A super-potent tetramerized ACE2 protein displays enhanced neutralization of SARS-CoV-2 virus infection

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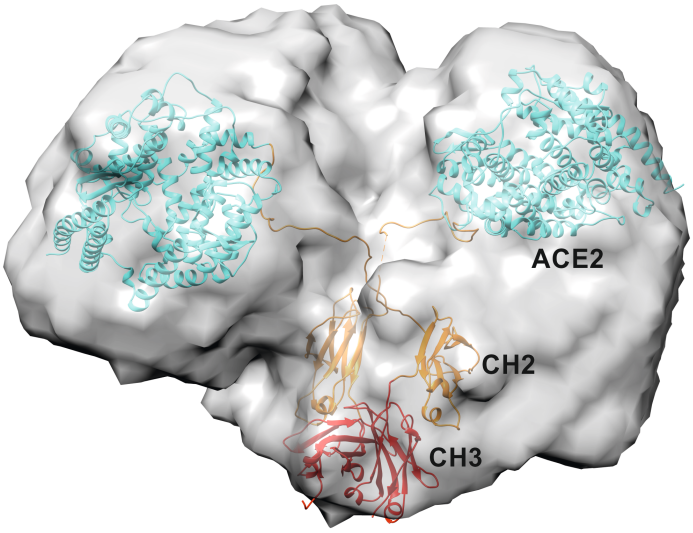
Supplementary Figure 1



Supplementary Figure 1. Structural analysis of ACE2-Fc protein

Representative model of chimaeric molecule ACE2-IgG fitted into the experimentally determined scattering envelope (represented in grey) determined by SEC-SAXS. A structural model of the components were fitted into the envelope (using UCSF chimera; J Comput Chem doi: 10.1002/jcc.20084) and comprise the ACE2 extracellular domain coloured in cyan, the IgG CH2 domain in orange and the IgG CH3 domain in red.

Supplementary Table 1: Biophysical determination of molecular weights for ACE2-Fc and ACE2-Fc-TD

A. Molecular weights determined by SEC-MALLS

Sample	Monomeric MW (kDa)	Concentration (mg/mL)	Mn (kDa)	Mw (kDa)	Mw/Mn
ACE2-Fc	95.3	1.0	211.8	211.9	1.000
ACE2-Fc-TD	100.2	1.0	447.9	449.2	1.114

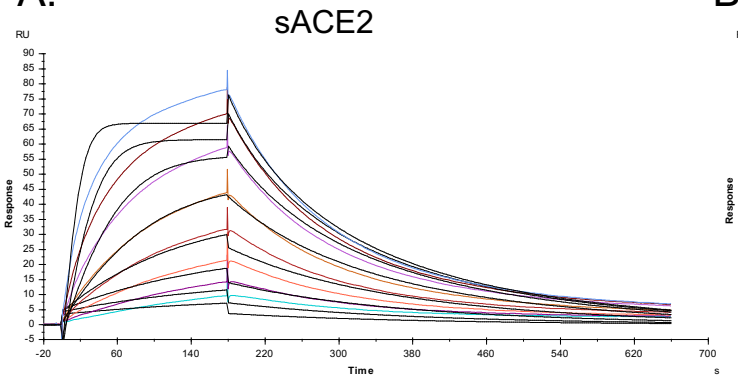
B. Molecular weights sedimentation co-efficient analysis

Sample	Monomeric MW (kDa)	Concentration (mg/mL)	MW (kDa)	Sed. Co (S)	f/f_0
ACE2-Fc	95.3	0.50	225	8.30	1.55
		0.25	221	8.38	1.52
		0.10	221	8.44	1.50
ACE2-Fc-TD	100.2	0.50	416	11.75	1.64
		0.25	386	11.83	1.56
		0.10	420	11.85	1.64

Note: For each sample concentration the signal-weighted sedimentation co-efficient and the estimated molecular weight of each species is shown, together with the best-fit frictional ratio for the distribution.

Supplementary Figure 2

A.



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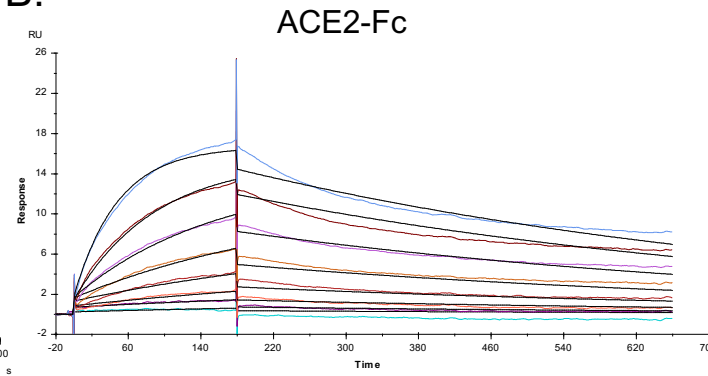
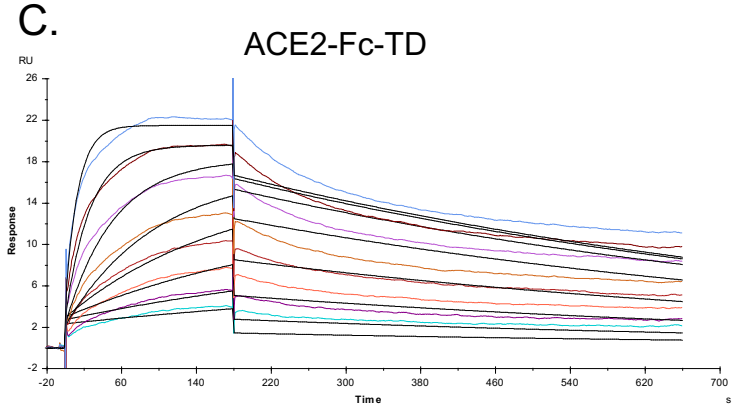


C.



D.

	K_d (nM)	k_{on} ($M^{-1}s^{-1}$)	k_{off} (s^{-1})
sACE2	22 ±3	5.21×10^5 $\pm 0.49 \times 10^5$	0.012 ±0.0007
ACE2-Fc	21 ±7	0.92×10^5 $\pm 0.06 \times 10^5$	0.0019 ±0.0006
ACE2-Fc-TD	3.9 ±0.3	4.55×10^5 $\pm 1.34 \times 10^5$	0.0017 ±0.0006

Supplementary Figure S2: SPR analysis of ACE2 proteins binding to SARS-Cov-2-RBD. Sensograms for sACE2 (A), ACE2-Fc (B) and ACE2-Fc-TD (C) binding to SARS-Cov-2-RBD-Biotin are shown in colour, together with data fitting to a 1:1 kinetics model shown in black. Biotinylated SARS-Cov-2-RBD was captured on a streptavidin-coated chip and ACE2 antibodies flowed over the surface at 1.56, 3.13, 6.25, 12.5, 25, 50, 100 and 200nM. Kinetic parameters are shown in (D). Sensograms shown are representative of two independent experiments and values are the mean averages of two experiments with errors the standard deviation from the mean.

Supplementary Figure 3: sequence of the coding regions of the proteins used

Sequence shown is nucleotides and derived amino-acids of ACE2-Fc-TD. All proteins were expressed by secretion from Expi293F cells using the pTT5 vector. Leader sequence for secretion from Expi293F cells and the p53 tetramerization domain are underlined in the ACE2-Fc-TD.

ACE2-Fc-TD in pTT5

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CR3022-Fab-TD(VH-CH1-TD + VL-CL)

CR3022 VH-CH1-TD

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CR3022 VL-CL.

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   210       220       230       240       250       260       270       280       290       300
 GCCTCCTAAGCTGCTGATCTACTGGGCCAGCACCAGAGAAAGCGGCGTGCCCGATAGATTTTCTGGCAGCGGCTCTGGCACCGACTTCACCCTGACAATT
 CGGAGGATTCGACGACTAGATGACCCGGTCGTGGTCTCTTTCGCCGCACGGGCTATCTAAAAGACCGTCGCCGAGACCGTGGCTGAAGTGGGACTGTTAA
  ProProLysLeuLeuIleTyrTrpAlaSerThrArgGluSerGlyValProAspArgPheSerGlySerGlySerGlyThrAspPheThrLeuThrIle>

   310       320       330       340       350       360       370       380       390       400
 AGCTCCCTGCAGGCCGAGGATGTGGCCGTGTACTACTGCCAGCAGTACTACAGCACCCCTTACACCTTTGGCCAGGGCACCAAGGTGGAAATCAAGCGTA
 TCGAGGGACGTCCGGCTCCTACACCGGCACATGATGACGGTCGTCATGATGTCGTGGGGAATGTGGAAACCGGTCCCGTGGTTCCACCTTTAGTTCGCAT
 SerSerLeuGlnAlaGluAspValAlaValTyrTyrCysGlnGlnTyrTyrSerThrProTyrThrPheGlyGlnGlyThrLysValGluIleLysArg>

   410       420       430       440       450       460       470       480       490       500
 CGGTGGCCGCTCCCTCCGTGTTCATCTTCCCACCTTCCGACGAGCAGCTGAAGTCCGGCACCGCTTCTGTCGTGTGCCTGCTGAACAACTTCTACCCCCG
 GCCACCGGCGAGGGAGGCACAAGTAGAAGGGTGGAAGGCTGCTCGTCGACTTCAGGCCGTGGCGAAGACAGCACACGGACGACTTGTTGAAGATGGGGGC
ThrValAlaAlaProSerValPheIlePheProProSerAspGluGlnLeuLysSerGlyThrAlaSerValValCysLeuLeuAsnAsnPheTyrProArg>

   510       520       530       540       550       560       570       580       590       600
 CGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGTCCGGCAACTCCCAGGAATCCGTGACCGAGCAGGACTCCAAGGACAGCACCTACTCCCTG
 GCTCCGGTTCCACGTCACCTTCCACCTGTTGCGGGACGTCAGGCCGTTGAGGGTCCTTAGGCACTGGCTCGTCCTGAGGTTCCTGTCGTGGATGAGGGAC
  GluAlaLysValGlnTrpLysValAspAsnAlaLeuGlnSerGlyAsnSerGlnGluSerValThrGluGlnAspSerLysAspSerThrTyrSerLeu>

   610       620       630       640       650       660       670       680       690       700
 TCCTCCACCCTGACCCTGTCCAAGGCCGACTACGAGAAGCACAAGGTGTACGCCTGCGAAGTGACCCACCAGGGCCTGTCTAGCCCCGTGACCAAGTCTT
 AGGAGGTGGGACTGGGACAGGTTCCGGCTGATGCTCTTCGTGTTCCACATGCGGACGCTTCACTGGGTGGTCCCGGACAGATCGGGGCACTGGTTCAGAA
 SerSerThrLeuThrLeuSerLysAlaAspTyrGluLysHisLysValTyrAlaCysGluValThrHisGlnGlyLeuSerSerProValThrLysSer>

   710       720
 TCAACCGGGGCGAGTGT
 AGTTGGCCCCGCTCACA
PheAsnArgGlyGluCys>
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CR3022-scFv-TD

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    10        20        30        40        50        60        70        80        90       100
 ATGGGATGGTCTTGTATAATTCTGTTCCTGGTGGCAACAGCAACAGGAGTGCATAGCCAGATGCAGCTGGTGCAGTCTGGCACCGAAGTGAAGAAGCCTG
 TACCCTACCAGAACATATTAAGACAAGGACCACCGTTGTCGTTGTCCTCACGTATCGGTCTACGTCGACCACGTCAGACCGTGGCTTCACTTCTTCGGAC
 MetGlyTrpSerCysIleIleLeuPheLeuValAlaThrAlaThrGlyValHisSerGlnMetGlnLeuValGlnSerGlyThrGluValLysLysPro>

   110       120       130       140       150       160       170       180       190       200
 GCGAGAGCCTGAAGATCAGCTGCAAAGGCAGCGGCTACGGCTTCATCACCTACTGGATCGGCTGGGTCCGACAGATGCCTGGCAAAGGCCTTGAGTGGAT
 CGCTCTCGGACTTCTAGTCGACGTTTCCGTCGCCGATGCCGAAGTAGTGGATGACCTAGCCGACCCAGGCTGTCTACGGACCGTTTCCGGAACTCACCTA
GlyGluSerLeuLysIleSerCysLysGlySerGlyTyrGlyPheIleThrTyrTrpIleGlyTrpValArgGlnMetProGlyLysGlyLeuGluTrpMet>
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   210       220       230       240       250       260       270       280       290       300
 GGGCATCATCTACCCCGGCGACAGCGAGACAAGATACAGCCCTAGCTTCCAGGGCCAAGTGACCATCAGCGCCGACAAGAGCATCAACACCGCCTACCTT
 CCCGTAGTAGATGGGGCCGCTGTCGCTCTGTTCTATGTCGGGATCGAAGGTCCCGGTTCACTGGTAGTCGCGGCTGTTCTCGTAGTTGTGGCGGATGGAA
  GlyIleIleTyrProGlyAspSerGluThrArgTyrSerProSerPheGlnGlyGlnValThrIleSerAlaAspLysSerIleAsnThrAlaTyrLeu>

   310       320       330       340       350       360       370       380       390       400
 CAGTGGTCCAGCCTGAAGGCCTCTGACACCGCCATCTACTATTGTGCCGGCGGAAGCGGCATCAGCACCCCTATGGATGTTTGGGGCCAGGGCACCACAG
 GTCACCAGGTCGGACTTCCGGAGACTGTGGCGGTAGATGATAACACGGCCGCCTTCGCCGTAGTCGTGGGGATACCTACAAACCCCGGTCCCGTGGTGTC
 GlnTrpSerSerLeuLysAlaSerAspThrAlaIleTyrTyrCysAlaGlyGlySerGlyIleSerThrProMetAspValTrpGlyGlnGlyThrThr>

   410       420       430       440       450       460       470       480       490       500
 TGACAGTTGGCGGAGGTGGAAGCGGAGGCGGAGGATCTGGTGGTGGTGGATCTGACATCCAGCTGACACAGAGCCCTGATAGCCTGGCCGTGTCTCTGGG
 ACTGTCAACCGCCTCCACCTTCGCCTCCGCCTCCTAGACCACCACCACCTAGACTGTAGGTCGACTGTGTCTCGGGACTATCGGACCGGCACAGAGACCC
ValThrValGlyGlyGlyGlySerGlyGlyGlyGlySerGlyGlyGlyGlySerAspIleGlnLeuThrGlnSerProAspSerLeuAlaValSerLeuGly>
 ____________________________________________320 aa____________________________________________>

   510       520       530       540       550       560       570       580       590       600
 AGAGAGAGCCACCATCAACTGCAAGAGCAGCCAGAGCGTGCTGTACTCCAGCATCAACAAGAACTACCTGGCCTGGTATCAGCAGAAGCCCGGCCAGCCT
 TCTCTCTCGGTGGTAGTTGACGTTCTCGTCGGTCTCGCACGACATGAGGTCGTAGTTGTTCTTGATGGACCGGACCATAGTCGTCTTCGGGCCGGTCGGA
  GluArgAlaThrIleAsnCysLysSerSerGlnSerValLeuTyrSerSerIleAsnLysAsnTyrLeuAlaTrpTyrGlnGlnLysProGlyGlnPro>

   610       620       630       640       650       660       670       680       690       700
 CCTAAGCTGCTGATCTACTGGGCCAGCACCAGAGAAAGCGGCGTGCCCGATAGATTTTCTGGCAGCGGCTCTGGCACCGACTTCACCCTGACAATTAGCT
 GGATTCGACGACTAGATGACCCGGTCGTGGTCTCTTTCGCCGCACGGGCTATCTAAAAGACCGTCGCCGAGACCGTGGCTGAAGTGGGACTGTTAATCGA
 ProLysLeuLeuIleTyrTrpAlaSerThrArgGluSerGlyValProAspArgPheSerGlySerGlySerGlyThrAspPheThrLeuThrIleSer>

   710       720       730       740       750       760       770       780       790       800
 CCCTGCAGGCCGAGGATGTGGCCGTGTACTACTGCCAGCAGTACTACAGCACCCCTTACACCTTTGGCCAGGGCACCAAGGTGGAAATCAAGCGTAAGAA
 GGGACGTCCGGCTCCTACACCGGCACATGATGACGGTCGTCATGATGTCGTGGGGAATGTGGAAACCGGTCCCGTGGTTCCACCTTTAGTTCGCATTCTT
SerLeuGlnAlaGluAspValAlaValTyrTyrCysGlnGlnTyrTyrSerThrProTyrThrPheGlyGlnGlyThrLysValGluIleLysArgLysLys>

   810       820       830       840       850       860       870       880       890       900
 GAAACCACTGGATGGAGAATATTTCACCCTTCAGATCCGTGGGCGTGAGCGCTTCGAGATGTTCCGAGAGCTGAATGAGGCCTTGGAACTCAAGGATGCC
 CTTTGGTGACCTACCTCTTATAAAGTGGGAAGTCTAGGCACCCGCACTCGCGAAGCTCTACAAGGCTCTCGACTTACTCCGGAACCTTGAGTTCCTACGG
  LysProLeuAspGlyGluTyrPheThrLeuGlnIleArgGlyArgGluArgPheGluMetPheArgGluLeuAsnGluAlaLeuGluLeuLysAspAla>

   910       920       930       940       950       960
 CAGGCTGGGAAGGAGCCAGGGGACTACAAGGACGACGACGACAAACACCACCATCACCACCAC
 GTCCGACCCTTCCTCGGTCCCCTGATGTTCCTGCTGCTGCTGTTTGTGGTGGTAGTGGTGGTG
 GlnAlaGlyLysGluProGlyAspTyrLysAspAspAspAspLysHisHisHisHisHisHis>
                           Flag Tag
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CR3014-Fab-TD (VH-CH1-TD + VL-CL)

CR3014 VH1-CH1-TD

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    10        20        30        40        50        60        70        80        90       100
 ATGGGATGGTCTTGTATAATTCTGTTCCTGGTGGCAACAGCAACAGGAGTGCATAGCGAGGTGCAGCTGGTTGAATCTGGCGGAGGACTGGTTCAGCCTG
 TACCCTACCAGAACATATTAAGACAAGGACCACCGTTGTCGTTGTCCTCACGTATCGCTCCACGTCGACCAACTTAGACCGCCTCCTGACCAAGTCGGAC
 MetGlyTrpSerCysIleIleLeuPheLeuValAlaThrAlaThrGlyValHisSerGluValGlnLeuValGluSerGlyGlyGlyLeuValGlnPro>
   110       120       130       140       150       160       170       180       190       200
 GCGGATCTCTGAGACTGTCTTGTGCCGCCAGCGGCTTCACCTTCAGCGACCACTATATGGACTGGGTCCGACAGGCCCCTGGCAAAGGACTTGAGTGGGT
 CGCCTAGAGACTCTGACAGAACACGGCGGTCGCCGAAGTGGAAGTCGCTGGTGATATACCTGACCCAGGCTGTCCGGGGACCGTTTCCTGAACTCACCCA
GlyGlySerLeuArgLeuSerCysAlaAlaSerGlyPheThrPheSerAspHisTyrMetAspTrpValArgGlnAlaProGlyLysGlyLeuGluTrpVal>

   210       220       230       240       250       260       270       280       290       300
 CGGACGGACCAGAAACAAGGCCAACAGCTACACCACAGAGTACGCCGCCTCTGTGAAGGGCAGATTCACCATCAGCCGGGACGACAGCAAGAACAGCCTG
 GCCTGCCTGGTCTTTGTTCCGGTTGTCGATGTGGTGTCTCATGCGGCGGAGACACTTCCCGTCTAAGTGGTAGTCGGCCCTGCTGTCGTTCTTGTCGGAC
  GlyArgThrArgAsnLysAlaAsnSerTyrThrThrGluTyrAlaAlaSerValLysGlyArgPheThrIleSerArgAspAspSerLysAsnSerLeu>

   310       320       330       340       350       360       370       380       390       400
 TACCTTCAGATGAACTCCCTGAAAACCGAGGACACCGCCGTGTACTACTGCGCCAGAGGCATCAGCCCCTTCTACTTCGATTATTGGGGCCAGGGCACCC
 ATGGAAGTCTACTTGAGGGACTTTTGGCTCCTGTGGCGGCACATGATGACGCGGTCTCCGTAGTCGGGGAAGATGAAGCTAATAACCCCGGTCCCGTGGG
 TyrLeuGlnMetAsnSerLeuLysThrGluAspThrAlaValTyrTyrCysAlaArgGlyIleSerProPheTyrPheAspTyrTrpGlyGlnGlyThr>

   410       420       430       440       450       460       470       480       490       500
 TGGTCACAGTTGCCTCCACTAAGGGGCCGAGTGTTTTTCCACTTGCCCCATCCAGTAAGAGCACCTCTGGAGGAACTGCCGCCCTGGGTTGCCTTGTTAA
 ACCAGTGTCAACGGAGGTGATTCCCCGGCTCACAAAAAGGTGAACGGGGTAGGTCATTCTCGTGGAGACCTCCTTGACGGCGGGACCCAACGGAACAATT
LeuValThrValAlaSerThrLysGlyProSerValPheProLeuAlaProSerSerLysSerThrSerGlyGlyThrAlaAlaLeuGlyCysLeuValLys>

   510       520       530       540       550       560       570       580       590       600
 GGATTACTTCCCTGAGCCAGTAACTGTTAGCTGGAACTCTGGCGCTCTGACCAGCGGAGTGCACACCTTCCCTGCTGTGCTGCAGTCCTCAGGGCTGTAC
 CCTAATGAAGGGACTCGGTCATTGACAATCGACCTTGAGACCGCGAGACTGGTCGCCTCACGTGTGGAAGGGACGACACGACGTCAGGAGTCCCGACATG
  AspTyrPheProGluProValThrValSerTrpAsnSerGlyAlaLeuThrSerGlyValHisThrPheProAlaValLeuGlnSerSerGlyLeuTyr>

   610       620       630       640       650       660       670       680       690       700
 TCCCTTTCTAGTGTCGTAACAGTGCCATCTTCTAGCCTGGGGACCCAGACGTACATCTGTAACGTGAATCATAAACCCAGTAACACAAAGGTAGATAAGA
 AGGGAAAGATCACAGCATTGTCACGGTAGAAGATCGGACCCCTGGGTCTGCATGTAGACATTGCACTTAGTATTTGGGTCATTGTGTTTCCATCTATTCT
 SerLeuSerSerValValThrValProSerSerSerLeuGlyThrGlnThrTyrIleCysAsnValAsnHisLysProSerAsnThrLysValAspLys>

   710       720       730       740       750       760       770       780       790       800
 AGGTTGAACCTAAGTCCTGCGATAAGACACATACCAAGAAGAAACCACTGGATGGAGAATATTTCACCCTTCAGATCCGTGGGCGTGAGCGCTTCGAGAT
 TCCAACTTGGATTCAGGACGCTATTCTGTGTATGGTTCTTCTTTGGTGACCTACCTCTTATAAAGTGGGAAGTCTAGGCACCCGCACTCGCGAAGCTCTA
LysValGluProLysSerCysAspLysThrHisThrLysLysLysProLeuAspGlyGluTyrPheThrLeuGlnIleArgGlyArgGluArgPheGluMet>
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   810       820       830       840       850       860       870       880
GTTCCGAGAGCTGAATGAGGCCTTGGAACTCAAGGATGCCCAGGCTGGGAAGGAGCCAGGGCACCACCACCATCACCAC
CAAGGCTCTCGACTTACTCCGGAACCTTGAGTTCCTACGGGTCCGACCCTTCCTCGGTCCCGTGGTGGTGGTAGTGGTG
 PheArgGluLeuAsnGluAlaLeuGluLeuLysAspAlaGlnAlaGlyLysGluProGlyHisHisHisHisHisHis>
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CR3014 VL-CL

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    10        20        30        40        50        60        70        80        90       100
ATGGGATGGTCTTGTATAATTCTGTTCCTGGTGGCAACAGCAACAGGAGTGCATAGCGAGCTGACACAGAGCCCTTCTAGCCTGTCTGCCAGCGTGGGCG
TACCCTACCAGAACATATTAAGACAAGGACCACCGTTGTCGTTGTCCTCACGTATCGCTCGACTGTGTCTCGGGAAGATCGGACAGACGGTCGCACCCGC
MetGlyTrpSerCysIleIleLeuPheLeuValAlaThrAlaThrGlyValHisSerGluLeuThrGlnSerProSerSerLeuSerAlaSerValGly>

   110       120       130       140       150       160       170       180       190       200
ACAGAGTGACCATCACATGTAGAGCCAGCCAGAGCATCAGCAGCTACCTGAACTGGTATCAGCAGAAGCCCGGCAAGGCCCCTAAACTGCTGATCTATGC
TGTCTCACTGGTAGTGTACATCTCGGTCGGTCTCGTAGTCGTCGATGGACTTGACCATAGTCGTCTTCGGGCCGTTCCGGGGATTTGACGACTAGATACG
AspArgValThrIleThrCysArgAlaSerGlnSerIleSerSerTyrLeuAsnTrpTyrGlnGlnLysProGlyLysAlaProLysLeuLeuIleTyrAla>

   210       220       230       240       250       260       270       280       290       300
CGCCAGCTCTCTGCAGTCTGGCGTGCCATCTAGATTTTCCGGCAGCGGCTCTGGCACCGACTTCACCCTGACCATATCTAGCCTGCAGCCTGAGGACTTC
GCGGTCGAGAGACGTCAGACCGCACGGTAGATCTAAAAGGCCGTCGCCGAGACCGTGGCTGAAGTGGGACTGGTATAGATCGGACGTCGGACTCCTGAAG
 AlaSerSerLeuGlnSerGlyValProSerArgPheSerGlySerGlySerGlyThrAspPheThrLeuThrIleSerSerLeuGlnProGluAspPhe>

   310       320       330       340       350       360       370       380       390       400
GCCACCTACTACTGCCAGCAGAGCTACAGCACCCCTCCTACATTTGGCCAGGGCACCAAGGTGGAAATCAAGCGTACGGTGGCCGCTCCCTCCGTGTTCA
CGGTGGATGATGACGGTCGTCTCGATGTCGTGGGGAGGATGTAAACCGGTCCCGTGGTTCCACCTTTAGTTCGCATGCCACCGGCGAGGGAGGCACAAGT
AlaThrTyrTyrCysGlnGlnSerTyrSerThrProProThrPheGlyGlnGlyThrLysValGluIleLysArgThrValAlaAlaProSerValPhe>

   410       420       430       440       450       460       470       480       490       500
TCTTCCCACCTTCCGACGAGCAGCTGAAGTCCGGCACCGCTTCTGTCGTGTGCCTGCTGAACAACTTCTACCCCCGCGAGGCCAAGGTGCAGTGGAAGGT
AGAAGGGTGGAAGGCTGCTCGTCGACTTCAGGCCGTGGCGAAGACAGCACACGGACGACTTGTTGAAGATGGGGGCGCTCCGGTTCCACGTCACCTTCCA
IlePheProProSerAspGluGlnLeuLysSerGlyThrAlaSerValValCysLeuLeuAsnAsnPheTyrProArgGluAlaLysValGlnTrpLysVal>

   510       520       530       540       550       560       570       580       590       600
GGACAACGCCCTGCAGTCCGGCAACTCCCAGGAATCCGTGACCGAGCAGGACTCCAAGGACAGCACCTACTCCCTGTCCTCCACCCTGACCCTGTCCAAG
CCTGTTGCGGGACGTCAGGCCGTTGAGGGTCCTTAGGCACTGGCTCGTCCTGAGGTTCCTGTCGTGGATGAGGGACAGGAGGTGGGACTGGGACAGGTTC
 AspAsnAlaLeuGlnSerGlyAsnSerGlnGluSerValThrGluGlnAspSerLysAspSerThrTyrSerLeuSerSerThrLeuThrLeuSerLys>

   610       620       630       640       650       660       670       680       690
GCCGACTACGAGAAGCACAAGGTGTACGCCTGCGAAGTGACCCACCAGGGCCTGTCTAGCCCCGTGACCAAGTCTTTCAACCGGGGCGAGTGT
CGGCTGATGCTCTTCGTGTTCCACATGCGGACGCTTCACTGGGTGGTCCCGGACAGATCGGGGCACTGGTTCAGAAAGTTGGCCCCGCTCACA
AlaAspTyrGluLysHisLysValTyrAlaCysGluValThrHisGlnGlyLeuSerSerProValThrLysSerPheAsnArgGlyGluCys>
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H4-Fab-TD (VH-CH-TD + VL-CL)

H4 VH1-CH1-TD

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    10        20        30        40        50        60        70        80        90       100
ATGGGCTGGTCCTGCATCATCCTGTTTCTGGTGGCCACAGCCACAGGCGTGCACTCTCAGGTTCAGCTGGTTCAGTCTGGCGCCGAAGTGAAGAAACCTG
TACCCGACCAGGACGTAGTAGGACAAAGACCACCGGTGTCGGTGTCCGCACGTGAGAGTCCAAGTCGACCAAGTCAGACCGCGGCTTCACTTCTTTGGAC
MetGlyTrpSerCysIleIleLeuPheLeuValAlaThrAlaThrGlyValHisSerGlnValGlnLeuValGlnSerGlyAlaGluValLysLysPro>

   110       120       130       140       150       160       170       180       190       200
GCGCCTCTGTGAAGGTGTCCTGCAAGGCCAGCGGCTACACCTTTACCGGCTACTACATGCACTGGGTCCGACAGGCTCCAGGACAGGGACTTGAGTGGAT
CGCGGAGACACTTCCACAGGACGTTCCGGTCGCCGATGTGGAAATGGCCGATGATGTACGTGACCCAGGCTGTCCGAGGTCCTGTCCCTGAACTCACCTA
GlyAlaSerValLysValSerCysLysAlaSerGlyTyrThrPheThrGlyTyrTyrMetHisTrpValArgGlnAlaProGlyGlnGlyLeuGluTrpMet>

   210       220       230       240       250       260       270       280       290       300
GGGCAGAATCAACCCCAATAGCGGCGGCACCAACTACGCCCAGAAATTCCAGGGCAGAGTGACCATGACCAGAGACACCAGCATCAGCACCGCCTACATG
CCCGTCTTAGTTGGGGTTATCGCCGCCGTGGTTGATGCGGGTCTTTAAGGTCCCGTCTCACTGGTACTGGTCTCTGTGGTCGTAGTCGTGGCGGATGTAC
 GlyArgIleAsnProAsnSerGlyGlyThrAsnTyrAlaGlnLysPheGlnGlyArgValThrMetThrArgAspThrSerIleSerThrAlaTyrMet>

   310       320       330       340       350       360       370       380       390       400
GAACTGAGCCGGCTGAGATCCGATGACACCGCCGTGTACTACTGCGCCAGAGTGCCTTACTGTAGCAGCACCAGCTGCCACAGAGACTGGTACTTCGACC
CTTGACTCGGCCGACTCTAGGCTACTGTGGCGGCACATGATGACGCGGTCTCACGGAATGACATCGTCGTGGTCGACGGTGTCTCTGACCATGAAGCTGG
GluLeuSerArgLeuArgSerAspAspThrAlaValTyrTyrCysAlaArgValProTyrCysSerSerThrSerCysHisArgAspTrpTyrPheAsp>

   410       420       430       440       450       460       470       480       490       500
TGTGGGGCAGAGGCACACTGGTCACAGTGTCTAGCGCCAGCACAAAGGGCCCTAGCGTTTTCCCACTGGCTCCCAGCAGCAAGTCTACCTCTGGTGGAAC
ACACCCCGTCTCCGTGTGACCAGTGTCACAGATCGCGGTCGTGTTTCCCGGGATCGCAAAAGGGTGACCGAGGGTCGTCGTTCAGATGGAGACCACCTTG
LeuTrpGlyArgGlyThrLeuValThrValSerSerAlaSerThrLysGlyProSerValPheProLeuAlaProSerSerLysSerThrSerGlyGlyThr>

   510       520       530       540       550       560       570       580       590       600
AGCCGCTCTGGGCTGCCTGGTCAAGGATTACTTTCCCGAGCCTGTGACCGTGTCCTGGAATAGCGGAGCACTGACAAGCGGCGTGCACACCTTTCCAGCT
TCGGCGAGACCCGACGGACCAGTTCCTAATGAAAGGGCTCGGACACTGGCACAGGACCTTATCGCCTCGTGACTGTTCGCCGCACGTGTGGAAAGGTCGA
 AlaAlaLeuGlyCysLeuValLysAspTyrPheProGluProValThrValSerTrpAsnSerGlyAlaLeuThrSerGlyValHisThrPheProAla>

   610       620       630       640       650       660       670       680       690       700
GTGCTGCAAAGCAGCGGCCTGTACTCTCTGAGCAGCGTCGTGACAGTGCCTAGCAGCTCTCTGGGCACCCAGACCTACATCTGCAATGTGAACCACAAGC
CACGACGTTTCGTCGCCGGACATGAGAGACTCGTCGCAGCACTGTCACGGATCGTCGAGAGACCCGTGGGTCTGGATGTAGACGTTACACTTGGTGTTCG
ValLeuGlnSerSerGlyLeuTyrSerLeuSerSerValValThrValProSerSerSerLeuGlyThrGlnThrTyrIleCysAsnValAsnHisLys>

   710       720       730       740       750       760       770       780       790       800
CTAGCAACACCAAGGTGGACAAGAAGGTGGAACCCAAGAGCTGCGACAAGACCCACACCAAGAAGAAGCCTCTGGACGGCGAGTACTTCACTCTGCAGAT
GATCGTTGTGGTTCCACCTGTTCTTCCACCTTGGGTTCTCGACGCTGTTCTGGGTGTGGTTCTTCTTCGGAGACCTGCCGCTCATGAAGTGAGACGTCTA
ProSerAsnThrLysValAspLysLysValGluProLysSerCysAspLysThrHisThrLysLysLysProLeuAspGlyGluTyrPheThrLeuGlnIle>
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   810       820       830       840       850       860       870       880       890       900
CCGGGGCAGAGAACGCTTCGAGATGTTTAGAGAGCTGAACGAGGCCCTGGAACTGAAGGATGCCCAGGCCGGAAAAGAGCCTGGACACCACCATCACCAT
GGCCCCGTCTCTTGCGAAGCTCTACAAATCTCTCGACTTGCTCCGGGACCTTGACTTCCTACGGGTCCGGCCTTTTCTCGGACCTGTGGTGGTAGTGGTA
 ArgGlyArgGluArgPheGluMetPheArgGluLeuAsnGluAlaLeuGluLeuLysAspAlaGlnAlaGlyLysGluProGly HisHisHisHisHis>

CAC
GTG
His>
___>
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H4 VL-CL

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    10        20        30        40        50        60        70        80        90       100
ATGGGCTGGTCCTGCATCATCCTGTTTCTGGTGGCCACAGCCACAGGCGTGCACAGCGATATCCAGATGACACAGAGCCCTCTGAGCCTGCCTGTGACAC
TACCCGACCAGGACGTAGTAGGACAAAGACCACCGGTGTCGGTGTCCGCACGTGTCGCTATAGGTCTACTGTGTCTCGGGAGACTCGGACGGACACTGTG
MetGlyTrpSerCysIleIleLeuPheLeuValAlaThrAlaThrGlyValHisSerAspIleGlnMetThrGlnSerProLeuSerLeuProValThr>

   110       120       130       140       150       160       170       180       190       200
CTGGCGAACCTGCCAGCATCAGCTGTAGAAGCAGCCAGAGCCTGCTGGACAGCGACGACGGCAATACCTACCTGGACTGGTATCTGCAGAAGCCCGGCCA
GACCGCTTGGACGGTCGTAGTCGACATCTTCGTCGGTCTCGGACGACCTGTCGCTGCTGCCGTTATGGATGGACCTGACCATAGACGTCTTCGGGCCGGT
ProGlyGluProAlaSerIleSerCysArgSerSerGlnSerLeuLeuAspSerAspAspGlyAsnThrTyrLeuAspTrpTyrLeuGlnLysProGlyGln>

   210       220       230       240       250       260       270       280       290       300
GTCTCCTCAGCTGCTGATCTACACCCTGAGCTACAGAGCCAGCGGCGTGCCCGATAGATTTTCTGGCTCTGGCAGCGGCACCGACTTCACCCTGAAGATC
CAGAGGAGTCGACGACTAGATGTGGGACTCGATGTCTCGGTCGCCGCACGGGCTATCTAAAAGACCGAGACCGTCGCCGTGGCTGAAGTGGGACTTCTAG
 SerProGlnLeuLeuIleTyrThrLeuSerTyrArgAlaSerGlyValProAspArgPheSerGlySerGlySerGlyThrAspPheThrLeuLysIle>

   310       320       330       340       350       360       370       380       390       400
TCTAGAGTGGAAGCCGAGGACGTGGGCGTGTACTACTGTATGCAGCGGATCGAGTTCCCTCTGACCTTTGGCGGCGGAACAAAGGTGGAAATCAAGCGGA
AGATCTCACCTTCGGCTCCTGCACCCGCACATGATGACATACGTCGCCTAGCTCAAGGGAGACTGGAAACCGCCGCCTTGTTTCCACCTTTAGTTCGCCT
SerArgValGluAlaGluAspValGlyValTyrTyrCysMetGlnArgIleGluPheProLeuThrPheGlyGlyGlyThrLysValGluIleLysArg>

   410       420       430       440       450       460       470       480       490       500
CAGTGGCCGCTCCTAGCGTGTTCATCTTTCCACCTAGCGACGAGCAGCTGAAGTCTGGCACAGCCTCTGTCGTGTGCCTGCTGAACAACTTCTACCCCAG
GTCACCGGCGAGGATCGCACAAGTAGAAAGGTGGATCGCTGCTCGTCGACTTCAGACCGTGTCGGAGACAGCACACGGACGACTTGTTGAAGATGGGGTC
ThrValAlaAlaProSerValPheIlePheProProSerAspGluGlnLeuLysSerGlyThrAlaSerValValCysLeuLeuAsnAsnPheTyrProArg>
   510       520       530       540       550       560       570       580       590       600
AGAAGCCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAATAGCCAAGAGAGCGTGACCGAGCAGGACAGCAAGGACTCTACCTACAGCCTG
TCTTCGGTTCCACGTCACCTTCCACCTGTTGCGGGACGTCTCGCCGTTATCGGTTCTCTCGCACTGGCTCGTCCTGTCGTTCCTGAGATGGATGTCGGAC
 GluAlaLysValGlnTrpLysValAspAsnAlaLeuGlnSerGlyAsnSerGlnGluSerValThrGluGlnAspSerLysAspSerThrTyrSerLeu>
   610       620       630       640       650       660       670       680       690       700
AGCAGCACCCTGACACTGAGCAAGGCCGACTACGAGAAGCACAAAGTGTACGCCTGCGAAGTGACCCACCAGGGCCTTTCTAGCCCTGTGACCAAGAGCT
TCGTCGTGGGACTGTGACTCGTTCCGGCTGATGCTCTTCGTGTTTCACATGCGGACGCTTCACTGGGTGGTCCCGGAAAGATCGGGACACTGGTTCTCGA
SerSerThrLeuThrLeuSerLysAlaAspTyrGluLysHisLysValTyrAlaCysGluValThrHisGlnGlyLeuSerSerProValThrLysSer>
   710       720
TCAACCGGGGCGAATGTT
AGTTGGCCCCGCTTACAA
PheAsnArgGlyGluCys>
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H4-scFv-TD

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    10        20        30        40        50        60        70        80        90       100
ATGGGCTGGTCCTGCATCATCCTGTTTCTGGTGGCCACAGCCACAGGCGTGCACTCTCAGGTTCAGCTGGTTCAGTCTGGCGCCGAAGTGAAGAAACCTG
TACCCGACCAGGACGTAGTAGGACAAAGACCACCGGTGTCGGTGTCCGCACGTGAGAGTCCAAGTCGACCAAGTCAGACCGCGGCTTCACTTCTTTGGAC
MetGlyTrpSerCysIleIleLeuPheLeuValAlaThrAlaThrGlyValHisSerGlnValGlnLeuValGlnSerGlyAlaGluValLysLysPro>

   110       120       130       140       150       160       170       180       190       200
GCGCCTCTGTGAAGGTGTCCTGCAAGGCCAGCGGCTACACCTTTACCGGCTACTACATGCACTGGGTCCGACAGGCTCCAGGACAGGGACTTGAGTGGAT
CGCGGAGACACTTCCACAGGACGTTCCGGTCGCCGATGTGGAAATGGCCGATGATGTACGTGACCCAGGCTGTCCGAGGTCCTGTCCCTGAACTCACCTA
GlyAlaSerValLysValSerCysLysAlaSerGlyTyrThrPheThrGlyTyrTyrMetHisTrpValArgGlnAlaProGlyGlnGlyLeuGluTrpMet>

   210       220       230       240       250       260       270       280       290       300
GGGCAGAATCAACCCCAATAGCGGCGGCACCAACTACGCCCAGAAATTCCAGGGCAGAGTGACCATGACCAGAGACACCAGCATCAGCACCGCCTACATG
CCCGTCTTAGTTGGGGTTATCGCCGCCGTGGTTGATGCGGGTCTTTAAGGTCCCGTCTCACTGGTACTGGTCTCTGTGGTCGTAGTCGTGGCGGATGTAC
 GlyArgIleAsnProAsnSerGlyGlyThrAsnTyrAlaGlnLysPheGlnGlyArgValThrMetThrArgAspThrSerIleSerThrAlaTyrMet>

   310       320       330       340       350       360       370       380       390       400
GAACTGAGCCGGCTGAGATCCGATGACACCGCCGTGTACTACTGCGCCAGAGTGCCTTACTGTAGCAGCACCAGCTGCCACAGAGACTGGTACTTCGACC
CTTGACTCGGCCGACTCTAGGCTACTGTGGCGGCACATGATGACGCGGTCTCACGGAATGACATCGTCGTGGTCGACGGTGTCTCTGACCATGAAGCTGG
GluLeuSerArgLeuArgSerAspAspThrAlaValTyrTyrCysAlaArgValProTyrCysSerSerThrSerCysHisArgAspTrpTyrPheAsp>

   410       420       430       440       450       460       470       480       490       500
TGTGGGGCAGAGGCACACTGGTCACAGTTTCTAGCGGAGGCGGAGGATCTGGTGGCGGAGGAAGTGGCGGAGGCGGTTCTGATATCCAGATGACACAGAG
ACACCCCGTCTCCGTGTGACCAGTGTCAAAGATCGCCTCCGCCTCCTAGACCACCGCCTCCTTCACCGCCTCCGCCAAGACTATAGGTCTACTGTGTCTC
LeuTrpGlyArgGlyThrLeuValThrValSerSerGlyGlyGlyGlySerGlyGlyGlyGlySerGlyGlyGlyGlySerAspIleGlnMetThrGlnSer>

   510       520       530       540       550       560       570       580       590       600
CCCTCTGAGCCTGCCTGTGACACCTGGCGAACCTGCCAGCATCTCCTGTAGAAGCTCTCAGAGCCTGCTGGACAGCGACGACGGCAACACATACCTGGAC
GGGAGACTCGGACGGACACTGTGGACCGCTTGGACGGTCGTAGAGGACATCTTCGAGAGTCTCGGACGACCTGTCGCTGCTGCCGTTGTGTATGGACCTG
 ProLeuSerLeuProValThrProGlyGluProAlaSerIleSerCysArgSerSerGlnSerLeuLeuAspSerAspAspGlyAsnThrTyrLeuAsp>

   610       620       630       640       650       660       670       680       690       700
TGGTATCTGCAGAAGCCCGGCCAGTCTCCTCAGCTGCTGATCTACACCCTGAGCTACAGAGCCAGCGGCGTGCCCGATAGATTTTCTGGCTCTGGCAGCG
ACCATAGACGTCTTCGGGCCGGTCAGAGGAGTCGACGACTAGATGTGGGACTCGATGTCTCGGTCGCCGCACGGGCTATCTAAAAGACCGAGACCGTCGC
TrpTyrLeuGlnLysProGlyGlnSerProGlnLeuLeuIleTyrThrLeuSerTyrArgAlaSerGlyValProAspArgPheSerGlySerGlySer>
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   710       720       730       740       750       760       770       780       790       800
 GCACCGACTTCACCCTGAAGATCTCTAGAGTGGAAGCCGAGGACGTGGGCGTGTACTATTGCATGCAGCGGATCGAGTTCCCTCTGACCTTTGGCGGCGG
 CGTGGCTGAAGTGGGACTTCTAGAGATCTCACCTTCGGCTCCTGCACCCGCACATGATAACGTACGTCGCCTAGCTCAAGGGAGACTGGAAACCGCCGCC
GlyThrAspPheThrLeuLysIleSerArgValGluAlaGluAspValGlyValTyrTyrCysMetGlnArgIleGluPheProLeuThrPheGlyGlyGly>

   810       820       830       840       850       860       870       880       890       900
 AACAAAGGTGGAAATCAAGAAGAAGAAGCCCCTGGACGGCGAGTACTTCACACTGCAGATCCGGGGCAGAGAACGCTTCGAGATGTTCAGAGAGCTGAAC
 TTGTTTCCACCTTTAGTTCTTCTTCTTCGGGGACCTGCCGCTCATGAAGTGTGACGTCTAGGCCCCGTCTCTTGCGAAGCTCTACAAGTCTCTCGACTTG
  ThrLysValGluIleLysLysLysLysProLeuAspGlyGluTyrPheThrLeuGlnIleArgGlyArgGluArgPheGluMetPheArgGluLeuAsn>

   910       920       930       940       950       960
 GAGGCCCTGGAACTGAAGGATGCCCAGGCCGGAAAAGAGCCTGGACACCACCATCACCATCACT
 CTCCGGGACCTTGACTTCCTACGGGTCCGGCCTTTTCTCGGACCTGTGGTGGTAGTGGTAGTGA
 GluAlaLeuGluLeuLysAspAlaGlnAlaGlyLysGluProGlyHisHisHisHisHisHis>
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B38-Fab-TD (VH-CH1-TD + VL-CL)

B38 VH-CH1-TD

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    10        20        30        40        50        60        70        80        90       100
 ATGGGCTGGTCCTGCATCATCCTGTTTCTGGTGGCCACAGCCACAGGCGTGCACTCTGAAGTGCAGCTGGTTGAGTCTGGCGGAGGACTGGTTCAACCTG
 TACCCGACCAGGACGTAGTAGGACAAAGACCACCGGTGTCGGTGTCCGCACGTGAGACTTCACGTCGACCAACTCAGACCGCCTCCTGACCAAGTTGGAC
 MetGlyTrpSerCysIleIleLeuPheLeuValAlaThrAlaThrGlyValHisSerGluValGlnLeuValGluSerGlyGlyGlyLeuValGlnPro>

   110       120       130       140       150       160       170       180       190       200
 GCGGAAGCCTGAGACTGTCTTGTGCCGCCTCTGGCTTCATCGTGTCCAGCAACTACATGAGCTGGGTCCGACAGGCCCCTGGCAAAGGACTTGAATGGGT
 CGCCTTCGGACTCTGACAGAACACGGCGGAGACCGAAGTAGCACAGGTCGTTGATGTACTCGACCCAGGCTGTCCGGGGACCGTTTCCTGAACTTACCCA
GlyGlySerLeuArgLeuSerCysAlaAlaSerGlyPheIleValSerSerAsnTyrMetSerTrpValArgGlnAlaProGlyLysGlyLeuGluTrpVal>

   210       220       230       240       250       260       270       280       290       300
 GTCCGTGATCTACAGCGGCGGCAGCACCTACTACGCCGATTCTGTGAAGGGCAGATTCACCATCAGCCGGCACAACAGCAAGAACACCCTGTACCTGCAG
 CAGGCACTAGATGTCGCCGCCGTCGTGGATGATGCGGCTAAGACACTTCCCGTCTAAGTGGTAGTCGGCCGTGTTGTCGTTCTTGTGGGACATGGACGTC
  SerValIleTyrSerGlyGlySerThrTyrTyrAlaAspSerValLysGlyArgPheThrIleSerArgHisAsnSerLysAsnThrLeuTyrLeuGln>

   310       320       330       340       350       360       370       380       390       400
 ATGAACAGCCTGAGAGCCGAGGACACCGCCGTGTACTACTGTGCCAGAGAAGCCTACGGCATGGACGTGTGGGGACAGGGAACAACCGTGACAGTGTCTA
 TACTTGTCGGACTCTCGGCTCCTGTGGCGGCACATGATGACACGGTCTCTTCGGATGCCGTACCTGCACACCCCTGTCCCTTGTTGGCACTGTCACAGAT
 MetAsnSerLeuArgAlaGluAspThrAlaValTyrTyrCysAlaArgGluAlaTyrGlyMetAspValTrpGlyGlnGlyThrThrValThrValSer>

   410       420       430       440       450       460       470       480       490       500
 GCGCCAGCACAAAGGGCCCTAGCGTTTTCCCACTGGCTCCCAGCAGCAAGTCTACCTCTGGTGGAACAGCCGCTCTGGGCTGCCTGGTCAAGGATTACTT
 CGCGGTCGTGTTTCCCGGGATCGCAAAAGGGTGACCGAGGGTCGTCGTTCAGATGGAGACCACCTTGTCGGCGAGACCCGACGGACCAGTTCCTAATGAA
SerAlaSerThrLysGlyProSerValPheProLeuAlaProSerSerLysSerThrSerGlyGlyThrAlaAlaLeuGlyCysLeuValLysAspTyrPhe>

   510       520       530       540       550       560       570       580       590       600
 TCCCGAGCCTGTGACCGTGTCCTGGAATTCTGGCGCTCTGACAAGCGGCGTGCACACCTTTCCAGCTGTGCTGCAAAGCAGCGGCCTGTACTCTCTGAGC
 AGGGCTCGGACACTGGCACAGGACCTTAAGACCGCGAGACTGTTCGCCGCACGTGTGGAAAGGTCGACACGACGTTTCGTCGCCGGACATGAGAGACTCG
  ProGluProValThrValSerTrpAsnSerGlyAlaLeuThrSerGlyValHisThrPheProAlaValLeuGlnSerSerGlyLeuTyrSerLeuSer>

   610       620       630       640       650       660       670       680       690       700
 AGCGTGGTCACAGTGCCTAGCTCTAGCCTGGGCACCCAGACCTACATCTGCAATGTGAACCACAAGCCTAGCAACACCAAGGTGGACAAGAAGGTGGAAC
 TCGCACCAGTGTCACGGATCGAGATCGGACCCGTGGGTCTGGATGTAGACGTTACACTTGGTGTTCGGATCGTTGTGGTTCCACCTGTTCTTCCACCTTG
 SerValValThrValProSerSerSerLeuGlyThrGlnThrTyrIleCysAsnValAsnHisLysProSerAsnThrLysValAspLysLysValGlu>
   710       720       730       740       750       760       770       780       790       800
 CCAAGAGCTGCGACAAGACCCACACCAAGAAGAAGCCTCTGGACGGCGAGTACTTCACTCTGCAGATCCGGGGCAGAGAACGCTTCGAGATGTTCAGAGA
 GGTTCTCGACGCTGTTCTGGGTGTGGTTCTTCTTCGGAGACCTGCCGCTCATGAAGTGAGACGTCTAGGCCCCGTCTCTTGCGAAGCTCTACAAGTCTCT
ProLysSerCysAspLysThrHisThrLysLysLysProLeuAspGlyGluTyrPheThrLeuGlnIleArgGlyArgGluArgPheGluMetPheArgGlu>

   810       820       830       840       850       860       870
 GCTGAACGAGGCCCTGGAACTGAAGGATGCCCAGGCCGGAAAAGAGCCTGGACACCACCATCACCATCACTG
 CGACTTGCTCCGGGACCTTGACTTCCTACGGGTCCGGCCTTTTCTCGGACCTGTGGTGGTAGTGGTAGTGAC
  LeuAsnGluAlaLeuGluLeuLysAspAlaGlnAlaGlyLysGluProGlyHisHisHisHisHisHis>
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B38 VL-CL

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         10        20        30        40        50        60        70        80        90       100
 AGCTTATGGGCTGGTCCTGCATCATCCTGTTTCTGGTGGCCACAGCCACAGGCGTGCACAGCGATATCGTGATGACCCAGTCTCCTAGCTTCCTGAGCGC
 TCGAATACCCGACCAGGACGTAGTAGGACAAAGACCACCGGTGTCGGTGTCCGCACGTGTCGCTATAGCACTACTGGGTCAGAGGATCGAAGGACTCGCG
      MetGlyTrpSerCysIleIleLeuPheLeuValAlaThrAlaThrGlyValHisSerAspIleValMetThrGlnSerProSerPheLeuSerAla>
        110       120       130       140       150       160       170       180       190       200
 CAGCGTGGGCGACAGAGTGACCATTACATGTAGAGCCAGCCAGGGCATCAGCAGCTACCTGGCTTGGTATCAGCAGAAGCCTGGCAAGGCCCCTAAACTG
 GTCGCACCCGCTGTCTCACTGGTAATGTACATCTCGGTCGGTCCCGTAGTCGTCGATGGACCGAACCATAGTCGTCTTCGGACCGTTCCGGGGATTTGAC
  SerValGlyAspArgValThrIleThrCysArgAlaSerGlnGlyIleSerSerTyrLeuAlaTrpTyrGlnGlnLysProGlyLysAlaProLysLeu>
        210       220       230       240       250       260       270       280       290       300
 CTGATCTACGCCGCCAGCACACTGCAGTCTGGCGTGCCATCTAGATTTTCCGGCAGCGGCTCTGGCACCGAGTTCACCCTGACCATATCTAGCCTGCAGC
 GACTAGATGCGGCGGTCGTGTGACGTCAGACCGCACGGTAGATCTAAAAGGCCGTCGCCGAGACCGTGGCTCAAGTGGGACTGGTATAGATCGGACGTCG
 LeuIleTyrAlaAlaSerThrLeuGlnSerGlyValProSerArgPheSerGlySerGlySerGlyThrGluPheThrLeuThrIleSerSerLeuGln>

        310       320       330       340       350       360       370       380       390       400
 CTGAGGACTTCGCCACCTACTACTGCCAGCAGCTGAACAGCTACCCTCCTTACACCTTTGGCCAGGGCACCAAGCTGGAAATCAAGCGGACAGTGGCCGC
 GACTCCTGAAGCGGTGGATGATGACGGTCGTCGACTTGTCGATGGGAGGAATGTGGAAACCGGTCCCGTGGTTCGACCTTTAGTTCGCCTGTCACCGGCG
ProGluAspPheAlaThrTyrTyrCysGlnGlnLeuAsnSerTyrProProTyrThrPheGlyGlnGlyThrLysLeuGluIleLysArgThrValAlaAla>

        410       420       430       440       450       460       470       480       490       500
 TCCTAGCGTGTTCATCTTTCCACCTAGCGACGAACAGCTGAAGTCCGGCACAGCCTCTGTCGTGTGCCTGCTGAACAACTTCTACCCCAGAGAAGCCAAG
 AGGATCGCACAAGTAGAAAGGTGGATCGCTGCTTGTCGACTTCAGGCCGTGTCGGAGACAGCACACGGACGACTTGTTGAAGATGGGGTCTCTTCGGTTC
  ProSerValPheIlePheProProSerAspGluGlnLeuLysSerGlyThrAlaSerValValCysLeuLeuAsnAsnPheTyrProArgGluAlaLys>
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        510       520       530       540       550       560       570       580       590       600
  GTGCAGTGGAAGGTGGACAACGCTCTGCAGTCCGGCAACTCCCAAGAGAGCGTGACAGAGCAGGACAGCAAGGACTCCACCTACAGCCTGAGCAGCACCC
  CACGTCACCTTCCACCTGTTGCGAGACGTCAGGCCGTTGAGGGTTCTCTCGCACTGTCTCGTCCTGTCGTTCCTGAGGTGGATGTCGGACTCGTCGTGGG
  ValGlnTrpLysValAspAsnAlaLeuGlnSerGlyAsnSerGlnGluSerValThrGluGlnAspSerLysAspSerThrTyrSerLeuSerSerThr>

        610       620       630       640       650       660       670       680       690       700
  TGACACTGAGCAAGGCCGACTACGAGAAGCACAAAGTGTACGCCTGCGAAGTGACCCACCAGGGCCTTTCTAGCCCTGTGACCAAGAGCTTCAACCGGGG
  ACTGTGACTCGTTCCGGCTGATGCTCTTCGTGTTTCACATGCGGACGCTTCACTGGGTGGTCCCGGAAAGATCGGGACACTGGTTCTCGAAGTTGGCCCC
 LeuThrLeuSerLysAlaAspTyrGluLysHisLysValTyrAlaCysGluValThrHisGlnGlyLeuSerSerProValThrLysSerPheAsnArgGly>
  CGAATGTTG
  GCTTACAAC
   GluCys>
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SARS-CoV2-S1

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30        40        50        60        70        80        90       100       110       120
  ATGGGATGGTCTTGTATAATTCTGTTCCTGGTGGCAACAGCAACAGGAGTGCATAGCGTGAACCTGACCACCAGAACACAGCTGCCTCCAGCCTACACCA
  TACCCTACCAGAACATATTAAGACAAGGACCACCGTTGTCGTTGTCCTCACGTATCGCACTTGGACTGGTGGTCTTGTGTCGACGGAGGTCGGATGTGGT
  MetGlyTrpSerCysIleIleLeuPheLeuValAlaThrAlaThrGlyValHisSerValAsnLeuThrThrArgThrGlnLeuProProAlaTyrThr>

130       140       150       160       170       180       190       200       210       220
  ACAGCTTCACCAGAGGCGTGTACTACCCCGACAAGGTGTTCAGATCCAGCGTGCACTCTACCCAGGACCTGTTCCTGCCTTTCTTCAGCAACGTGAC
  TGTCGAAGTGGTCTCCGCACATGATGGGGCTGTTCCACAAGTCTAGGTCGCACGACGTGAGATGGGTCCTGGACAAGGACGGAAAGAAGTCGTTGCACTG
 AsnSerPheThrArgGlyValTyrTyrProAspLysValPheArgSerSerValLeuHisSerThrGlnAspLeuPheLeuProPhePheSerAsnValThr>

230       240       250       260       270       280       290       300       310       320
  CTGGTTCCACGCCATCCACGTGTCCGGCACCAATGGCACCAAGAGATTCGACAACCCCGTGCTGCCCTTCAACGACGGGGTGTACTTTGCCAGCACCGAG
  GACCAAGGTGCGGTAGGTGCACAGGCCGTGGTTACCGTGGTTCTCTAAGCTGTTGGGGCACGACGGGAAGTTGCTGCCCCACATGAAACGGTCGTGGCTC
   TrpPheHisAlaIleHisValSerGlyThrAsnGlyThrLysArgPheAspAsnProValLeuProPheAsnAspGlyValTyrPheAlaSerThrGlu>

330       340       350       360       370       380       390       400       410       420
  AAGTCCAACATCATCAGAGGCTGGATCTTCGGCACCACACTGGACAGCAAGACCCAGAGCCTGCTGATCGTGAACAACGCCACCAACGTGGTCATCAAAG
  TTCAGGTTGTAGTAGTCTCCGACCTAGAAGCCGTGGTGTGACCTGTCGTTCTGGGTCTCGGACGACTAGCACTTGTTGCGGTGGTTGCACCAGTAGTTTC
  LysSerAsnIleIleArgGlyTrpIlePheGlyThrThrLeuAspSerLysThrGlnSerLeuLeuIleValAsnAsnAlaThrAsnValValIleLys>

430       440       450       460       470       480       490       500       510       520
  TGTGCGAGTTCCAGTTCTGCAACGACCCCTTCCTGGGCGTCTACTACCACAAGAACAACAAGAGCTGGATGGAAAGCGAGTTCCGGGTGTACAGCAGCGC
  ACACGCTCAAGGTCAAGACGTTGCTGGGGAAGGACCCGCAGATGATGGTGTTCTTGTTGTTCTCGACCTACCTTTCGCTCAAGGCCCACATGTCGTCGCG
 ValCysGluPheGlnPheCysAsnAspProPheLeuGlyValTyrTyrHisLysAsnAsnLysSerTrpMetGluSerGluPheArgValTyrSerSerAla>

530       540       550       560       570       580       590       600       610       620
  CAACAACTGCACCTTCGAGTACGTGTCCCAGCCTTTCCTGATGGACCTGGAAGGCAAGCAGGGCAACTTCAAGAACCTGCGCGAGTTCGTGTTCAAGAAC
  GTTGTTGACGTGGAAGCTCATGCACAGGGTCGGAAAGGACTACCTGGACCTTCCGTTCGTCCCGTTGAAGTTCTTGGACGCGCTCAAGCACAAGTTCTTG
   AsnAsnCysThrPheGluTyrValSerGlnProPheLeuMetAspLeuGluGlyLysGlnGlyAsnPheLysAsnLeuArgGluPheValPheLysAsn>

630       640       650       660       670       680       690       700       710       720
  ATCGACGGCTACTTCAAGATCTACAGCAAGCACACCCCTATCAACCTCGTGCGGGATCTGCCTCAGGGCTTCTCTGCTCTGGAACCCCTGGTGGATCTGC
  TAGCTGCCGATGAAGTTCTAGATGTCGTTCGTGTGGGGATAGTTGGAGCACGCCCTAGACGGAGTCCCGAAGAGACGAGACCTTGGGGACCACCTAGACG
  IleAspGlyTyrPheLysIleTyrSerLysHisThrProIleAsnLeuValArgAspLeuProGlnGlyPheSerAlaLeuGluProLeuValAspLeu>

730       740       750       760       770       780       790       800       810       820
  CCATCGGCATCAACATCACCCGGTTTCAGACACTGCTGGCCCTGCACAGAAGCTACCTGACACCTGGCGATAGCAGCTCTGGATGGACAGCTGGCGCCGC
  GGTAGCCGTAGTTGTAGTGGGCCAAAGTCTGTGACGACCGGGACGTGTCTTCGATGGACTGTGGACCGCTATCGTCGAGACCTACCTGTCGACCGCGGCG
 ProIleGlyIleAsnIleThrArgPheGlnThrLeuLeuAlaLeuHisArgSerTyrLeuThrProGlyAspSerSerSerGlyTrpThrAlaGlyAlaAla>

830       840       850       860       870       880       890       900       910       920
  TGCCTACTATGTGGGATACCTGCAGCCTCGGACCTTCCTGCTGAAGTACAACGAGAACGGCACCATCACCGACGCCGTGGATTGTGCTCTGGATCCTCTG
  ACGGATGATACACCCTATGGACGTCGGAGCCTGGAAGGACGACTTCATGTTGCTCTTGCCGTGGTAGTGGCTGCGGCACCTAACACGAGACCTAGGAGAC
   AlaTyrTyrValGlyTyrLeuGlnProArgThrPheLeuLeuLysTyrAsnGluAsnGlyThrIleThrAspAlaValAspCysAlaLeuAspProLeu>

930       940       950       960       970       980       990      1000      1010      1020
  AGCGAGACAAAGTGCACCCTGAAGTCCTTCACCGTGGAAAAGGGCATCTACCAGACCAGCAACTTCCGGGTGCAGCCCACCGAATCCATCGTGCGGTTCC
  TCGCTCTGTTTCACGTGGGACTTCAGGAAGTGGCACCTTTTCCCGTAGATGGTCTGGTCGTTGAAGGCCCACGTCGGGTGGCTTAGGTAGCACGCCAAGG
  SerGluThrLysCysThrLeuLysSerPheThrValGluLysGlyIleTyrGlnThrSerAsnPheArgValGlnProThrGluSerIleValArgPhe>

030      1040      1050      1060      1070      1080      1090      1100      1110      1120
  CCAATATCACCAATCTGTGCCCCTTCGGCGAGGTGTTCAATGCCACCAGATTCGCCTCTGTGTACGCCTGGAACCGGAAGCGGATCAGCAATTGCGTGGC
  GGTTATAGTGGTTAGACACGGGGAAGCCGCTCCACAAGTTACGGTGGTCTAAGCGGAGACACATGCGGACCTTGGCCTTCGCCTAGTCGTTAACGCACCG
 ProAsnIleThrAsnLeuCysProPheGlyGluValPheAsnAlaThrArgPheAlaSerValTyrAlaTrpAsnArgLysArgIleSerAsnCysValAla>

130      1140      1150      1160      1170      1180      1190      1200      1210      1220
  CGACTACTCCGTGCTGTACAACTCCGCCAGCTTCAGCACCTTCAAGTGCTACGGCGTGTCCCCTACCAAGCTGAACGACCTGTGCTTCACAAACGTGTAC
  GCTGATGAGGCACGACATGTTGAGGCGGTCGAAGTCGTGGAAGTTCACGATGCCGCACAGGGGATGGTTCGACTTGCTGGACACGAAGTGTTTGCACATG
   AspTyrSerValLeuTyrAsnSerAlaSerPheSerThrPheLysCysTyrGlyValSerProThrLysLeuAsnAspLeuCysPheThrAsnValTyr>

230      1240      1250      1260      1270      1280      1290      1300      1310      1320
  GCCGACAGCTTCGTGATCCGGGGAGATGAAGTGCGGCAGATTGCCCCTGGACAGACAGGCAAGATCGCCGACTACAACTACAAGCTGCCCGACGACTTCA
  CGGCTGTCGAAGCACTAGGCCCCTCTACTTCACGCCGTCTAACGGGGACCTGTCTGTCCGTTCTAGCGGCTGATGTTGATGTTCGACGGGCTGCTGAAGT
  AlaAspSerPheValIleArgGlyAspGluValArgGlnIleAlaProGlyGlnThrGlyLysIleAlaAspTyrAsnTyrLysLeuProAspAspPhe>

330      1340      1350      1360      1370      1380      1390      1400      1410      1420
  CCGGCTGTGTGATTGCCTGGAACAGCAACAACCTGGACTCCAAAGTCGGCGGCAACTACAATTACCTGTACCGGCTGTTCCGGAAGTCCAATCTGAAGCC
  GGCCGACACACTAACGGACCTTGTCGTTGTTGGACCTGAGGTTTCAGCCGCCGTTGATGTTAATGGACATGGCCGACAAGGCCTTCAGGTTAGACTTCGG
 ThrGlyCysValIleAlaTrpAsnSerAsnAsnLeuAspSerLysValGlyGlyAsnTyrAsnTyrLeuTyrArgLeuPheArgLysSerAsnLeuLysPro>

430      1440      1450      1460      1470      1480      1490      1500      1510      1520
  CTTCGAGCGGGACATCTCCACCGAGATCTATCAGGCCGGCAGCACCCCTTGTAACGGCGTGGAAGGCTTCAACTGCTACTTCCCACTGCAGTCCTACGGC
  GAAGCTCGCCCTGTAGAGGTGGCTCTAGATAGTCCGGCCGTCGTGGGGAACATTGCCGCACCTTCCGAAGTTGACGATGAAGGGTGACGTCAGGATGCCG
   PheGluArgAspIleSerThrGluIleTyrGlnAlaGlySerThrProCysAsnGlyValGluGlyPheAsnCysTyrPheProLeuGlnSerTyrGly>
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530       1540       1550       1560       1570       1580       1590       1600       1610       1620
  TTTCAGCCCACAAATGGCGTGGGCTACCAGCCTTACAGAGTGGTGGTGCTGAGCTTCGAGCTGCTGCATGCTCCTGCCACAGTGTGCGGCCCTAAGAAAA
  AAAGTCGGGTGTTTACCGCACCCGATGGTCGGAATGTCTCACCACCACGACTCGAAGCTCGACGACGTACGAGGACGGTGTCACACGCCGGGATTCTTTT
  PheGlnProThrAsnGlyValGlyTyrGlnProTyrArgValValValLeuSerPheGluLeuLeuHisAlaProAlaThrValCysGlyProLysLys>

630       1640       1650       1660       1670       1680       1690       1700       1710       1720
  GCACCAATCTCGTGAAGAACAAATGCGTGAACTTCAACTTCAACGGCCTGACCGGCACCGGCGTGCTGACAGAGAGCAACAAGAAGTTCCTGCCATTCCA
  CGTGGTTAGAGCACTTCTTGTTTACGCACTTGAAGTTGAAGTTGCCGGACTGGCCGTGGCCGCACGACTGTCTCTCGTTGTTCTTCAAGGACGGTAAGGT
 SerThrAsnLeuValLysAsnLysCysValAsnPheAsnPheAsnGlyLeuThrGlyThrGlyValLeuThrGluSerAsnLysLysPheLeuProPheGln>

730       1740       1750       1760       1770       1780       1790       1800       1810       1820
  GCAGTTCGGCCGGGATATCGCCGATACCACAGATGCCGTCAGAGATCCCCAGACACTGGAAATCCTGGACATCACCCCTTGCAGCTTCGGCGGAGTGTCT
  CGTCAAGCCGGCCCTATAGCGGCTATGGTGTCTACGGCAGTCTCTAGGGGTCTGTGACCTTTAGGACCTGTAGTGGGGAACGTCGAAGCCGCCTCACAGA
   GlnPheGlyArgAspIleAlaAspThrThrAspAlaValArgAspProGlnThrLeuGluIleLeuAspIleThrProCysSerPheGlyGlyValSer>

830       1840       1850       1860       1870       1880       1890       1900       1910       1920
  GTGATCACCCCTGGCACCAACACCAGCAATCAGGTGGCAGTGCTGTACCAGGACGTGAACTGTACCGAAGTGCCCGTGGCCATTCACGCCGATCAGCTGA
  CACTAGTGGGGACCGTGGTTGTGGTCGTTAGTCCACCGTCACGACATGGTCCTGCACTTGACATGGCTTCACGGGCACCGGTAAGTGCGGCTAGTCGACT
  ValIleThrProGlyThrAsnThrSerAsnGlnValAlaValLeuTyrGlnAspValAsnCysThrGluValProValAlaIleHisAlaAspGlnLeu>

930       1940       1950       1960       1970       1980       1990       2000       2010       2020
  CACCTACATGGCGGGTGTACTCCACCGGCAGCAATGTGTTTCAGACCAGAGCCGGCTGTCTGATCGGAGCCGAGCACGTGAACAATAGCTACGAGTGCGA
  GTGGATGTACCGCCCACATGAGGTGGCCGTCGTTACACAAAGTCTGGTCTCGGCCGACAGACTAGCCTCGGCTCGTGCACTTGTTATCGATGCTCACGCT
 ThrProThrTrpArgValTyrSerThrGlySerAsnValPheGlnThrArgAlaGlyCysLeuIleGlyAlaGluHisValAsnAsnSerTyrGluCysAsp>

030       2040       2050       2060       2070       2080       2090       2100       2110       2120
  CATCCCCATCGGCGCTGGCATCTGCGCCTCTTACCAGACACAGACAAACAGCCCCAGACGGGCCAGATCTGTGGCTTCTCAGGGCCTGAACGACATCTTC
  GTAGGGGTAGCCGCGACCGTAGACGCGGAGAATGGTCTGTGTCTGTTTGTCGGGGTCTGCCCGGTCTAGACACCGAAGAGTCCCGGACTTGCTGTAGAAG
   IleProIleGlyAlaGlyIleCysAlaSerTyrGlnThrGlnThrAsnSerProArgArgAlaArgSerValAlaSerGlnGlyLeuAsnAspIlePhe>

130       2140       2150       2160       2170       2180
  GAGGCTCAGAAAATCGAATGGCACGAGCACCACCACCATCACCACTGAGCG
  CTCCGAGTCTTTTAGCTTACCGTGCTCGTGGTGGTGGTAGTGGTGACTCGC
  GluAlaGlnLysIleGluTrpHisGluHisHisHisHisHisHis***>
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SARS-CoV2-RBD

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     10         20         30         40         50         60         70         80         90        100
  ATGGGATGGTCTTGTATAATTCTGTTCCTGGTGGCAACAGCAACAGGAGTGCATAGCAATATCACCAATCTGTGCCCCTTCGGCGAGGTGTTCAATGCCA
  TACCCTACCAGAACATATTAAGACAAGGACCACCGTTGTCGTTGTCCTCACGTATCGTTATAGTGGTTAGACACGGGGAAGCCGCTCCACAAGTTACGGT
  MetGlyTrpSerCysIleIleLeuPheLeuValAlaThrAlaThrGlyValHisSerAsnIleThrAsnLeuCysProPheGlyGluValPheAsnAla>

    110        120        130        140        150        160        170        180        190        200
  CCAGATTCGCCTCTGTGTACGCCTGGAACCGGAAGCGGATCAGCAATTGCGTGGCCGACTACTCCGTGCTGTACAACTCCGCCAGCTTCAGCACCTTCAA
  GGTCTAAGCGGAGACACATGCGGACCTTGGCCTTCGCCTAGTCGTTAACGCACCGGCTGATGAGGCACGACATGTTGAGGCGGTCGAAGTCGTGGAAGTT
 ThrArgPheAlaSerValTyrAlaTrpAsnArgLysArgIleSerAsnCysValAlaAspTyrSerValLeuTyrAsnSerAlaSerPheSerThrPheLys>

    210        220        230        240        250        260        270        280        290        300
  GTGCTACGGCGTGTCCCCTACCAAGCTGAACGACCTGTGCTTCACAAACGTGTACGCCGACAGCTTCGTGATCCGGGGAGATGAAGTGCGGCAGATTGCC
  CACGATGCCGCACAGGGGATGGTTCGACTTGCTGGACACGAAGTGTTTGCACATGCGGCTGTCGAAGCACTAGGCCCCTCTACTTCACGCCGTCTAACGG
   CysTyrGlyValSerProThrLysLeuAsnAspLeuCysPheThrAsnValTyrAlaAspSerPheValIleArgGlyAspGluValArgGlnIleAla>

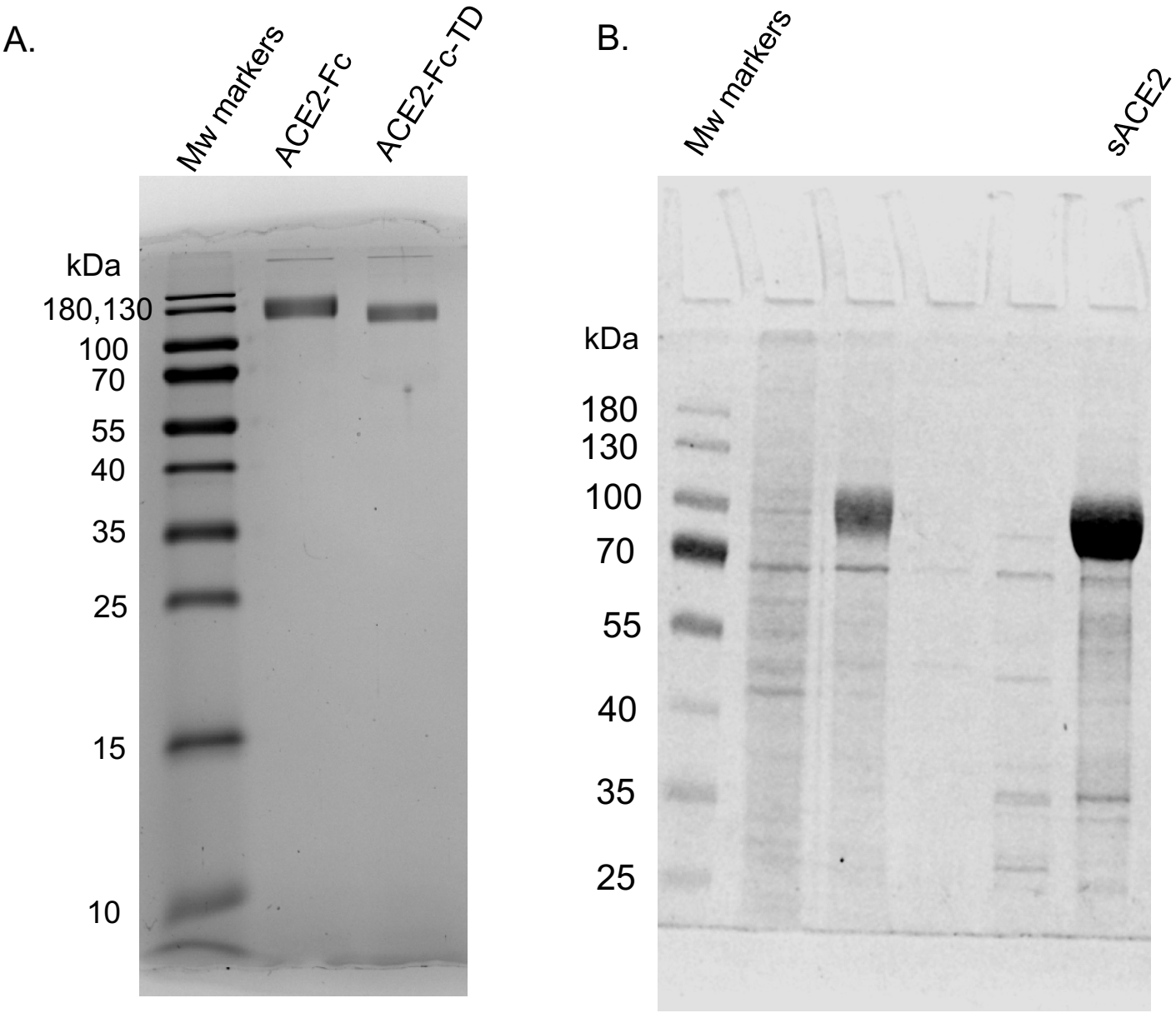
    310        320        330        340        350        360        370        380        390        400
  CCTGGACAGACAGGCAAGATCGCCGACTACAACTACAAGCTGCCCGACGACTTCACCGGCTGTGTGATTGCCTGGAACAGCAACAACCTGGACTCCAAAG
  GGACCTGTCTGTCCGTTCTAGCGGCTGATGTTGATGTTCGACGGGCTGCTGAAGTGGCCGACACACTAACGGACCTTGTCGTTGTTGGACCTGAGGTTTC
  ProGlyGlnThrGlyLysIleAlaAspTyrAsnTyrLysLeuProAspAspPheThrGlyCysValIleAlaTrpAsnSerAsnAsnLeuAspSerLys>

    410        420        430        440        450        460        470        480        490        500
  TCGGCGGCAACTACAATTACCTGTACCGGCTGTTCCGGAAGTCCAATCTGAAGCCCTTCGAGCGGGACATCTCCACCGAGATCTATCAGGCCGGCAGCAC
  AGCCGCCGTTGATGTTAATGGACATGGCCGACAAGGCCTTCAGGTTAGACTTCGGGAAGCTCGCCCTGTAGAGGTGGCTCTAGATAGTCCGGCCGTCGTG
 ValGlyGlyAsnTyrAsnTyrLeuTyrArgLeuPheArgLysSerAsnLeuLysProPheGluArgAspIleSerThrGluIleTyrGlnAlaGlySerThr>

    510        520        530        540        550        560        570        580        590        600
  CCCTTGTAACGGCGTGGAAGGCTTCAACTGCTACTTCCCACTGCAGTCCTACGGCTTTCAGCCCACAAATGGCGTGGGCTACCAGCCTTACAGAGTGGTG
  GGGAACATTGCCGCACCTTCCGAAGTTGACGATGAAGGGTGACGTCAGGATGCCGAAAGTCGGGTGTTTACCGCACCCGATGGTCGGAATGTCTCACCAC
   ProCysAsnGlyValGluGlyPheAsnCysTyrPheProLeuGlnSerTyrGlyPheGlnProThrAsnGlyValGlyTyrGlnProTyrArgValVal>

    610        620        630        640        650        660
  GTGCTGAGCTTCGAGCTGCTGCATGCTCCTGCCACAGTGCACCACCACCATCACCAC
  CACGACTCGAAGCTCGACGACGTACGAGGACGGTGTCACGTGGTGGTGGTAGTGGTG
  ValLeuSerPheGluLeuLeuHisAlaProAlaThrValHisHisHisHisHisHis
```

Supplementary Figure 4



Supplementary Figure 4. Uncropped SDS-PAGE gel images shown in Figure 1A.

The images show full length Coomassie stained SDS-PAGE gels (with indicated stained molecular weight markers).