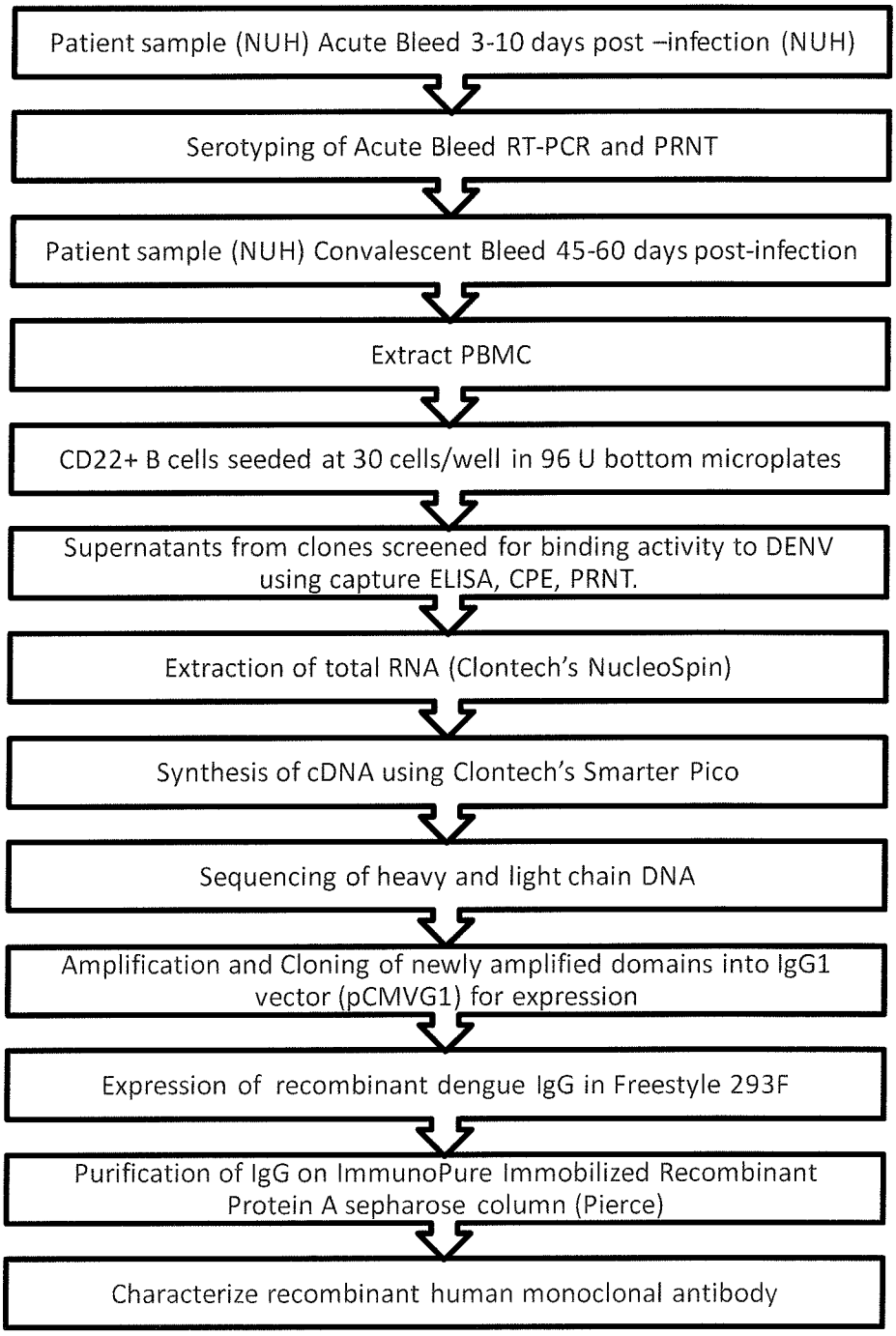


Figure 1: Flowchart of the process of antibody screening, expression and characterization

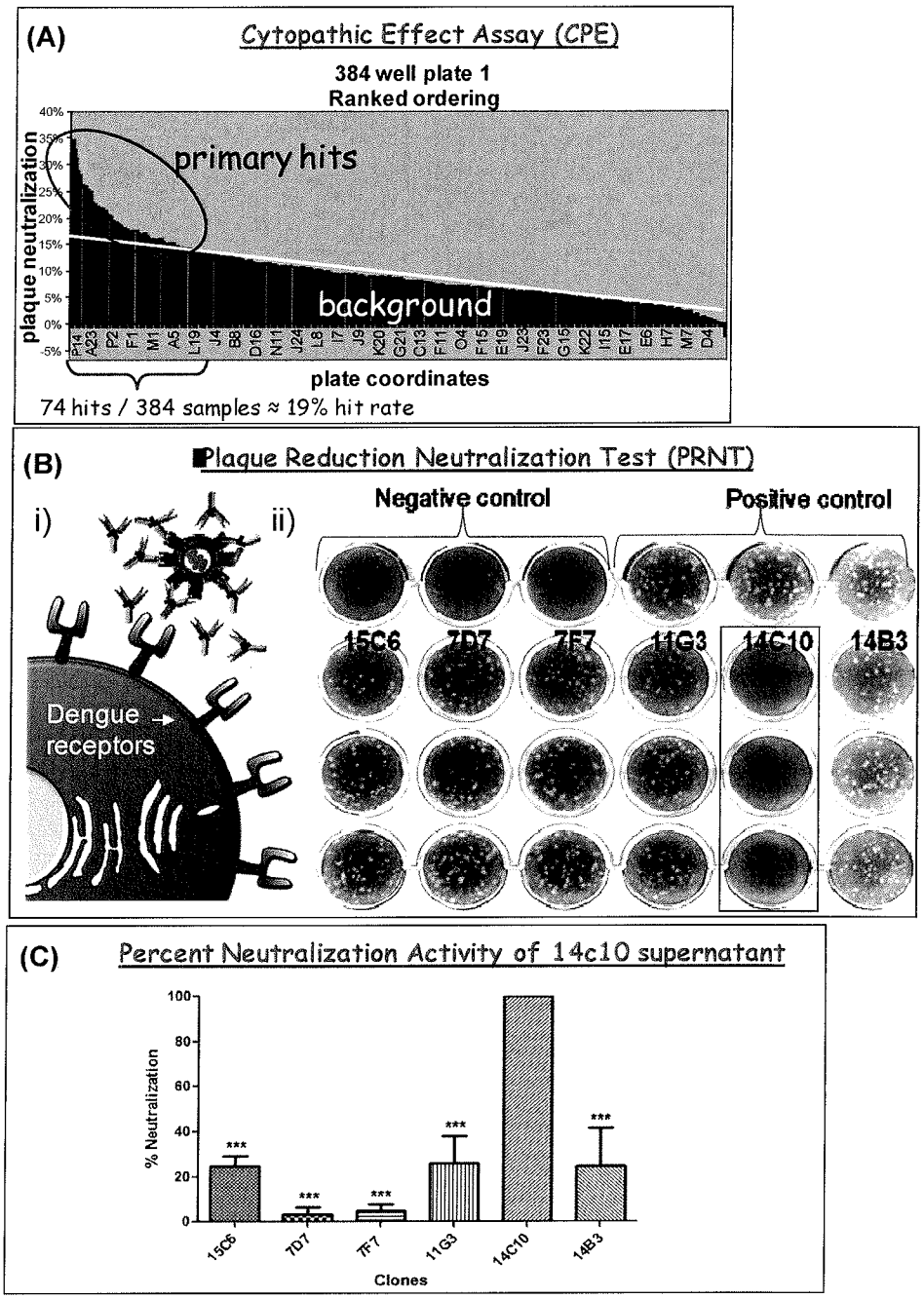
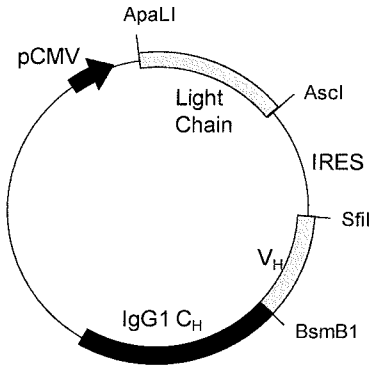


Figure 2: Screening of supernatants from immortalized B cell clones by CPE and PRNT assay.

(A)

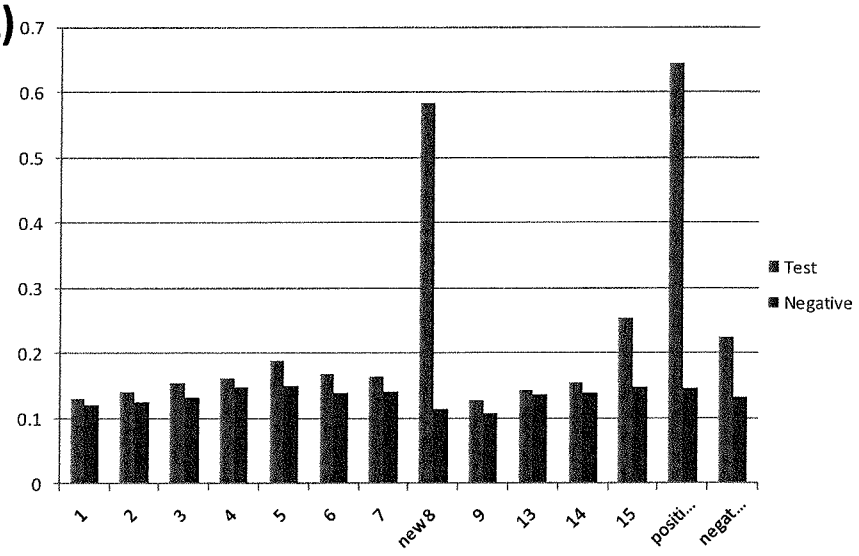


(B)

Clone	Light Chain Sequence	Heavy Chain Sequence
1	DIVMTQSPLSLSVTPGQPASISCRSSQSLLHSDGRT SLDWFLLRPGQFPQVKISELSRRFSGVPDRVSGSG SGTDFTLKISRGEAEDVRAFYCIYGIYVGRSAKGPS WRSN	QVQLVQSGAEVKKPGTSVKVSCKASGYNFTDYYVHWVRQ APGQGLEWMAWINPNSGGSKYAQMFQGRISLTRDTSISTA YLELFSLTSDDTAVYYCADLTAFDVWGQGTLVTVSSGTTV TVSS
2	DIVMTQSPLSLSVTPGQPASISCRSSQSLLHSDGRT SLDWFLLRPGQFPQVKISELSRRFSGVPDRVSGSG SGTDFTLKISRGEAEDVRAFYCIYGIYVGRSAKGPS WRSN	EVQLVESGGGVVQPGRSLRLSCAASGFSFSSYGMHWVR QAPGKGLEWVAVIWYDGSKTYYGDSVKGRFTISKDNSKK MVNLQMDSLGVEDTAFYYCARGIAGGWAFWGIDLWGQGT LVTVSS
3	DIVMTQSPLSLSVTPGQPASISCRSSQSLLHSDGRT SLDWFLLRPGQFPQVKISELSRRFSGVPDRVSGSG SGTDFTLKISRGEAEDVRAFYCIYGIYVGRSAKGPS WRSN	EVQLVQSGGGVVRPGKSLRLSCAASGFTFDDYGMSWVR QAPGKGLEWVSGINWNGGSTGYADSVKGRFTISRDNAKN SLYLQMNSLRAEDTAFYYCAREYGSGSYINWFDPWGQGT LVTVSS
4	DIQMTQSPLSLPVTPGEPASISCRSSQSLLHTNGNN YLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGS GSGTDFTLKISRVEAEDVGVYYCVQALQTKTTFGQ GTKLEIKR	QVQLVQSGAEVKKPGTSVKVSCKASGYNFTDYYVHWVRQ APGQGLEWMAWINPNSGGSKYAQMFQGRISLTRDTSISTA YLELFSLTSDDTAVYYCADLTAFDVWGQGTLVTVSSGTTV TVSS
5	DIQMTQSPLSLPVTPGEPASISCRSSQSLLHTNGNN YLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGS GSGTDFTLKISRVEAEDVGVYYCVQALQTKTTFGQ GTKLEIKR	EVQLVESGGGVVQPGRSLRLSCAASGFSFSSYGMHWVR QAPGKGLEWVAVIWYDGSKTYYGDSVKGRFTISKDNSKK MVNLQMDSLGVEDTAFYYCARGIAGGWAFWGIDLWGQGT LVTVSS
6	DIQMTQSPLSLPVTPGEPASISCRSSQSLLHTNGNN YLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGS GSGTDFTLKISRVEAEDVGVYYCVQALQTKTTFGQ GTKLEIKR	EVQLVQSGGGVVRPGKSLRLSCAASGFTFDDYGMSWVR QAPGKGLEWVSGINWNGGSTGYADSVKGRFTISRDNAKN SLYLQMNSLRAEDTAFYYCAREYGSGSYINWFDPWGQGT LVTVSS
7	DIVMTQSPGTLSLSPGERATLSCRASQNVYSYLGW YQHKPGRSPRLLIFGVTSRATGVPDRFSGSGSGTD FTLTISRLEPEDFAVYYCQQYAGSAYTFGQGTKVEI K	QVQLVQSGAEVKKPGTSVKVSCKASGYNFTDYYVHWVRQ APGQGLEWMAWINPNSGGSKYAQMFQGRISLTRDTSISTA YLELFSLTSDDTAVYYCADLTAFDVWGQGTLVTVSSGTTV TVSS
8*	DIVMTQSPGTLSLSPGERATLSCRASQNVYSYLGW YQHKPGRSPRLLIFGVTSRATGVPDRFSGSGSGTD FTLTISRLEPEDFAVYYCQQYAGSAYTFGQGTKVEI K	EVQLVESGGGVVQPGRSLRLSCAASGFSFSSYGMHWVR QAPGKGLEWVAVIWYDGSKTYYGDSVKGRFTISKDNSKK MVNLQMDSLGVEDTAFYYCARGIAGGWAFWGIDLWGQGT LVTVSS
9	DIVMTQSPGTLSLSPGERATLSCRASQNVYSYLGW YQHKPGRSPRLLIFGVTSRATGVPDRFSGSGSGTD FTLTISRLEPEDFAVYYCQQYAGSAYTFGQGTKVEI K	EVQLVQSGGGVVRPGKSLRLSCAASGFTFDDYGMSWVR QAPGKGLEWVSGINWNGGSTGYADSVKGRFTISRDNAKN SLYLQMNSLRAEDTAFYYCAREYGSGSYINWFDPWGQGT LVTVSS
10	DIVMTQSPDSLAVSLGERATINCKSSQSVLHSSNNK NYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSG SGSGTDFTLTISSLQAEDVAVYYCQQYYSAPHKFG QGTKLEIK	QVQLVQSGAEVKKPGTSVKVSCKASGYNFTDYYVHWVRQ APGQGLEWMAWINPNSGGSKYAQMFQGRISLTRDTSISTA YLELFSLTSDDTAVYYCADLTAFDVWGQGTLVTVSSGTTV TVSS
11	DIVMTQSPDSLAVSLGERATINCKSSQSVLHSSNNK NYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSG SGSGTDFTLTISSLQAEDVAVYYCQQYYSAPHKFG QGTKLEIK	EVQLVESGGGVVQPGRSLRLSCAASGFSFSSYGMHWVR QAPGKGLEWVAVIWYDGSKTYYGDSVKGRFTISKDNSKK MVNLQMDSLGVEDTAFYYCARGIAGGWAFWGIDLWGQGT LVTVSS
12	DIVMTQSPDSLAVSLGERATINCKSSQSVLHSSNNK NYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSG SGSGTDFTLTISSLQAEDVAVYYCQQYYSAPHKFG QGTKLEIK	EVQLVQSGGGVVRPGKSLRLSCAASGFTFDDYGMSWVR QAPGKGLEWVSGINWNGGSTGYADSVKGRFTISRDNAKN SLYLQMNSLRAEDTAFYYCAREYGSGSYINWFDPWGQGT LVTVSS

Figure 3: Identification and recombinant expression of antibody Heavy and Light Chain Templates from B-cell line 14c10.

(A)



(B)

Heavy Chain: IGHV1-2*02

```
GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAG   70
 E  V  Q  L  V  E  S  G  G  G  V  V  Q  P  G  R  S  L  R  L  S  C  A

CGTCTGGATTCAGCTTCAGCAGTTATGGCATGCACTGGGTCCGCCAGGCCCCAGGCAAGGGGCTGGAGTG  140
 A  S  G  F  S  F  S  S  Y  G  M  H  W  V  R  Q  A  P  G  K  G  L  E  W

GGTGGCAGTGATATGGTATGATGGAAGTAAAACGTATTATGGAGACTCCGTGAAGGGCCGATTCACCATC  210
   V  A  V  I  W  Y  D  G  S  K  T  Y  Y  G  D  S  V  K  G  R  F  T  I

TCCAAAGACAATTCCAAGAAAATGGTGAATCTCCAAATGGACAGCCTGGGAGTCGAGGACACGGCTTTTT  280
 S  K  D  N  S  K  K  M  V  N  L  Q  M  D  S  L  G  V  E  D  T  A  F

ATTACTGTGCAAGAGGGATAGCCGGTGGCTGGGCGTTTTGGGGGATTGACCTCTGGGGCCAGGGAACCCT  350
 Y  Y  C  A  R  G  I  A  G  G  W  A  F  W  G  I  D  L  W  G  Q  G  T  L

GGTCACCGTCTCCTCA                                                        366
   V  T  V  S  S
```

Light Chain: IGKV3-20*01

```
GATGTTGTGATGACTCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCA   70
 D  V  V  M  T  Q  S  P  G  T  L  S  L  S  P  G  E  R  A  T  L  S  C

GGGCCAGCCAGAATGTTTACAGCTACTTAGGCTGGTACCAGCACAAACCTGGCCGGTCTCCCAGGCTCCT  140
 R  A  S  Q  N  V  Y  S  Y  L  G  W  Y  Q  H  K  P  G  R  S  P  R  L  L

CATCTTTGGTGTCACCAGCAGGGCCACTGGCGTCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGAC  210
   I  F  G  V  T  S  R  A  T  G  V  P  D  R  F  S  G  S  G  S  G  T  D

TTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCGGTGTACTACTGTCAGCAGTACGCTGGCT  280
 F  T  L  T  I  S  R  L  E  P  E  D  F  A  V  Y  Y  C  Q  Q  Y  A  G

CAGCGTACACTTTTGGCCAGGGGACCAAGGTGGAGATCAAACGT                            324
 S  A  Y  T  F  G  Q  G  T  K  V  E  I  K  R
```

Figure 4: Recombinant antibody no: 8 from B cell line 14C10 has neutralizing activity for Dengue serotype 1.

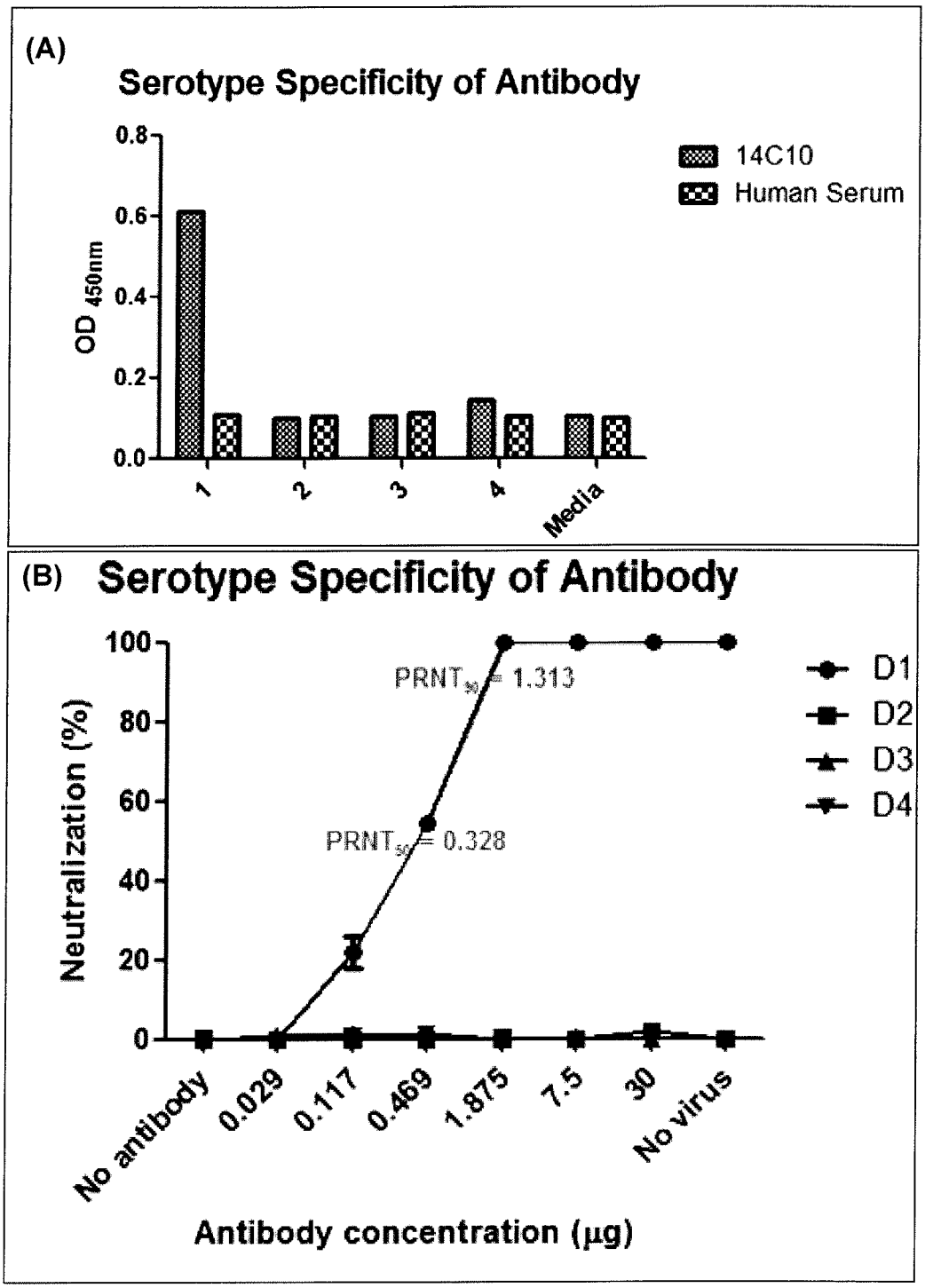


Figure 5: Serotype specificity of recombinant 14C10.8 antibody tested by PRNT and ELIZA.

(C)

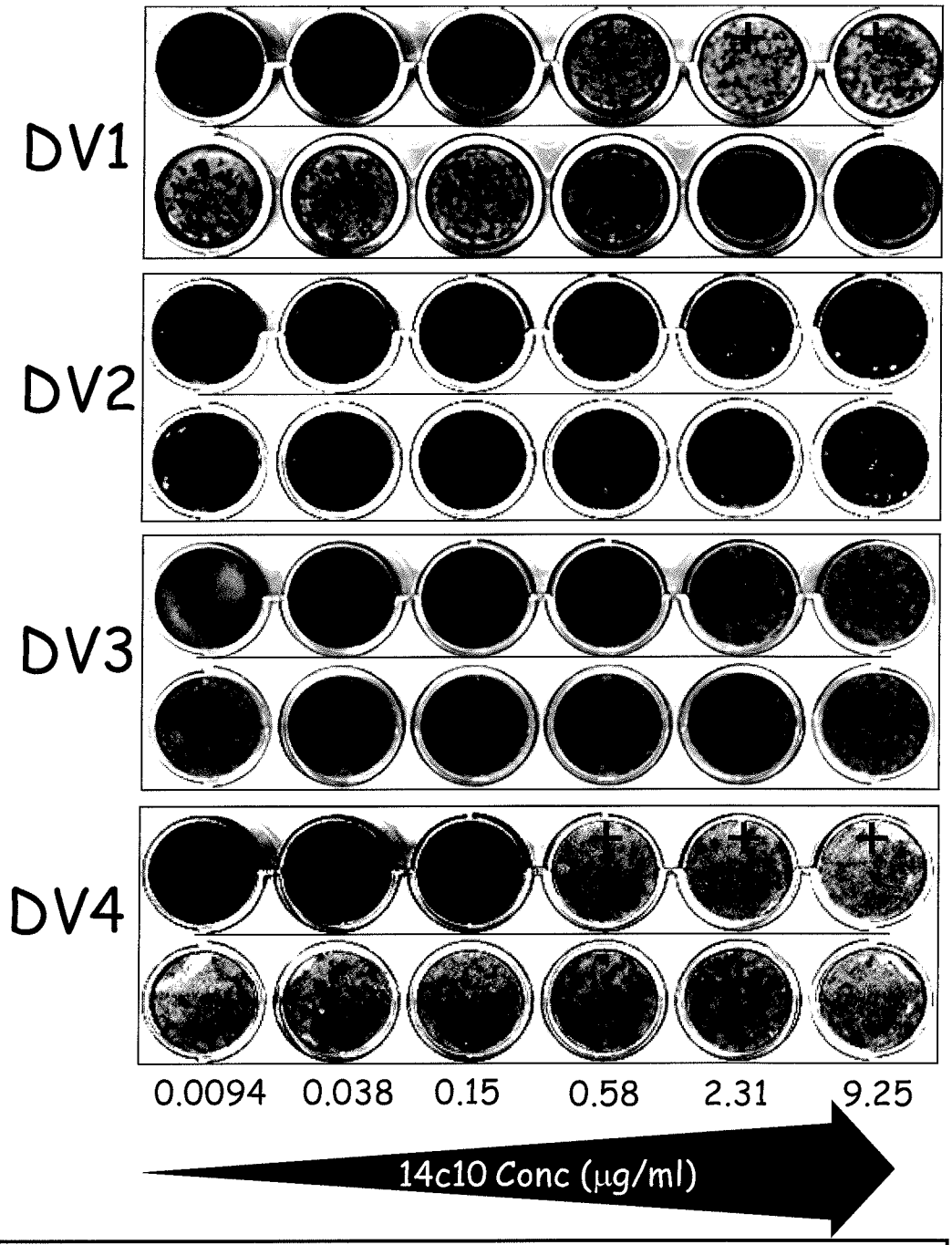


Figure 5 contd: Serotype specificity of recombinant 14C10.8 antibody with PRNT and ELIZA.

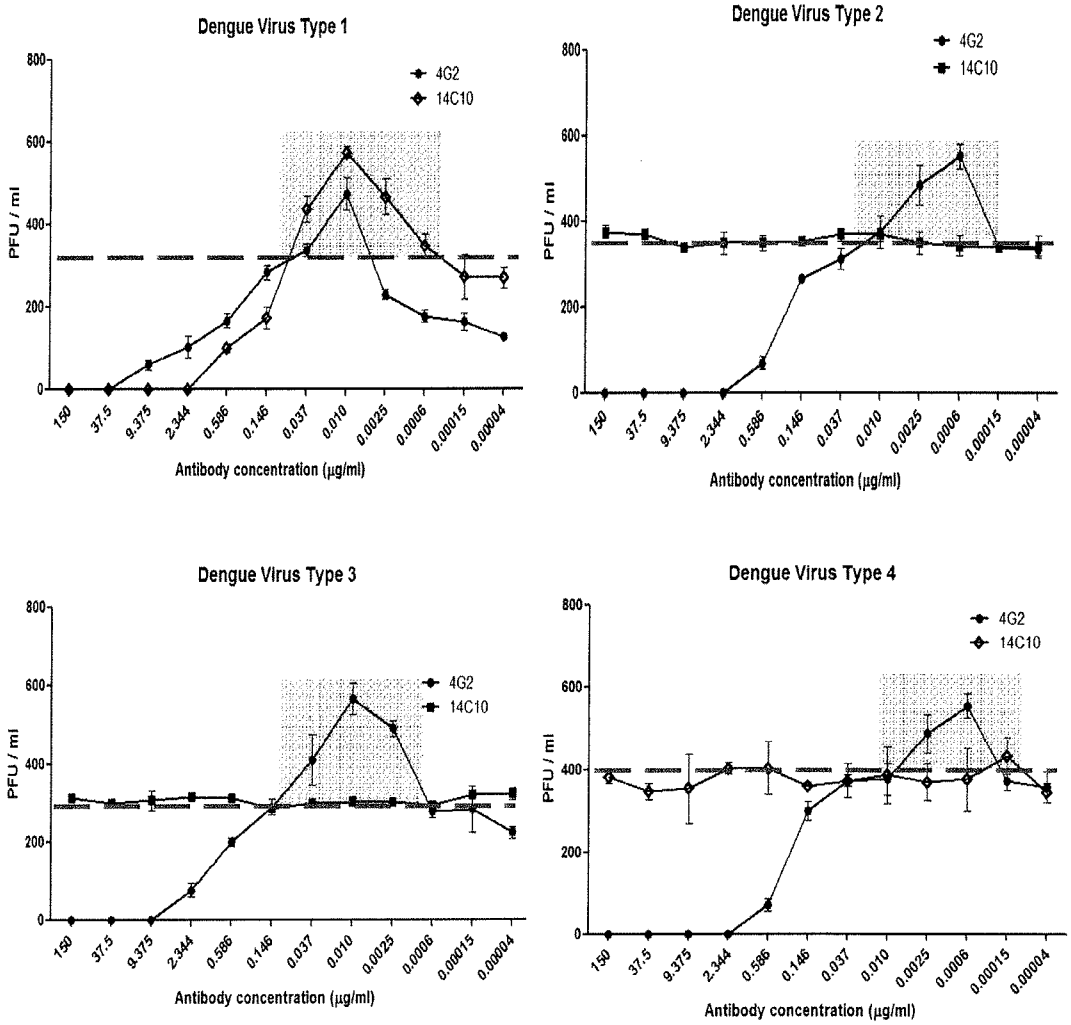
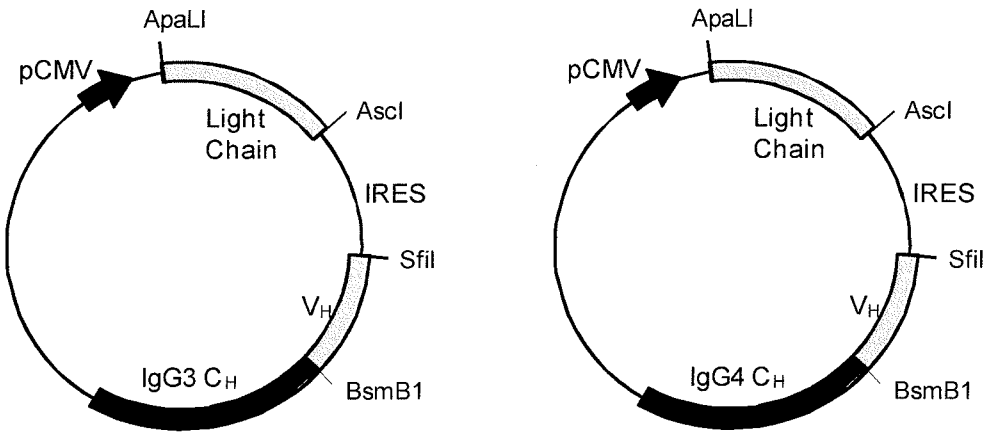


Figure 6: In vitro Antibody Dependent Enhancement of Dengue serotype 1, 2, 3 and 4 infection of K562 Cells by 14c10 Versus 4G2.



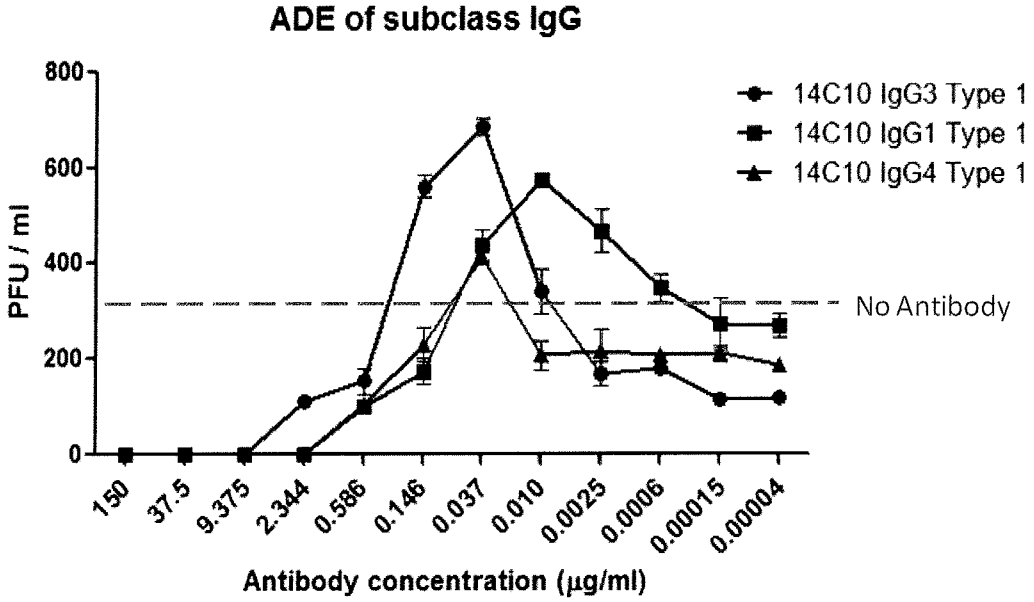


Figure 7: In vitro Antibody Dependent Enhancement of Dengue serotype 1, infection of K562 Cells by 14c10.8 Expressed as recombinant human IgG1, IgG3 or IgG4.

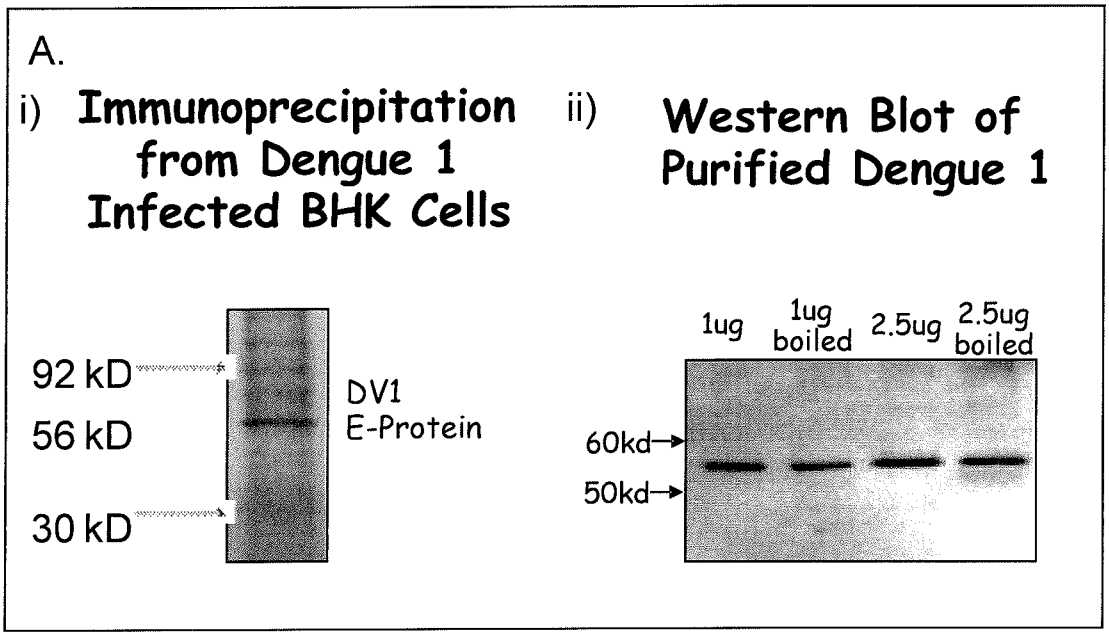
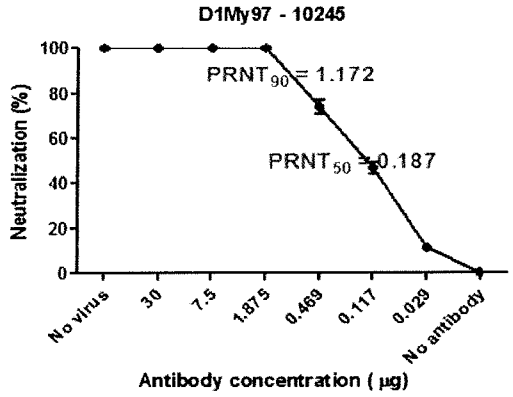


Figure 8: 14c10.8 is specific for a linear epitope on Dengue Serotype 1 E-Protein

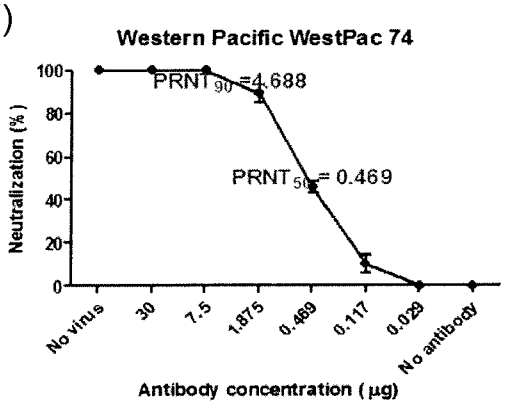
i)



EU448410:

MRCVGIGNRDFVEGLSGATWVDVVLEHGSCVT
TMAKDKPTLDIELLKTEVTNPAVLRKLCIEAKIS
NTTTDSRCPTQGEATLVEEQDTNFVCRRTFVDR
GWGNGCGLFGKGSLITCAKFKCVTKLEGKIVQ
YENLKYSVIVTVHTGDQHQVGNETTEHGTIATIT
PQAPTSEIQLTDYGALTLDCSPRTGLDFNEMVL
LTMKEKSWLVHKQWFLDLPLPWTSGASTSQE
TWNRQDLLVTFKTAHAKKQEVVVLGSQEGAM
HTALTGATEIQTSGTTTIFAGHLKCRLKMDKLTL
KGMSYVMCTGPFKLEKEMAETQHGTVLVQVKY
EGTDAPCKIPFSSQDEKGVTQNGRLVTANPIVT
DKEKPINIEAEPPFGESYIVVGAGEKALKLSWFK
KGSSIGKMFEATARGARRMAILGDTAWDFGSI
GGVFTSVGKLVHQIFGTAYGVLFSGVSWTMKI
GIGILLTWLGLNSRSTSLSMTCIAVGMVTLYLG
VMVQA

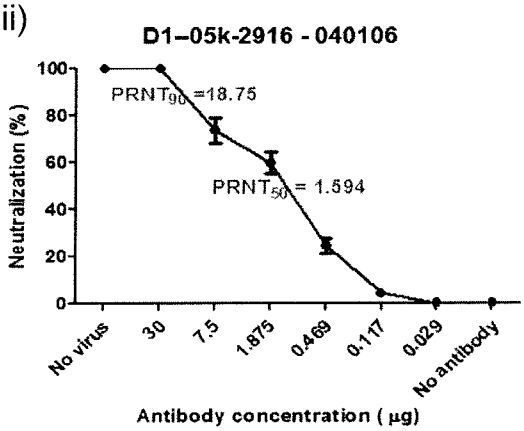
ii)



DVU88535:

MRCVGIGNRDFVEGLSGATWVDVVLEHGSCVT
TMAKDKPTLDIELLKTEVTNPAVLRKLCIEAKISN
TTTDSRCPTQGEATLVEEQDTNFVCRRTFVDRG
WGNGCGLFGKGSLITCAKFKCVTKLEGKIVQYE
NLKYSVIVTVHTGDQHQVGNETTEHGTTATITPQ
APTSEIQLTDYGALTLDCSPRTGLDFNEMVLLT
MEKKSWLVHKQWFLDLPLPWTSGASTSQETW
NRQDLLVTFKTAHAKKQEVVVLGSQEGAMHTA
LTGATEIQTSGTTTIFAGHLKCRLKMDKLTLKG
MSYVMCTGSFKLEKEVAETQHGTVLVQVKYEG
TDAPCKIPFSSQDEKGVTQNGRLITANPIVTDKE
KPVNIEAEPPFGESYIVVGAGEKALKLSWFKKG
SSIGKMFEATARGARRMAILGDTAWDFGSIGGV
FTSVGKLIHQIFGTAYGVLFSGVSWTMKIGIGIL
LTWLGLNSRSTSLSMTCIAVGMVTLYLGVMVQ
A

iii)

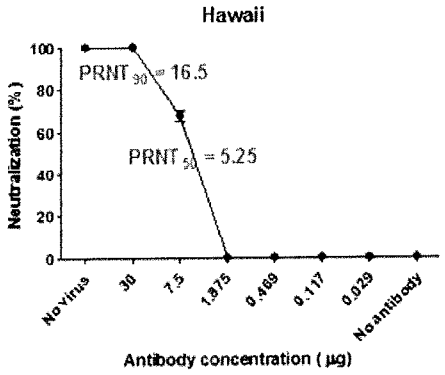


EU081234:

MRCVGIGSRDFVEGLSGATWVDVVLEHGSCV
TTMAKDKPTLDIELLKTEVTNPAVLRKLCIEAKI
SNTTTDSRCPTQGEATLVEEQDANFVCRRTFV
DRGWGNGCGLFGKGSLITCAKFKCVTKLEGKI
VQYENLKYSVIVTVHTGDQHQVGNESTEHGTT
ATITPQAPTTEIQLTDYGALTLDCSPRTGLDFN
EMVLLTMKEKSWLVHKQWFLDLPLPWTSGA
STSQETWNRQDLLVTFKTAHAKKQEVVVLGS
QEGAMHTALTGATEIQTSGTTTIFAGHLKCRLK
MDKLTLKGMSYVMCTGSFKLEKEVAETQHGT
VLVQIKYEGTDAPCKIPFLTQDEKGVTQNGRLI
TANPIVTDKEKPVNIEAEPPFGESYIVIGAGEKA
LKLSWFKKGSSIGKMFEATARGARRMAILGDT
AWDFGSIGGVFTSVGKLVHQIFGTAYGVLFSG
VSWTMKIGIGVLLTWLGLNSRSTSLSMTCIAV
GLVTLYLGVMVQA

Figure 9: Neutralization activity of recombinant 14c10 against various genotypes.

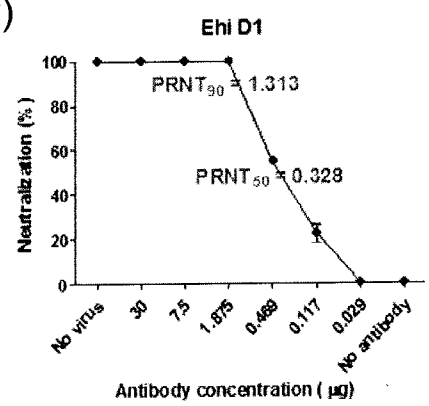
iv)



AF425619:

MRCVGIGNRDFVEGLSGATWVDVVLEHGSCVTTMAK
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QGEATLVEEQDANFVCRRTFVDRGWGNGCGLFGKGS
LITCAKFKCVTKLEGKIVQYENLKYSVIVTVHTGDQHQV
GNETTEHGTIATITPQAPTSEIQLTDYGALTLDCSPRTG
LDFNEMVLLTMKEKSWLVHKQWFLDLPLPWTSGAST
PQETWNREDLLVTFKTAHAKKQEVAVLGSQEGAMHT
ALTGATEIQTSGTTKIFAGHLKCRLKMDKLTLKGMSYV
MCTGSFKLEKEVAETQHGTVLVQVKYEGTDAPCKIPFS
TQDEKGVTQNGRLITANPIVTDKEKPVNIEAEPPFGESY
IVVGAGEKALKLSWFKKGSSIGKMLEATARGARRMAI
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SWTMKIGIGILLTWLGLNSRSASLSMTCIAVGMVTLYL
GVMVQA

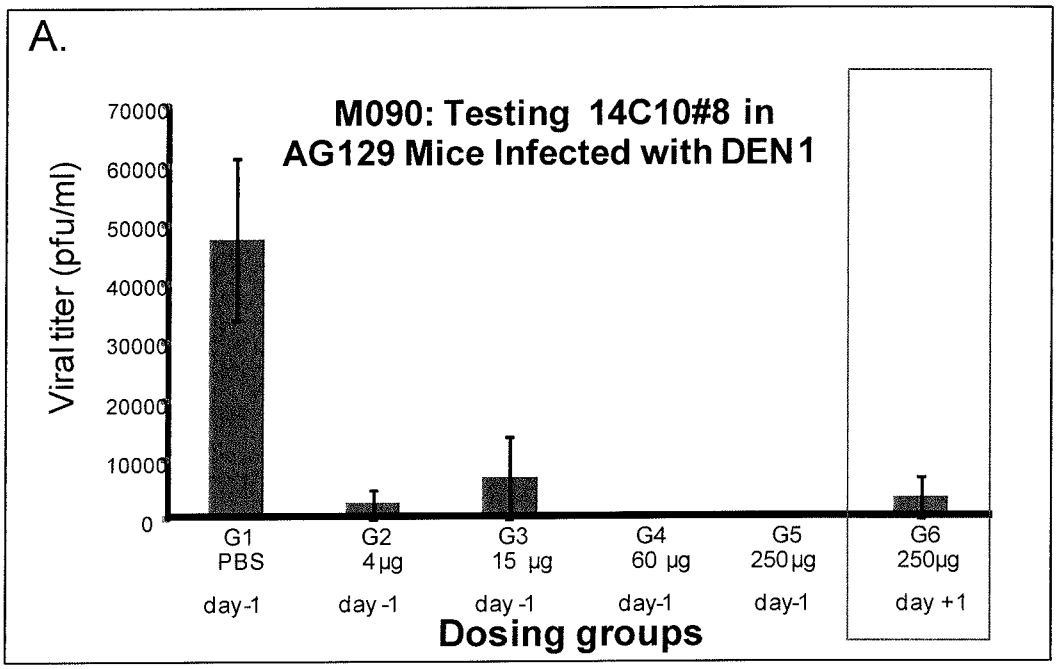
v)



GQ357687:

MRCVGIGSRDFVEGLSGATWVDVVLEHGSCVTTMA
KDKPTLDIELLKTEVTNPAVLRKLCIEAKISNTTTDSRC
PTQGEATLVEEQDANFVCRRTFVDRGWGNGCGLFG
KGSLITCAKFKCVTKLEGKIVQYENLKYSVIVTVHTGD
QHQVGNESTEHGTTATITPQAPTTEIQLTDYGALTLD
CSPRTGLDFNEMVLLTMKEKSWLVHKQWFLDLPLP
WTSGASTSQETWNRQDLLVTFKTAHAKKQEVVVLG
SQEGAMHTALTGATEIQTSGTTTIFAGHLKCRLKMDK
LTLKGMSYVMCTGSFKLEKEVAETQHGTVLVQIKYE
GTDAPCKIPFSTQDEKGVTQNGRLITANPIVTDKEKP
VNIEAEPPFGESYIVIGAGEKALKLSWFKKGSSIGKM
FEATARGARRMAILGDTAWDFGSIGGVFTSVGKLVH
QIFGTAYGVLFSGVSWTMKIGIGVLLTWLGLNSRST
SLSMTCIAVGLVTLYLGVMVQA

Figure 9 contd: Neutralization activity of recombinant 14c10.8 against various genotypes.



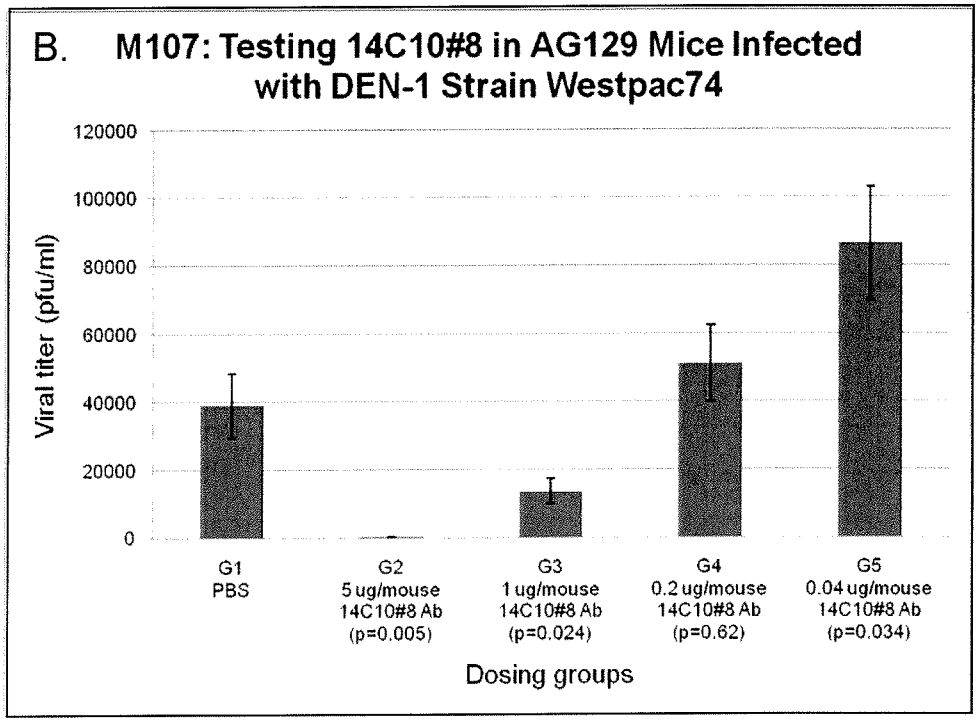


Figure 10: 14c10.8 has prophylactic and therapeutic activity *in vivo*.

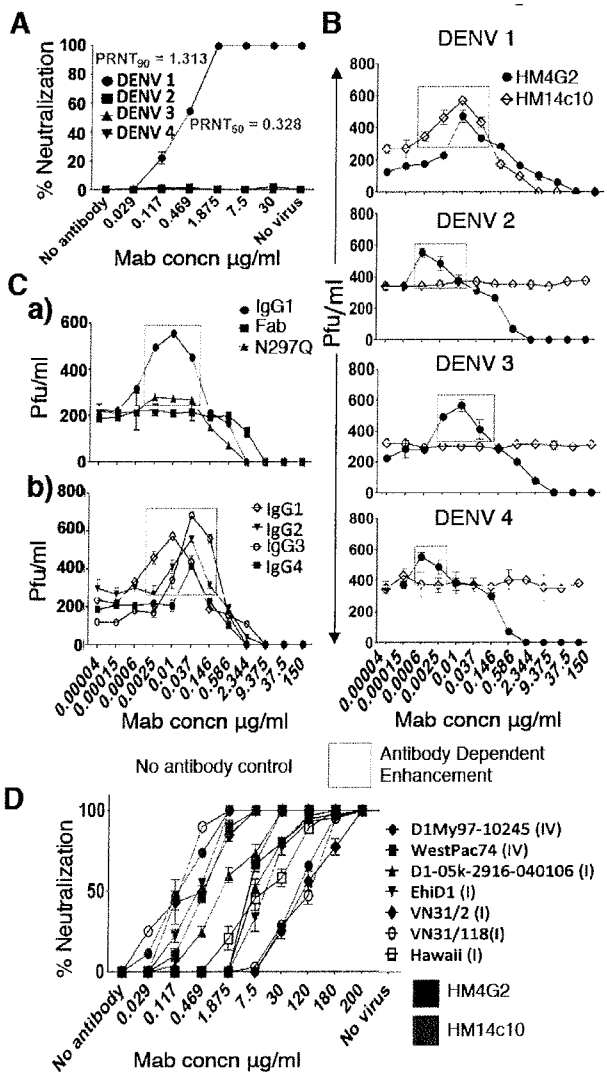

A
% Neutralization
PRNT90 = 1.313
DENV 1
DENV 2
DENV 3
DENV 4
PRNT50 = 0.328
No antibody
0.029
0.117
0.469
1.875
7.5
30
No virus
Mab concn µg/ml
B
DENV 1
HM4G2
HM14c10
DENV 2
DENV 3
DENV 4
Pfu/ml
C
a)
IgG1
Fab
N297Q
b)
IgG1
IgG2
IgG3
IgG4
Pfu/ml
Mab concn µg/ml
No antibody control
Antibody Dependent Enhancement
D
% Neutralization
D1My97-10245 (IV)
WestPac74 (IV)
D1-05k-2916-040106 (I)
EhiD1 (I)
VN31/2 (I)
VN31/118(I)
Hawaii (I)
HM4G2
HM14c10
Mab concn µg/ml

Figure 11

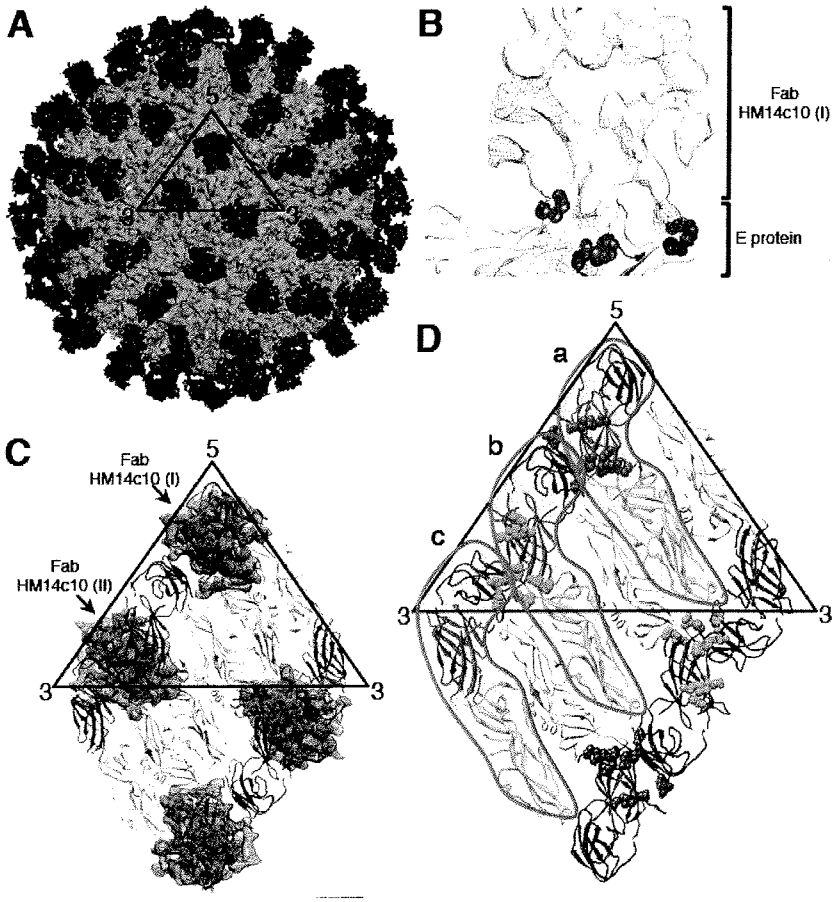

A
5
3
3
B
Fab
HM14c10 (I)
E protein
C
Fab
HM14c10 (I)
Fab
HM14c10 (II)
5
3
3
D
5
a
b
c
3
3

Figure 12

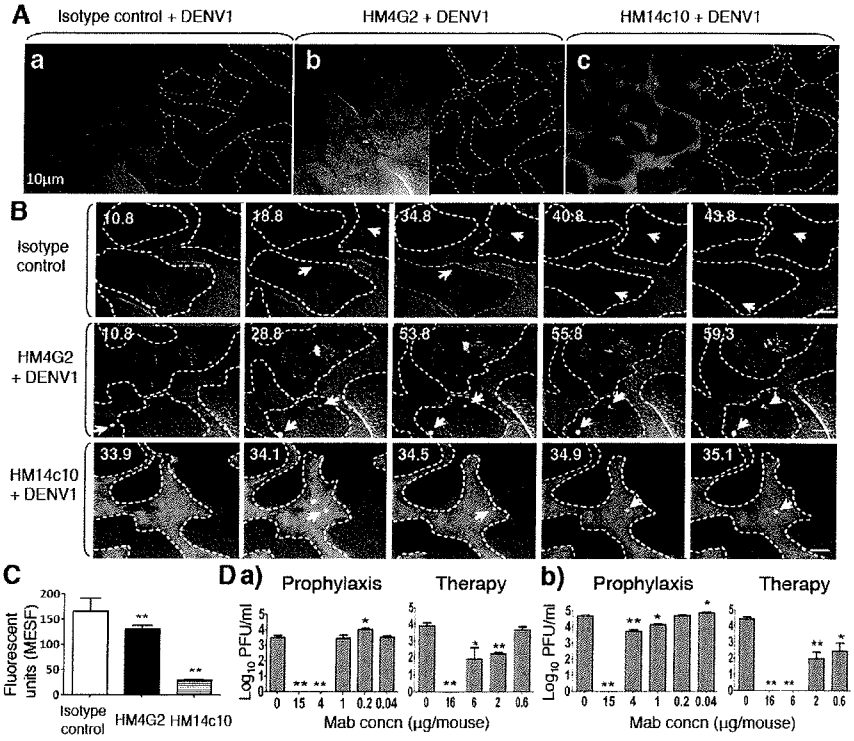
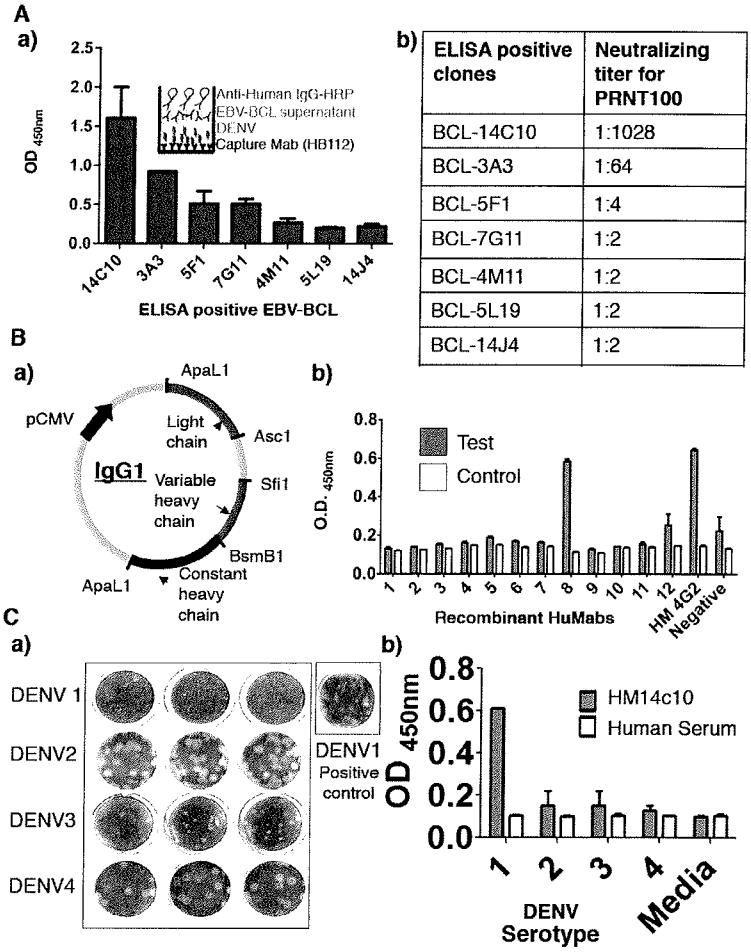

A
Isotype control + DENV1
HM4G2 + DENV1
HM14c10 + DENV1
a
b
c
10μm
B
Isotype control
HM4G2 + DENV1
HM14c10 + DENV1
10.8
18.8
34.8
40.8
43.8
10.8
28.8
53.8
55.8
59.3
33.9
34.1
34.5
34.9
35.1
C
Fluorescent units (MESF)
Isotype control
HM4G2
HM14c10
D a)
Prophylaxis
Therapy
Log10 PFU/ml
Mab concn (μg/mouse)
b)
Prophylaxis
Therapy
Log10 PFU/ml
Mab concn (μg/mouse)

Figure 13



b) ELISA positive clones	Neutralizing titer for PRNT100
BCL-14C10	1:1028
BCL-3A3	1:64
BCL-5F1	1:4
BCL-7G11	1:2
BCL-4M11	1:2
BCL-5L19	1:2
BCL-14J4	1:2

Figure 14

Identification and recombinant expression of a fully human antibody with neutralizing activity for Dengue Virus.

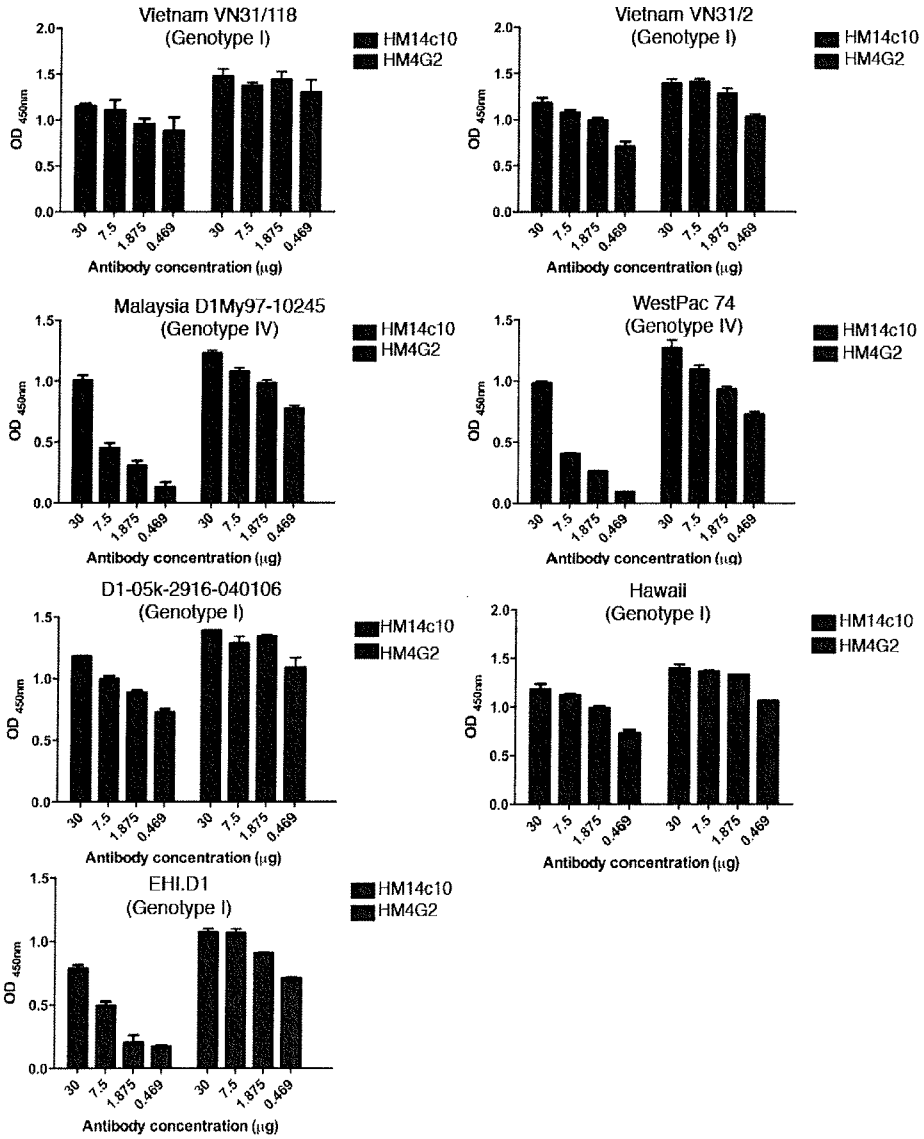


Figure 15

HM14c10 exhibits binding activity for multiple DENV1 clinical isolates.

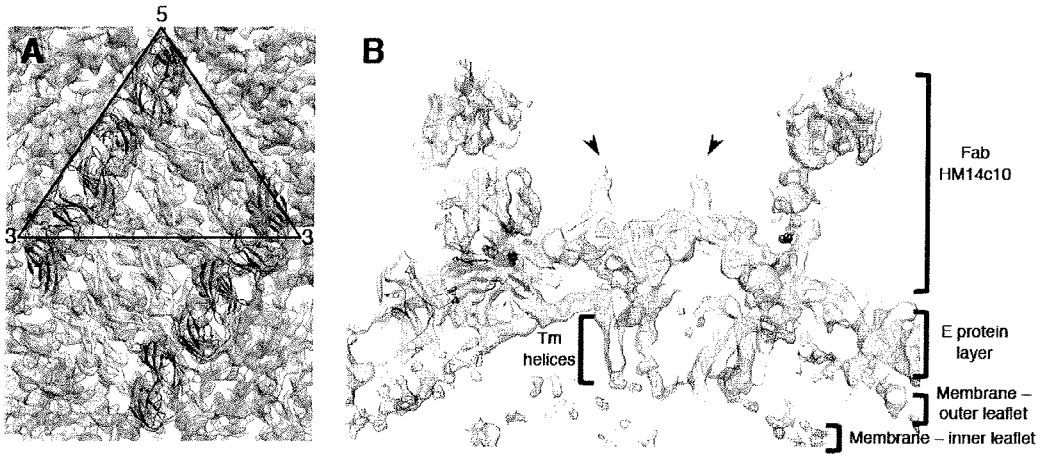


Figure 16

Fit of the post-fusion crystal structure of DENV1 E proteins into the cryoEM map of Fab HM14c10 complexed with Dengue 1 virus.

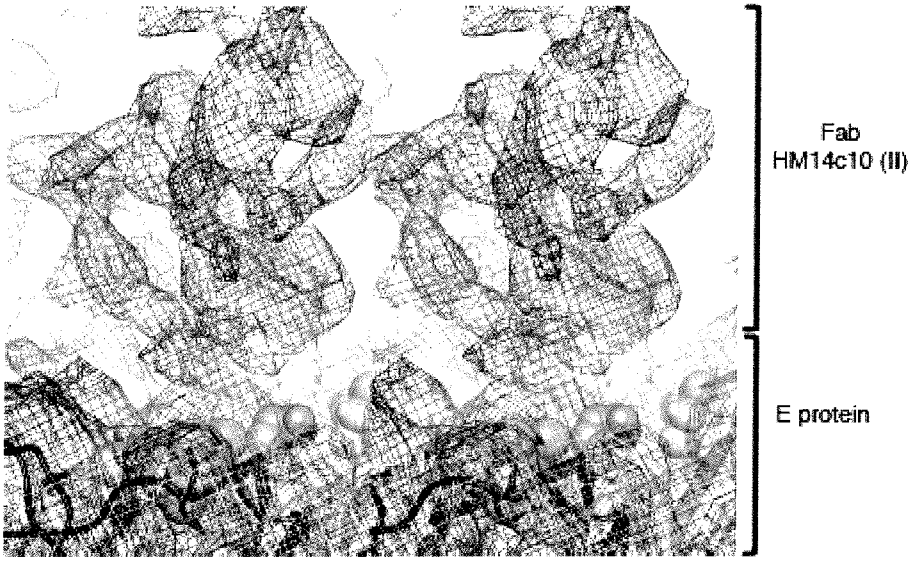


Figure 17

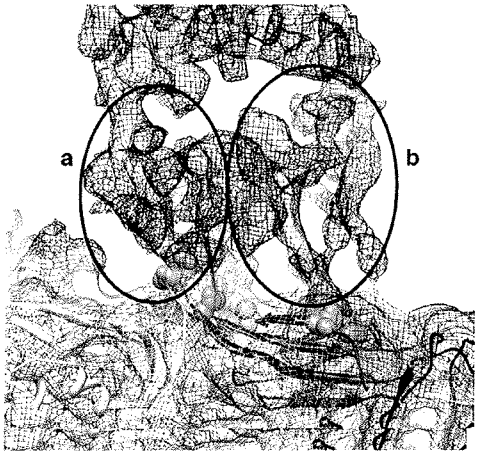
Stereo-diagram of the Fab HM14c10 and E protein binding interface.



Figure 18

Superposition of the variable regions of homology model of HM14c10 (green) with reference human monoclonal antibody (PDB code 2GHW) (blue). Figure is showing (**A**) side and (**B**) top view of the antibody variable regions.

A



B

Fab position [a]	Fab density [b]	Antibody chain	Number of fitted atoms / number of atoms outside contour after fitting [c]	Average map value at atom positions after fitting
I	a	light	834 / 584	2.077
	b	heavy	936 /663	2.074
I	a	heavy	936 /666	1.791
	b	light	834 / 580	2.117
II	a	light	834 / 533	2.286
	b	heavy	936 / 676	1.936
II	a	heavy	936 / 640	2.022
	b	light	834 / 629	1.909

C

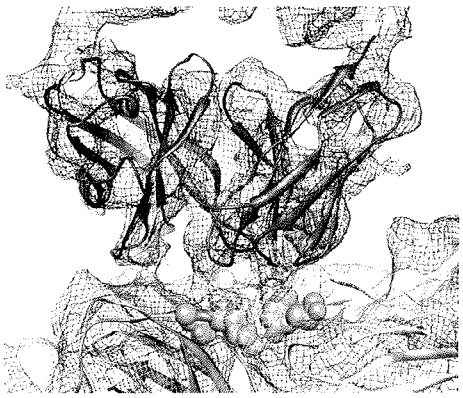


Figure 19

Fitting of the homology model of HM14c10 variable region into HM14c10:DENV1 cryoEM density map.

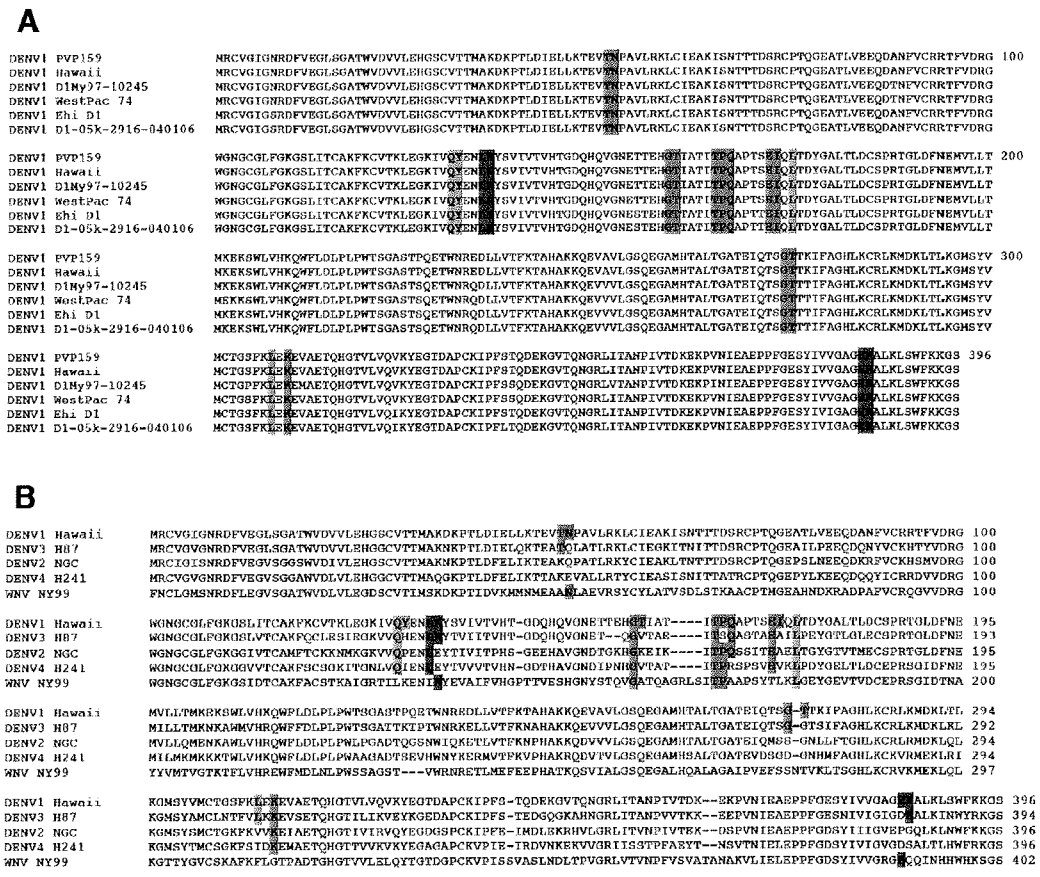


Figure 20

HM14c10 epitope on dengue serotype 1 (genotype PVP159) and comparison of the epitope with (A) other DENV1 genotypes and (B) dengue serotypes and West Nile virus (WNV).

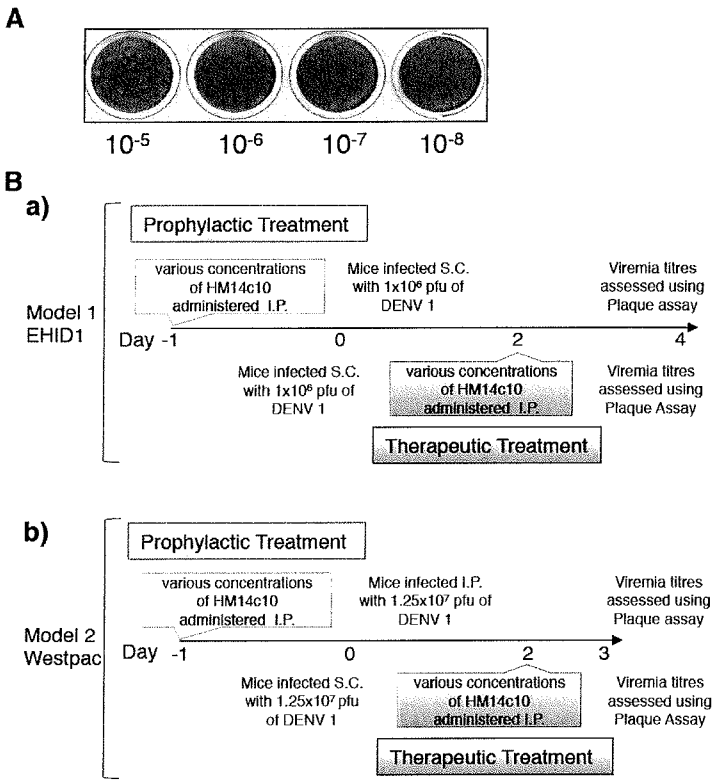


Figure 21

Infectivity and *in vivo* efficacy of labeled DENV1.

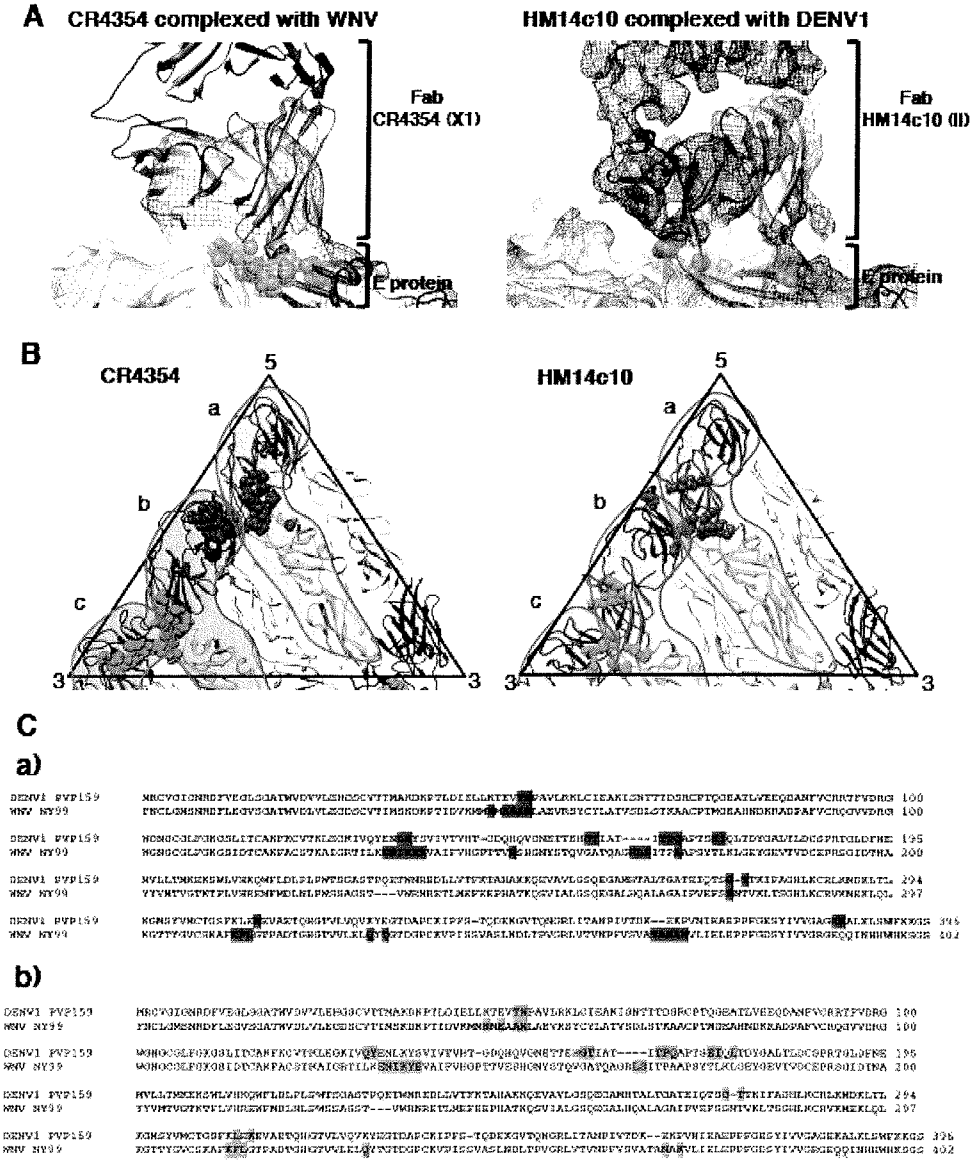


Figure 22

Comparison of epitope bound by a West Nile virus antibody CR4354 and dengue 1 specific HM14c10.