	Binding (EC50, ng/ml)										Neut. (IC50, ng/ml)		
	ZIKV E	DENV1 E	DENV2 E	DENV3 E	DENV4 E	DENV1 VLP	DENV2 VLP	DENV3 VLP	DENV4 VLP	DIII ZKA	ZIKV neut	DENV1 neut	
ZKA3	172	510	108	17	134	12	28	10	7	-	411	346	
ZKA4	172	135	23	9	22	9	11	10	8	-	961	592	
ZKA5	243	877	133	22	123	37	32	25	31	-	1978	-	
ZKA6	79	355	28	13	58	13	14	9	10	-	1661	-	
ZKA7	112	329	74	11	95	9	18	8	7	-	646	513	
ZKA8	70	136	31	8	28	8	11	7	11	-	1336	102	
ZKA76	408	-	-	-	-	-	-	-	-	3756	62	nd	
ZKA78	2759	1407	982	33	385	158	83	131	136	-	2863	266	
ZKA117	376	1780	341	49	391	142	86	36	158	-	1945	83	
ZKB27	225	-	-	-	-	nd	nd	nd	nd	-	257	nd	
ZKB29	285	-	-	-	-	nd	nd	nd	nd	-	-	nd	
ZKB30	1560	2011	2320	344	459	nd	nd	nd	nd	-	-	nd	
ZKB32	1668	-	-	-	-	nd	nd	nd	nd	-	545	nd	
ZKB34	122	-	-	-	-	nd	nd	nd	nd	-	-	nd	
ZKB39	136	-	-	-	-	nd	nd	nd	nd	-	667	nd	
ZKB41	241	-	-	-	-	nd	nd	nd	nd	-	-	nd	
ZKB45	125	-	-	-	-	nd	nd	nd	nd	-	1461	nd	
ZKB46	3238	-	-	-	-	nd	nd	nd	nd	-	-	nd	
ZKB51	645	220	115	66	62	nd	nd	nd	nd	-	-	nd	EDII/II
ZKB52	3398	-	-	-	-	nd	nd	nd	nd	-	-	nd	
ZKB53	59	-	-	-	-	nd	nd	nd	nd	-	-	nd	
ZKB84	4373	-	-	-	-	nd	nd	nd	nd	-	-	nd	
ZKC21	2069	4201	3659	877	1252	nd	nd	nd	nd	-	-	nd	
ZKC22	161	347	133	330	75	nd	nd	nd	nd	-	-	nd	
ZKC23	87	2162	97	37	21	nd	nd	nd	nd	-	-	nd	
ZKC24	92	177	71	240	55	nd	nd	nd	nd	-	-	nd	
ZKC26	52	150	61	21	28	nd	nd	nd	nd	-	420	nd	
ZKD4	20	80	24	8	11	nd	nd	nd	nd	-	-	nd	
ZKD5	42	254	103	17	41	nd	nd	nd	nd	-	-	nd	
ZKD6	115	585	600	31	96	nd	nd	nd	nd	-	-	nd	
ZKD7	33	474	147	12	44	nd	nd	nd	nd	-	-	nd	
ZKD8	24	169	62	12	25	nd	nd	nd	nd	-	-	nd	
ZKD15	581	-	-	-	-	nd	nd	nd	nd	-	-	nd	
ZKD16	62	692	475	10	27	nd	nd	nd	nd	-	-	nd	
ZKD17	14	93	32	7	12	nd	nd	nd	nd	-	-	nd	
ZKD20	565	-	-	50	-	nd	nd	nd	nd	-	-	nd	
ZKD21	53	63	189	13	17	nd	nd	nd	nd	-	-	nd	
ZKA64	65	-	-	-	-	-	-	-	-	161	155	-	
ZKA134	168	-	-	-	-	-	-	-	-	626	432	nd	
ZKA190	113	-	-	-	-	-	-	-	-	444	12	nd	
ZKA246	473	-	-	-	-	-	-	-	-	5974	243	nd	
ZKA256	115	-	-	-	-	-	-	-	-	214	224	nd	
ZKB31	73	-	-	-	-	nd	nd	nd	nd	18	-	nd	
ZKB42	5561	7073	6485	12065	6884	nd	nd	nd	nd	5158	-	nd	EDIII
ZKB50	653	10000	-	-	-	nd	nd	nd	nd	-	-	nd	
ZKB85	953	-	-	-	-	nd	nd	nd	nd	2400	2387	nd	
ZKB47	13	-	-	-	-	nd	nd	nd	nd	574	-	nd	
ZKC6	8575	-	-	-	-	nd	nd	nd	nd	5533	32	nd	
ZKC25	162	144	147	150	158	nd	nd	nd	nd	200	-	nd	
ZKD18	17	-	-	-	-	nd	nd	nd	nd	12	-	nd	
ZKA81	-	-	-	-	-	nd	nd	nd	nd	-	243	nd	
ZKA144	-	-	-	-	-	nd	nd	nd	nd	-	48	nd	
ZKA146	-	-	-	-	-	nd	nd	nd	nd	-	45	nd	
ZKA155	-	-	-	-	-	nd	nd	nd	nd	-	99	nd	
ZKA160	-	-	-	-	-	nd	nd	nd	nd	-	38	26	
ZKA167	-	-	-	-	-	nd	nd	nd	nd	-	121	nd	
ZKA169	-	-	-	-	-	nd	nd	nd	nd	-	321	nd	
ZKA171	-	-	-	-	-	nd	nd	nd	nd	-	47	nd	
ZKA172	-	-	-	-	-	nd	nd	nd	nd	-	9	nd	
ZKA174	-	-	-	-	-	nd	nd	nd	nd	-	55	-	
ZKA183	-	-	-	-	-	nd	nd	nd	nd	-	34	nd	
ZKA185	-	-	-	-	-	nd	nd	nd	nd	-	13	-	
ZKA189	-	-	-	-	-	nd	nd	nd	nd	-	273	nd	
ZKA191	-	-	-	-	-	nd	nd	nd	nd	-	52	nd	
ZKA195	-	-	-	-	-	nd	nd	nd	nd	-	33	-	NNB
ZKA207	-	-	-	-	-	nd	nd	nd	nd	-	43	nd	
ZKA215	-	-	-	-	-	nd	nd	nd	nd	-	26	nd	
ZKA218	-	-	-	-	-	nd	nd	nd	nd	-	14	nd	
ZKA228	-	-	-	-	-	nd	nd	nd	nd	-	36	nd	
ZKA230	-	-	-	-	-	nd	nd	nd	nd	-	10	nd	
ZKB75	-	-	-	-	-	nd	nd	nd	nd	-	190	nd	
ZKB79	-	-	-	-	-	nd	nd	nd	nd	-	391	nd	
ZKB83	-	-	-	-	-	nd	nd	nd	nd	-	59	nd	
ZKC3	-	-	-	-	-	nd	nd	nd	nd	-	170	nd	
ZKC8	-	-	-	-	-	nd	nd	nd	nd	-	762	nd	
ZKC15	-	-	-	-	-	nd	nd	nd	nd	-	15	nd	
ZKC18	-	-	-	-	-	nd	nd	nd	nd	-	662	nd	
ZKD1	-	-	-	-	-	nd	nd	nd	nd	-	1141	nd	

Figure 1

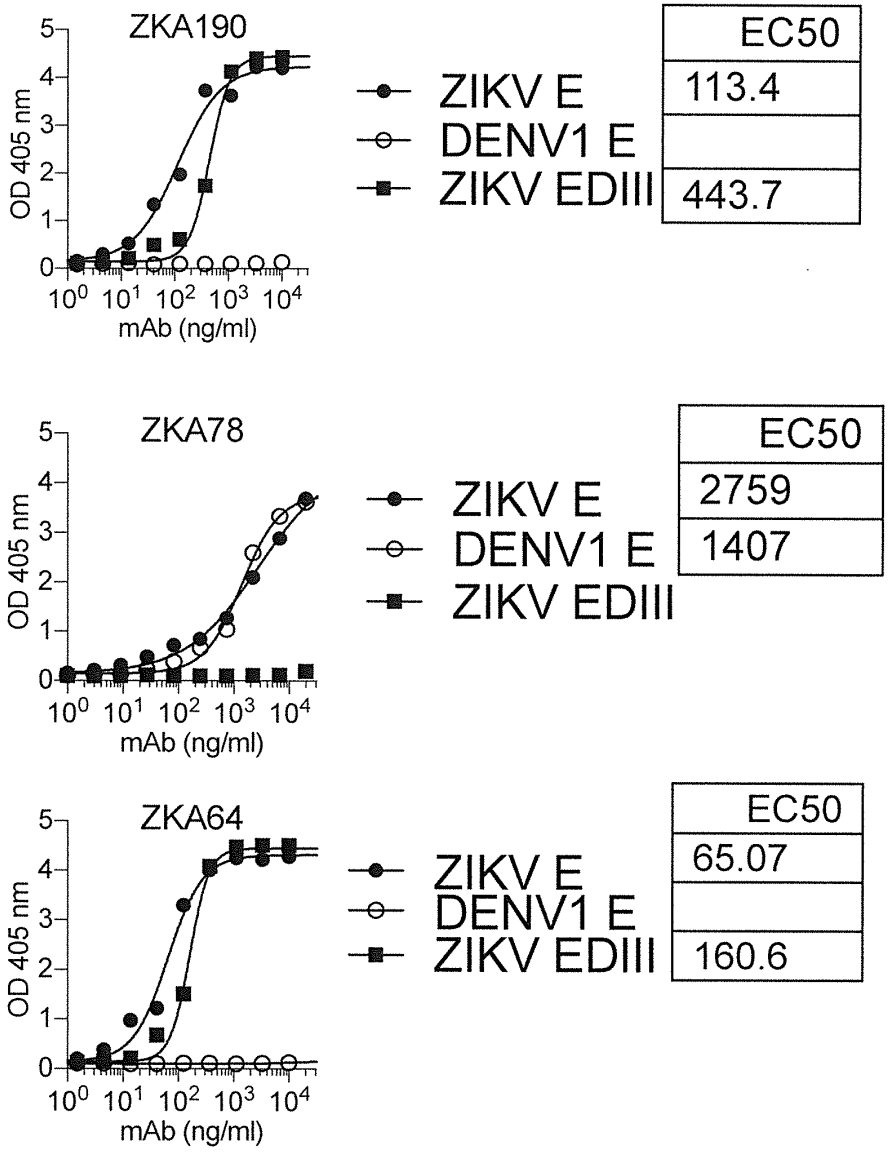

ZKA190
OD 405 nm
mAb (ng/ml)
ZIKV E
DENV1 E
ZIKV EDIII
EC50
113.4
443.7
ZKA78
2759
1407
ZKA64
65.07
160.6

Figure 2

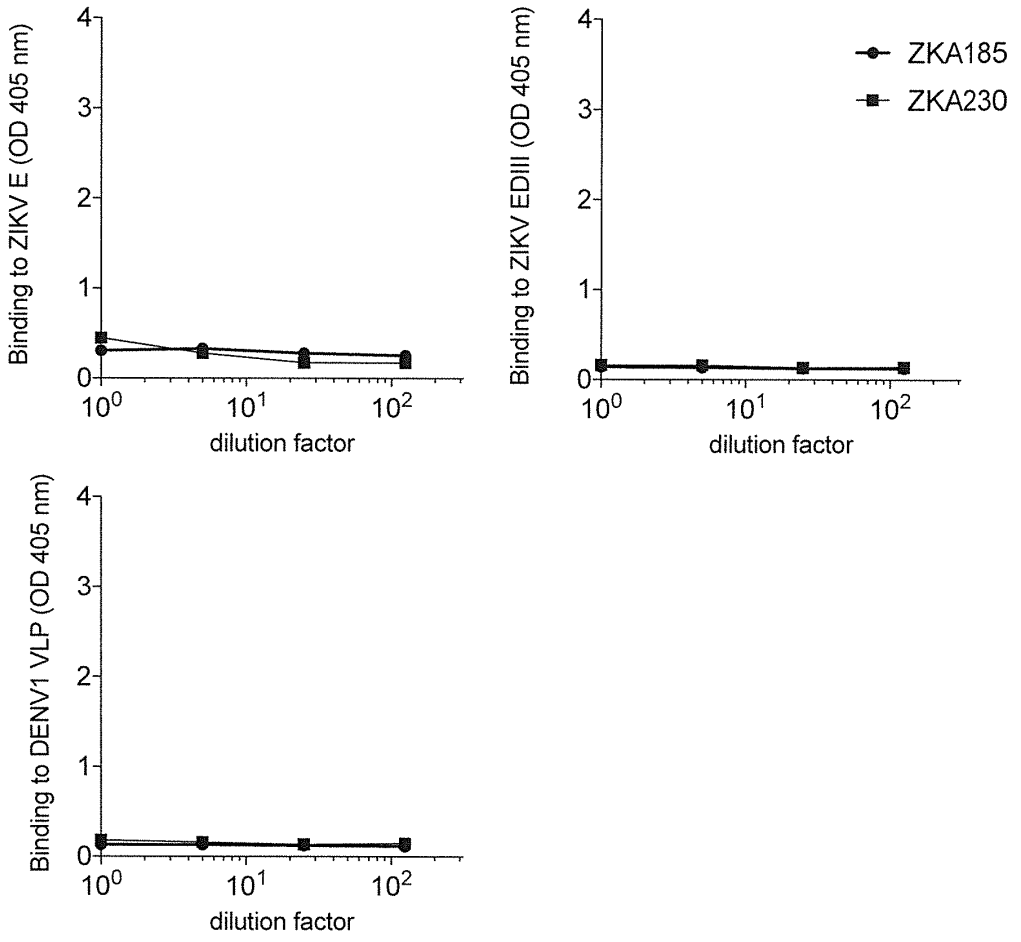
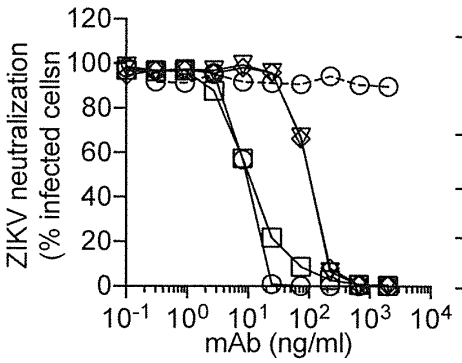

Binding to ZIKV E (OD 405 nm)
Binding to ZIKV EDIII (OD 405 nm)
Binding to DENV1 VLP (OD 405 nm)
dilution factor
ZKA185
ZKA230

Figure 3



	IC50
ZKA190	8.868
ZKA64 wt	93.27
ZKA64 LALA	94.01
ZKA230	10.31

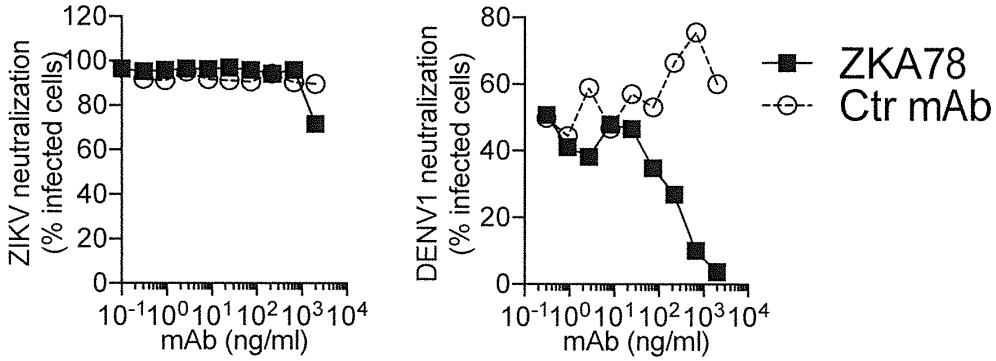
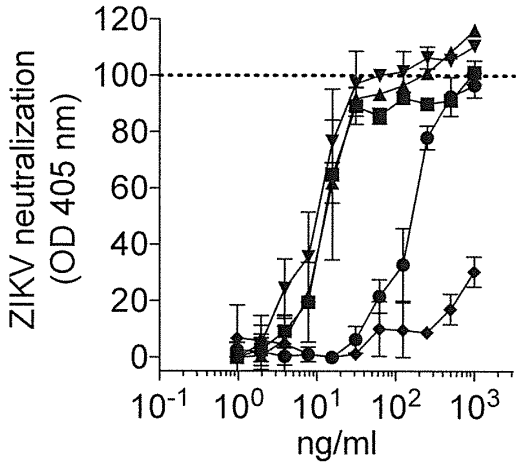


Figure 4



	EC50
ZKA64	150.7
ZKA190	12.9
ZKA185	12.85
ZKA230	8.999
ZKA78	4072

Figure 5

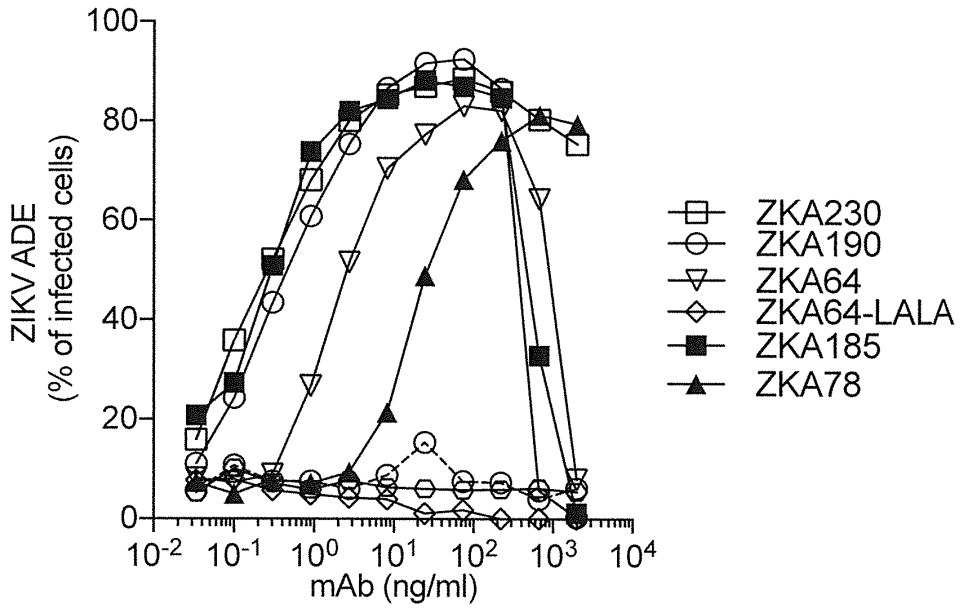

ZIKV ADE
(% of infected cells)
100
80
60
40
20
0
10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4}
mAb (ng/ml)
ZKA230
ZKA190
ZKA64
ZKA64-LALA
ZKA185
ZKA78

Figure 6

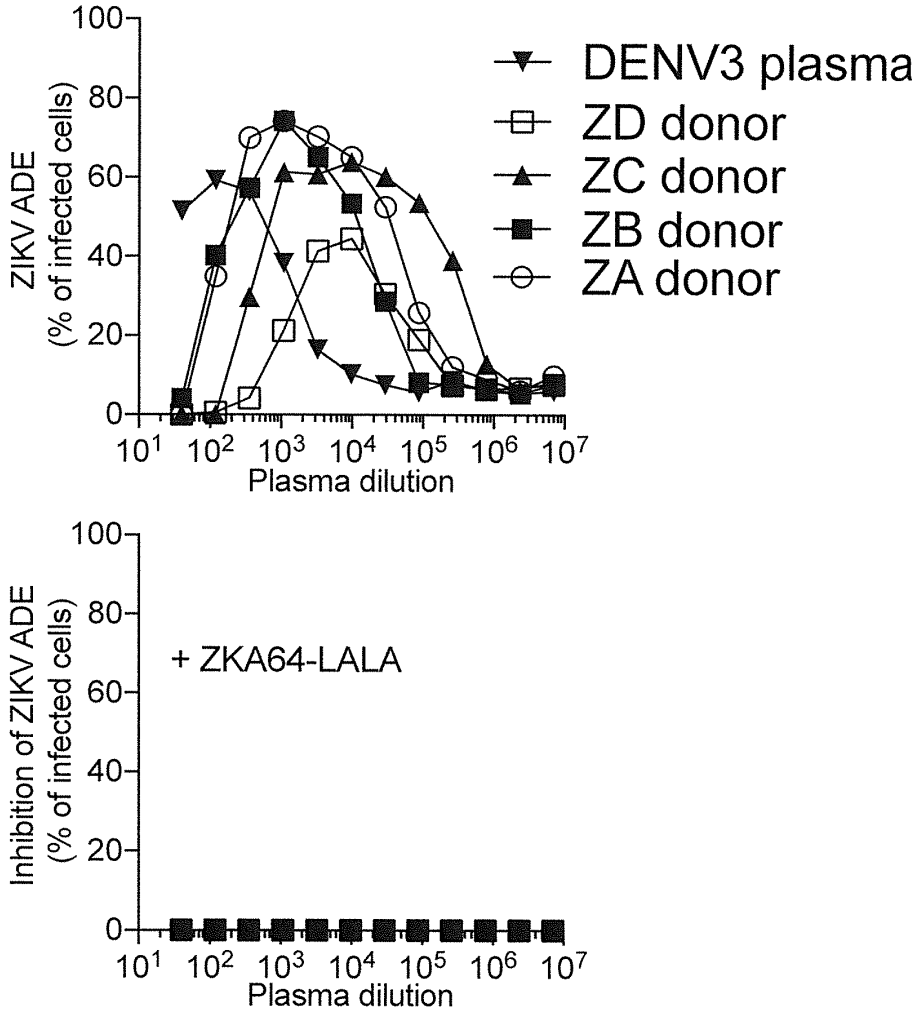

100
80
60
40
20
0
ZIKV ADE
(% of infected cells)
DENV3 plasma
ZD donor
ZC donor
ZB donor
ZA donor
10^1 10^2 10^3 10^4 10^5 10^6 10^7
Plasma dilution
100
80
60
40
20
0
Inhibition of ZIKV ADE
(% of infected cells)
+ ZKA64-LALA
10^1 10^2 10^3 10^4 10^5 10^6 10^7
Plasma dilution

Figure 7

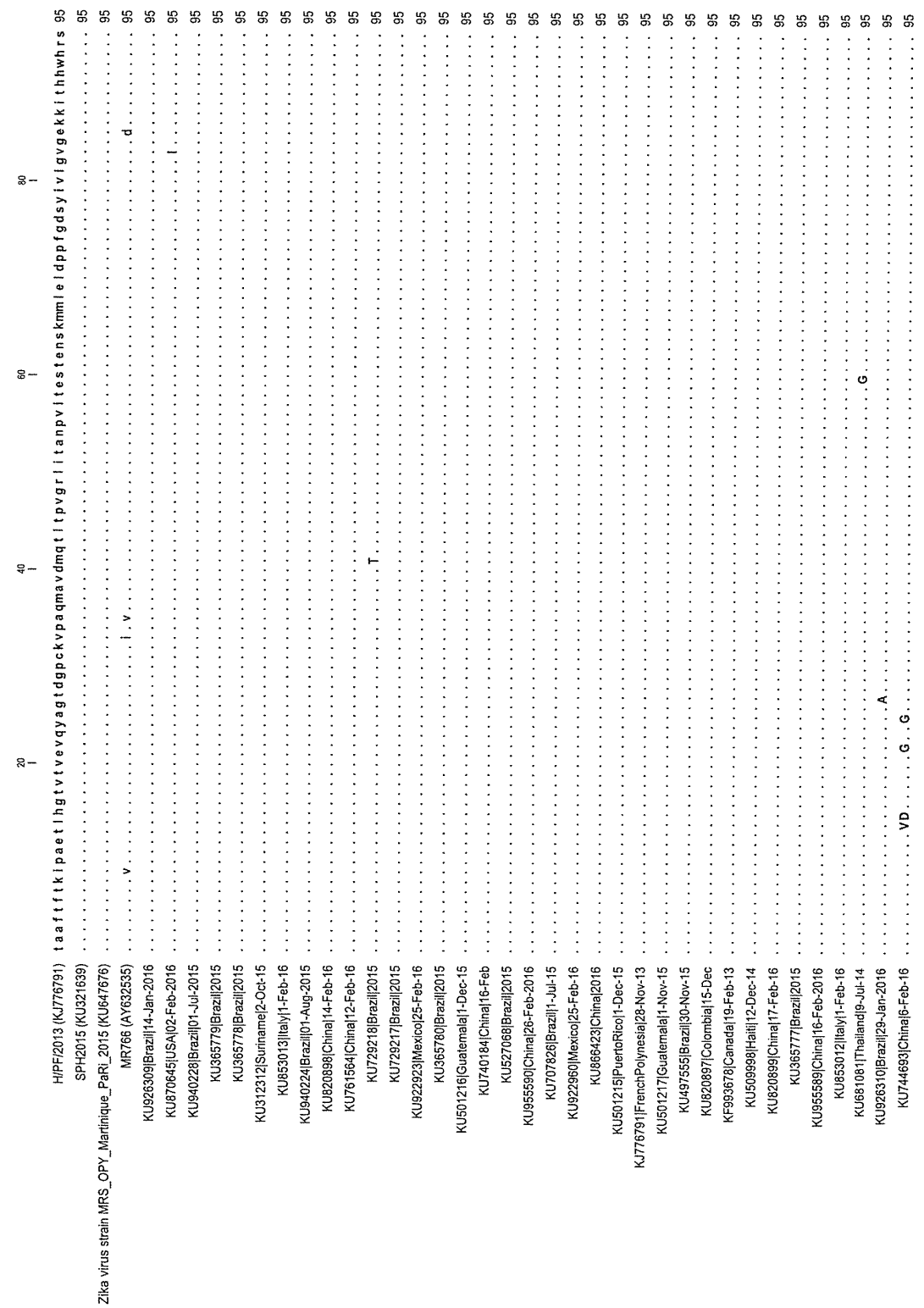

20
40
60
80
H/PF/2013 (KJ776791) t a a f t f t k i p a e t l h g t v t v e v q y a g t d g p c k v p a q m a v d m q t l t p v g r l i t a n p v i t e s t e n s k m m l e l d p p f g d s y i v i g v g e k k i t h h w h r s 95
SPH2015 (KU321639) 95
Zika virus strain MRS_OPY_Martinique_PaRi_2015 (KU647676) 95
MR766 (AY632535) 95
KU926309|Brazil|14-Jan-2016 95
KU870645|USA|02-Feb-2016 95
KU940228|Brazil|01-Jul-2015 95
KU365779|Brazil|2015 95
KU365778|Brazil|2015 95
KU312312|Suriname|2-Oct-15 95
KU853013|Italy|1-Feb-16 95
KU940224|Brazil|01-Aug-2015 95
KU820898|China|14-Feb-16 95
KU761564|China|12-Feb-16 95
KU729218|Brazil|2015 95
KU729217|Brazil|2015 95
KU922923|Mexico|25-Feb-16 95
KU365780|Brazil|2015 95
KU501216|Guatemala|1-Dec-15 95
KU740184|China|16-Feb 95
KU527068|Brazil|2015 95
KU955590|China|26-Feb-2016 95
KU707826|Brazil|1-Jul-15 95
KU922960|Mexico|25-Feb-16 95
KU866423|China|2016 95
KU501215|PuertoRico|1-Dec-15 95
KJ776791|FrenchPolynesia|28-Nov-13 95
KU501217|Guatemala|1-Nov-15 95
KU497555|Brazil|30-Nov-15 95
KU820897|Colombia|15-Dec 95
KF993678|Canada|19-Feb-13 95
KU509998|Haiti|12-Dec-14 95
KU820899|China|17-Feb-16 95
KU365777|Brazil|2015 95
KU955589|China|16-Feb-2016 95
KU853012|Italy|1-Feb-16 95
KU681081|Thailand|9-Jul-14 95
KU926310|Brazil|29-Jan-2016 95
KU744693|China|6-Feb-16 95

Figure 8

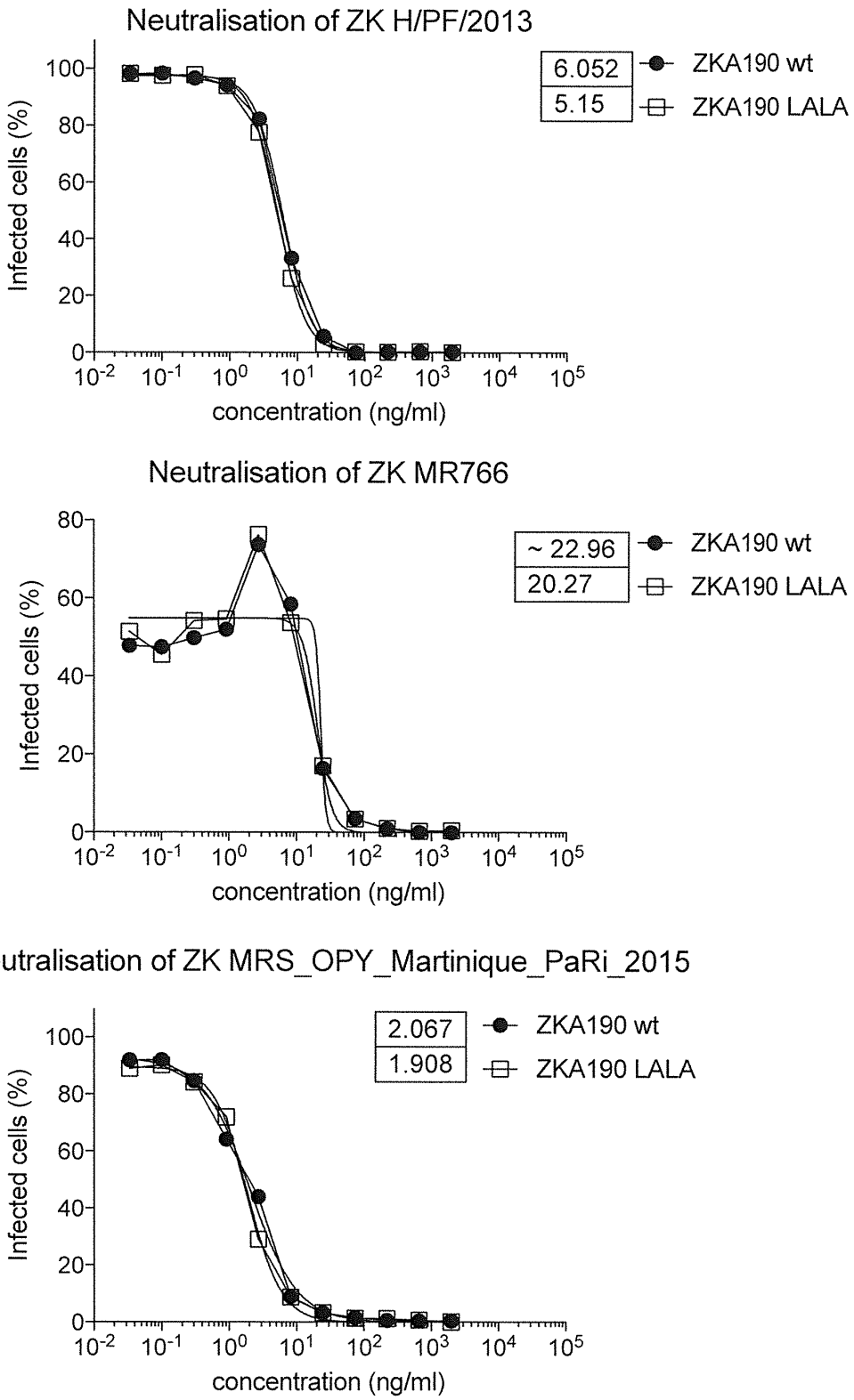
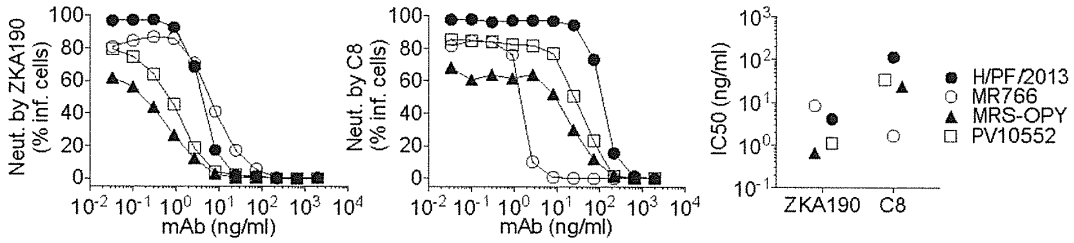

Neutralisation of ZK H/PF/2013
6.052
5.15
ZKA190 wt
ZKA190 LALA
Infected cells (%)
concentration (ng/ml)
Neutralisation of ZK MR766
~ 22.96
20.27
ZKA190 wt
ZKA190 LALA
Infected cells (%)
concentration (ng/ml)
Neutralisation of ZK MRS_OPY_Martinique_PaRi_2015
2.067
1.908
ZKA190 wt
ZKA190 LALA
Infected cells (%)
concentration (ng/ml)

Figure 9

A



B

	IC50 (ng/ml)	
ZIKV strain	ZKA190	C8
H/PF/2013	4,09	115,80
MR766	8,37	1,67
MRS-OPY	0,65	23,48
PV10552	1,09	34,60

C

	ZKA190	C8
Number of values	4	4
Minimum	0,6484	1,665
25% Percentile	0,7581	7,119
Median	2,586	29,04
75% Percentile	7,302	95,5
Maximum	8,374	115,8
Mean	3,549	43,89
Std. Deviation	3,561	49,86
Std. Error of Mean	1,781	24,93
Lower 95% CI of mean	-2,118	-35,45
Upper 95% CI of mean	9,215	123,2
Coefficient of variation	100,35%	113,60%
Geometric mean	2,216	19,89
Geometric SD factor	3,246	5,977
Sum	14,19	175,5

Figure 10

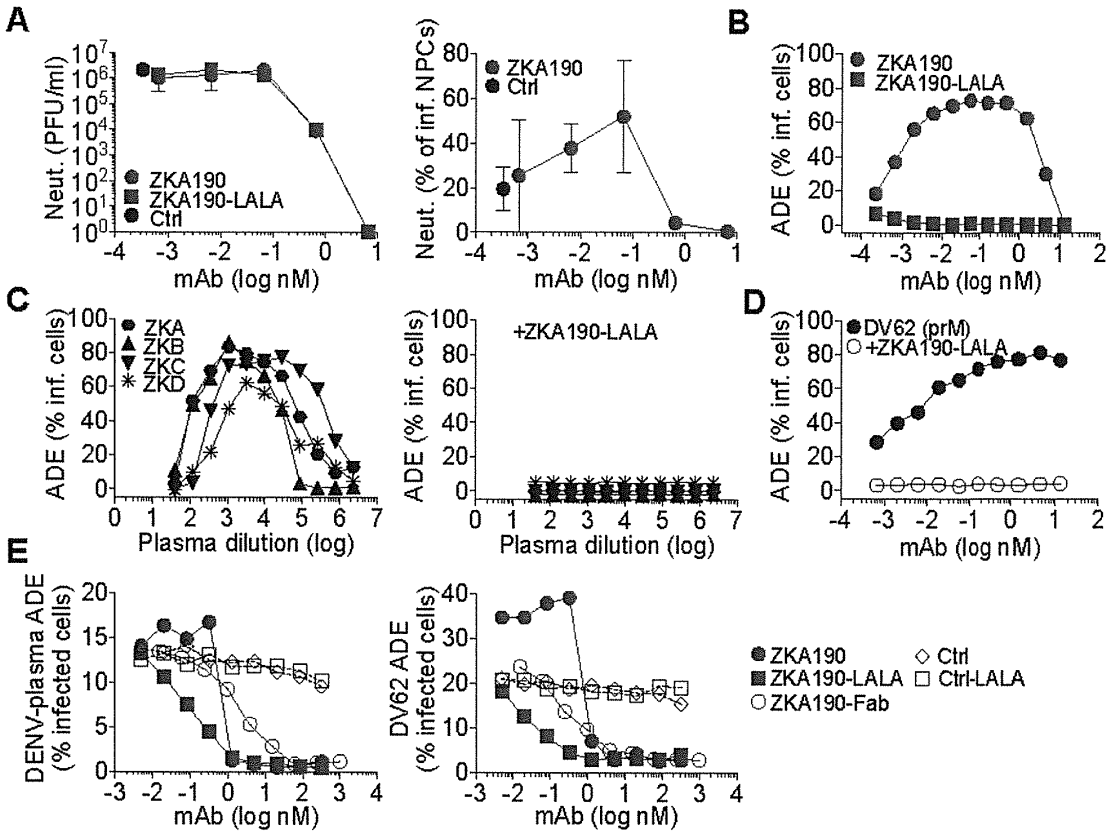

A
Neut. (PFU/ml)
ZKA190
ZKA190-LALA
Ctrl
mAb (log nM)
Neut. (% of inf. NPCs)
ZKA190
Ctrl
mAb (log nM)
B
ADE (% inf. cells)
ZKA190
ZKA190-LALA
mAb (log nM)
C
ADE (% inf. cells)
ZKA
ZKB
ZKC
ZKD
Plasma dilution (log)
+ZKA190-LALA
Plasma dilution (log)
D
ADE (% inf. cells)
DV62 (prM)
+ZKA190-LALA
mAb (log nM)
E
DENV-plasma ADE (% infected cells)
mAb (log nM)
DV62 ADE (% infected cells)
mAb (log nM)
ZKA190
ZKA190-LALA
ZKA190-Fab
Ctrl
Ctrl-LALA

Figure 11

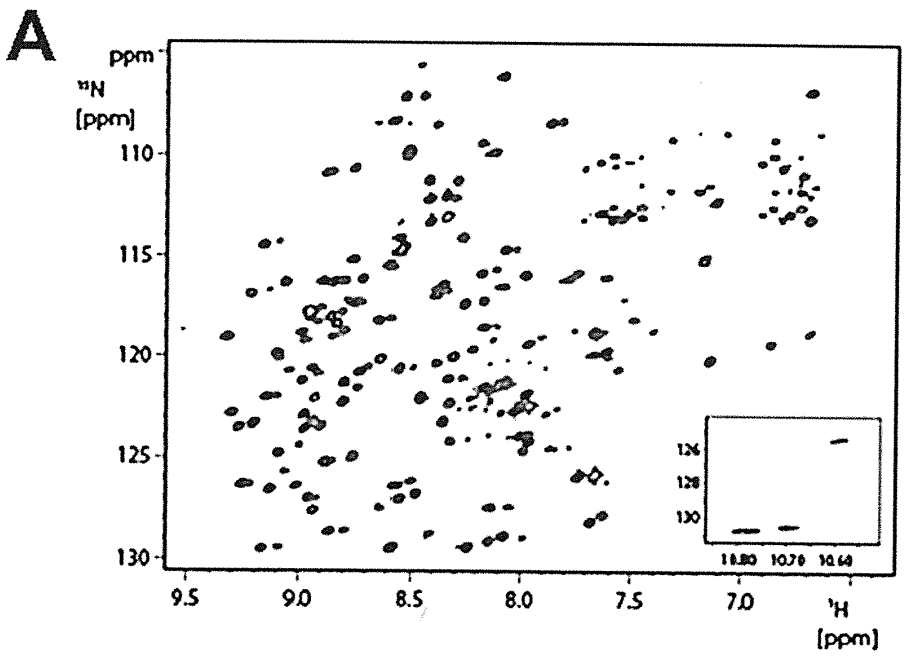


Figure 12

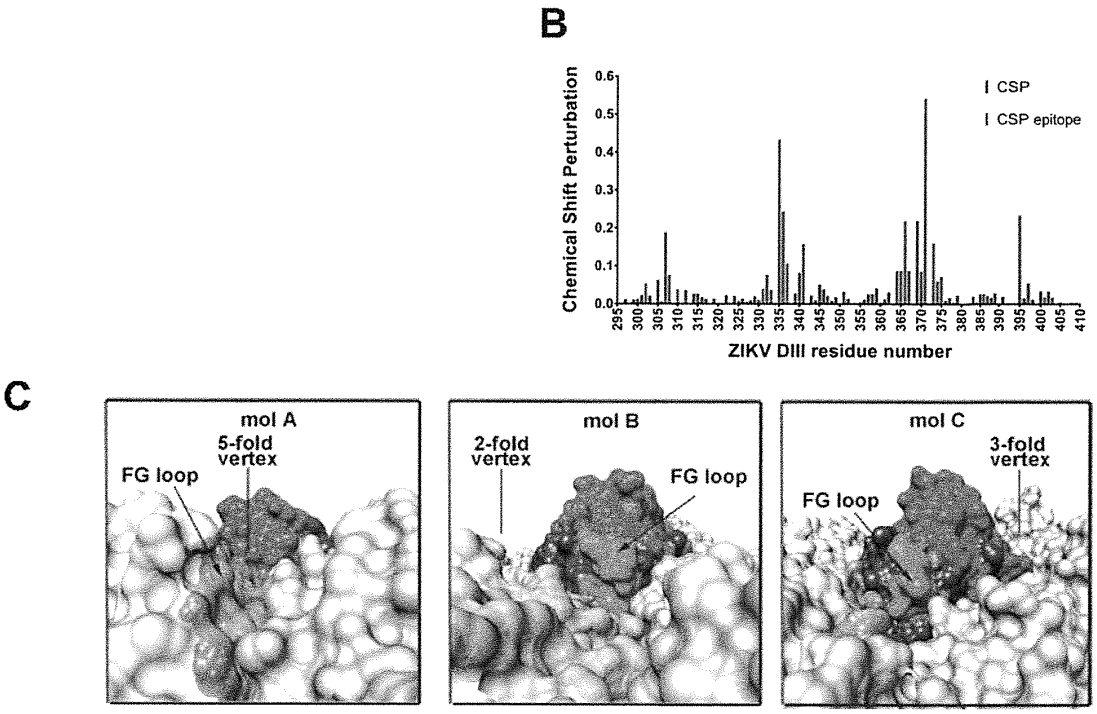


Figure 12 (continued)

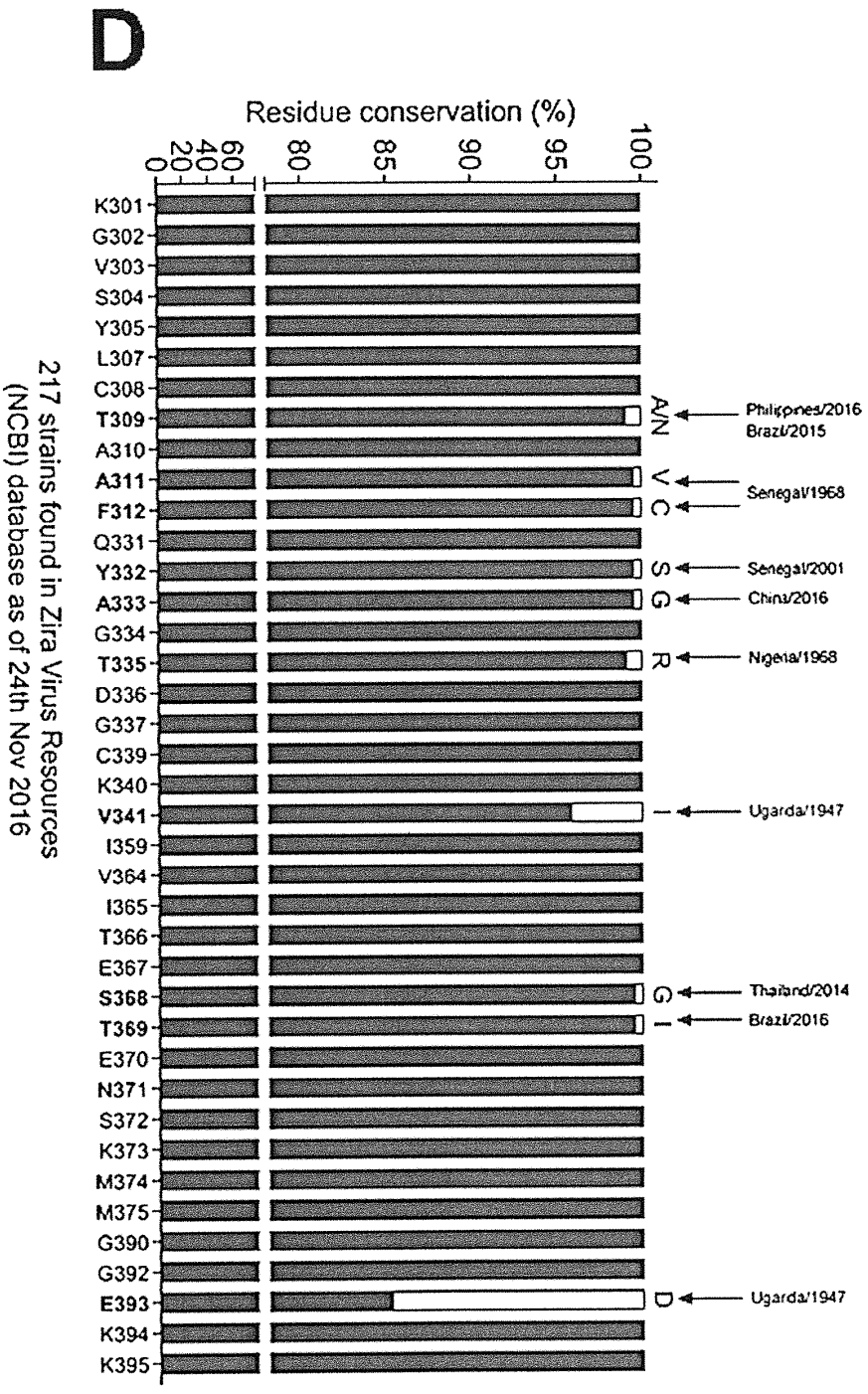


Figure 12 (continued)

E

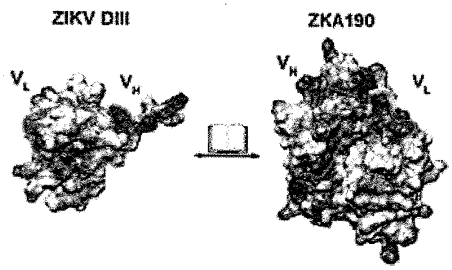


Figure 12 (continued)

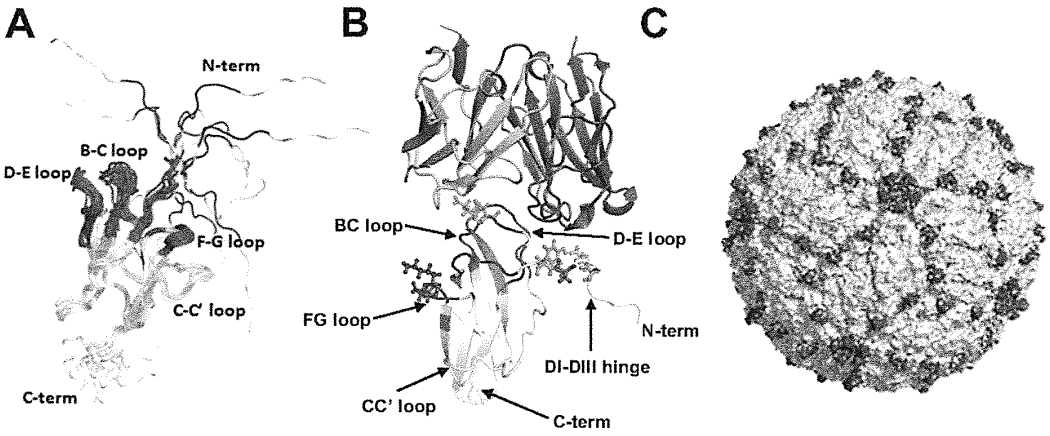
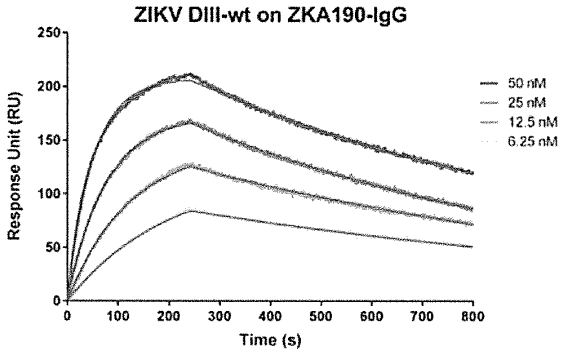
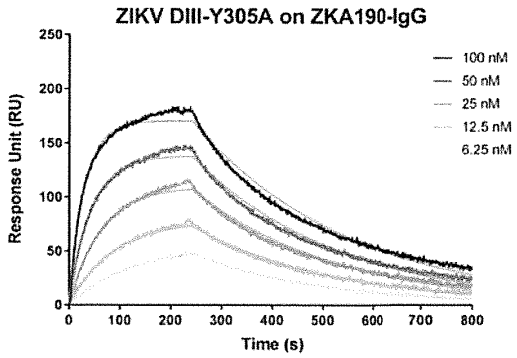
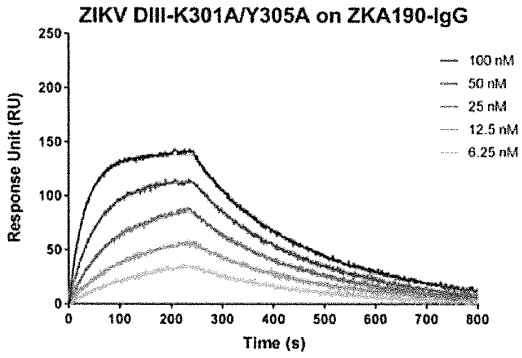
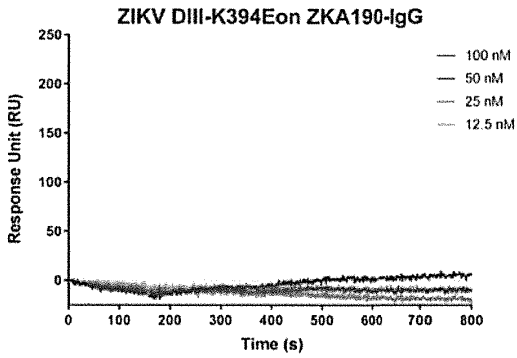

A
N-term
B-C loop
D-E loop
F-G loop
C-C' loop
C-term
B
BC loop
D-E loop
FG loop
N-term
DI-DIII hinge
CC' loop
C-term
C

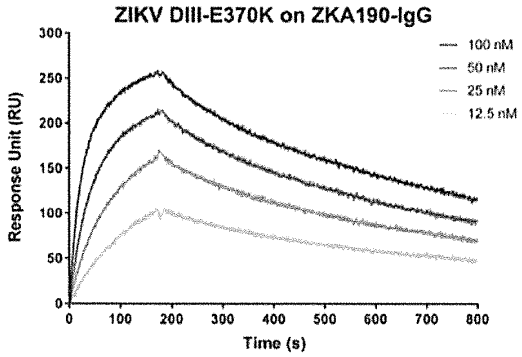
Figure 13











	k_a (1/Ms)	k_d (1/s)	K_D (M)
Wild-type	5,3E+05	1,0E-03	2,0E-09
K301A	4,4E+05	1,1E-03	2,5E-09
K301E	5,8E+05	1,5E-03	2,6E-09
V303F	5,1E+05	5,9E-04	1,1E-09
V303L	4,4E+05	1,2E-03	2,8E-09
K301A/Y305A	3,0E+05	4,6E-03	1,5E-08
S304F	5,4E+05	1,5E-03	2,7E-09
Y305A	5,6E+05	3,7E-03	6,6E-09
E393A	5,7E+05	1,2E-03	2,1E-09
E393K	5,9E+05	1,2E-03	2,1E-09
E393A/K394A	4,8E+05	7,0E-04	1,5E-09
K394A	3,3E+05	1,3E-03	4,0E-09
T335R		No binding	
E370K	5,6E+05	1,3E-03	2,5E-09

Figure 14

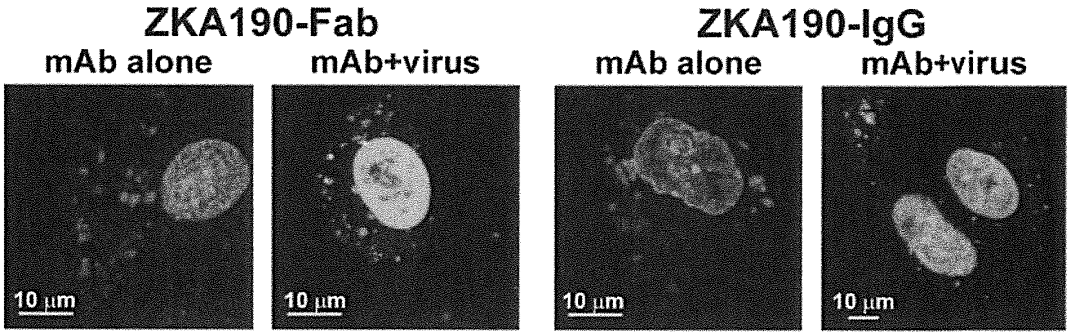

ZKA190-Fab
mAb alone
mAb+virus
ZKA190-IgG
mAb alone
mAb+virus
10 µm
10 µm
10 µm
10 µm

Figure 15

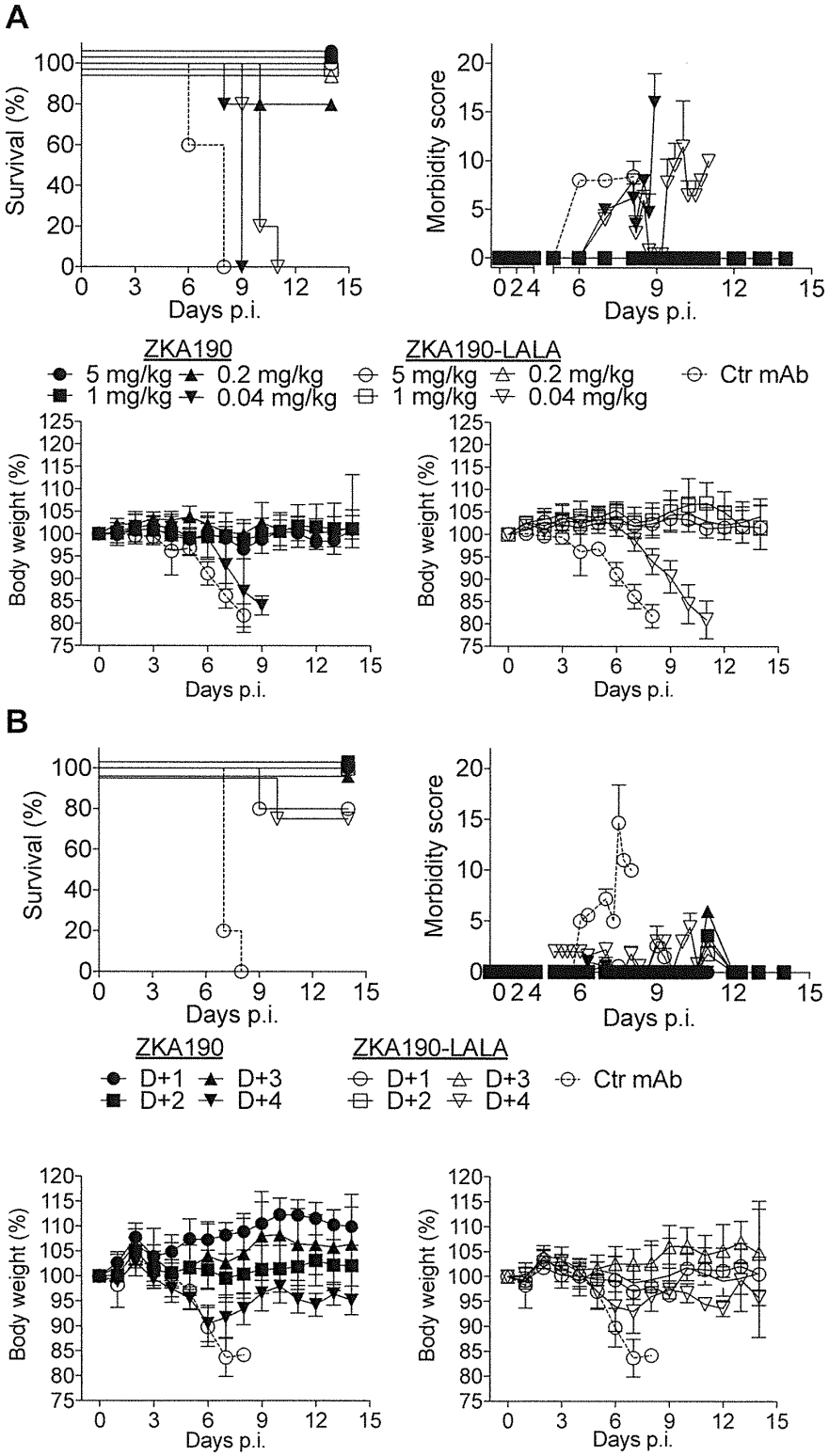

A
Survival (%)
Days p.i.
Morbidity score
Days p.i.
ZKA190
5 mg/kg
0.2 mg/kg
1 mg/kg
0.04 mg/kg
ZKA190-LALA
5 mg/kg
0.2 mg/kg
1 mg/kg
0.04 mg/kg
Ctr mAb
Body weight (%)
Days p.i.
Body weight (%)
Days p.i.
B
Survival (%)
Days p.i.
Morbidity score
Days p.i.
ZKA190
D+1
D+3
D+2
D+4
ZKA190-LALA
D+1
D+3
D+2
D+4
Ctr mAb
Body weight (%)
Days p.i.
Body weight (%)
Days p.i.

Figure 16

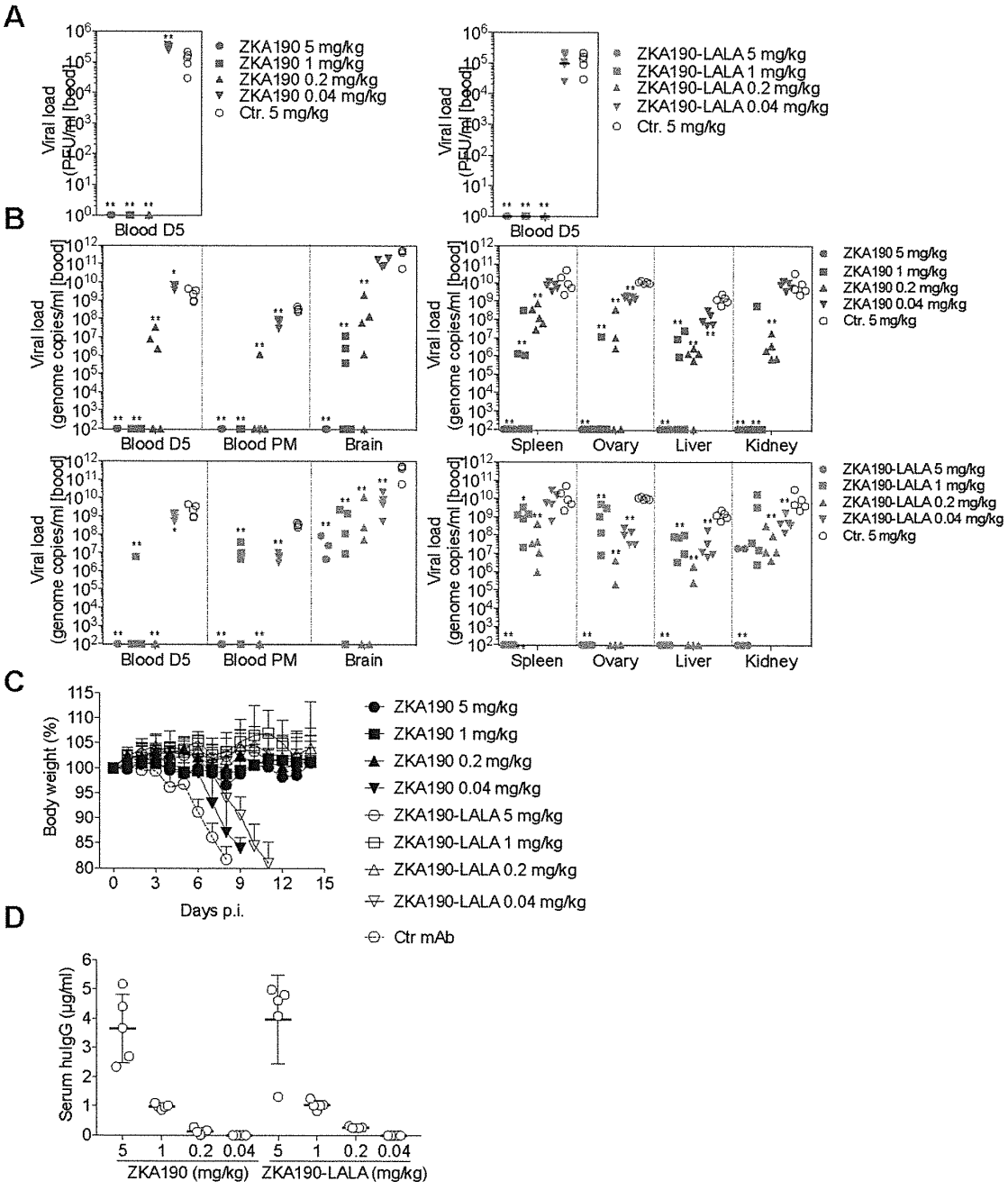

A
Viral load (PFU/ml [blood])
ZKA190 5 mg/kg
ZKA190 1 mg/kg
ZKA190 0.2 mg/kg
ZKA190 0.04 mg/kg
Ctr. 5 mg/kg
Blood D5
ZKA190-LALA 5 mg/kg
ZKA190-LALA 1 mg/kg
ZKA190-LALA 0.2 mg/kg
ZKA190-LALA 0.04 mg/kg
B
Viral load (genome copies/ml [blood])
Blood D5
Blood PM
Brain
Spleen
Ovary
Liver
Kidney
C
Body weight (%)
Days p.i.
Ctr mAb
D
Serum huIgG (µg/ml)
ZKA190 (mg/kg)
ZKA190-LALA (mg/kg)

Figure 17

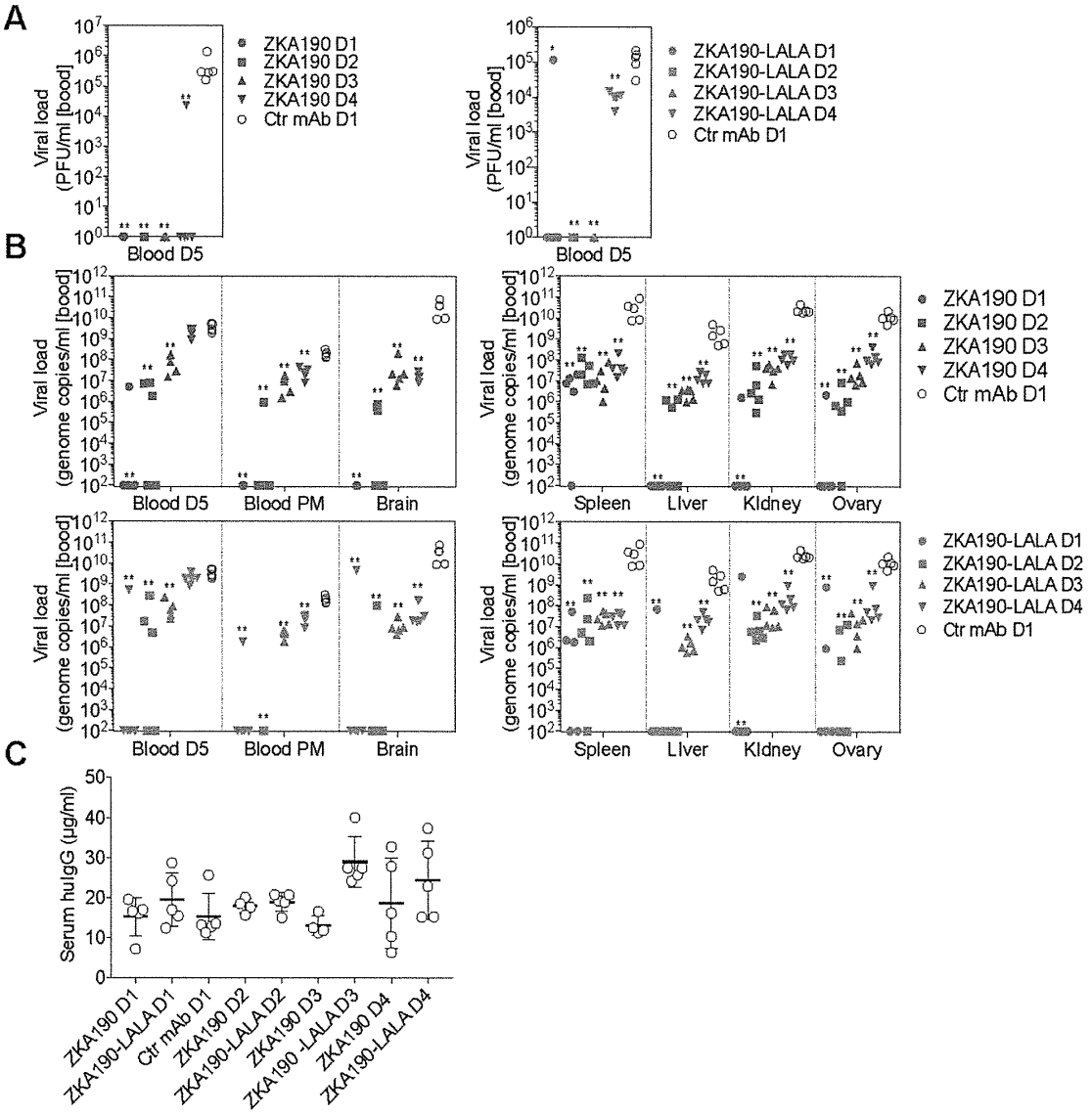

A
Viral load (PFU/ml [bood])
Blood D5
ZKA190 D1
ZKA190 D2
ZKA190 D3
ZKA190 D4
Ctr mAb D1
ZKA190-LALA D1
ZKA190-LALA D2
ZKA190-LALA D3
ZKA190-LALA D4
B
Viral load (genome copies/ml [bood])
Blood D5
Blood PM
Brain
Spleen
Liver
Kidney
Ovary
C
Serum huIgG (µg/ml)
ZKA190 D1
ZKA190-LALA D1
Ctr mAb D1
ZKA190 D2
ZKA190-LALA D2
ZKA190 D3
ZKA190 -LALA D3
ZKA190 D4
ZKA190-LALA D4

Figure 18

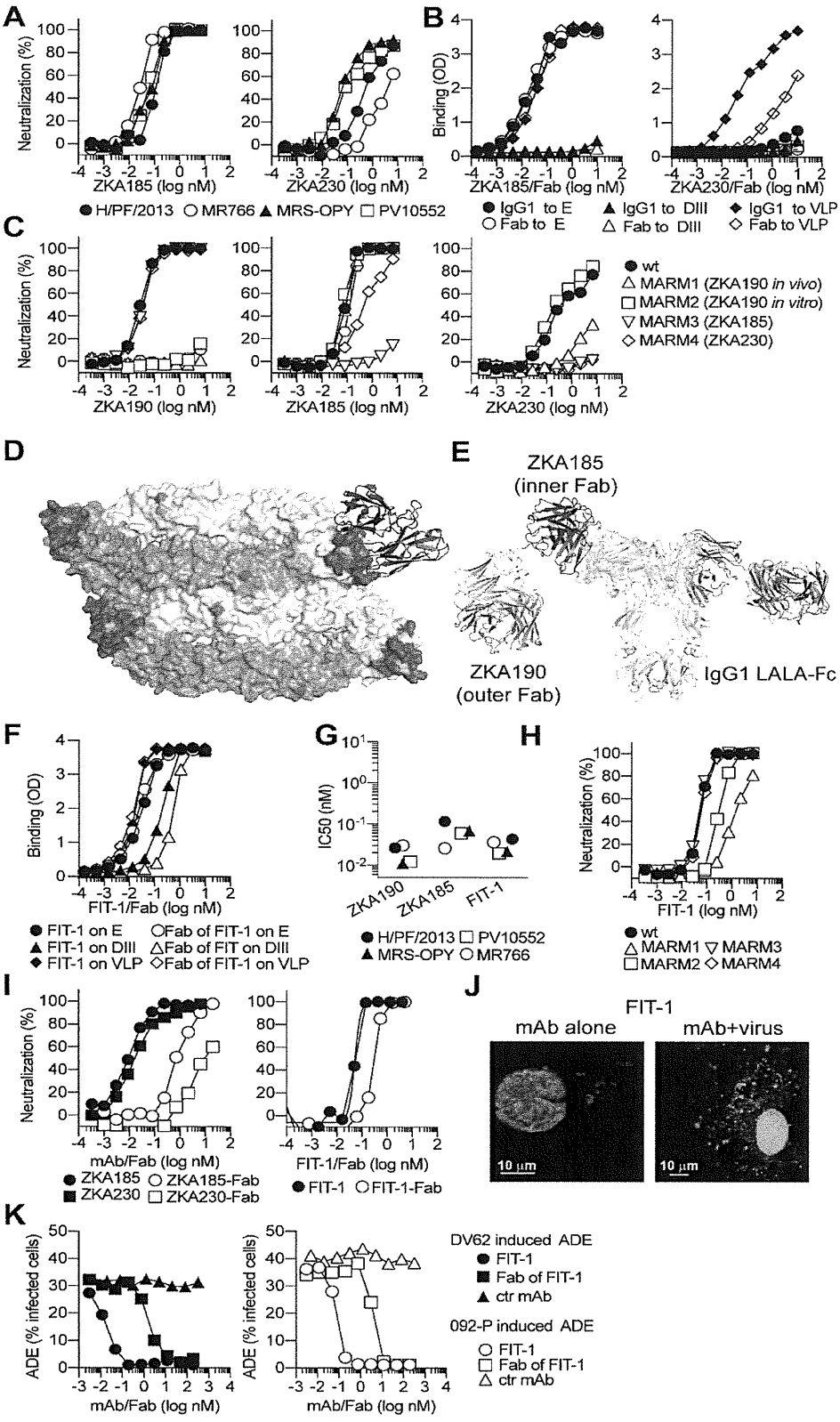

A
Neutralization (%)
ZKA185 (log nM)
ZKA230 (log nM)
H/PF/2013 MR766 MRS-OPY PV10552
B
Binding (OD)
ZKA185/Fab (log nM)
ZKA230/Fab (log nM)
IgG1 to E
Fab to E
IgG1 to DIII
Fab to DIII
IgG1 to VLP
Fab to VLP
C
Neutralization (%)
ZKA190 (log nM)
ZKA185 (log nM)
ZKA230 (log nM)
wt
MARM1 (ZKA190 in vivo)
MARM2 (ZKA190 in vitro)
MARM3 (ZKA185)
MARM4 (ZKA230)
D
E
ZKA185
(inner Fab)
ZKA190
(outer Fab)
IgG1 LALA-Fc
F
Binding (OD)
FIT-1/Fab (log nM)
FIT-1 on E
Fab of FIT-1 on E
FIT-1 on DIII
Fab of FIT on DIII
FIT-1 on VLP
Fab of FIT-1 on VLP
G
IC50 (nM)
ZKA190
ZKA185
FIT-1
H/PF/2013 PV10552
MRS-OPY MR766
H
Neutralization (%)
FIT-1 (log nM)
wt
MARM1 MARM3
MARM2 MARM4
I
Neutralization (%)
mAb/Fab (log nM)
ZKA185 ZKA185-Fab
ZKA230 ZKA230-Fab
FIT-1/Fab (log nM)
FIT-1 FIT-1-Fab
J
FIT-1
mAb alone
mAb+virus
10 µm
10 µm
K
ADE (% infected cells)
mAb/Fab (log nM)
DV62 induced ADE
FIT-1
Fab of FIT-1
ctr mAb
092-P induced ADE
FIT-1
Fab of FIT-1
ctr mAb

Figure 19

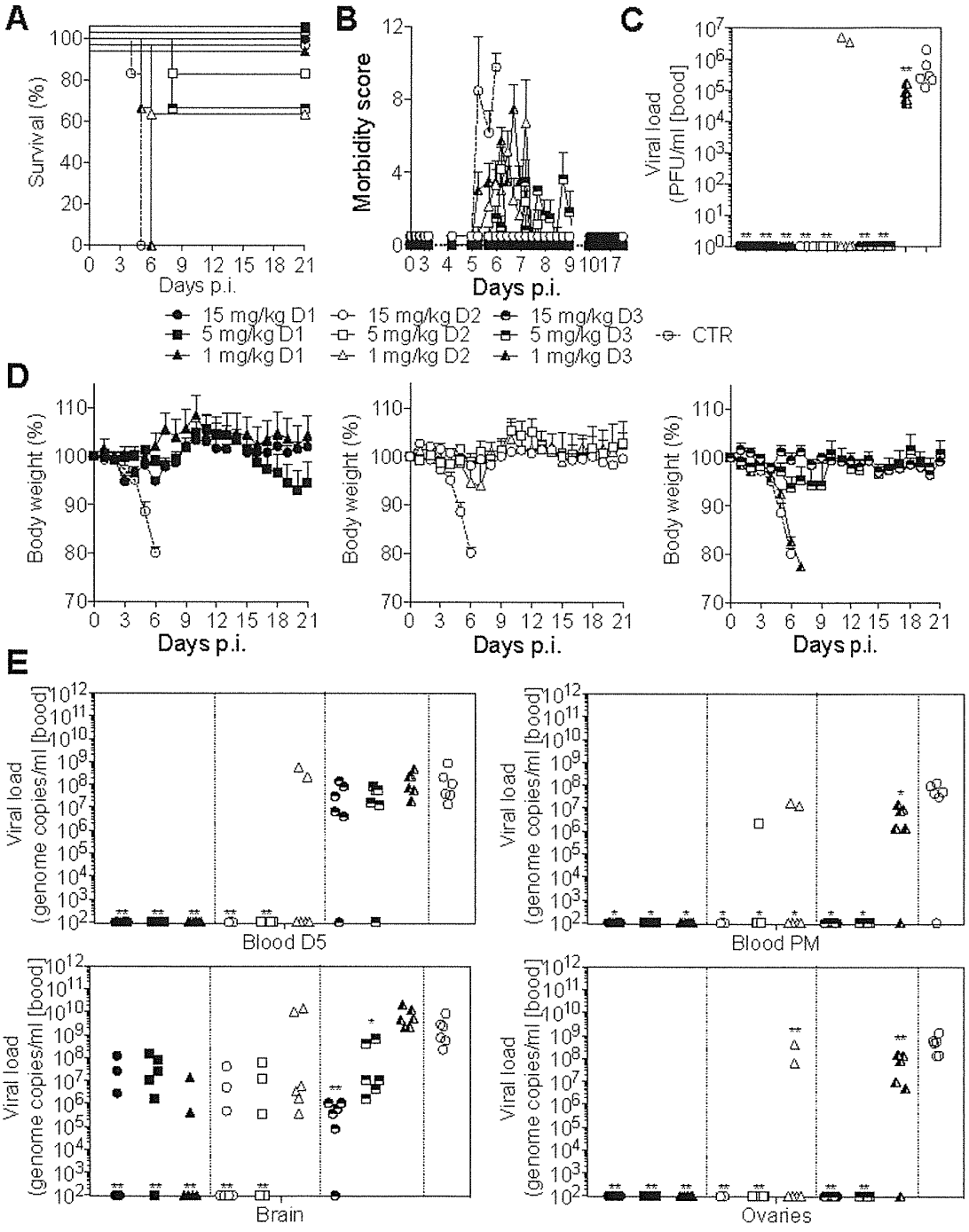

A
Survival (%)
Days p.i.
B
Morbidity score
Days p.i.
C
Viral load (PFU/ml [blood])
15 mg/kg D1
5 mg/kg D1
1 mg/kg D1
15 mg/kg D2
5 mg/kg D2
1 mg/kg D2
15 mg/kg D3
5 mg/kg D3
1 mg/kg D3
CTR
D
Body weight (%)
Days p.i.
E
Viral load (genome copies/ml [blood])
Blood D5
Blood PM
Brain
Ovaries

Figure 20

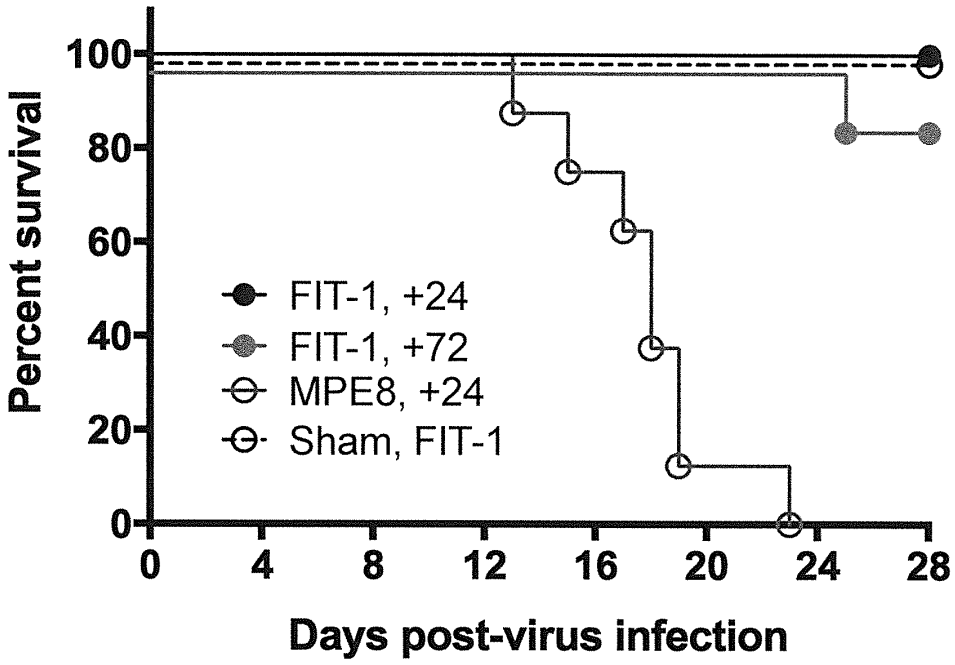

Percent survival
100
80
60
40
20
0
0
4
8
12
16
20
24
28
Days post-virus infection
FIT-1, +24
FIT-1, +72
MPE8, +24
Sham, FIT-1

Figure 21

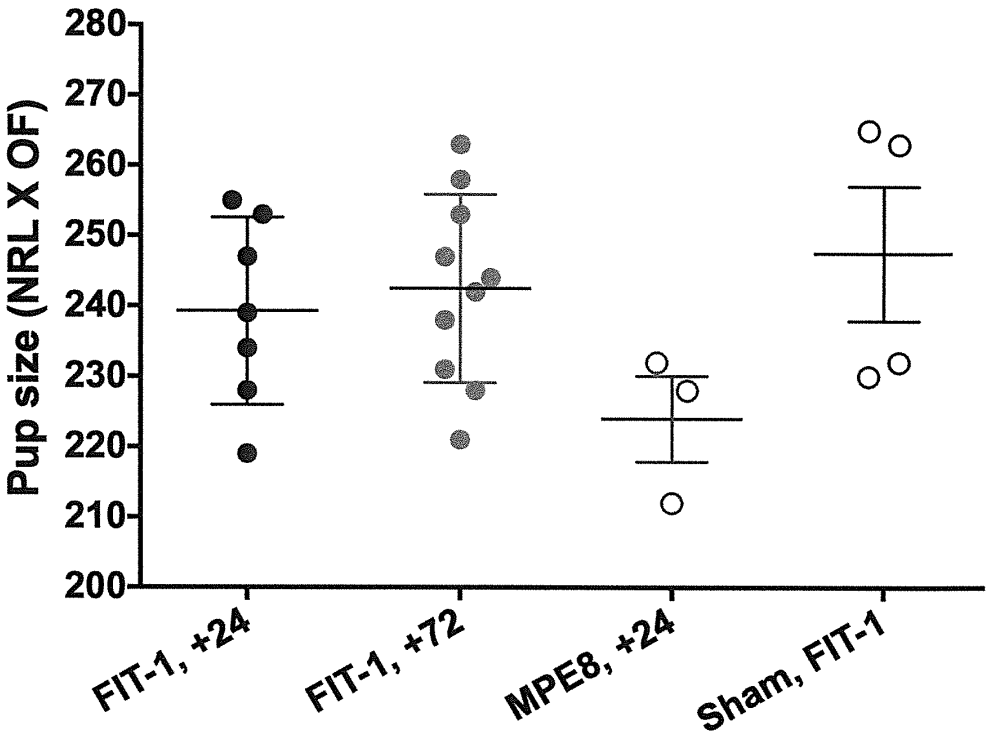

Pup size (NRL X OF)
280
270
260
250
240
230
220
210
200
FIT-1, +24
FIT-1, +72
MPE8, +24
Sham, FIT-1

Figure 22

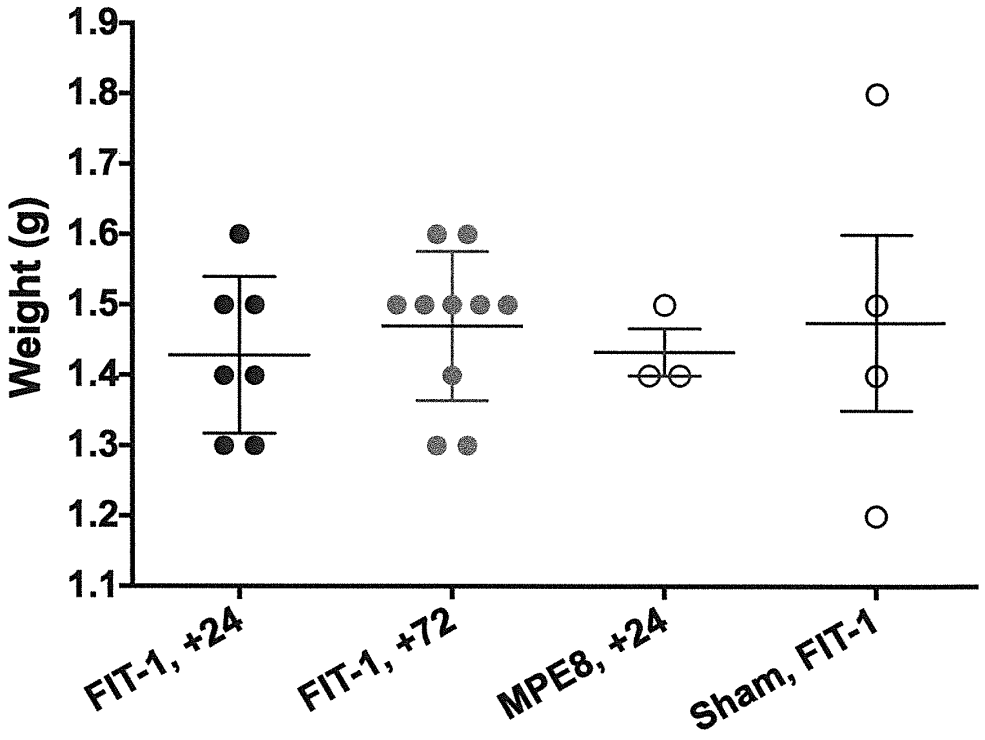

Weight (g)
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
FIT-1, +24
FIT-1, +72
MPE8, +24
Sham, FIT-1

Figure 23

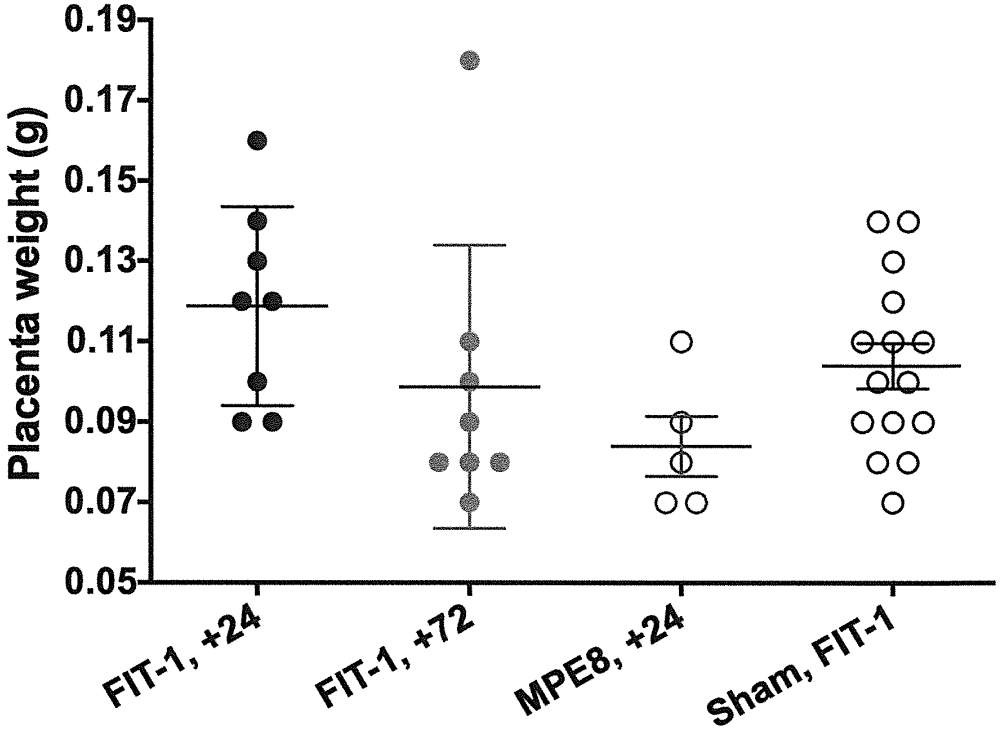

Placenta weight (g)
0.19
0.17
0.15
0.13
0.11
0.09
0.07
0.05
FIT-1, +24
FIT-1, +72
MPE8, +24
Sham, FIT-1

Figure 24

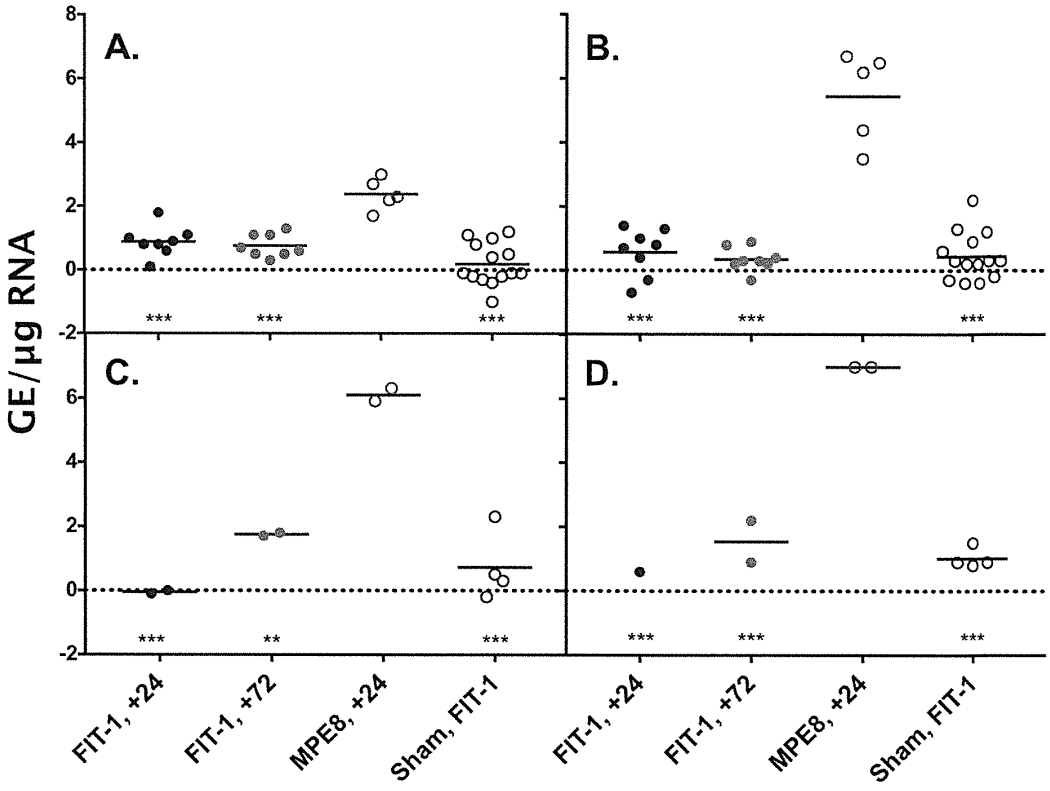


Figure 25

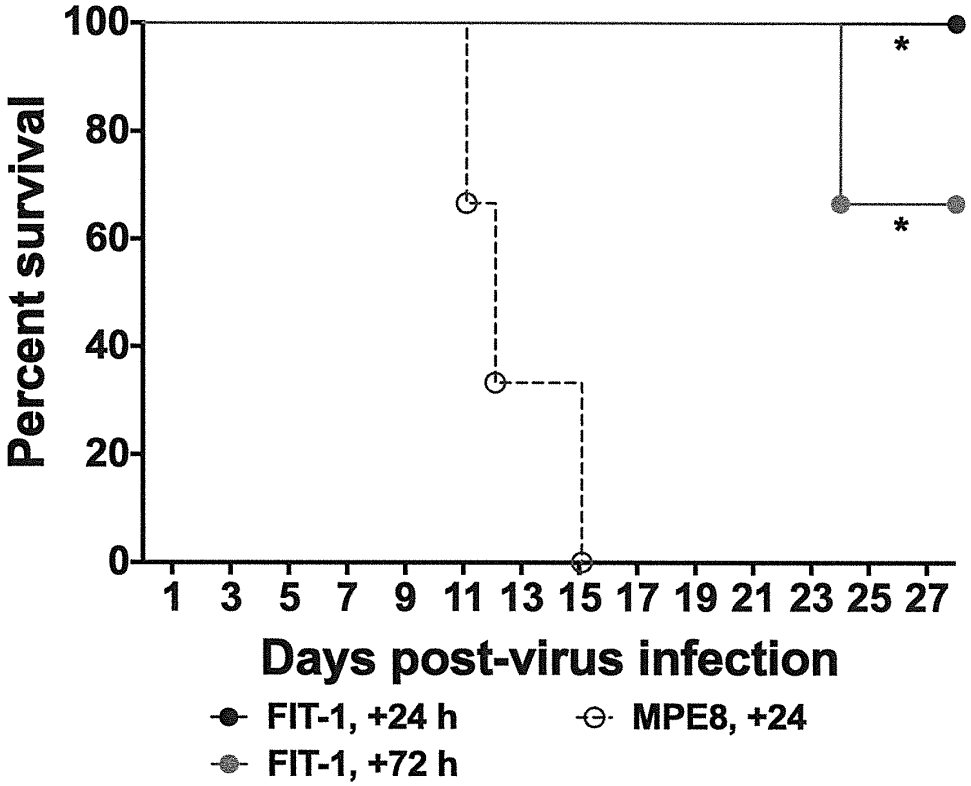

100
80
60
40
20
0
Percent survival
1 3 5 7 9 11 13 15 17 19 21 23 25 27
Days post-virus infection
FIT-1, +24 h
MPE8, +24
FIT-1, +72 h
*
*

Figure 26

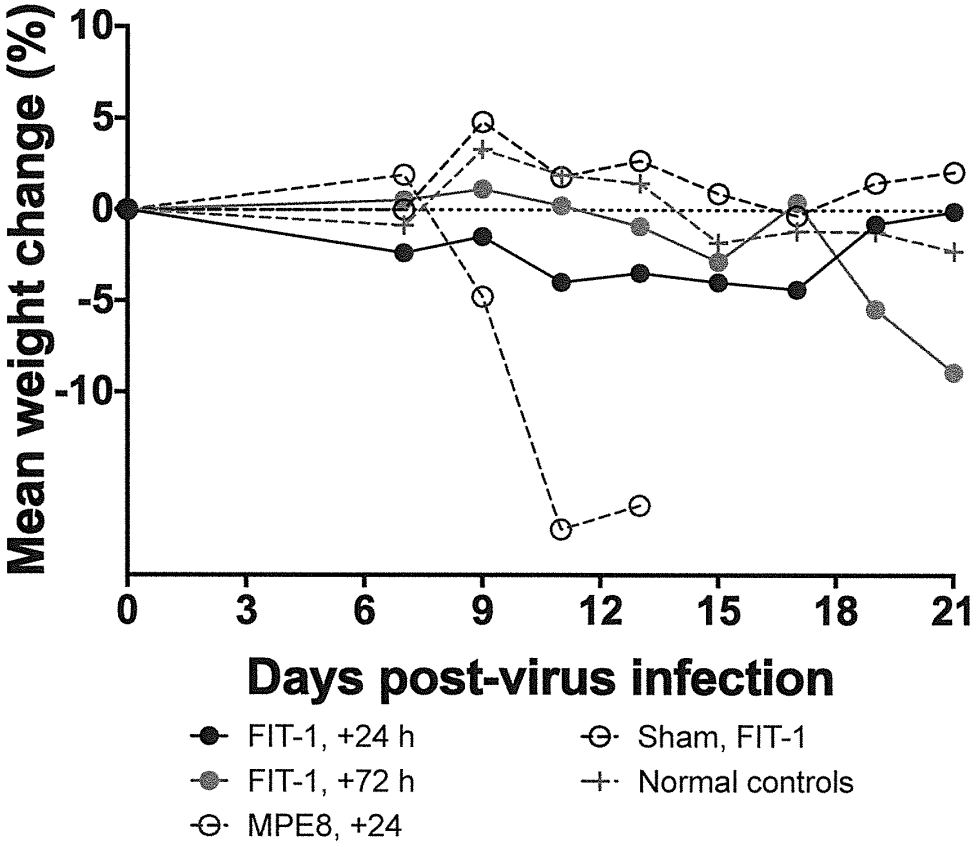

Mean weight change (%)
10
5
0
-5
-10
0
3
6
9
12
15
18
21
Days post-virus infection
FIT-1, +24 h
FIT-1, +72 h
MPE8, +24
Sham, FIT-1
Normal controls

Figure 27

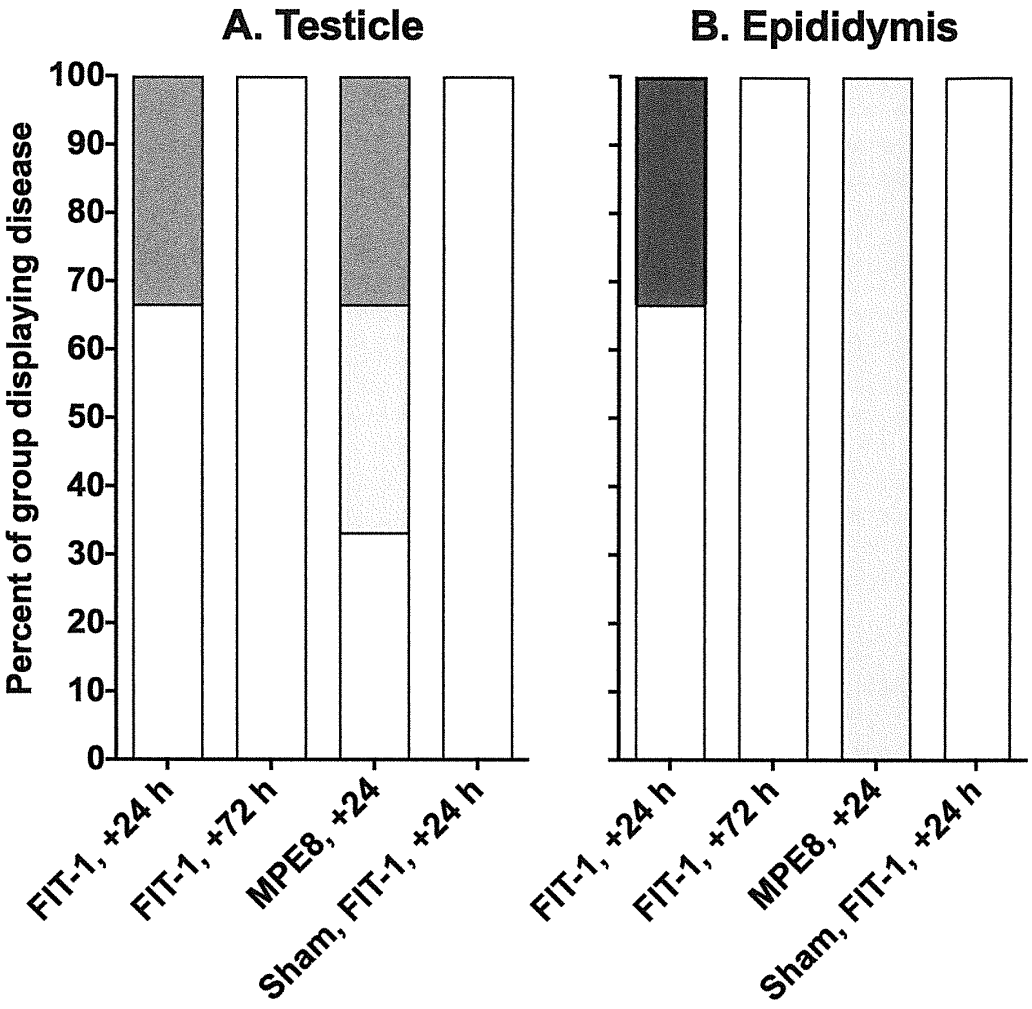

A. Testicle
B. Epididymis
Percent of group displaying disease
100
90
80
70
60
50
40
30
20
10
0
FIT-1, +24 h
FIT-1, +72 h
MPE8, +24
Sham, FIT-1, +24 h
FIT-1, +24 h
FIT-1, +72 h
MPE8, +24
Sham, FIT-1, +24 h

Figure 28

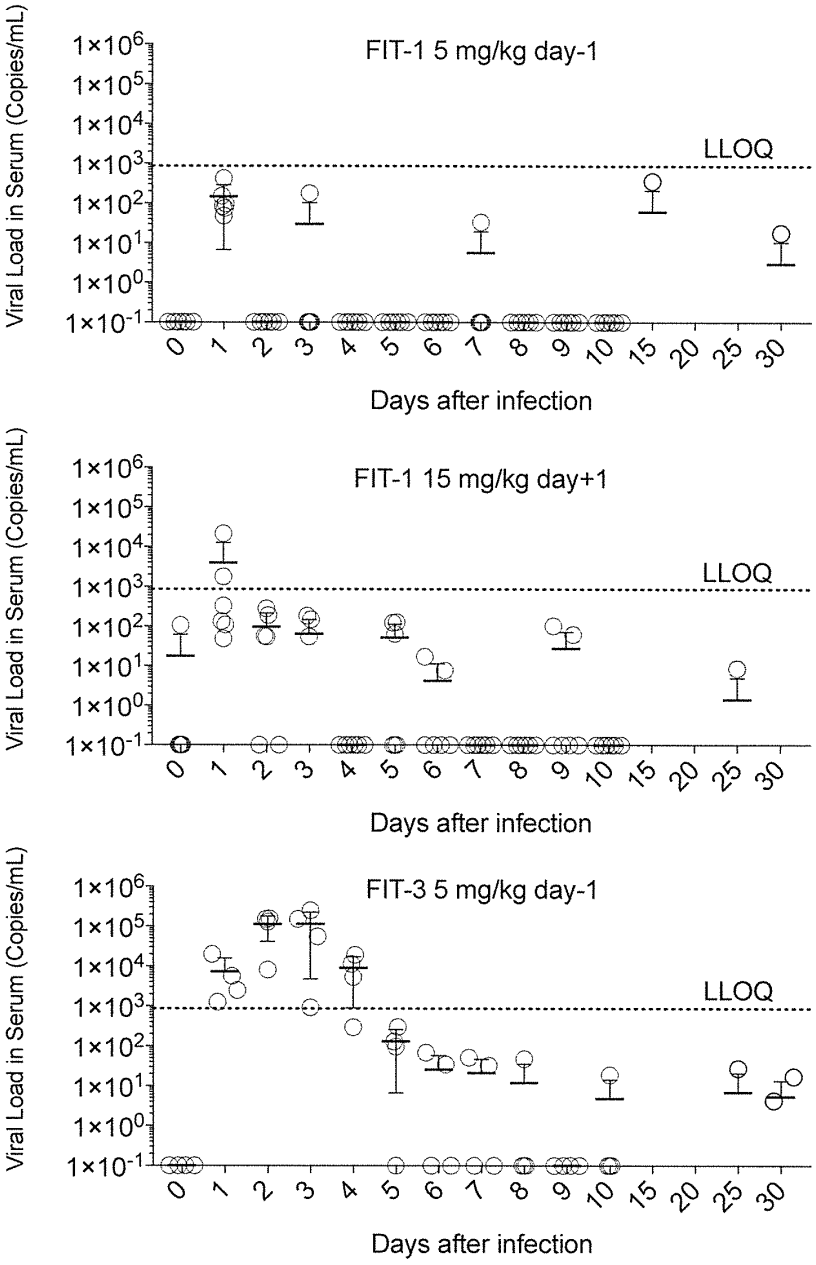

FIT-1 5 mg/kg day-1
Viral Load in Serum (Copies/mL)
1×10^6
1×10^5
1×10^4
1×10^3
1×10^2
1×10^1
1×10^0
1×10^-1
LLOQ
0 1 2 3 4 5 6 7 8 9 10 15 20 25 30
Days after infection
FIT-1 15 mg/kg day+1
Viral Load in Serum (Copies/mL)
LLOQ
Days after infection
FIT-3 5 mg/kg day-1
Viral Load in Serum (Copies/mL)
LLOQ
Days after infection

Figure 29