 4050

<212> TYPE: DNA

<213> ORGANISM: Porcine hemagglutinating encephalomyelitis coronavirus

<400> SEQUENCE: 10

```

atgtttttta tacttttaat ctccctgcct tctgcttttg cagttatagg ggatttaaag 60
tgtactactt cattaattaa tgacgttgac actggtgtgc catctattag ctctgaagtt 120
gttgatgtca ctaatgggtt ggggactttc tatgttttag atcgtgtcta tttaaatacc 180
acattgttgc tcaatgggta ttacccaatt tcagggtgcta catttcgtaa tatggctctg 240
aaaggaaactc gattattgag caccttgtgg ttttaagccgc cttttttatc accttttaat 300
gatggtatgt ttgccaaagt taaaacacgc agattttcta aagatggtgt tatttatagt 360
gagtttcctg ctattactat aggtagtact tttgtaaata cttcctatag catagtagta 420
gagcctcata cctcacttat taatggtaat ttacaaggtt tgttgcaaat ttctgtttgt 480
caatacacta tgttgtgaata cccacatact atttgcac ctaatttggg taatcaacgc 540
atagaattat ggcattatga cacagatgtt gtttcttgtt tatacaggcg taatttcaca 600
tatgatgtga atgctgatta tttatatatt cactttttatc aggaaggttg cactttttat 660
gcatacttta cagatactgg ttttgtgacc aagtttctgt ttaagttgta tttaggcact 720
gtgctgtcac attattatgt tatgccattg acttgaata gogctttatc tttagaatac 780
tgggttacac ctctcactac tagacaattt cttctagcct ttgaccagga tgggttttta 840
taccatgctg ttgattgtgc tagtgatttt atgagtgaga ttatgtgtaa aacttcttca 900
attacaccac ctactggtgt ttatgaacta aacggttaca cagttcaacc tgttgccact 960
gtatatcgta gaatacctga tttaccaaat tgcgatatcg aagcttggct taattctaag 1020
accgtttctt cgcctcttaa ttgggaacgt aaaatttttt ctaattgtaa ttttaacatg 1080
ggcaggctga tgtcttttat tcaggctgac tcttttggtt gtaacaatat tgatgcttct 1140
cgcttatatg gtatgtgttt tggtagcatt actattgata agtttgctat acccaatagt 1200
agaaagggtg atctgcaagt gggtaaatct ggttatttac aatcttttaa ttataagatt 1260
gacactgctg ttagcagttg tcaactctat tatagtttgc ctgcagcaaa cgtatctgtc 1320
actcattata atccttcac ttggaataga aggtatgggt ttaataatca gagttttggt 1380
tccagaggcc ttcattgatgc tgtttattca cagcaatgtt ttaatacacc taacacatat 1440
tgtccttgta gaacaagtca atgcataggt ggtgcaggca caggaaactg tcctgtaggc 1500
accactgtgc gcaagtgttt tgctgcagtt acaaaagcta ctaagtgtac ttgctgggtg 1560
caaccagatc ctccacata taaagggtga aacgcctgga cttgtccgca atctaaagtt 1620

```


-continued

tctatacaac caggtcagca ttgccctggt ttgggtcttg tggaggatga ttgctctggc	1680
aacccttgca cttgtaaac accaggctttc ataggctgga gttcagaaac ttgtttgcaa	1740
aatggtaggt gtaatatattt tgctaatttt attctgaatg atgttaatag cggtaacaacc	1800
tgttctactg atttacaaca gggtaatact attattacta ctgatgtttg tgttaattat	1860
gacctatatg gcattacagg ccagggcata cttatagaag ttaatgccac ttattataat	1920
agttggcaga atcttcttta tgattctagt ggtaatctct atggctttag agattattta	1980
tcaaatagaa cttttcttat tcgtagctgc tatagtggaa gagtttcagc agtttttcat	2040
gctaactcat ctgaaccagc tttgatgttt cgtaacttta aatgcagcca cgtttttaat	2100
aataccattt taagacaaat acagcttggt aactattttg atagttacct tggttgtgtt	2160
gttaatgctt ataataatac agctagtgtt gtaagtactt gtgatttaac cgttggtagc	2220
ggctattgtg ttgattatgt tacagcactt agatcacgta gatcttttac tacaggttat	2280
cgtttacta attttgaacc atttgccgtt aatttggtta atgatagtat agaacctgtt	2340
ggtggtttgt atgaaataca gataccttca gagtttacca ttggttaatt agaagagttc	2400
attcaaacga gatcccttaa ggttactata gactgtgcta catttgtttg tggtgactat	2460
gcagcatgta gacaacagtt agctgagtat ggtagttttt gtgagaacat taatgctata	2520
ctcacagaag taaatgaact acttgacact acacagttgc aagtagctaa tagtttaatg	2580
aatggagtc aacctagtac caagattaag gatggcatta atttcaatgt tgacgatatc	2640
aacttctccc ctgtattagg ttgttttaga agcgaatga atagagcttc cactagatct	2700
gctatagagg atttactttt tgataaaagta aaattgtctg atgtcggctt tgtacaggcc	2760
tataataact gcactggagg tgccgaaatt agggatctca tttgtgtgca aagttataat	2820
ggtatcaaag tgttgccctc attgttatct gaaaatcaga tcagtggcta cactttggca	2880
gccaccgctg ctagcttatt ccctccttg acagctgcag caggtgtacc attttattta	2940
aatgttcagt atcgtataaa tgggcttggc gtcactatgg atgtgctaag tcaaaaccaa	3000
aagcttattg ctagtgcatt taacaatgct cttgatgcta tcaggaagg gttcgacgca	3060
accaattctg ctttagttaa aattcaggct gttgttaatg caaatgctga agcacttaat	3120
aacttattgc agcaactctc taacagattt ggtgccataa gtgcctcttt acaagaaatt	3180
ttatccaggc tcgatgctct tgaagctaaa gtcagatag acagacttat caatgggcgt	3240
ctcaccgctc ttaatgctta tgtttctcag cagcttagtg attctacact agtaaaattt	3300
agtgcagcac aagctattga gaaagttaat gaatgtgta aaagccaatc atctaggata	3360
aatttctgtg gtaatggtaa tcatattata tcattagtac agaatgctcc atatggtttg	3420
tattttatcc attttagcta tgtccccacc aagtatgtta cagcaaagg tagtcctggt	3480
ttgtgcattg ctggcgatat aggaatatcg cctaagagtg gttattttat taatgtaaat	3540
aattcttggg tgttactgtg tagtagctat tactaccctg aacctataac ccaaaataat	3600
gttggttgta tgagtacctg tgctgttaat tatactaaag caccggatct aatgctgaac	3660
acatcgacac ccaaccttcc tgacttcaag gaagaattgt atcaatggtt taaaaaccaa	3720
tcttcagtgg caccagattt gtcacttgat tatattaatg ttacgttctt ggacctacaa	3780
gatgaaatga ataggttaca agaggctata aaagttttta atcagagcta catcaatctc	3840
aaggacattg gtacatatga gtattatgtg aaatggcctt ggtatgtatg gcttttaatt	3900

-continued

```

ggccttgctg gtgtagctat gcttgtttta ctattcttca tatgctgctg tacaggatgt 3960
gggactagtt gttttaagaa atgtggcggt tgttgtagtg attatactgg acaccaggag 4020
tttghtaatca aaacttcaca tgacgattaa 4050

```

```

<210> SEQ ID NO 11
<211> LENGTH: 4086
<212> TYPE: DNA
<213> ORGANISM: Murine hepatitis virus

```

```

<400> SEQUENCE: 11

```

```

atgctattcg tgtttttaac cttgttgccc tcttctctag ggtatattgg tgattttaga 60
tgtatccaac ttgtaaatac cgacacctct aatgccagcg ctccaagcgt tagtacagag 120
gtagttgatg ttccaaaagg gattggtact tattatgttt tagatcgagt ctattttaa 180
gccacactat tgcttactgg ttattacct gtagatgggt ccatgtatag aaacatggct 240
ctaacgggaa ttaataccat aagccttaat tggtaaaaac cacccttttt atcagagttt 300
aatgatggca tatttgctaa ggtaaaagac cttaaagcat ctttgcccaa agattctatt 360
tcatatattcc ctactataat tataggtagt aattttgtca ccacttccta tactgtagta 420
ttggaaccgt ataatgggtat aattatggca tccatttgcc agtataccat ttgtcaacta 480
ccgtacacgg attgcaaac gaatacgggc ggtaataagt taattggctt ttggcacaca 540
gagctaaaat cccctgtgtg cattttaaag cgtaatttta cgtttaatgt taatgccgaa 600
tggctttatt ttcattttta ccagcagggt ggtacttttt atgcgtatta tgcggatgtt 660
tcttctgcta ctacgttttt gtttagtagt tatattgggt atgtgttaac acaatatatt 720
gtgttgccct atagtgttac tctcactaca acagggtgtc tttcaccgca gtattgggtt 780
acacctcttg tcaagcgcca atatttattt aattttaatc aaaagggtat tattactagt 840
gctgttgatt gtgctagtag ttataccagc gaaataaagt gtaagacca aagtatgaat 900
cccaatacgg gagtttatga tttatccggt tacaccgtcc aacctgtagg attagtgtac 960
cggcgtgtta gaaatttgcc tgattgtaaa attgaggaat ggctaactgc taagtctgta 1020
ccttctctc tcaattggga gcgcaaaaca tttcaaaatt gtaacttcga cctgagcagt 1080
ctattaagat ttgttcaggc tgagtcactc tcatgtagta atatagatgc ttccaagggt 1140
tatggtatgt gctttgtagt tatatctata gacaagttag cgatacccaa tagacgccga 1200
gttgatttgc agctaggcaa ctctgggttt ttgcaatcct ttaattacaa aatagataga 1260
agagctactt cgtgtcagct ctattatagt cttgcaaaaa ataatgtcac tgtcaataac 1320
cataaccogt cctcttgga caggcggtat gggttcaatg atgtggctac atttggaact 1380
ggtaaacatg acgttgctta tgctgaggct tgttttaccg tgggagcatc atattgccct 1440
tgcggaacc ccagcatagt gtgcgccatg accactggaa aacctaactt tgccaattgc 1500
cctacaggca cctcgaaatg tgagtgcact gttatgcat ttggtaataa tcaatttaag 1560
tgtgattgca cttgtaaccc tagtctctca accacctatg atcttagatg tctccaagca 1620
agaagcatgc ttggcgtagg tgatcattgt gaaggcttag gagttttaga agataaatgt 1680
gggtggcagca acacctgcaa ttgttctgct catgcctttg ttggtggggc taaggatagt 1740
tgcttggtca atggccgctg tcacattttt agtaatttga tgttaaatgg cattaatagt 1800
ggtactacat gttccatgga tttgcaattg cctaatactg aagtggtcac tggcgtctgc 1860

```

-continued

gtcaaatatg acctctacgg tataacaggc caaggtatgt ttaaggaggt taaggctgac	1920
tattatcata gttggcaaaa cctcttatat gatgttaatg gcaacttaat cggatttcgc	1980
gattttgttg ctaataagag ttatactatt cgaagttgct atagtggcg ggtctcggct	2040
gcataatcatc aagatgcacc agaaccagcg ctactatata gcaatttaaa atgtgactat	2100
gtctttaaca acaacatata ccgtgaggag acaccactta actatttcga tagttatctt	2160
ggttggtgtg ttaatgctga caactcaact gaagaagctg ttgacgcgtg tgatttgctg	2220
atgggtagtg ggctttgtgt caactattca acgtctcacc ggcctcgcag ctctgtcagc	2280
acgggttata aattaactac ttttgaacca ttacagtcgc gcaattgtcaa tgatagtgtt	2340
gagctctgtg atgggttata tgagctgcaa ataccaacca actttactat agctagccat	2400
caggagttcg ttcaaacgag gtctccaaag gttactatag actgtgctgc atttgtctgt	2460
ggtggccaca cagcatgccg tcagcagttg gttgagtacg gctcattctg tgataatatt	2520
aatgccattc ttggcgaggt aaataacctc atagatacta tgcaacttca agtgcaagt	2580
gctttaatcc aaggtgtcac gttaaagctc cgcttatcgg atggcattgg tggtaaata	2640
gatgatatta attttagtcc tctgcttggt tgtttaggtt ctgactgtgg cgaagtacc	2700
atggcagctc aaaccggagc atctgctata gaggatgtat tatttgaaa agtcaaaactc	2760
tctgatgttg gctttgtcga agcatataac aattgcaact gaggcgaaga agttagagac	2820
ctactttgtg tgcaatcttt taatggcacc aaagtgtcac cgctgtgtt gtctgagaat	2880
caaatttctg gttatacagc gggagctact gtatctgcta tgttccatg gtctgcagct	2940
gcagggtgac cattttcttt aagtgttcaa tatagaatta atggctcttg tgcactatg	3000
aatgttctta gtgaaatca gaaatgata gcaagtgcac ttaacaacgc gataggtgct	3060
atacaggaag ggtttgctgc aaccaattct gccttagcaa aaatgcagtt cgttgtcaat	3120
gcaaatgcgg aagcactcaa taatttatta aaccagcttt ccaataggtt tggtgcaatt	3180
agtgtctctt tacaagaaat tctatctcgc ctagatgtc ttgaagcga ggctcagata	3240
gaccgtctta ttaatggcag attaaactga cttaatgcac atgtctctaa gcagctgagt	3300
gacatgacct ttgttaaggt gagtgcagcc caggctatag agaaagttaa tgagtgtgtt	3360
aaaagccaat catctaggat aaatttctgt ggcaatggca atcatatatt gtcattagtc	3420
cagaatgcgc cttatggttt atattttatt catttcagct atgtgcctac ttcctttaca	3480
acggcaaatg tgagtctctg gctatgcatt tctgggtgata gaggattagc acctaaagct	3540
ggatattttg ttcaagatga tggagagtgg aagttcacag gtagtaatta ttattaccct	3600
gaaccattta cagataaaaa tagtgtcgtg atgagtagtt gcgcagcaaa ctacacaaag	3660
gcacctgaag ttttcttgaa cacttcaata cctaactcac ccgactttaa ggaggagtta	3720
gataaatggt ttaaaaatca gacgtctatt gcgcctgatt tatctctcga tttcgagaaa	3780
ttaaacgtta ccctcctgga cctgactgat gagatgaaca ggattcagga tgcaattaag	3840
aagttaaatg agagttacat caacctcaag gacgttgcca catatgaaat gtatgtgaaa	3900
tggccttggt atgtgtggtt gctaattgga ttagctgggt tagctgtttg tgtgtgttta	3960
tttttcatat gttgctgcac ggggtgtggc tcatgttgtt tcaagaagtg tggaaattgt	4020
tgtgatgagt gtggaggaca ccaggacagt attgtgatac ataatatatt ctctcatgag	4080
gattga	4086

-continued

<210> SEQ ID NO 12

<211> LENGTH: 4083

<212> TYPE: DNA

<213> ORGANISM: Rat coronavirus

<400> SEQUENCE: 12

atgctattcg tgtttttaac cctattgccc tcttgctag ggtatattgg tgattttaga	60
tgtatcaacc ttgtaaacac ccgcatttct aatgcgcgcg caccagtggt tagcacagag	120
gtagttgatg tttctaagg tcttggtaca tattacgttt tagatcgtgt ttattttaa	180
gccacgttat tgcttactgg ttactacct gtagatgggt coactgtatc taacatggct	240
ctaattggga ctaataacct aagccttaat tggtttgaa cgccttttt atcagagttt	300
aacgatggca tatatgctaa ggtaagaac ctcaaagcat cttgcccac aggcctggct	360
tcatactttc ctactataat tataggtagt aattttgta atacttccta tactgtagta	420
ttggaacct acaatgggtat tattatggca tctatttgc agtataccat ttgtcaatta	480
ccgcacacgg attgcaaacc taacacgggc ggtaacacgc taattggttt ttggcacaca	540
gatttaaggc ctccggtgtg cattttaaag cgtaatttta cgtttaatgt taatgccga	600
tggctttatt ttcatTTTT ctagcagggt ggtacttttt atgcgtatta tgcagatgtt	660
tcttctgcc ctacgttttt gtttagttcg tatattgtg ctgtgttaac acagtatttt	720
gtgttgccct atagtgtag tccactacc tcagggtttt cctcaccga gtattgggtt	780
acaccacttg ttaagcgcca atatttattt aattttaacc aaaagggtat tattactagc	840
gctgttgatt gtgctagtag ttataccagt gaaataaagt gtaagactca aagtatgaat	900
cccaatacgg gagtctatga tttatccggt tacaccgtcc aacctgtagg actagtgtac	960
cggcgtgtta gaaatttgc tgattgtaaa attgaggaat ggttggctgc taacacagta	1020
ccctctctc tcaattggga gcgcaaaaca tttcaaaatt gtaacttcaa cctgagcagt	1080
ctattaagat ttgttcaggc tgagtcactc tcatgtagta atatagatgc ttccaagggt	1140
tatggaatgt gctttggtag catatctata gataaattg caatacccaa cagtcgccgt	1200
gttgatcttc agctaggtaa atcgggtctt ttgcaatctt ttaattataa aattgataca	1260
agagcgacct cgtgtcagct ctattacagt cttgcacaag ataatgtcac tgcattaac	1320
cacaacccat cctcctggaa taggcgttat ggatttaatg acgtggctac atttcatagt	1380
ggatgaacatg acgttgctta tgcagaggca tgtttcactg ttggagcttc atattgccct	1440
tgtgcgaagc ccagcacagt ctattcatgt gtcacaggta aacctaatgc tgctaattgc	1500
ccaacaggta cctcgaatcg tgagtgtaat gttcaggctt caggttttaa gtctaagtgc	1560
gattgcacat gtaaccctag tcctctaacc acctatgac ctatagttct tcaagcgcg	1620
agcatgcttg gcgtagggtg tcattgtgaa ggtctaggta ttttagaaga taaatgtggt	1680
ggcagcaaca tatgcaattg ttccggtgat gcctttgtg gctgggctat ggacagctgt	1740
ctatctaattg cccgctgcca ttttttagt aatttgatgt taaatggcat taatagtgg	1800
actacatgtt ccacggattt tcaattgcct aatacgaag tggcactgg cgtttgtgtc	1860
aagtatgacc tctacggtag tacaggccaa ggtgttttta aggaggttaa ggctgattat	1920
tacaatagtt ggcaaacct cttatatgat gttaattgta acttaaatgg tttccgtgac	1980
attgttacca ataagactta tttattaaga agttgctata gtgggcgcgt ttccgctgca	2040

-continued

tatcatcaag atgcacctga accagcgcta ctatatcgca atttaaaatg tgattatgtg	2100
tttaataaca acatatcccg tgaggagaca ccacttaact attttgatag ttatttgggt	2160
tgtgttatta atgctgataa ctcaactgag cagtctgttg acgcgtgtga ttgctgtatg	2220
ggtagtgggc tttgtgtcaa ctattcaatc gtcaccgtg cgcgaggtc tgcagtacg	2280
ggttataaat taactacttt tgaacctatt acagtcagca ttgtcaatga tagtgttgag	2340
tctgttgggt gattatatga gatgcaata cctactaatt ttactatagc tagccatcag	2400
gagttcattc aaacgaggto tccgaagggt actatagatt gtgctgcatt tgtctgtggt	2460
gattatacag cgtgtagaca acagttgggt gattatggct ctttttgtga taatattaat	2520
gccattcttg gcgaggtgaa taacctcata gatactatgc aattacaagt tgctagtgtc	2580
ctgatccaag gtgtcacgct aagttcacgc ttggcagatg gcctctcagg tcagattgat	2640
gatattaatt ttagtcctct tctaggttgc cttggctcag attgtagcga aggcaccaag	2700
gcagcgcaag ggcgatctgc tatagaggat gtattatttg ataaggtaa actctctgat	2760
gttggctttg tcgaatcata taataattgc actggaggto aagaagttag agacctactt	2820
tgtgtgcaat cttttaatgg cattaaagt ctaccgcctg tattatccga gagtcaaatc	2880
tctggttata cagcgggagc tactgcatct gctatgttcc ctccatggtc tgcagctgca	2940
ggtgtgccaat ttgctttaag tgttcaatat agaattaatg gtcttggtgt cactatgaat	3000
gttcttagtg aaaaccagaa aatgatagct agttcattta acaacgcgat aggtgctata	3060
caggaagggt tcgatgcaac caattctgct ttagcgaataa ttcagtcctg tgcacgca	3120
aatgcagaag cactcaataa ccttttgaat cagctttcca ataggtttg tgcaattagt	3180
gcttctttac aggaaattct atctgcctc gatgctcttg aagctcaggc tcagatagac	3240
cgtcttatta atggcagatt aactgcactt aatgcatatg tctctaagca gctgagcgac	3300
atgacctta ttaagtgtag tgctgccag gctatagaga aagttaatga gtgtgttaaa	3360
agccaatcac ctaggataaa tttctgtggc aatggcaatc atatattgtc attagtccag	3420
aatgcgcctt acggtttata ttttattcat ttcagctatg tgcctacatc ctttacaacg	3480
gtaaatgtga gtctggact atgcatttct ggtgatagag gattagcacc taaagctgga	3540
tattttgttc aagatcatgg agaattgaag ttcacaggta gcaattatta ctaccctgaa	3600
tcattacag ataaaaacag tgctgtgatg agtagttgcg cagtaaaact cacaaaggca	3660
cctgaagttt tcttgaacac ttcaataact aatctaccg actttaagga ggagttagat	3720
aatggttta agaatcagac gtctattgtg cctgatttat ctttcgatat cgggaaatta	3780
aatgttcat tccttgacct gtcctatgag atgaacagga ttcaggatgc aattaagaat	3840
ttaaatgaga gttacatcaa cctcaaggaa attggcacat atgagatgta tgtgaaatgg	3900
ccttggtatg tttggctgct aattggatta gctggtgtag ctgtttgtgt tttgtattt	3960
tttatatgtt gctgcacagg ttgtggctct tgtgtttta agaaatgtgg aaattgttgt	4020
gatgagtatg gaggacgtca ggcaggatatt gtgatacata atatttcctc tcatgaggat	4080
tga	4083

<210> SEQ ID NO 13

<211> LENGTH: 3489

<212> TYPE: DNA

<213> ORGANISM: Infectious bronchitis virus

-continued

<400> SEQUENCE: 13

atgttggttaa cacctctttt actagtgact cttttgtgtg cactatgtag tgctgttttg	60
tatgacagta gttcttacgt ttactactac caaagtgcct tcagaccacc tagtggttg	120
catttacaag ggggtgctta tgcggtagtt aacatttcta gcgaatttaa taatgcaggc	180
tcttcacag ggtgtactgt tgggtattatt catgggtggtc gtgttggtta tgcttcttct	240
atagctatga cggcaccgtc atcaggtagt gcttggtcta gcagtcagtt ttgtactgca	300
cactgtaatt tttcagatac tacagtgttt gttacacatt gttataaaca tggtggtgt	360
cctttaactg gcatgcttca acagaatcct atacgtgttt ctgctatgaa aaatggccag	420
cttttctata atttaacagt tagtgtagct aagtacccta ctttttagatc atttcagtgt	480
gttaataatt taacatccgt atattttaa ggtgatcttg tttacacctc taatgagacc	540
atagatgtta catctgcagg tgtttatttt aaagctggtg gacctataac ttataaagtt	600
atgagagaag ttaaagccct ggcttatttt gttaatggta ctgcacaaga tgttattttg	660
tgtgatggat cacctagagg cttgttagca tgccagtata atactggcaa ttttccagat	720
ggcttttctc cttttactaa tagtagttta gttaagcaga agtttattgt ctatcgtgaa	780
aatagtgtta atactacttg tacgtttcac aatttcattt ttcataatga gactggcgcc	840
aacctaatc ctagtggtgt tcagaatatt caaacttacc aaacaaaaac agctcagagt	900
ggttattata attttaattt ttctttctcg agtagttttg tttataagga gtctaatttt	960
atgtatggat cttatcacc aagttgtaaa tttagactag aaactattaa taatggcttg	1020
tggtttaatt cactttcagt ttcaattgct tacggctcctc ttcaaggtgg ttgcaagcaa	1080
tctgtcttta aaggtagagc aacttggtgt tatgcttatt catatggagg tccttcgctg	1140
tgtaaagggtg tttattcagg tgagttagat cataattttg aatgtggact gttagtttat	1200
gttactaaga gcgggtggtc tcgtatacaa acagccaactg aaccgccagt tataactcaa	1260
aacaattata ataataattac tttaaatact tgtgttgatt ataatatata tggcagaact	1320
ggccaagggt ttattactaa tgtgaccgac tcagctgtta gttataatta tctagcagac	1380
gcaggtttgg ctattttaga tacatctggt tccatagaca tctttgttgt acaaggtgaa	1440
tatggtctta attattataa ggtaaaccct tgcgaagatg tcaaccagca gttttagtt	1500
tctggtggtta aattagtagg tattottact tcacgtaatg agactggttc tcagcttctt	1560
gagaaccagt tttacatcaa aatcactaat ggaacacgtc gttttagacg ttctattact	1620
gaaaatgttg caaattgcc ttatgttagt tatggtaagt tttgtataaa acctgatggc	1680
tcaattgcc caatagtacc aaaacaattg gaacagtttg tggcaccttt atttaatgtt	1740
actgaaaatg tgctcatacc taacagtttc aacttaactg ttacagatga gtacatacaa	1800
acgcgtatgg ataaggtcca aattaattgc ctgcagtatg tttgtggcag ttctctggat	1860
tgtagaaagt tgtttcaaca atatgggacct gtttgcgaca acatattgtc ttagtaaat	1920
agtgttggtc aaaaagaaga tatggaactt ttgaatttct attcttctac taaaccggct	1980
ggttttaata caccagtctt tagtaatgtt agcactggtg agtttaatat ttctcttctg	2040
ttaacaaatc ctagtagtcg tagaaagcgt tctcttattg aagaccttct atttacaagc	2100
gttgaatctg ttggactacc aacaaatgac gcatataaaa attgcactgc aggaccttta	2160
ggctttttta aggaccttgc gtgtgctcgt gaatataatg gtttgcttgt gttgcctcct	2220

-continued

```

atcataacag cagaaatgca agctttgtat actagttctc tagtagcttc tatggctttt 2280
ggtgggtatta ctgcagctgg tgctatacct ttgcccacac aactgcaggc tagaattaat 2340
cacttgggta ttaccagtc acttttgttg aagaatcaag aaaaaattgc tgcttccttt 2400
aataaggcca ttggtcatat gcaggaaggt tttagaagta catctctagc attacaacaa 2460
attcaagatg ttgttagtaa acagagtgtt attcttactg agactatggc atcacttaat 2520
aaaaattttg gtgctatttc ttctgtgatt caagaaatct accagcaatt tgacgccata 2580
caagcaaatg ctcaagtga tcgtcttata actggtagat tgcctcact ttctgtttta 2640
gcactctgta agcaggcgga gtatattaga gtgtcacaac agcgtgagtt agctactcag 2700
aaaattaatg agtgtgttaa gtcacagtct attaggtact ccttttgttg taatggacga 2760
catgttctaa ccataccgca aaatgcacct aatggtatag tgtttatata cttttcttat 2820
actccagata gttttgttaa tggtactgca atagtgggtt tttgtgtaaa gccagctaata 2880
gctagtcagt atgcaatagt gcccgctaata ggtaggggta tttttatata agttaatggt 2940
agttactaca tcactgcacg agatatgtat atgccaagag ctattactgc aggagatgta 3000
gttacgctta cttcttgtca agcaaatat gtaagtgtaa ataagaccgt cattactaca 3060
ttcgtagaca atgatgattt tgattttaat gacgaattgt caaaatggtg gaatgatact 3120
aagcatgagc taccagactt tgacaaattc aattacacag tacctatact tgacattgat 3180
agtgaattg atcgtattca aggcgttata cagggtctta atgactctct aatagacctt 3240
gaaaaacttt caatactcaa aacttatatt aagtggcctt ggtatgtgtg gttagccata 3300
gcttttgcca ctattatctt catcttaata ctaggatggg ttttcttcat gactggttgt 3360
tgtggttgtt gttgtggatg ctttggcatt atgcctctaa tgagtaagtg tggtaagaaa 3420
tcttcttatt acacgacttt tgataacgat gtggtaactg aacaatacag acctaaaaag 3480
tctgtttga 3489

```

```

<210> SEQ ID NO 14
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: SARS coronavirus GD69

```

```

<400> SEQUENCE: 14

```

```

cccacgccag aaggtagatc acgaactaca cgtggg 36

```

```

<210> SEQ ID NO 15
<211> LENGTH: 95
<212> TYPE: DNA
<213> ORGANISM: SARS coronavirus GD69

```

```

<400> SEQUENCE: 15

```

```

ctctatgttt ataagggcta tcaacctata gatgtagttc gtgatctacc ttctggtttt 60
aacactttga aacctatttt taagttgact cttgg 95

```

```

<210> SEQ ID NO 16
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
      primer

```

-continued

<400> SEQUENCE: 16

ctctatgttt ataagggtta tcaacc

26

<210> SEQ ID NO 17

<211> LENGTH: 27

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 17

ccaagaggca acttaaaaat aggtttc

27

<210> SEQ ID NO 18

<211> LENGTH: 12

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 18

aggctgtaag aa

12

<210> SEQ ID NO 19

<211> LENGTH: 38

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 19

gcccacgcca gaaggtagat cacgaactac acgtgggc

38

<210> SEQ ID NO 20

<211> LENGTH: 45

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 20

taatacgact cactataggc tctatgttta taagggtat caacc

45

<210> SEQ ID NO 21

<211> LENGTH: 39

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 21

aggctgtaag aaccaaggc caacttaaaa ataggtttc

39

<210> SEQ ID NO 22

<211> LENGTH: 231

<212> TYPE: DNA

<213> ORGANISM: SARS coronavirus urbani

<400> SEQUENCE: 22

-continued

```

atgtactcat tcgtttcggg agaaacaggt acgttaatag ttaatagcgt acttcttttt 60
cttgctttcg tggatttctt gctagtcaca ctagccatcc ttactgcgct tcgattgtgt 120
gcgtactgct gcaatattgt taacgtgagt ttagtaaaac caacgggtta cgtctactcg 180
cgtgttaaaa atctgaactc ttctgaagga gttcctgata ttctgggtcta a 231

```

```

<210> SEQ ID NO 23
<211> LENGTH: 231
<212> TYPE: DNA
<213> ORGANISM: SARS coronavirus Tor2

```

```

<400> SEQUENCE: 23

```

```

atgtactcat tcgtttcggg agaaacaggt acgttaatag ttaatagcgt acttcttttt 60
cttgctttcg tggatttctt gctagtcaca ctagccatcc ttactgcgct tcgattgtgt 120
gcgtactgct gcaatattgt taacgtgagt ttagtaaaac caacgggtta cgtctactcg 180
cgtgttaaaa atctgaactc ttctgaagga gttcctgata ttctgggtcta a 231

```

```

<210> SEQ ID NO 24
<211> LENGTH: 234
<212> TYPE: DNA
<213> ORGANISM: Human coronavirus OC43

```

```

<400> SEQUENCE: 24

```

```

atgttcctta agctagtggg tgatcatgct ttggttgta atgtactact ctggtgtgtg 60
gtgcttatag tgatactact agtgtgtatt acaataatta aactaattaa gctttgtttc 120
acttgccata tgttttgtaa tagaacaggt tatggcccca ttaaaatgt gtaccacatt 180
taccaatcat atatgcacat agaccctttc cctaaacgag ttattgattt ctaa 234

```

```

<210> SEQ ID NO 25
<211> LENGTH: 231
<212> TYPE: DNA
<213> ORGANISM: Porcine epidemic diarrhea virus

```

```

<400> SEQUENCE: 25

```

```

atgctacaat tagtgaatga taatgggtcta gtagttaatg ttatactttg gcttttcgta 60
ctctttttcc tgcttattat aagcattacc ttcgccaat tggtaaatct gtgcttcact 120
tgtcaccggt tgtgtaatag cgcagtttat acacctatag ggcgcctgta tagagtttat 180
aagtcttaca tgcgaattga cccctcccc agtactgtta ttgacgtata a 231

```

```

<210> SEQ ID NO 26
<211> LENGTH: 249
<212> TYPE: DNA
<213> ORGANISM: Transmissible gastroenteritis virus

```

```

<400> SEQUENCE: 26

```

```

atgacgtttc ctagggcatt gactgtcata gatgacaatg gaatggatcat taacatcatt 60
ttctggtttc tgttgataat tatattgata ttactttcaa tagcattgct aaatataatt 120
aagctatgca tgggtgtgtg caatttagga aggacagtta ttattgttcc agcgcaacat 180
gcttacgatg cctataagaa ttttatgcga attaaagcat acaacccgga tggagcactc 240
cttgcttga 249

```

-continued

```

<210> SEQ ID NO 27
<211> LENGTH: 249
<212> TYPE: DNA
<213> ORGANISM: Porcine respiratory coronavirus

<400> SEQUENCE: 27
atgacgtttc ctagggcatt gactgtcata gatgacaacg gaatgggcat tagcatcatt    60
ttttggttcc tgttgataat tatattgata ttactttcaa tagcattgct aaatataatt    120
aagctatgca tgggtgtgtg caatttagga aggacagtta ttattgttcc agtgcaacat    180
gottacgatg cctataagaa ttttatgcga attaaagcat acaaccctga tggagcactc    240
cttgtttga                                     249

<210> SEQ ID NO 28
<211> LENGTH: 249
<212> TYPE: DNA
<213> ORGANISM: Canine coronavirus

<400> SEQUENCE: 28
atgacgttcc ctccggcatt gactgtcata gatgacaatg gaatgggcat tagtatcatt    60
ttctggttcc tgttgataat tatattgata ttattttcaa tagcattgct aaatataatt    120
aagctatgca tgggtatgtg caatttagga agaacagtta ttattgttcc agctcgacat    180
gcctatgatg cctataagaa ttttatgcaa attagagcat acaaccctga tgaagcactc    240
cttgtttga                                     249

<210> SEQ ID NO 29
<211> LENGTH: 249
<212> TYPE: DNA
<213> ORGANISM: Feline coronavirus

<400> SEQUENCE: 29
atgacgttcc ctagggcatt tactatcata gatgaccatg gcattggtgt tagcgtcttc    60
ttctggctcc tgttgataat tatattgata ttgttttcaa tagcattgct aaatgttatt    120
aaattgtgca tgggtatgtg caatttgggt aagactatta tagtactacc tgcacgccat    180
gcatatgatg cctataagac ctttatgcaa accaaggcat ataatcccga cgaagcattt    240
ttggtttga                                     249

<210> SEQ ID NO 30
<211> LENGTH: 267
<212> TYPE: DNA
<213> ORGANISM: Murine hepatitis virus

<400> SEQUENCE: 30
atgtttaatt tattccttac agatacagta tgggtatgtg ggcagattat ttttatagtc    60
gcagtgtgtt tgatgggtcac cataatagtg gttgccttcc ttgcgtctat caaactttgt    120
attcaacttt gcggtttgtg taatactttg ttgctgtctc cttctatttg tgtgtataat    180
aggagtaagc agctttataa gtattataat gaagaagtga gaccgcccc gttagagggtg    240
gatgatataa taatccaaac attatga                                     267

<210> SEQ ID NO 31
<211> LENGTH: 267
<212> TYPE: DNA
<213> ORGANISM: Rat coronavirus

```

-continued

<400> SEQUENCE: 31

```
atgtttaatt tattccttat agacacagta tggtagctgg ggcagattat ttttatagtc      60
gcagtgtggt tgatgggtcac cataattgtg gttgccttcc ttgcgtctat taaactttgt      120
attcaacttt gcggtttgtg taatactttg ttgctgtctc ctctatttta tgtgtataat      180
aggagtaagc agctttataa gtattataat gaagaagtga gaccgcccc gttagagggtg      240
gatgatataa taatccaaac attatga                                           267
```

<210> SEQ ID NO 32

<211> LENGTH: 255

<212> TYPE: DNA

<213> ORGANISM: Bovine coronavirus

<400> SEQUENCE: 32

```
atgtttatgg ctgatgctta tttgcagac actgtgtggt atgtggggca aataatTTTT      60
atagttgccA tttgtttatt ggttataata gttgtagtgg catTTTTggc aactTTTaaa      120
ttgtgtattc aactttgcgg tatgtgtaat accttagtac tgtccccttc tatttatgtg      180
tttaatagag gtaggcagtt ttatgagttt tacaacgatg taaaaccacc agttcttgat      240
gtggatgacg tttag                                           255
```

<210> SEQ ID NO 33

<211> LENGTH: 327

<212> TYPE: DNA

<213> ORGANISM: Infectious bronchitis virus

<400> SEQUENCE: 33

```
atgaatttat tgaataagtc gctagaggag aatggaagtt ttctaacagc gctttacata      60
attgtaggat ttttagcact ttatcttcta ggtagagcac ttcaagcatt tgtacaggct      120
gctgatgctt gttgtttatt ttggtatata tgggtagtaa ttccaggagc taagggtaca      180
gcctttgtat acaagtatac atatggtaga aaacttaaca atccggaatt agaagcagtt      240
attgttaacg agtttcctaa gaacggttgg aataataaaa atccagcaaa ttttcaagat      300
gccaacgag acaaattgta ctcttga                                           327
```

<210> SEQ ID NO 34

<211> LENGTH: 38

<212> TYPE: DNA

<213> ORGANISM: SARS coronavirus GD69

<400> SEQUENCE: 34

```
cctccgcacg aaagcaagaa aaagaagtac gccggagg                               38
```

<210> SEQ ID NO 35

<211> LENGTH: 95

<212> TYPE: DNA

<213> ORGANISM: SARS coronavirus GD69

<400> SEQUENCE: 35

```
cggaagaaac aggtacgtta atagttaata gcgtacttct ttttcttgct ttcgtggtat      60
tcttgctagt cacactagcc atccttactg cgctt                                   95
```

<210> SEQ ID NO 36

<211> LENGTH: 24

-continued

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 36

cggaagaaac aggtacgtta atag 24

<210> SEQ ID NO 37
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 37

aagcgagta aggatggcta 20

<210> SEQ ID NO 38
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 38

tattgcagca gtac 14

<210> SEQ ID NO 39
<211> LENGTH: 40
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 39

gcctccgcac gaaagcaaga aaaagaagta cgccggaggc 40

<210> SEQ ID NO 40
<211> LENGTH: 43
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 40

taatacgact cactataggc ggaagaaaca ggtacgttaa tag 43

<210> SEQ ID NO 41
<211> LENGTH: 34
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 41

tattgcagca gtacaagcgc agtaaggatg gcta 34

-continued

<210> SEQ ID NO 42

<211> LENGTH: 789

<212> TYPE: DNA

<213> ORGANISM: Transmissible gastroenteritis virus

<400> SEQUENCE: 42

```
atgaagattt tgttaatat agcgtgtgtg attgcatgcg catgtggaga acgctattgt    60
gctatgaaat ccgatacaga tttgtcatgt cgcaatagta cagcgtctga ttgtgagtca    120
tgcttcaacg gaggcgatct tatttggcat cttgcaaact ggaacttcag ctggctctata    180
atattgatcg tttttataac tgtgctacaa tatggaagac ctcaattcag ctgggtcgtg    240
tatggcatta aaatgcttat aatgtggcta ttatggcccg ttgttttggc tcttacgatt    300
tttaatgcat actcgaata ccaagtgtcc agatatgtaa tgttcggctt tagtattgca    360
ggtgcaattg ttacatttgt actctggatt atgtattttg taagatccat tcagttgtac    420
agaaggacta agtcttgggtg gtccttcaac cctgaaacta aagcaattct ttgcgttagt    480
gcattaggaa gaagctatgt gcttctctc gaaggtgtgc caactggtgt cactctaact    540
ttgctttcag ggaatttgta cgctgaaggg ttcaaaattg caggtggtat gaacatcgac    600
aatttaccaa aatacgtaat ggttgcatta cctagcagga ctattgtcta cacacttggt    660
ggcaagaagt tgaagcaag tagtgcgact ggatgggctt actatgtaaa atctaaagct    720
ggtgattact caacagaggc aagaactgat aatttgagtg agcaagaaaa attattacat    780
atggtataa                                     789
```

<210> SEQ ID NO 43

<211> LENGTH: 789

<212> TYPE: DNA

<213> ORGANISM: Porcine respiratory coronavirus

<400> SEQUENCE: 43

```
atgaagattt tgttgatatt agcgtgtgcg attgcatgca catgtggaga acgctattgt    60
gctatgaaag acgatacagg tttgtcatgt cgcaatggca cggcgtctga ttgtgagtca    120
tgcttcaaca gaggcgatct tatttggctt cttgcaaact ggaacttcag ctggctctata    180
atattgatca tttttattac tgtgctacaa tatggaagac ctcaattcag ctgggtcgtg    240
tatggcatta aaatgcttat aatgtggcta ttatggccga ttgttttggc tcttacgatt    300
tttaatgcat actcgaata ccaagtgtcc aggtatgtaa tgttcggctt tagtattgca    360
ggtgcaattg ttacatttgt actctggatt atgtattttg taagatccat tcagttgtac    420
agaaggacta agtcttgggtg gtccttcaac cctgaaacta acgcaattct ttgcgttagt    480
gcattaggaa gaagctatgt gcttctctc gaaggtgtgc caactggtgt cactctaact    540
ttgctttcag ggaatttgta cgctgaaggg ttcaaaattg caggtggtat gaccatcgac    600
aatttgccaa aatacgtaat ggttgcatta cccagcagga ctattgttta cacacttggt    660
ggcaagaagt tgaagcaag tagtgcgact ggatgggctt actatgtaaa atctaaagct    720
ggtgattact caacagaggc aagaactgat aatttgagtg agcaagaaaa attattacat    780
atggtataa                                     789
```

<210> SEQ ID NO 44

<211> LENGTH: 789

<212> TYPE: DNA

<213> ORGANISM: Canine coronavirus

-continued

<400> SEQUENCE: 44

```
atgaagaaaa ttttgtttt actagcgtgt gcaattgcat gcgtctatgg agaacgctat    60
tgtgccatga ctgaaagtto tacgtcatgt cgtaatagca cggctggcaa ctgtgcttca    120
tgcttcgaaa caggtgatct tatttggcat cttgcaaact ggaacttcag ctggctctgta    180
atattgatca tttttataac agtgttataa tatggaagac ctcaatttag ctggctctgtg    240
tgtggcatta aaatgcttat tatgtggctg ttatggccca ttgttttagc tcttacgatt    300
tttaatgcat acctggaata cagagtttcc agatatgtaa tgctcggctt tagtgttgca    360
ggcgcaactg ttacatttat actttggatt atgtattttg ttagatccat tcagttatac    420
agaaggacta agtcttgggt gtctttcaac cctgaaacta gcgcaattct ttgcgttagt    480
gcgttaggaa gaagctatgt gcttctctct gaagggtgtg caactgggtg cactctaaca    540
ttgctttcag ggaatttggt tgctgaaggg ttcaaaattg caggtgggtat gaacatcgac    600
aatttaccaa aatagttaat ggttgcatca cctgtcagaa ccatagtcta cacacttggt    660
ggcaagaaat tgaagcaag tagtgcaaca ggatgggctt actatgtaaa gtctaaagct    720
ggtgattact caacagatgc acgaactgat aatttgagtg agcatgaaaa attattacat    780
atggtataa                                     789
```

<210> SEQ ID NO 45

<211> LENGTH: 870

<212> TYPE: DNA

<213> ORGANISM: Feline coronavirus

<400> SEQUENCE: 45

```
atgcatatga tgcctataag acctttatgc aaaccaaggc atataatccc gacgaagcat    60
ttttggtttg aactaaacaa aatgaagtac attttgctaa tactcgcgtg cataattgca    120
tgcgtttatg gtgaacgcta ctgtgccatg caagacagtg gcttcagtg tattaatggc    180
acaaattcaa gatgtcaaac ctgctttgaa cgtgggtgat ttatttggca tcttgctaac    240
tggaacttca gctggctctgt aatattgatt gtttttataa cagtgttaca atatggcaga    300
ccacaattta gctggctcgt ttatggcatt aaaatgctga tcatgtggct attatggcct    360
attgttctag cgcttacgat ttttaatgca tactctgagt accaagtttc cagatatgta    420
atgttcggct ttagtggttg aggtgcagtt gtaacgtttg cactttggat gatgtatatt    480
gtgagatctg ttcagctata tagaagaacc aaatcatggt ggtcttttaa tcctgagact    540
aatgcaattc tttgtgttaa tgcattgggt agaagttatg tgcttccctt agatgttact    600
cctacaggtg ttacccttac tctactttca ggaaatctat atgctgaagg tttcaaaatg    660
gctgggtggt taaccatcga gcaattgcct aaatacgtca tgattgctac acctagtaga    720
accatcggtt ataccattagt tggaaaacaa ttaaaagcaa ctactgccac aggatgggct    780
tactacgtaa aatctaaagc tgggtgattac tcaacagaag cacgtactga caatttgagt    840
gaacatgaaa aattattaca tatggtgtaa                                     870
```

<210> SEQ ID NO 46

<211> LENGTH: 678

<212> TYPE: DNA

<213> ORGANISM: Human coronavirus OC43

<400> SEQUENCE: 46

-continued

```

atgtcaaatg acaattgtac gggtagacatt gtcacccatt tgaagaattg gaatttttgt    60
tggaatgtta ttctaaccat attcattggtt attcttcagt ttggacacta taaatactcc    120
agattgtttt atggtttgaa gatgcttgta ctgtggcttc tttggccact cgtacttgct    180
ttgtcaatct ttgacacctg ggctaattgg gattctaatt gggcctttgt tgcatttagc    240
ttttttatgg ccgtatcaac actcgttatg tgggtgatgt acttcgcaaa cagtttcaga    300
cttttccgac gtgctcgaac tttttgggca tggaatcctg aggttaatgc aatcactgtc    360
acaaccgtgt tgggacagac atactatcaa cccattcaac aagctccaac aggcattact    420
gtgaccttgc tgagcggcgt gctttacgtt gacggacata gattggcttc aggtgttcag    480
gttcataacc tacctgaata catgacagtt gccgtgccga gcactactat aatttatagt    540
agagtcggaa ggtccgtaaa ttcacaaaat agcacaggct gggttttcta cgtacgagta    600
aaacacgggtg atttttctgc agtgagctct cccatgagca acatgacaga aaacgaaaga    660
ttgcttcatt ttttctaa                                         678

```

```

<210> SEQ ID NO 47
<211> LENGTH: 681
<212> TYPE: DNA
<213> ORGANISM: Porcine epidemic diarrhea virus

```

```

<400> SEQUENCE: 47

```

```

atgtctaacg gttctattcc cgttgatgag gtgattgaac acctagaaa ctggaatttc    60
acatggaata tcatactgac gatactactt gtagtgcttc agtatggcca ttacaagtac    120
tctgtgttct tgtatggtgt caagatggct attctatgga tactttggcc tcttgtgttg    180
gcactgtcac tttttgacgc atgggctagc ttccagggtca actgggtctt ttcgctttc    240
agcatcctta tggcttgcat cactcttatg ctgtggataa tgtattttgt caatagcatt    300
cggttgtggc gcaggacaca ttcttgggtg tctttcaatc ctgaaactga cgcgcttctc    360
actacttctg tgatgggccc acaggtctgc attccagtgc ttggagcacc aactggtgta    420
acgctaacac tccttagtgg tacattgctt gtagagggtc ataaggttgc tactggcgta    480
caggtaagtc aattacctaa tttcgtcaca gtcgccaagg ccactacaac aattgtctac    540
ggacgtgttg gtcgttcagt caatgcttca tctggcactg gttgggcttt ctatgtccgg    600
tcaaaacacg gcgactatto agctgtgagt aatccgagtg cggttctcac agatagtgag    660
aaagtgcctc atttagtcta a                                         681

```

```

<210> SEQ ID NO 48
<211> LENGTH: 693
<212> TYPE: DNA
<213> ORGANISM: Bovine coronavirus

```

```

<400> SEQUENCE: 48

```

```

atgagtagtg taactacacc agcaccagtt tacacctgga ctgctgatga agctattaaa    60
ttcctaaagg aatggaactt ttctttgggt attatactac tttttattac aatcatattg    120
caatttggtt atacaagtcg cagtatgttt gtttatgtta ttaagatgat cattttgttg    180
cttatgtggc cccttactat catcttaact attttcaatt gcgtgtatgc gttgaataat    240
gtgtatcttg gcttttctat agttttcact atagtggcca ttatcatgtg gattgtgtat    300
tttgtgaata gtatcagggt gtttattaga actggaagtt ggtggagttt caaccagaa    360

```

-continued

```

acaacaact tgatgtgtat agatatgaag ggaaggatgt atgttaggcc gataattgag    420
gactaccata cccttacggt cacaataata cgtgggcato tttacatgca aggtataaaa    480
ctaggtactg gctattcttt gtcagatttg ccagcttatg tgactgttgc taaggcttca    540
cacctgtcga cgtataagcg tggttttctt gacaagatag gcgatactag tggttttgct    600
gtttatgtta agtccaaagt cggttaattac cgactgccat caacccaaaa gggttctggc    660
atggacaccg cattgttgag aaataatata taa                                693

```

<210> SEQ ID NO 49

<211> LENGTH: 693

<212> TYPE: DNA

<213> ORGANISM: Porcine hemagglutinating encephalomyelitis coronavirus

<400> SEQUENCE: 49

```

atgagtagtc caactacacc agtaccagtt attagctgga ctgctgatga agctattaaa    60
ttcctaaagg aatggaattt ttctttgggt ataatagtag tctttatcac aatcatactt    120
caatttggtat atacaagtcg cagtatgttt gtttatgtta ttaagatggt tattctgtgg    180
ctcatgtggc ctcttactat aattttaact atcttcaact gcgtatacgc gttgaataat    240
gtgtaccttg gcttctctat agtttttact atagtggcca ttattatgtg ggttgtttat    300
tttgtgaata gtatcagggt gtttattaga actggaagtt ggtggagttt caaccagaa    360
acaacaact tgatgtgtat agatatgaag ggaagaatgt atgttaggcc gattattgag    420
gactaccaca cccttactgc cacaataata cgtggccacc tctacatcca aggtataaaa    480
ctaggtactg gctattcttt gtcagatttg cctgcttatg tgaccgttgc taaggttaca    540
cacctgtcga catataagcg tggttttctt gataggatag gcgatactag tggttttgct    600
gtttatgtta agtccaaagt cggttaattat cgattgcctt caaccataa gggctcaggc    660
atggacaccg cattgttgag aaataatata taa                                693

```

<210> SEQ ID NO 50

<211> LENGTH: 687

<212> TYPE: DNA

<213> ORGANISM: Murine hepatitis virus

<400> SEQUENCE: 50

```

atgactagta ccactcaggc tccacagcct gtttatcagt ggacggctga tgaggcaatt    60
cgattcctta aggaatggaa tttctctctc ggcaattata tactttttgt tactatcata    120
ctacagttcg gttacacgag ccgtagcatg tttgtttatg ttgtgaaat gatacttttg    180
tggcttatgt ggccactaac tattgttttg tgtattttta actgcgtcta tgcgctaaat    240
aatgtgtatc ttggattttc tatagtgttt actatagtgt ccattataat gtggattatg    300
tattttgtta atagcatcag gttgtttatc aggactggca gctgggtggag cttcaacccc    360
gaaacaaaca acctaatgtg tatagatatg aaaggtagtg tgtatgttag acccattata    420
gaggattacc atacactaac agccactatc attcgtggc acctctatat gcaagggttt    480
aagctaggca ctggcttctc tttgtctgat ttgcctgctt atgttacagt tgctaagggtg    540
tctcaccttt gcacttataa gcgcgcattc ttagacaagg tagacggtgt tagcggtttt    600
gctgtttatg tgaagtccaa ggtcggaaat taccgactgc cctcaataa accgagtggc    660
atggacaccg cattgttgag aatctaa                                687

```

-continued

<210> SEQ ID NO 51
<211> LENGTH: 687
<212> TYPE: DNA
<213> ORGANISM: Rat coronavirus

<400> SEQUENCE: 51

```
atgagtagta ccactccagc cccccagact gtctatcaat ggacggccga tgtggcagtt    60
cgattcctta aggaatggaa cttcttggtg ggcatatac tactctttat tactatcata    120
ctacagttcg gttacacgag ccgtagcatg ttatatatg ttgtgaaat gataatcttg    180
tggttaatgt ggccactgac tattgttttg tgtattttta attgcgtgta tgcgctaaat    240
aatgtgtatc ttggattttc tatagtgttt actatagtgt ccattgtaat gtggattatg    300
tattttgtta atagcataag gttgtttatc aggactggtg gctggtggag cttcaaccct    360
gaaacaaaca acctaattgt tatagatgtg aaaggtagtg tgtatgttag acccattatt    420
gaagattacc atacactaac agccacaaat gtacgtggcc acctttatat gcaagggttt    480
aagctaggca ctggcttctc tttgtctgat ttgccgctt atgttacagt tgctaagggtg    540
tcgcaccttt gcacttataa gcgcgcattt ttagacaagg ttgacggtgt tagcggtttt    600
gctgtttatg tgaagtccaa ggtcggtaat taccgactgc cctcaaataa accgagtggc    660
gcggacaccc cattgttgag aatctaa                                     687
```

<210> SEQ ID NO 52
<211> LENGTH: 675
<212> TYPE: DNA
<213> ORGANISM: SARS coronavirus urbani

<400> SEQUENCE: 52

```
ttgcttatca tggcagacaa cggtagctatt accgttgagg agcttaaaca actcctggaa    60
caatggaacc tagtaatagg ttccctatcc ctacgctgga ttatgttact acaatttgcc    120
tattctaata ggaacaggtt tttgtacata ataaagcttg ttttcctctg gctcttggtg    180
ccagtaacac ttgcttggtt tgtgctgct gctgtctaca gaattaattg ggtgactggc    240
gggattgcga ttgcaatggc ttgtattgta ggcttgatgt ggcttagcta cttcgttgct    300
tccttcaggc tgtttgctcg taccgctca atgtggtcat tcaaccaga aacaaacatt    360
cttctcaatg tgcctctccg ggggacaatt gtgaccagac cgctcatgga aagtgaactt    420
gtcattgggt ctgtgatcat tcgtggtcac ttgcgaatgg ccggacaccc cctagggcgc    480
tgtgacatta aggacctgcc aaaagagatc actgtggcta catcacgaac gctttcttat    540
tacaaattag gagcgtcgca gcgtgtaggc actgattcag gttttgctgc atacaaccgc    600
taccgtattg gaaactataa attaaataca gaccacgccg gtacgaacga caatattgct    660
ttgctagtac agtaa                                             675
```

<210> SEQ ID NO 53
<211> LENGTH: 675
<212> TYPE: DNA
<213> ORGANISM: SARS coronavirus Tor2

<400> SEQUENCE: 53

```
ttgcttatca tggcagacaa cggtagctatt accgttgagg agcttaaaca actcctggaa    60
caatggaacc tagtaatagg ttccctatcc ctacgctgga ttatgttact acaatttgcc    120
```

-continued

tattctaatac ggaacaggtt tttgtacata ataaagcttg ttttctctcg gctcttgttg	180
ccagtaacac ttgcttggtt tgtgcttgct gctgtctaca gaattaattg ggtgactggc	240
gggattgcga ttgcaatggc ttgtattgta ggcttgatgt ggcttagcta cttcgttgct	300
tccttcaggc tgtttgctcg taccgctca atgtggatcat tcaaccaga aacaaacatt	360
cttctcaatg tgcctctccg ggggacaatt gtgaccagac cgctcatgga aagtgaactt	420
gtcattgggtg ctgtgatcat tcgtgggtcac ttgcgaatgg ccggacactc cctaggggcg	480
tgtgacatta aggacctgcc aaaagagatc actgtggcta catcacgaac gctttcttat	540
tacaaattag gagcgctgca gcgtgtaggc actgattcag gttttgtgc atacaaccgc	600
taccgtattg gaaactataa attaaataca gaccacgccg gtagcaacga caatattgct	660
ttgctagtac agtaa	675

<210> SEQ ID NO 54
 <211> LENGTH: 678
 <212> TYPE: DNA
 <213> ORGANISM: Infectious bronchitis virus

<400> SEQUENCE: 54

atgccaacg agacaaattg tactcttgac tttgaacagt cagttcagct ttttaagag	60
tataatttat ttataactgc attcttggtt ttcttaacca taatacttca gtatggctat	120
gcaacaagaa gtaaggttat ttataactg aaaatgtag tgttatgggtg cttttggccc	180
cttaacattg cagtaggtgt aatttcattg acataccac caaacacagg aggtcttgct	240
gcagcgataa tacttcacgt gtttgctgt ctgtcttttg taggttattg gatccagagt	300
attagactct ttaagcgggtg taggtcatgg tggtcattta atccagaatc taatgccgta	360
ggttcaatac tcctaactaa tggccaacaa tgtaatttg ctatagagag tgtgccaatg	420
gtgctttctc caattataaa gaatgggtgt ctttattgtg agggtcagtg gcttgctaag	480
tgtgaaccag accacttgcc taaagatata tttgtttgta caccgtag acgtaatatc	540
taccgtatgg tgcagaaata tactggtgac caaagcggaa ataagaaaag gtttgctacg	600
tttgcttatg caaagcagtc agtagatact ggcgagctag aaagtgtagc aacaggagga	660
agtagtcttt acacataa	678

<210> SEQ ID NO 55
 <211> LENGTH: 38
 <212> TYPE: DNA
 <213> ORGANISM: SARS coronavirus GD69

<400> SEQUENCE: 55

cctccgaccc aattaattct gtagacagca gccggagg	38
---	----

<210> SEQ ID NO 56
 <211> LENGTH: 107
 <212> TYPE: DNA
 <213> ORGANISM: SARS coronavirus GD69

<400> SEQUENCE: 56

cttggtttcc tctggctctt gtggccagta acacttgctt gttttgtgct tgctgctgtc	60
tacagaatta attgggtgac tggcgggatt gcgattgcaa tggcttg	107

-continued

<210> SEQ ID NO 57
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 57

cttggtttcc tctggctctt g 21

<210> SEQ ID NO 58
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 58

caagccattg caatcgcaat c 21

<210> SEQ ID NO 59
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 59

aagcaacgaa gtag 14

<210> SEQ ID NO 60
<211> LENGTH: 40
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 60

gcctccgacc caattaatto tgtagacagc agccggaggc 40

<210> SEQ ID NO 61
<211> LENGTH: 40
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 61

taatacgact cactataggc ttgttttcct ctggctcttg 40

<210> SEQ ID NO 62
<211> LENGTH: 35
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 62

aagcaacgaa gtagcaagcc attgcaatcg caatc 35

-continued

<210> SEQ ID NO 63

<211> LENGTH: 1149

<212> TYPE: DNA

<213> ORGANISM: Transmissible gastroenteritis virus

<400> SEQUENCE: 63

```
atggccaacc agggacaacg tgtcagttgg ggagatgaat ctacccaaac acgtggtcgt    60
tccaattccc gtggtcggaa gaataataac atacctcttt cattcttcaa ccccataacc    120
ctccaacaag gttcaaaatt ttggaactta tgtccgagag actttgtacc caaaggaata    180
ggtaacaggg atcaacagat tggttattgg aatagacaaa ctgcgtatcg catggtgaag    240
ggccaacgta aagagcttcc tgaaaggtag ttcttctact acttaggtac tggacctcat    300
gcagatgcc aatttaaga taaattagat ggagttgtct gggttgccaa ggatggtgcc    360
atgaacaaac caaccacgct tggtagtcgt ggtgctaata atgaatccaa agctttgaaa    420
ttcgatggta aagtgccagg cgaatttcaa cttgaagtta atcaatcaag agacaattca    480
aggtcacgct ctcaatctag atctcgtctc agaaatagat ctcaatctag aggcaggcaa    540
caattcaata acaagaagga tgacagtgtg gaacaagctg ttcttgccgc acttaaaaag    600
ttaggtgttg acacagaaaa acaacagcaa cgctctcgtt ctaaatctaa agaacgtagt    660
aactctaaga caagagatac tacacctaa gaaataaaca aacacacctg gaagagaact    720
gcaggtaaag gtgatgtgac aagattttat ggagctagaa gcagttcagc caattttggt    780
gacactgacc tcgttgccaa tgggagcagt gccaaagcatt acccacaact ggctgaatgt    840
gttccatctg tgtctagcat tctgtttgga agctattgga cttcaaagga agatggcgac    900
cagatagaag tcacgttcac acacaaatac cacttgccaa aggatgatcc taagactgga    960
caattccttc agcagattaa tgcctatgct cgtccatcag aagtggcaaa agaacagaga   1020
aaaagaaaat ctggttctaa atctgcagaa aggtcagagc aagatgtggt acctgatgca   1080
ttaatagaaa attatacaga tgtgtttgat gacacacagg ttgagataat tgatgaggta   1140
acgaactaa                                     1149
```

<210> SEQ ID NO 64

<211> LENGTH: 1149

<212> TYPE: DNA

<213> ORGANISM: Porcine respiratory coronavirus

<400> SEQUENCE: 64

```
atggccaacc agggacaacg tgtcagttgg ggggatgaat ccacccaaat acgtggtcgc    60
tccaattccc gtggtcggaa gattaataac atacctcttt cattcttcaa ccccataacc    120
ctccagcaag gtgcaaaatt ttggaactca tgtccgagag attttgtacc caaaggaata    180
ggtaaatagg atcaacagat tggttattgg aatagacaaa ctgcgtatcg catggtgaag    240
ggccaacgta aagagcttcc tgaaaggtag ttcttttact acttaggcac tggacctcat    300
gcagatgcc aatttaaga taaattagat ggagttgtct gggttgccaa ggatggtgcc    360
atgaacaaac caaccacgct tggtagtcgt ggtgctaata atgaatccaa agctttgaaa    420
ttcgatggta aagtgccagg cgaatttcaa cttgaagtta accagtctag ggacaactca    480
aggtcacgct ctcaatctag atcgcgtctc agaaacagat ctcaatctag aggtaggcaa    540
caatccaata acaagaagga tgacagtgtg gaacaagctg ttcttgccgc acttaaaaag    600
```

-continued

```

ttaggtgttt acacagaaaa acaacagcaa cgctctcggt ctaaatctaa agaacgtagt    660
aactctaaaa caagagatac tacgcctaag aatgaaaaca aacacacctg gaagagaact    720
gcaggtaaag gtgatgtgac aagattttat ggagctagaa gcagctcagc caattttggt    780
gacagtgacc tcgttgccaa tgggagcagt gccaaagcatt acccacaatt ggctgaatgt    840
gttccatctg tgtctagcat tttgtttgga agctattgga cttcaaagga agatggcgac    900
cagatagaag tcacgttcac acacaaatac cacttgccaa aggatcatcc taaaactgaa    960
caattccttc agcagattaa tgcctatgct agcccatcag aattggcaaa agaacagaga   1020
aaaagaaagt ctcgttctaa atctgcagaa aggtcagagc aagagggtgt acctgattca   1080
ttaatagaaa actatacaga tgtgtttgat gacacacagg ttgagatgat tgacgaggta   1140
acgaactaa                                     1149

```

```

<210> SEQ ID NO 65
<211> LENGTH: 1146
<212> TYPE: DNA
<213> ORGANISM: Canine coronavirus

```

```

<400> SEQUENCE: 65

```

```

atggcctctc agggacaacg tgtcagttgg ggagatgaat ccaccaagag acgcggtcgt    60
tctaattctc gtggccggaa gaataatgat atacctcttt cattottcaa cccattacc    120
ctcgagcaag gatcaaagtt ttgggactta tgtccgagag actttgtacc caaaggaata    180
ggtaataagg atcaacaaat tggttattgg aacaggcaaa cccgttatcg catggtgaag    240
ggtcgacgta aaaatcttcc tgaaaagtgg ttcttctact atttaggaac tggacctcat    300
gctgatgcca aatttaagca aaaattagat ggagttgtct gggttgctag gggagattcc    360
atgactaagc caacaactct tggttactcg ggcactaata atgaatcaaa ggctttgaaa    420
ttcgatgtca aagtaccatc agaatttcac cttgaagtga accaattaag ggacaattca    480
aggtctaggt ctcaatctag atctcagtc agaaataggt ctcaatctag aggaaggcaa    540
ctatccaata ataagaagga tgacaatggt gaacaagctg ttcttgctgc actcaaaaag    600
ttaggtgttg acacagaaaa acaacaaaga tctcgttcca aatctaagga acgtagcagc    660
tctaagacaa gagatactac ccctaagaat gaaaacaaac acacctggaa gagaactgca    720
ggtaaaagtg atgtgacaaa attttatgga gctagaagta gttcagccaa ttttggtgac    780
agcgatcttg ttgccaatgg gaacggtgcc aagcattacc cacaactggc tgaatgtgtt    840
ccatctgtat ctagcattct gtttggaagc cattggactg ctaaggaaga tggtgaccag    900
attgaagtca cattcacaca caaataccac ttgccaaagg atgaccta gactggacaa    960
ttccttcagc agattaatgc atacgcccg ccatcagagg tggctaaaga acagagacaa   1020
cgcaaagctc gttctaaatc tgtagaaagg gtagagcaag aggttgtagc tgatgcatta   1080
acagaaaatt acacagatgt gtttgatgac acacaggttg agattattga tgaggtaacg   1140
aactaa                                     1146

```

```

<210> SEQ ID NO 66
<211> LENGTH: 1134
<212> TYPE: DNA
<213> ORGANISM: Feline coronavirus

```

```

<400> SEQUENCE: 66

```

-continued

atggccacac agggacaacg cgtcaactgg ggagatgaac cttccaaaag acgtggctcg	60
tctaactctc gtggctggaa gaataatgat atacctttgt cattctacaa cccattacc	120
ctcgaacaag gatctaaatt ttggaattta tgtccgagag acctgttcc caaaggaata	180
ggtaataagg atcaacaaat tggttattgg aatagacaga ttcgttatcg tattgtaaaa	240
ggccagcgta aggaactcgc tgagaggtgg ttcttttact tcttaggtac aggacctcat	300
gctgatgcta aattcaaaga caagattgat ggagtcttct ggggtgcaag ggatggtgcc	360
atgaacaagc ccacaacgct tggcactcgt ggaaccaata acgaatcaa accactgaga	420
tttgatggta agataccgcc acagtttcag cttgaagtga accgttctag gaacaattca	480
aggctcggtt ctacgtctag atctgtttca agaaacagat ctcaatctag aggaagacac	540
cattccaata accagaataa taatgttgag gatacaattg tagccgtgct tgaataatta	600
gggtttactg acaacaaaag gtcacgttct aaacctagag aacgtagtga ttccaaacct	660
agggacacaa cacctaagaa tgccaacaaa cacacctgga agaaaactgc aggcaaggga	720
gatgtgacaa ctttctatgg tgctagaagt agttcagcta actttggtga tagtgatctc	780
gttgccaatg gtaacgctgc caaatgtac cctcagatag ctgaatgtgt tccatcagt	840
tctagcataa tctttggcag tcaatgtct gctgaagaag ctggtgatca agtgaaagtc	900
acgctcactc acacctacta cctgccaaag gatgatgcca aaactagtca attcctagaa	960
cagattgacg cttacaagcg accttctgaa gtggctaagg atcagaggca aagaagatcc	1020
cgttctaagt ctgctgataa gaagcctgag gagttgtctg taactcttgt ggaggcatac	1080
acagatgtgt ttgatgacac acaggttgag atgattgatg aggttacgaa ctaa	1134

<210> SEQ ID NO 67

<211> LENGTH: 1269

<212> TYPE: DNA

<213> ORGANISM: SARS coronavirus urbani

<400> SEQUENCE: 67

atgtctgata atggacccca atcaaaccaa cgtagtgcgc cccgcattac atttgggtgga	60
cccacagatt caactgacaa taaccagaat ggaggacgca atggggcaag gccaaaacag	120
cgccgacccc aaggtttacc caataaact gcgctcttgg tccacagctct cactcagcat	180
ggcaaggagg aacttagatt ccctcgaggc cagggcgctc caatcaacac caatagtgg	240
ccagatgacc aaattggcta ctaccgaaga gctacccgac gagttcgtgg tggtagcggc	300
aaaatgaaag agctcagccc cagatgttac ttctattacc taggaactgg ccagaagct	360
tcacttcctc acggcgctaa caaagaaggc atcgtatggg ttgcaactga gggagccttg	420
aatacaccca aagaccacat tggcaccgcg aatcctaata acaatgtgc caccgtgcta	480
caacttcctc aaggaacaac attgccaaa ggcttctacg cagagggaag cagaggcggc	540
agtcaagcct cttctcgctc ctcatcagct agtcgcggtt attcaagaaa ttcaactcct	600
ggcagcagta ggggaaattc tcctgctcga atggctagcg gaggtggtga aactgccctc	660
gcgctattgc tgctagacag attgaaccag cttgagagca aagtttcttg taaaggccaa	720
caacaacaag gccaaactgt cactaagaaa tctgctgctg aggcattctaa aaagcctcgc	780
caaaaacgta ctgccacaaa acagtacaac gtcactcaag catttgggag acgtggtcca	840
gaacaaaccc aaggaaattt cggggaccaa gacctaatca gacaaggaac tgattacaaa	900

-continued

```

cattggccgc aaattgcaca atttgtcca agtgcctctg cattcttttg aatgtcacgc   960
attggcatgg aagtcacacc ttcggaaca tggctgactt atcatggagc cattaaattg   1020
gatgacaaag atccacaatt caaagacaac gtcatactgc tgaacaagca cattgacgca   1080
tacaaaacat tcccaccaac agagcctaaa aaggacaaaa agaaaaagac tgatgaagct   1140
cagcctttgc cgcagagaca aaagaagcag cccactgtga ctcttcttcc tgcggctgac   1200
atggatgatt tctccagaca acttcaaaat tccatgagtg gagcttctgc tgattcaact   1260
caggcataa                                     1269

```

```

<210> SEQ ID NO 68
<211> LENGTH: 1269
<212> TYPE: DNA
<213> ORGANISM: SARS coronavirus Tor2

```

```

<400> SEQUENCE: 68

```

```

atgtctgata atggacccca atcaaaccaa cgtagtgcc cccgcattac atttgggtgga   60
cccacagatt caactgacaa taaccagaat ggaggacgca atggggcaag gccaaaacag   120
cgccgacccc aaggtttacc caataatact gcgtcttggt tcacagctct cactcagcat   180
ggcaaggagg aacttagatt ccctcgaggg cagggcggtc caatcaacac caatagtgg   240
ccagatgacc aaattggcta ctaccgaaga gctaccgac gagttcgtgg tggtagcggc   300
aaaatgaaag agctcagccc cagatggtag ttctattacc taggaactgg cccagaagct   360
tcacttcctt acggcgctaa caaagaaggc atcgtatggg ttgcaactga gggagccttg   420
aatacaccca aagaccacat tggcaccgc aatcctaata acaatgctgc caccgtgcta   480
caacttcctc aaggaacaac attgccaaa ggcttctacg cagagggag cagaggcggc   540
agtcaagcct ctctcgtctc ctcatcagct agtcgcggtt attcaagaaa ttcaactcct   600
ggcagcagta ggggaaattc tcctgctcga atggctagcg gaggtggtga aactgccctc   660
gcgctattgc tgctagacag attgaaccag cttgagagca aagtttcttg taaaggccaa   720
caacaacaag gccaaactgt cactaagaaa tctgctgctg aggcattctaa aaagcctcgc   780
caaaaacgta ctgccacaaa acagtacaac gtcactcaag catttgggag acgtggtcca   840
gaacaaaccc aaggaaattt cggggaccaa gacctaatca gacaaggaa tgattacaaa   900
cattggccgc aaattgcaca atttgtcca agtgcctctg cattcttttg aatgtcacgc   960
attggcatgg aagtcacacc ttcggaaca tggctgactt atcatggagc cattaaattg   1020
gatgacaaag atccacaatt caaagacaac gtcatactgc tgaacaagca cattgacgca   1080
tacaaaacat tcccaccaac agagcctaaa aaggacaaaa agaaaaagac tgatgaagct   1140
cagcctttgc cgcagagaca aaagaagcag cccactgtga ctcttcttcc tgcggctgac   1200
atggatgatt tctccagaca acttcaaaat tccatgagtg gagcttctgc tgattcaact   1260
caggcataa                                     1269

```

```

<210> SEQ ID NO 69
<211> LENGTH: 1347
<212> TYPE: DNA
<213> ORGANISM: Bovine coronavirus

```

```

<400> SEQUENCE: 69

```

```

atgtctttta ctctggtaa gcaatccagt agtagagcgt cctttgaaa tcgttctggt   60

```

-continued

```

aatggcatcc ttaagtgggc cgatcagtc gaccaatcta gaaatgttca aaccaggggt 120
agaagagctc aaccaagca aactgctact tctcagctac catcaggagg gaatgttgta 180
ccctactatt cttggttctc tggaattact cagtttcaaa aaggaaagga gtttgaattt 240
gcagagggac aaggtgtgcc tattgcacca ggagtcccag ctactgaagc taaggggtac 300
tggtacagac acaacagacg ttcttttaaa acagccgatg gcaaccagcg tcaactgctg 360
ccacgatggg atttttacta tcttgaaca ggaccgatg ccaaagacca gtatggcacc 420
gatattgacg gagtcttctg ggtcgctagt aaccaggctg atgtcaatac cccggctgac 480
attctcgatc gggacccaag tagcgatgag gctattccga ctaggtttcc gcctggcacg 540
gtactccctc agggttacta tattgaaggc tcaggaaggt ctgctcctaa ttccagatct 600
acttcacgcg catccagtag agcctctagt gcaggatcgc gtagtagagc caattctggc 660
aacagaaccc ctacctctgg tgtaaacacct gatatggctg atcaaattgc tagtcttgtt 720
ctggcaaac ttggcaagga tgccactaag ccacagcaag taactaagca gactgccaaa 780
gaaatcagac agaaaatttt gaataagccc cgccagaaga ggagcccaa taaacaatgc 840
actgttcagc agtggttttg gaagagaggc cccaatcaga attttggtgg tggagaaatg 900
ttaaaacttg gaactagtga cccacagttc cccattcttg cagaactcgc acccacagct 960
ggtgcgtttt tctttggatc aagattagag ttggccaaag tgcagaattt gtctgggaat 1020
cttgacgagc ccagaaagga tgtttatgaa ttgcgctata atggtgcaat tagatttgac 1080
agtacacttt caggttttga gaccataatg aaggtgttga atgagaattt gaatgcatat 1140
caacaacaag atggtatgat gaatatgagt ccaaaaccac agcgtcagcg tggtcagaag 1200
aatggacaag gagaaaatga taatataagt gttgcagcgc ctaaaagccg tgtgcagcaa 1260
aataagagta gagagttgac tgcagaggac atcagccttc ttaagaagat ggatgagccc 1320
tatactgaag acacctcaga aatataa 1347

```

<210> SEQ ID NO 70

<211> LENGTH: 1350

<212> TYPE: DNA

<213> ORGANISM: Porcine hemagglutinating encephalomyelitis coronavirus

<400> SEQUENCE: 70

```

atgtctttca ctctggcaa gcagtcagc agtagagcgt cctctggaaa tcgttctggt 60
aatggcatcc ttaagtgggc cgatcagtc gaccagtcta gaaatgttca aaccaggggt 120
agaagagttc aatccaagca aactgctact tctcagcaac catcaggagg gactgttgta 180
ccctactatt cttggttctc tggaattact cagtttcaaa agggaaagga gtttgaattt 240
gcagagggac aaggtgtgcc tattgcacca ggagtcccat ctactgaagc taaggggtac 300
tggtacagac acaacagacg ttcttttaaa acagccgacg gcaatcagcg tcaactgctg 360
ccacgatggg acttttacta cctgggaaca ggaccgatg ccaaagacca gtacggcacc 420
gacattgacg gagtcttctg ggtcgctagt aaccaggctg atattaatac cccggctgac 480
attgtcgatc gggatccaag tagcgatgag gctattccga ctaggtttcc gcctggcacg 540
gtactccctc aaggttacta tattgaaggc tcaggaaggt ctgctcctaa ttccagatct 600
acttcgcgtg caccacaatag agcccttagt gcaggatcgc gtagtagagc caattctggc 660
aatagaacct ctacccttgg tgtaaacacct gacatggctg atcaaattgc tagtcttgtt 720

```


-continued

ctggcaaac ttggcaagga tgccactaag cctcagcaag taactaagca gactgccaaa	780
gaggtcagac agaaaaatctt gaataagccc cgccagaaga ggagcccaa caaacaatgc	840
actgttcagc agtgttttgg gaagagaggc cccaatcaga attttgggtg tgagagaaatg	900
ttaaaacttg gaactagtga cccacagttc cccattcttg cagaactcgc acccacagct	960
ggtgcgtttt tctttggatc aagattagag ttggccaaag tgcagaatgt gtctgggaat	1020
cctgacgagc cccagaagga tgtttatgaa ttgcgctata atggcgcgat tagatttgac	1080
agcacactct caggttttga aaccattatg aaggtgctta accagaatgt gaatgcctat	1140
caacatcagg aagatgggat gatgaatatt agtcctaac cacagcggca gcgtggtcag	1200
aagaatggac aagtagaaaa tgataatgta agtgttgca cgcctaaaag ccgtgtgcag	1260
caaaaataaga gttagagagt gacagcagag gacatcagcc ttcttaagaa gatggatgag	1320
ccctatactg aagatacctc agaaatataa	1350

<210> SEQ ID NO 71

<211> LENGTH: 1356

<212> TYPE: DNA

<213> ORGANISM: Murine hepatitis virus

<400> SEQUENCE: 71

atgtcttttg ttctctggga agaaaatgcc ggtagcagaa gctcctcttg aaaccgcgct	60
ggtaaatggca tcctcaagaa gaccacttgg gctgacccaa ccgagcgttg aaatagaggc	120
agaaggaacc atccaagca gactgcaact actcagccca atgccgggag tgtggttccc	180
cattactctt ggttttcggg catcaccagc ttcaaaaagg gaaaggagtt ccagtttgca	240
caaggacagg gagtgcctat tgccagtggc atccccgctt cagagcaaaa gggatatttg	300
tatagacaca accgacgttc ttttaaaaca cctgatggcc agcacaagca gctactgccc	360
agatgggtatt tttactatct tggaacaggc ccccatgctg gcgcagagta tggcgacgat	420
atcgaaggag ttgtctgggt cgcaagccaa caggccgaca ctaagaccac tgccgatgtt	480
gttgaaaggg acccaagcag tcatgaggct attcctacta ggtttgcgcc cggcacggta	540
ttgcctcagg gcttttatgt agaaggctcg ggaaggctcg cacctgctag tcgatctggt	600
tcgcggctac aatcccgttg gccaaataat cgcgctagaa gcagttccaa ccagcgccag	660
cctgcctctg ctgtaaaac tgacatggcc gaagaaattg ctgctcttgt tttggctaag	720
cttggttaaag atgccggcca gcccaagcag gtaactaagc aaagcgccaa agaagtcagg	780
cagaaaatgt taactaagcc tcgtcaaaag aggactccaa acaagcagtg cccagtgcag	840
cagtgttttg ggaagagagg ccctaatacag aactttggag gctctgaaat gttaaaactt	900
ggaactagtg atccgcagtt cccattctt gcagagtttg ctccaacacc tagtgcttcc	960
ttctttggat ctaaaattaga attggtcaaa aagaactctg gtggtgctga tgaacccacc	1020
aaagatgttt atgaattgca gtattcaggt gcaattagat ttgatagtac tctaccgggt	1080
tttgagacta tcatgaaagt gttgactgag aatttgaatg cctaccagga ccaagctggt	1140
agtgtagatc tagtgagccc aaagcctcca agaagaggtc gtagacaggc tcaagaaaag	1200
aaagatgaag tagataatgt aagcgttgca aagcccaaaa gcttgggtgca gcgaaatgta	1260
agtagagaat taacccccga ggatcgtagc ctgctggctc agatcctaga cgatggcggt	1320
gtgccagatg ggttgaaga tgactctaata gtgtaa	1356

-continued

<210> SEQ ID NO 72
<211> LENGTH: 1365
<212> TYPE: DNA
<213> ORGANISM: Rat coronavirus

<400> SEQUENCE: 72

```
atgtcttttg ttcccgaca agaaaacgcc ggtagcagaa gtcctcttg aaaccgcgt      60
ggtaatggaa tcctcaagaa gaccacttgg gctgaccaa cagagcgcg aaaaaataat    120
ggaaatagag gcagaaggaa tcagcccaag cagactgcaa ctactcagcc caataccggg    180
agtgtggttc ccattactc ttggttttcg ggcattaccc aattccagaa gggaaaagag    240
ttccagtttg cagggtggaa aggagtgcct attgccaatg gaatcccacc ttctgagcaa    300
aagggatatt ggtatagaca caaccgtcgt tcttttaaaa cacctgatgg gcagcagaag    360
caactactcc ccagatggta tttttactat cttgggacgg gcccctatgc tggagccagt    420
ttcggagaca gcattgagg agtcttcttg gttgcaaata gtcaggcgga taccaacacc    480
tctgctgaca ttgttgaaag ggacccaagt agccatgagg ctattcctac taggtttgcg    540
cccgtacgg tattgcctca gggtttctat gttgaaggct cgggaaggtc tgcacctgct    600
agtcgatctg gttcgcggtc acaatccgtt gggccaaata atcgcgctag aagcagttcc    660
aaccagcgcc agcctgcctc tactgtaaaa cctgatatgg ccgaagaaat tctgctctt    720
gttttggtta atctaggcaa agatgccga cagcctaagc aagtaactaa gcaaagtgcc    780
aaagaagtca ggcagaaaat tttaaataag cctcgccaaa agaggactcc aaacaagcag    840
tgcccagtgc agcagtgttt tggaaagaga ggcccaatc agaatttttg aggccctgaa    900
atgttaaaac ttggaactag tgatccacag ttcccatto ttgcagagt ggcccaaca    960
cctggtgcct tcttcttttg atctaaatta gaattggtca aaaagaattc tggtgcggt    1020
gatgaaccca ccaaatgtgt gtatgagctg caatattcag gtgcagtcag attgatagt    1080
actctacctg gttttgagac tatcatgaaa gtgttgaatg agaatttgaa tgcctaccag    1140
aatcaagctg gtggtgcaga tgtagtgagc ccaaagcccc aaagaagag agggacgaaa    1200
caaacggctc agaaaagaag attagatagt ataagcgttg caaagcccaa aagtgcctg    1260
cagcgaatg taagcagaga attaaccca gaggatagaa gcctgttggc gcagatccta    1320
gatgatggcg ttgtgcctga tgggttagat gactctaatt tgtaa                    1365
```

<210> SEQ ID NO 73
<211> LENGTH: 1111
<212> TYPE: DNA
<213> ORGANISM: Human coronavirus OC43

<400> SEQUENCE: 73

```
atggctacag tcaaatgggc tgatgcatct gaaccacaac gtggtcgtca ggtagaata      60
ccttattctc ttatagccc ttgtcttgtt gatagtgaac aaccttgaa ggtgatacct    120
cgtaatttgg tacccatcaa caagaaagac aaaaataagc ttataggcta ttggaatgtt    180
caaaaacgtt tcagaactag aaagggcaaa cgggtggatt tgtcaccaa gctgcatttt    240
tattatcttg gcacaggacc ccataaagat gcaaaattta gagagcgtgt tgaagtgctc    300
gtctgggttg ctgttgatgg tgctaaaact gaacctacag gttacggtgt taggcgcaag    360
aattcagaac cagagatacc acacttcaat caaagctcc caaatggtgt tactgttgtt    420
```

-continued

gaagaacctg actcccgtgc tccttcccgg tctcagtcga ggtcgagag tcgcggtcgt	480
ggtgaatcca aacctcaatc tcggaatcct tcaagtgaac gaaaccataa cagtcaggat	540
gacatcatga aggcagttgc tgcggctcctt aaatcttttag gttttgacaa gcctcaggaa	600
aaagataaaa agtcagcgaa aacgggtact cctaagcctt ctcgtaatca gagtccctgct	660
tcttctcaaa cttctgccaa gagtcttgct cgttctcaga gttctgaaac aaaagaacaa	720
aagcatgaaa tgcaaaagcc acgggtggaaa agacagccta atgatgatgt gacatctaata	780
gtcacacaat gttttggccc cagagacctt gaccacaact ttggaagtgc aggtgtgtgtg	840
gccaatgggtg ttaaagctaa aggcatacca caatttgctg agcttggtgc gtcaacagct	900
gctatgtgtg ttgatagtca cattgtttcc aaagagtcag gcaacactgt ggtcttgact	960
ttcactacta gagtgaactg gcccaaagac catccacact tgggtaagtt tcttgaggag	1020
ttaaatgcat tcactagaga aatgcaacaa cactgaacca gtgcgtgatg aagtttctat	1080
tgaaactgac ataattgatg aagtaacta a	1111

<210> SEQ ID NO 74

<211> LENGTH: 1326

<212> TYPE: DNA

<213> ORGANISM: Porcine epidemic diarrhea virus

<400> SEQUENCE: 74

atggcttctg tcagctttca ggatcgtggc cgcaaacggg tgccattatc tctctatgcc	60
cctcttaggg ttactaatga caagcccctt tctaaggtac ttgcaacaa cgctgtaccc	120
actaacaagg ggaataagga ccagcaaat gggtactgga atgagcaaat tcgctggcgc	180
atgcgccgtg gtgagcgaat tgaacaacct tccaattggc atttctacta cctcggaaca	240
ggacctcacg gcgacctccg ttataggact cgtactgagg gtgttttctg ggttgctaaa	300
gaaggcgcaa agactgaacc cactaatttg ggtgtcagaa aggcgtctga aaagccaatc	360
attccaaaat tctctcaaca gctccccagt gtagttgaga ttgttgaacc taacacacct	420
cctgcttcac gtgcaaatc gcgtagcagg agtcgtggca atggcaacaa taggtctaga	480
tctccaagta acaacagagg caataaccag tcccgtggta attcacagaa tcgtggaaat	540
aaccagggtc gtggagcttc tcagaacaga ggaggcaata ataatacaa taacaagtct	600
cgtaaccagt ccaataacag gaaccagtca aatgaccgtg gtggtgtaac atcacgcgat	660
gatctggtgg ctgctgtcaa ggatgcactt aaatcttttg gtattggaga aaatcctgac	720
aggcataagc aacagcagaa gcctaagcag gaaaagtctg acaacagcgg caaaaataca	780
cctaagaaga acaaatccag ggccacttcg aaggaaactg acctcaaaga catcccagag	840
tggaggagaa ttccaaggg cgaaaatagc gtagcagctt gcttcggacc cagagggggc	900
ttcaaaaact ttggagatgc ggaatttgct gaaaaaggtg ttgatgcgtc aggctatgct	960
cagatcgcca gtttagcacc aaatggtgca gcattgctct ttggtggtaa tgtggtgtt	1020
cgtgagctag cggaactcta cgagattaca tacaactata aaatgactgt gccaaagtca	1080
gatccaaatg ttgagcttct tgtttcacag gtggatgcat ttaaaactgg gaatgcaaaa	1140
ctccagagaa agaagaaaa gaagaacaag cgtgaaacca cgctgcagca gcatgaagag	1200
gccatctacg atgatgtggg tgcgccatct gatgtgacct atgccaatct ggaatgggac	1260
acagctgttg atgggtgtga tacggccgtt gaaattatca acgagatctt cgatacagga	1320

-continued

aattaa 1326

<210> SEQ ID NO 75
<211> LENGTH: 1230
<212> TYPE: DNA
<213> ORGANISM: Infectious bronchitis virus

<400> SEQUENCE: 75

atggcaagcg gtaaagcagc tggaaaaaca gacgccccag cgccagtcac taaactagga 60
ggacaaaac cacctaaagt cggttcttct ggaaatgcat cttgggttca agcaataaaa 120
gccaagaagt taaatacacc tccgccaag tttgaaggta gcggtgttcc tgataacgaa 180
aacattaagc caagccagca acatgggatac tggagacgcc aagccagggt taagccaggc 240
aaaggtggaa gaaaaccagt ccagatgctt tggactttt actatactgg aacaggacct 300
gccgctgacc tgaactgggg tgatactcaa gatggtatag tgtgggttgc tgctaagggt 360
gctgatacta aatctagatc caatcagggt acaagagatc ctgataagtt tgaccaatac 420
ccactacgat tctcgatgg cggaacctgat ggtaatttcc gttgggactt cattccccctg 480
aaccgtggta ggagtggaa atcaacagca gcttcacgag cagcagctag tagagcacca 540
tcacgtgaag gttcgcgtgg tcgtagaagt gattctggag atgaccttat tgctcgtgca 600
gcaaagataa tccaggatca gcagaaaaag ggctctcgca ttaccaaggc aaaggcagat 660
gaaatggctc atcgccggta ttgcaagcgc actatccac ctaattatag ggttgatcaa 720
gtgtttggtc cccgtactaa aggtaaggag gggaattttg gtgatgacaa gatgaatgag 780
gaaggtatta aggatgggcg tgttacagca atgctcaacc tagtccttag cagccatgct 840
tgtctttttg gaagtagagt gacacccaaa cttcaactag atgggcttca cttgagattt 900
gaatttacta ctgtggtccc atgtgatgac ccgcagtttg ataattatgt gaaaatttgt 960
gatcagtgtg tcgatgggtg aggaacgcgt ccaaaagatg acgaaccaa accaaagtca 1020
cgctcaagtt caagacctgc tacaagagga aattctccag cgccaagaca acagcgccca 1080
aagaaggaga aaaagctaaa gaagcaggat gatgaagcag ataaagcatt gacctcagat 1140
gaggagagga acaatgcaca gctggaattt tatgatgagc ccaaggtaat taactggggg 1200
gatgcagctc taggagagaa tgaactttga 1230

<210> SEQ ID NO 76
<211> LENGTH: 38
<212> TYPE: DNA
<213> ORGANISM: SARS coronavirus GD69

<400> SEQUENCE: 76

cctccgtacc atctggggct gagctctttc atcgaggg 38

<210> SEQ ID NO 77
<211> LENGTH: 95
<212> TYPE: DNA
<213> ORGANISM: SARS coronavirus GD69

<400> SEQUENCE: 77

acgagttcgt ggtggtgacg gcaaaatgaa agagctcagc ccagatgggt acttctatta 60
cctaggaact ggccagaag cttcacttcc ctacg 95

-continued

<210> SEQ ID NO 78
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 78

acgagttcgt ggtggtgac 19

<210> SEQ ID NO 79
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 79

cgtagggaag tgaagcttc 19

<210> SEQ ID NO 80
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 80

gccttctttg ttag 14

<210> SEQ ID NO 81
<211> LENGTH: 40
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 81

gcctccgtac catctggggc tgagctcttt catcgaggc 40

<210> SEQ ID NO 82
<211> LENGTH: 38
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 82

taatacgact cactatagga cgagttcgtg gtggtgac 38

<210> SEQ ID NO 83
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

<400> SEQUENCE: 83

gccttctttg ttagcgtagg gaagtgaagc ttc 33

-continued

<210> SEQ ID NO 84
<211> LENGTH: 40
<212> TYPE: DNA
<213> ORGANISM: SARS coronavirus GD69

<400> SEQUENCE: 84

gcccacgtac catctggggc tgtagacagc agccgtgggc 40

<210> SEQ ID NO 85
<211> LENGTH: 98
<212> TYPE: DNA
<213> ORGANISM: SARS coronavirus GD69

<400> SEQUENCE: 85

ctctatgttt ataaggcta tcaacctata gatgctgctg tctacagccc cagatggtag 60

tattcttgct agtcacacta gccatcctta ctgcgctt 98

<210> SEQ ID NO 86
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 86

tacacacctc agcggtg 17

<210> SEQ ID NO 87
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 87

cacgaacgtg acgaat 16

<210> SEQ ID NO 88
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (21)..(26)
<223> OTHER INFORMATION: a, c, g, t, unknown, or other

<400> SEQUENCE: 88

gccggagctc tgcagaattc nnnnnn 26

<210> SEQ ID NO 89
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 89

-continued

gccggagctc tgcagaattc 20

<210> SEQ ID NO 90
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 90

gggttgggac taccctaagt gtga 24

<210> SEQ ID NO 91
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (11)
<223> OTHER INFORMATION: i

<400> SEQUENCE: 91

taacacacaa ncccatcatc a 21

<210> SEQ ID NO 92
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 92

ctaacatgct taggataatg g 21

<210> SEQ ID NO 93
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 93

gcctctcttg ttcttgcctg c 21

<210> SEQ ID NO 94
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 94

caggttaagcg taaaactcat c 21

1. In an assay for coronaviruses wherein the improvement comprises detectants specific for at least two genes selected from the group consisting of spike (S), envelope (E), membrane (M), and nucleocapsid (N).

2. The assay of claim 1 wherein the corona virus is a SARS virus.

3. The assay of claim 2 wherein the SARS virus is SARS-CoV.

4. The assay of claim 1 wherein the assay is a molecular-beacon-based multi-allelic RT-real-time-PCR assay.

5. The assay of claim 4 wherein the detectant is a molecular-beacon.

6. The assay of claim 5 wherein the molecular beacon is a mismatch-tolerant molecular beacons.

7. The assay of claim 1 wherein the assay is a PCR assay.

8. The assay of claim 7 wherein there are four sets of PCR primers for four different viral genes, and four different molecular beacons.

9. The assay of claim 8 wherein each molecular beacon is labeled with the same fluorophore.

10. The assay of claim 8 wherein each molecular beacon is specific for a different SARS-CoV gene.

11. The assay of claim 7 wherein the improvement further comprises an exogenous RNA standard that is added to the sample that can be reverse-transcribed and amplified by one of the primer sets.

12. The assay of claim 11 wherein the improvement further comprises the inclusion of a fifth molecular beacon that is labeled with a different fluorophore that is specific for the exogenous RNA standard.

13. The assay of claim 1 wherein the improvement further comprises RNA isolation from clinical samples

14. The assay of claim 13 wherein the sample includes blood, tissue, sputum, or nasopharyngeal aspiration samples.

15. The assay of claim 1 or 12 wherein the improvement further includes reverse transcription, PCR amplification and simultaneous automated amplicon detection in a spectrofluorometric thermal cycler that measures the fluorescence intensity of each color during the annealing phase of each thermal cycle.

16. The assay of claim 1 wherein the improvement further comprises the selection and detection of four target sequences that uniquely identify SARS-CoV.

17. The assay of claim 1 wherein the improvement further comprises including specific amplicon, primers and IPC standard along with the detectant for each gene.

18. The assay of claim 17 wherein the primers, amplicon and detectant include those having the formulas shown in FIGS. 3, 7, 11 and 15 for each gene and an IPC standard selected from those shown in FIG. 17.

19. The assay of claim 17 wherein the primers, amplicon and detectant include those having the formulas shown in FIGS. 4, 8, 12 and 16 for each gene and an IPC standard selected from those shown in FIG. 18.

20. The assay of claim 1 wherein the improvement further comprises a PCR multiplex format.

21. A kit for performing the assay of any one of claims 1-20.

22. The kit of claim 21 wherein the reagents are contained in individual containers.

23. The kit of claim 22 wherein the reagents are sufficient in amount to perform an assay of single sample.

24. The kit of claim 21 wherein the kit contains written instructions.

25. A reagent composition comprising one or more of the following reagent groups

S Gene	
LK249	5'-FAM- <u>CCCACGCCAGAAGGTAGATCACGA</u> ACTACA CGTGGG-3'-Dubcyl
LK249.N	5'-FAM- <u>GCCCCAGCCAGAGGTAGATCACGA</u> ACTACA CGTGGG-3'-Dubcyl
LK250	5'-CTCTATGTTTATAAGGGCTATCAACCTATAGATGTAGTT CGTGATCTACCTTCTGGTTTAACTTTGAAACCTATTTT AAGTTGCTCTTGG-3'
LK251	5'-CTCTATGTTTATAAGGGCTATCAACC-3'
LK251-T7	5'- <u>TAATACGACTCACTATAGG</u> CTCTATGTTTATAAGGGCTAT CAACC-3'
LK252	5'-CCAAGAGGCAACTTAAAAATAGTTTC-3'
LK252-RT	5'- <u>AGGCTGTAAGAA</u> CCAAGAGGCAACTTAAAAAT AGTTTC-3'
S-RT	5'-AGGCTGTAAGAA-3';
E Gene	
LK253	5'-FAM- <u>CCTCCGCACGAAAGCAAGAAAAAG</u> AAGTACGC XCGGAGG-3'-Dubcyl
LK253.N	5'-FAM- <u>GCCTCCGCACGAAAGCAAGAAAAAG</u> AAGTACGC CGGAGG-3'-Dubcyl
LK254	5'-CGGAAGAAACAGGTACGTTAATAGTTAATAGCGTACTTC TTTTCTTGCTTCTCGTGGTATTCTTGCTAGTCACACTAGCCA TCCTTACTGCGCTT-3'
LK255	5'-CGGAAGAAACAGGTACGTTAATAG-3'
LK255-T7	5'- <u>TAATACGACTCACTATAGG</u> CGGAAGAAACAGGT ACGTTAATAG-3'
LK256	5'-AAGCGCAGTAAGGATGGCTA-3'
LK256-RT	5'- <u>TATTGCAGCAGTACAAGCGCAGTAAGGATGGCTA</u> -3'
E-RT	5'-TATTGCAGCAGTAC-3';
M Gene	
LK257	5'-FAM- <u>CCTCCGACCCAATTAATTCTGTAGACAGCAGC</u> CGGAGG-3'-Dubcyl
LK257.N	5'-FAM- <u>GCCTCCGACCCAATTAATTCTGTAGACAGCAGC</u> CGGAGG-3'-Dubcyl
LK258	5'-CTTGTTTTCTCTGGCTCTTGTTGGCCAGTAACACTTGTCT TGTTTTGTGCTTGTCTGTCTACAGAATTAATTGGGTGACT GGCGGGATTGCGATTGCAATGGCTTG-3'
LK259	5'-CTTGTTTTCTCTGGCTCTTG-3'
	5'- <u>TAATACGACTCACTATAGG</u> CTTGTTCCT CTGGCTCTTG-3'
LK260	5'-CAAGCCATTGCAATCGCAATC-3'
LK260-RT	5'- <u>AAGCAACGAAGTAGCAAGCCATTGCAATCGCAATC</u> -3'

-continued

M-RT 5'-AAGCAACGAAGTAG-3';
or

IPC

LK265 5'-FAM-GCCACGTACCATCTGGGGCTGTAGACAGCAGC
CGTGGGC-3'-Dabcyl

LK266 5'-CTCTATGTTTATAAGGGCTATCAACCTATAGATGCTGCT
GTCTACAGCCCAGATGGTAGTATTCTTGCTAGTCACACTAG
CCATCCTTACTGCGCTT-3'

LK251 5'-CTCTATGTTTATAAGGGCTATCAACC-3'

-continued

LK251-T7 5'-TAATACGACTCACTATAGGCTCTATGTTTATAAGGGCTA
TCAACC-3'

LK256 5'-AAGCGCAGTAAGGATGGCTA-3'

LK256-RT 5'-TATTGCAGCAGTACAAGCGCAGTAAGGATGGCTA-3'

E-RT 5'-TATTGCAGCAGTAC-3'.

26. A kit containing the reagent composition of claim 25.

* * * * *

专利名称(译)	SARS相关冠状病毒的多等位基因分子检测		
公开(公告)号	US20060003340A1	公开(公告)日	2006-01-05
申请号	US10/917421	申请日	2004-08-13
申请(专利权)人(译)	桦木生物医学研究，有限责任公司		
当前申请(专利权)人(译)	桦木生物医学研究有限责任公司		
[标]发明人	KOSTRIKIS LEONDIOS G		
发明人	KOSTRIKIS, LEONDIOS G.		
IPC分类号	C12Q1/70 C12Q1/68 G01N33/53 C12N7/00 C12N7/01		
CPC分类号	C12Q1/70 G01N33/56983 C12Q1/701		
优先权	60/496995 2003-08-22 US 60/576314 2004-06-03 US		
外部链接	Espacenet USPTO		

摘要(译)

本发明涉及包括SARS病毒在内的冠状病毒的多等位基因RT-实时聚合酶链反应 (PCR) 测定。鉴定了SARS-CoV，S，E，M和N基因内的多个靶序列。四种不同靶标的使用增强了病毒的基本遗传漂变不会导致假阴性结果的可能性。设想了用于测定的多重测定形式。因此，本发明允许早期诊断SARS感染。该测定法可用于监测治疗方案，筛选潜在的抗SARS药剂以及需要定性和定量测定的类似应用。

