Supplemental Information

Neutralization of Zika virus by germline-like human monoclonal antibodies targeting cryptic epitopes on envelope domain III

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FIGURE LEGENDS

Figure S1: Immunogenetic analysis of the heavy and light chain variable regions of m303 and m304 using the IMGT tool.

Figure S2: Immunogenetic analysis of the m301 similar sequences from the IgM repertoire from healthy human neonates and adults. Sequence ID started with CB representing sequences derived from the library of the neonates, and started with HH representing sequences derived from the library of the adults.

(a): Amino acid sequences of HCDR3s that were found similar to that of m301 from the deep sequencing analysis of IgM libraries derived from 33 healthy human adults and 10 neonates, which were analyzed by Clusteral W2.

(b): Germline-rooted circular phylogenetic tree of m301 like antibody sequences found in IgM libraries derived from 33 healthy human adults and 10 newborn babies. The phylogenetic tree was constructed by the Neighbor-Joining method. The numbers labeled on the branch in red representing the probability to gain the topological structure, only the probabilities more than 50% were labeled that means the structures were more reliable.

Figure S3: Immunogenetic analysis of the m302 similar sequences from the IgM repertoire from healthy human neonates and adults.

(a): Amino acid sequences of HCDR3s that were found similar to that of m302 from the deep sequencing analysis of IgM libraries derived from the libraries of the healthy human neonates and adults.

(b): Germline-rooted circular phylogenetic tree of m302 like antibody sequences found in IgM libraries derived from the libraries of the healthy human neonates and adults.

Figure S4: Immunogenetic analysis of the m304 similar sequences from the IgM repertoire from healthy human neonates and adults.

(a): Amino acid sequences of HCDR3s that were found similar to that of m304 from the deep sequencing analysis of IgM libraries derived from the libraries of the healthy human neonates and adults.

(b): Germline-rooted circular phylogenetic tree of m304 like antibody sequences found in IgM libraries derived from the libraries of the healthy human neonates and adults.

Figure S5: Immunogenetic analysis of the m303 similar sequences from the IgM repertoire from healthy human neonates and adults.

(a): Amino acid sequences of HCDR3s that were found similar to that of m303 from the deep sequencing analysis of IgM libraries derived from the libraries of the healthy human neonates and adults.

(b): Germline-rooted circular phylogenetic tree of m303 like antibody sequences found in IgM libraries derived from the libraries of the healthy human neonates and adults.

Figure S6: Alignment of E protein DIII of ZIKV isolated circulating in 2015-2016 ZIKV outbreak.
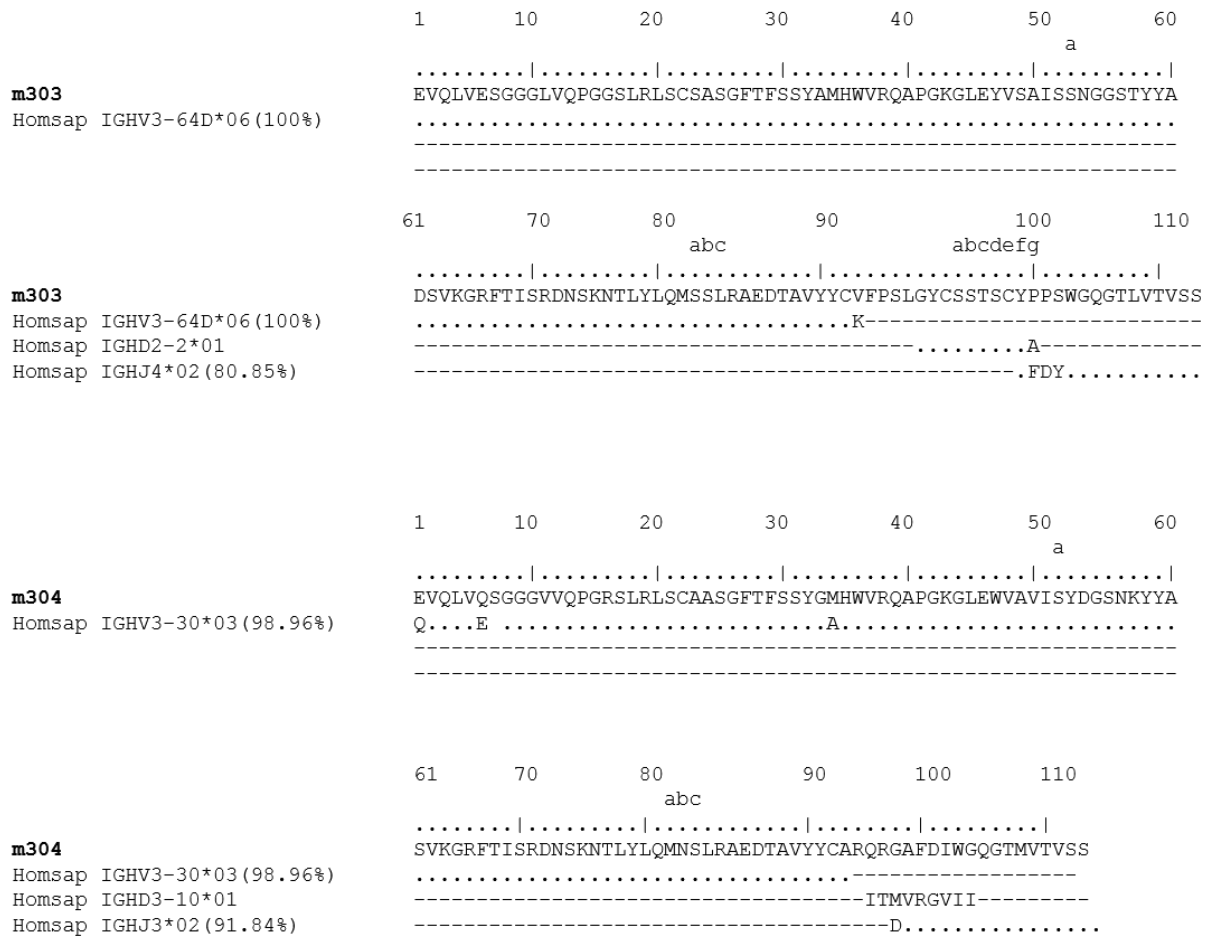
Figure S1

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                        1         10        20        30        40        50        60
                                                                                    a
                        .........|.........|.........|.........|.........|.........|
m303                    EVQLVESGGGLVQPGGSLRLSCSASGFTFSSYAMHWVRQAPGKGLEYVSAISSNGGSTYYA
Homsap IGHV3-64D*06(100%)  ............................................................
                        ------------------------------------------------------------
                        ------------------------------------------------------------


                        61        70        80        90        100       110
                                            abc                 abcdefg
                        .........|.........|...........|................|.........|
m303                    DSVKGRFTISRDNSKNTLYLQMSSLRAEDTAVYYCVFPSLGYCSSTSCYPPSWGQGTLVTVSS
Homsap IGHV3-64D*06(100%)  ...............................K-------------------------
Homsap IGHD2-2*01       ----------------------------------------.........A-------------
Homsap IGHJ4*02(80.85%) -----------------------------------------------.FDY...........




                        1         10        20        30        40        50        60
                                                                                    a
                        .........|.........|.........|.........|.........|.........|
m304                    EVQLVQSGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
Homsap IGHV3-30*03(98.96%) Q....E ..........................A...........................
                        ------------------------------------------------------------
                        ------------------------------------------------------------


                        61        70        80        90        100       110
                                            abc
                        ........|.........|...........|........|.........|
m304                    SVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARQRGAFDIWGQGTMVTVSS
Homsap IGHV3-30*03(98.96%) ....................................-----------------
Homsap IGHD3-10*01      -------------------------------------ITMVRGVII---------
Homsap IGHJ3*02(91.84%) --------------------------------------D...............
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Figure S2

M301	AKEVGRSYFDY
CB_M301_sm_521251801014941	AKESGSYYFDY
CB_M301_sm_512162673729430	AKEVRSYYFDY
CB_M301_sm_52206679634125	AKEVGATYFDY
CB_M301_sm_52209324713178	AKEMAGWYFDY
CB_M301_sm_512047446116893	AKEHSGSYFDY
CB_M301_sm_512021468110124	AKESGGSYFDY
CB_M301_sm_512091228642337	AKEVPLGYFDY
HH_M301_sm_121012706238222	AKSIVEGYFDY
HH_M301_sm_12214977046451	AKDANGGCFDY
CB_M301_sm_51107272728024	AKETEGGYFDY
CB_M301_sm_521193122337273	AKERNGDYFDY
CB_M301_sm_512211981614555	AKEGLGYYFDY
CB_M301_sm_512042919322467	AKELLGAYFDY
CB_M301_sm_522261242822995	AKERLQYYFDY
CB_M301_sm_511202546913236	AKEAEDYYFDY
CB_M301_sm_51123417813341	AKEAHGYYFDY
CB_M301_sm_511161095729483	AKEGQGWYFDY
CB_M301_sm_512262328726090	AKEGQLVYFDY
CB_M301_sm_511172327722344	AKEGNWHYFDY
HH_M301_sm_322252190720709	AKVRDSSLFDY
HH_M301_sm_311092372325931	AKESPTVAFDY
HH_M301_sm_321211820330081	AKDSRRWSFDY
HH_M301_sm_12105493910053	AKDLDNWEFDY
HH_M301_sm_32227325438679	AKDRNWLGFDY
HH_M301_sm_111112631117368	AKDRRTTVFDY
HH_M301_sm_311123002535972	AKGSSWYPFDY
HH_M301_sm_322121011512269	AKDSYDYPFDY
HH_M301_sm_121122956938662	AKSKQAIPFDY
HH_M301_sm_3122699736994	AKNGAYNDFDY
HH_M301_sm_32214300259702	AKVGVVNHFDY
HH_M301_sm_11109244853231	AKDGHSNTFDY
HH_M301_sm_121123142613781	AKRGYSYGFDY
	** ***

Tree labels:
CB M301 sm 512047446016788
CB M301 sm 512047446016893
CB M301 sm 522012082139868
CB M301 sm 51209380592
CB M301 sm s22066796634125
CB M301 sm 512042919322467
CB M301 sm 512211981614555
CB M301 sm 51123417813341 3226
HH M301 sm 121123142613781
HH M301 sm 111112631117368
HH M301 sm 32227 325438679
CB M301 sm 511181652812972
CB M301 sm 511 72327722344
CB M301 sm 512262328726090
HH M301 sm 311092372325931
HH M301 sm 12105493910053
HH M301 sm 321211820330081
HH M301 sm 11109244853231
CB M301 sm 52209324713178
CB M301 sm 52112284033796
HH M301 sm 12214977046451
HH M301 sm 322121011512269
CB M301 sm 511161095729483
HH M301 sm 3122699736994
HH M301 sm 32214300259702
CB M301 sm 512073159896308
HH M301 sm 311123002535972
CB M301 sm 522612242822995
HH M301 sm 511202546913236
CB M301 sm 52116267372930
CB M301 sm 52125180 1014941
CB M301 sm 512091228842337
CB M301 sm 511 09301474456 2
CB M301 sm 511 0727272 8024
HH M301 sm 121122956938 662
HH M301 sm 12 1012706238222
CB M301 sm 521193122337273
M301
HH M301 sm 322252190720709

59
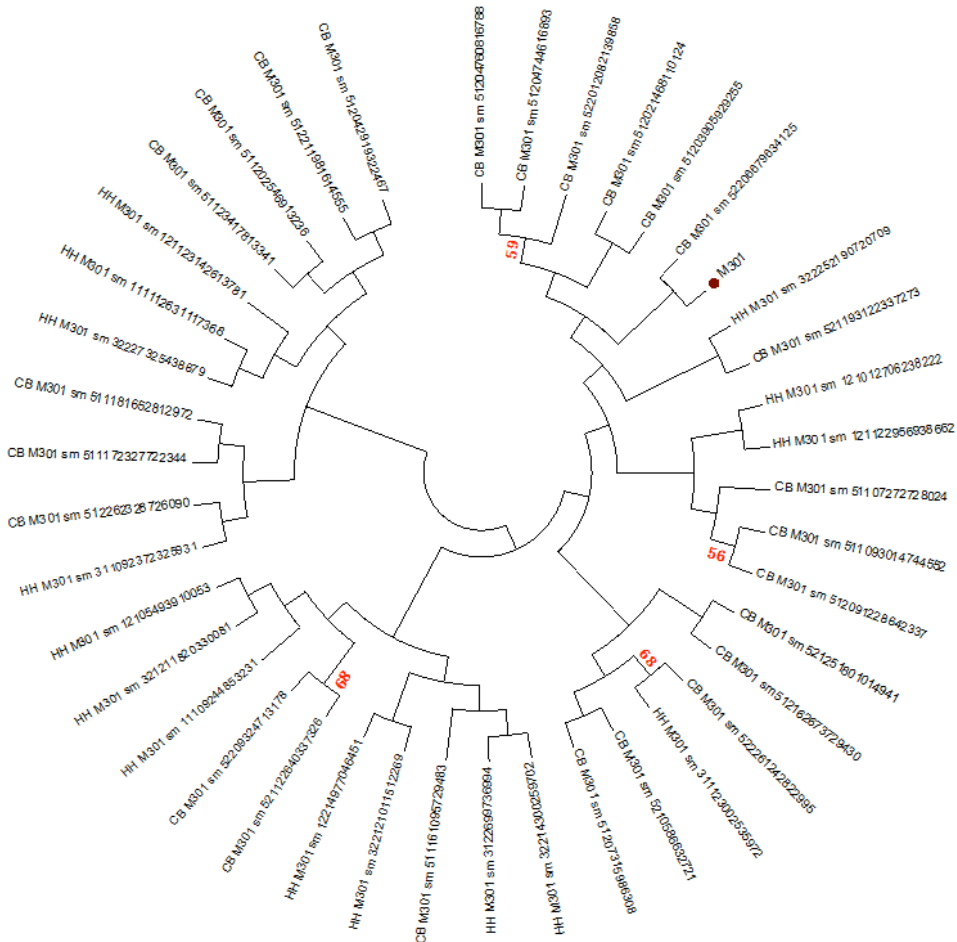56
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68

Figure S3

M302	AREIGDYYYYGMDV
CB_M302_sm_511062610848245	ARENGVYYYYGMDV
HH_M302_sm_12124250321447	AREWGYYYYYGMDV
HH_M302_sm_311011389017368	AREHGHYYYYGMDV
HH_M302_sm_121151203314607	ARESGSYYYYGMDV
CB_M302_sm_52101686729466	ARELGDFYYYYGMDV
HH_M302_sm_122172396738205	AREAPFYYYYGMDV
HH_M302_sm_11209345721342	AREAYYYYYGMDV
HH_M302_sm_122163110130943	AREAAHYYYYGMDV
HH_M302_sm_311192840228797	ARESAHYYYYGMDV
HH_M302_sm_112191441819056	AREAASYYYYGMDV
HH_M302_sm_1221222508664	AREPDTYYYYGMDV
HH_M302_sm_111212038517579	AREPDAYYYYGMDV
HH_M302_sm_31220181722914	AREPMGYYYYGMDV
HH_M302_sm_312011817232701	ARELSPYYYYGMDV
HH_M302_sm_32221465513359	ARECIPYYYYGMDV
HH_M302_sm_122251814225369	ARERRAHYYYYGMDV
HH_M302_sm_312022250633176	ARERGAYYYYGMDV
HH_M302_sm_312122499245467	AREKGGSYYYYGMDV
HH_M302_sm_31114984122344	AREEDGDYYYYGMDV
HH_M302_sm_312271226642372	AREGDGAYYYYGMDV
HH_M302_sm_122052136943304	AREVWFAYYYYGMDV
HH_M302_sm_3222828996941	ARENNRSYYYYGMDV
HH_M302_sm_12105530440543	AREELRFYYYYGMDV
HH_M302_sm_112231057142917	ARELTRPYYYYGMDV
HH_M302_sm_322031089628569	ARELLSPYYYYGMDV
HH_M302_sm_311272458618423	AREGTHDYYYYGMDV
HH_M302_sm_121182204917087	AREGLHDYYYYGMDV
HH_M302_sm_112271073416753	ARELRLKYYYYGMDV
HH_M302_sm_12112569031787	AREGQLVYYYYGMDV
HH_M302_sm_12218191471789	AREGRSYYYYGMDV
HH_M302_sm_311272437339225	AREGSSSYYYYGMDV
CB_M302_sm_512201458038363	AREGDSTYYYYGMDV
CB_M302_sm_521233008622678	AREGGSTVLGGMDV
	*** ****

Figure S4
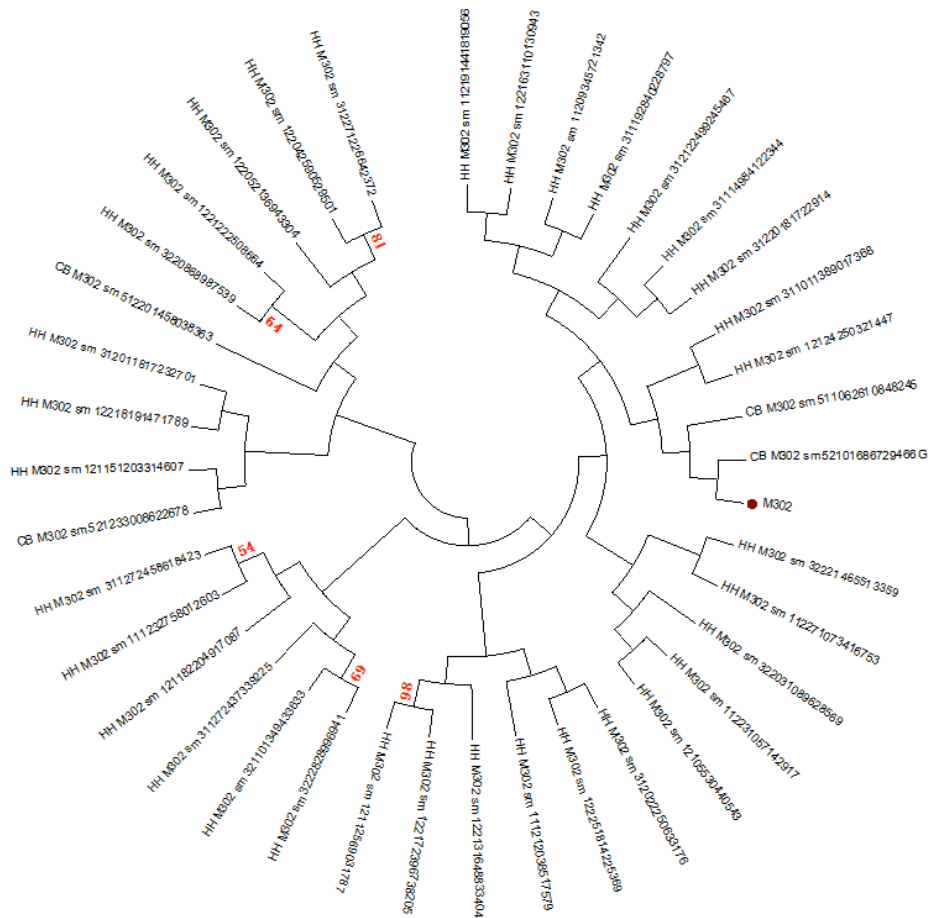
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M304                            ARQRGAFDI
CB_M304_sm_51221291324842       ARQRGAFDI
CB_M304_sm_52122250734177       ARERGAFDI
HH_M304_sm_31205139203655       ARERGAFDI
CB_M304_sm_51205130981578       ARSRGAFDI
HH_M304_sm_12124231042067       ARSRGAFDI
CB_M304_sm_52120171377627       ARKRGAFDI
HH_M304_sm_11110165082971       ARDRGAFDI
CB_M304_sm_51203252461211       ARDRGAFDI
HH_M304_sm_12105202938066       ARTRGAFDI
HH_M304_sm_1110282983108        ARVRGAFDI
HH_M304_sm_12219245054275       ARNRGAFDI
HH_M304_sm_32117323902132       ARIRGAFDI
CB_M304_sm_51226934342794       ARARGAFDI
HH_M304_sm_12128983119478       ARARGAFDI
HH_M304_sm_11114225162201       ARGRGAFDI
CB_M304_sm_51224136973532       ARGRGAFDI
                                **  ******
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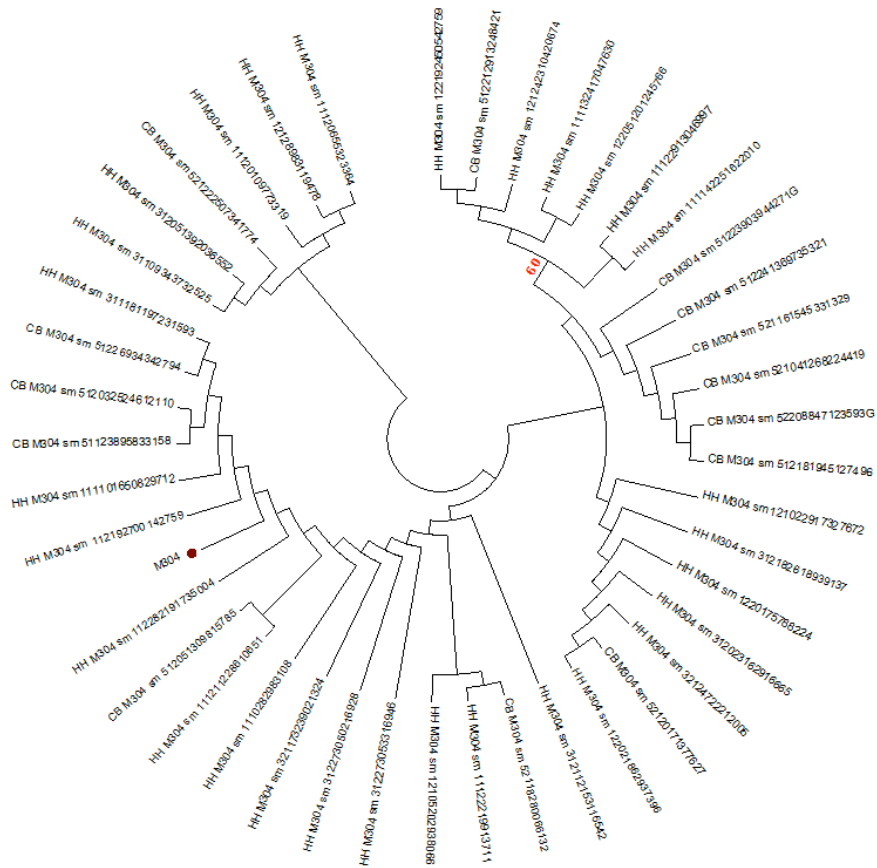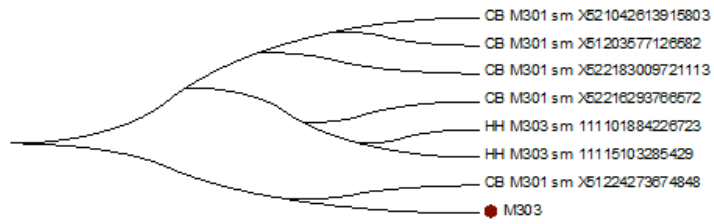
Figure S5

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m303                              VFPSLG--YCSSTSCYP-PS--
CB_M303_sm_522183009721113        --AKYHR-YCSSTSCP--EFDY
CB_M303_sm_51224273674848         --AKELG-YCSSTSCY--AFDY
CB_M303_sm_521042613915803        --ARAG--YCSSTSCFT-PFDY
CB_M303_sm_52216293766572         --ARRG--YCSSTSCYW-DFDY
CB_M303_sm_51203577126582         --ARVGGGYCSSTSCY---FDY
HH_M303_sm_111101884226723        --ARVG---CSSTSCYAAGFDY
HH_M303_sm_11115103285429         --ARGD---CSSTSCYVGEFDY
                                  .       ******
```


*CB: data from newborn babies

 HH: data from healthy adult donors

Figure S6

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            303    310        320        330        340        350        360
            .........|.........|.........|.........|.........|.........|
SZ01        VSYSLCTAAFTFTKIPAETLHGTVTVEVQYAGTDGPCKVPAQMAVDMQTLTPVGRLITAN
FLR         -------------------------V----------------------------------
PAN2015     -------------------------V----------------------------------
R103451     -------------------------V----------------------------------
PRVABC59    -------------------------L----------------------------------


                   370        380        390        400
            .........|.........|.........|.........|...
SZ01        PVITESTENSKMMLELDPPFGDSYIVIGVGEKKITHHWHRSG
FLR         -----------------------------------------
PAN2015     -----------------------------------------
R103451     -----------------------------------------
PRVABC59    -----------------------------------------
```