

Supplementary Information

T cell immunity to Zika virus targets immunodominant epitopes that show cross-reactivity with other Flaviviruses

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Supplementary Table 1. ZIKV protein sequences: Env, NS1, NS3, and NS5

ZIKV protein	AA sequence				
Env	IRCIGVSNRD	FVEGMSGGTW	VDVVLEHGGC	VTVMAQDKPT	
	VDIELVTTTV	SNMAEVRSYC	YEASISDMAS	DSRCPTQGEA	
	YLDKQSDTQY	VCKRTLVDRG	WGNGCGLFGK	GSLVTCAKFA	
	CSKKMTGKSI	QPENLEYRIM	LSVHGSQHSG	MIVNDTGHET	
	DENRAKVEIT	PNSPRAEATL	GGFGSLGLDC	EPRTGLDFSD	
	LYYLTMNNKH	WLVHKEWFHD	IPLPWHAGAD	TGTPHWNNE	
	ALVEFKDAHA	KRQTVVVLGS	QEGAVHTALA	GALEAEMDGA	
	KGRLSSGHLK	CRLKMDKLRL	KGVSYSLCTA	AFTFTKIPAE	
	TLHGTVTVEV	QYAGTDGPCK	VPAQMAVDMQ	TLTPVGRLLIT	
	ANPVITESTE	NSKMMELEDP	PFGDSYIVIG	VGEKKITHHW	
	HRSGSTIGKA	FEATVRGAKR	MAVLGDTAWD	FGSVGGALNS	
	LKGKIHQIFG	AAFKSLFGGM	SWFSQILIGT	LLMWLGLNTK	
	NGSISLMCLA	LGGVLIFLST	AVSA		
	NS1	DVGCSVDFSK	KETRCGTGVF	VYNDVEAWRD	RYKYHPDSPR
		RLAAAVKQAW	EDGICGISSV	SRMENIMWRS	VEGELNAILE
		ENGVQLTVVV	GSVKNPMWRG	PQRLPVPVNE	LPHGWKAWGK
		SYFVRAAKTN	NSFVVDGDTL	KECPLKHRAW	NSFLVEDHGF
GVFHTSVWLK		VREDYSLECD	PAVIGTAVKG	KEAVHSDLGY	
WIESEKNDTW		RLKRAHLIEM	KTCEWPKSHT	LWTDGIEESD	
LIIPKSLAGP		LSHHNTREGY	RTQMKGPPWS	EELEIRFEEC	
PGTKVHVEET		CGTRGPSLRS	TTASGRVIEE	WCCRECTMPP	
LSFRAKDGCW		YGMEIRPRKE	PESNLVRSMV	TA	
NS3		SGALWDVPAP	KEVKKGETTD	GVYRVMTRRL	LGSTQVGVGV
		MQEGVFHTMW	HVTKGSALRS	GEGRLDPYWG	DVKQDLVSYC
	GPWKLDAAWD	GHSEVQLLAV	PPGERARNIQ	TLPGIFKTKD	
	GDIGAVALDY	PAGTSGSPIL	DKCGRVIGLY	GNGVVIKNGS	
	YVSAITQGRR	EEETPVECFE	PSMLKKKQLT	VLDLHPGAGK	
	TRRVLPEIVR	EAIKTRLRTV	ILAPTRVVAA	EMEEALRGLP	
	VRYMTTAVNV	THSGTEIVDL	MCHATFTSRL	LQPIRVPNYN	
	LYIMDEAHFT	DPSSIAARGY	ISTRVEMGEA	AAIFMTATPP	
	GTRDAFPDSN	SPIMDTEVEV	PERAWSSGFD	WVTDHSGKTV	
	WVFPVSRNGN	EIAACLTKAG	KRVIQLSRKT	FETEFQKTKH	
	QEWDFVVTDD	ISEMGANFKA	DRVIDSRRL	KPVILDGERV	
	ILAGPMPVTH	ASAAQRRGRI	GRNPNKPGDE	YLYGGCAET	
	DEDHAHWLEA	RMLLDNIYLQ	DGLIASLYRP	EADKVA AIEG	
	EFKLRTEQRK	TFVELMKRGD	LPVWLAYQVA	SAGITYTDRR	
	WCFDGTNNNT	IMEDSVPAEV	WTRHGEKRVL	KPRWMDARVC	

SDHAALKSFK EFAAGKR

NS5

GGGTGETLGE KWKARLNQMS ALEFYSSYKKS GITEVCREEA
RRALKDGVAT GGHAVSRGSA KLRWLVERGY LQPYGKVIDL
GCGRGGWSYY AATIRKVQEV KGYTKGGPGH EEPVLVQSYG
WNIVRLKSGV DVFHMAAEPD DTLLCDIGES SSSPEVEEAR
TLRVLSMVGD WLEKRPGAFC IKVLCPYTST MMETLERLQR
RYGGGLVRVP LSRNSTHEMY WVSGAKSNTI KSVSTTSQLL
LGRMDGPRRP VKYEEDVNLG SGTRAVVSCA EAPNMKIIGN
RIERIRSEHA ETWFFDENHP YRTWAYHGSY EAPTQGSASS
LINGVVRLLS KPWDVVTGVT GIAMTDTPY GOQRVFKKVV
DTRVPDPQEG TRQVMSMVSS WLWKELGKHK RPRVCTKEEF
INKVRSNAAL GAIFEEEEKEW KTAVEAVNDP RFWALVDKER
EHHLRGECQS CVYNNMMGKRE KKQGEFGKAK GSRAIWYMWL
GARFLEFEAL GFLNEDHWMG RENSGGGVEG LGLQRLGYVL
EEMSRIPEGGR MYADDTAGWD TRISRFDLEN EALITNQMEK
GHRALALAI KYTYQNKVVK VLRPAEKGKT VMDIISRQDQ
RSGSQVVTYA LNTFTNLVVQ LIRNMEAEV LEMQDLWLLR
RSEKVTNWLQ SNGWDRLKRM AVSGDDCVVK PIDDRFAHAL
RFLNDMGKVR KDTQEWKPST GWDNWEEVPF CSHHFNKLHL
KDGRSIVVPC RHQDELIGRA RVSPGAGWSI RETACLAKSY
AQMWOQLLYFH RRDRLMANA ICSSVPVDWV PTGRTTWSIH
GKGEWMTTED MLVVWNRVWI EENDHMEDKT PVTKWTDIPY
LGKREDLWCG SLIGHRPRTT WAENIKNTVN MVRRIIGDEE
KYMDYLSTQV RYLGEESTP GVL

Supplementary Table 2. ZIKV protein antigen peptide panels for NS1, NS3, NS5, and Env

ZIKV NS1 (10AA OVERLAP)		
PEPTIDE NO.	peptide name	peptide sequence
1	Zika NS1 [1-20]	DVGCSVDFSKKETRCGTGVF
2	Zika NS1 [11-30]	KETRCGTGVFVYNDVEAWRD
3	Zika NS1 [21-40]	VYNDVEAWRDRYKYHPDSPR
4	Zika NS1 [31-50]	RYKYHPDSPRRLAAAVKQAW
5	Zika NS1 [41-60]	RLAAAVKQAWEDGICGISSV
6	Zika NS1 [51-70]	EDGICGISSVSRMENIMWRS
7	Zika NS1 [61-80]	SRMENIMWRSVEGELNAILE
8	Zika NS1 [71-90]	VEGELNAILEENGVQLTVVV
9	Zika NS1 [81-100]	ENGVQLTVVVGSVKNPMWRG
10	Zika NS1 [91-110]	GSVKNPMWRGPQRLPVPVNE
11	Zika NS1 [101-120]	PQRLPVPVNELPHGWKAWGK
12	Zika NS1 [111-130]	LPHGWKAWGKSYFVRAAKTN
13	Zika NS1 [121-140]	SYFVRAAKTNNSFVVDGDTL
14	Zika NS1 [131-150]	NSFVVDGDTLKECPLKHRAW
15	Zika NS1 [141-160]	KECPLKHRAWNSFLVEDHGF
16	Zika NS1 [151-170]	NSFLVEDHGFVGFHTSVWLK
17	Zika NS1 [161-180]	GVFHTSVWLKVREDYSLECD
18	Zika NS1 [171-190]	VREDYSLECDPAVIGTAVKG
19	Zika NS1 [181-200]	PAVIGTAVKGKEAVHSDLGY
20	Zika NS1 [191-210]	KEAVHSDLGYWIESEKNDTW
21	Zika NS1 [201-220]	WIESEKNDTWRLKRAHLIEM
22	Zika NS1 [211-230]	RLKRAHLIEMKTCEWPKSHT
23	Zika NS1 [221-240]	KTCEWPKSHTLWTDGIEESD
24	Zika NS1 [231-250]	LWTDGIEESDLIIPKSLAGP
25	Zika NS1 [241-260]	LIIPKSLAGPLSHHNTREGY
26	Zika NS1 [251-270]	LSHHNTREGYRTQMKGPHWS
27	Zika NS1 [261-280]	RTQMKGPHWSEELEIRFEEC
28	Zika NS1 [271-290]	EELEIRFEECPGTKVHVEET
29	Zika NS1 [281-300]	PGTKVHVEETCGTRGPSLRS
30	Zika NS1 [291-310]	CGTRGPSLRSTTASGRVIEE
31	Zika NS1 [301-320]	TTASGRVIEEWCCRECTMPP
32	Zika NS1 [311-330]	WCCRECTMPPLSFRAKDGCW
33	Zika NS1 [321-340]	LSFRAKDGCWYGMEIRPRKE
34	Zika NS1 [331-350]	YGMEIRPRKEPESNLVRSMV
35	Zika NS1 [333-352]	MEIRPRKEPESNLVRSMVTA

ZIKV NS3 (10AA OVERLAP)

PEPTIDE NO.	peptide name	peptide sequence
1	Zika NS3 [1-20]	SGALWDVPAPKEVKKGETTD
2	Zika NS3 [11-30]	KEVKKGETTDGVYRVMTRRL
3	Zika NS3 [21-40]	GVYRVMTRRLLGSTQVGVGV
4	Zika NS3 [31-50]	LGSTQVGVGVMQEGVFHTMW
5	Zika NS3 [41-60]	MQEGVFHTMWHVTKGSALRS
6	Zika NS3 [51-70]	HVTKGSALRSGEGRLDPYWG
7	Zika NS3 [61-80]	GEGRLDPYWGDKVQDLVSYC
8	Zika NS3 [71-90]	DVKQDLVSYCGPWKLDAAWD
9	Zika NS3 [81-100]	GPWKLDAAWDGHSEVQLLAV
10	Zika NS3 [91-110]	GHSEVQLLAVPPGERARNIQ
11	Zika NS3 [101-120]	PPGERARNIQTLPGIFKTKD
12	Zika NS3 [111-130]	TLPGIFKTKDGDIGAVALDY
13	Zika NS3 [121-140]	GDIGAVALDYPAGTSGSPIL
14	Zika NS3 [131-150]	PAGTSGSPILDKCGRVIGLY
15	Zika NS3 [141-160]	DKCGRVIGLYGNGVVIKNGS
16	Zika NS3 [151-170]	GNGVVIKNGSYVSAITQGRR
17	Zika NS3 [161-180]	YVSAITQGRREEETPVECFE
18	Zika NS3 [171-190]	EEETPVECFEPSMLKKKQLT
19	Zika NS3 [181-200]	PSMLKKKQLTVLDLHPGAGK
20	Zika NS3 [191-210]	VLDLHPGAGKTRRVLPEIVR
21	Zika NS3 [201-220]	TRRVLPEIVREAIKTRLRTV
22	Zika NS3 [211-230]	EAIKTRLRTVILAPTRVVAA
23	Zika NS3 [221-240]	ILAPTRVVAAEMEEALRGLP
24	Zika NS3 [231-250]	EMEEALRGLPVRYMTTAVNV
25	Zika NS3 [241-260]	VRYMTTAVNVTHSGTEIVDL
26	Zika NS3 [251-270]	THSGTEIVDLMCHATFTSRL
27	Zika NS3 [261-280]	MCHATFTSRLLOPIRVPNYN
28	Zika NS3 [271-290]	LQPIRVPNYNLYIMDEAHFT
29	Zika NS3 [281-300]	LYIMDEAHFTDPSSIAARGY
30	Zika NS3 [291-310]	DPSSIAARGYISTRVEMGEA
31	Zika NS3 [301-320]	ISTRVEMGEAAAIFMTATPP
32	Zika NS3 [311-330]	AAIFMTATPPGTRDAFPDSN
33	Zika NS3 [321-340]	GTRDAFPDSNSPIMDTEVEV
34	Zika NS3 [331-350]	SPIMDTEVEVPERAWSSGFD
35	Zika NS3 [341-360]	PERAWSSGFDWVTDHSGKTV
36	Zika NS3 [351-370]	WVTDHSGKTVWFVPSVRNGN
37	Zika NS3 [361-380]	WFVPSVRNGNEIAACLTKAG
38	Zika NS3 [371-390]	EIAACLTKAGKRVIQLSRKT
39	Zika NS3 [381-400]	KRVIQLSRKTFETEFQKTKH
40	Zika NS3 [391-410]	FETEFQKTKHQEWDFVVTTD
41	Zika NS3 [401-420]	QEWDFVVTTDISEMGANFKA

42	Zika NS3 [411-430]	I SEMGANFKADRVIDSRRL
43	Zika NS3 [421-440]	DRVIDSRRLKPVILDGERV
44	Zika NS3 [431-450]	KPVILDGERVILAGPMPVTH
45	Zika NS3 [441-460]	ILAGPMPVTHASAAQRRGRI
46	Zika NS3 [451-470]	ASAAQRRGRIGRNPKNKPGDE
47	Zika NS3 [461-480]	GRNPKNKPGDEYLYGGGCAET
48	Zika NS3 [471-490]	YLYGGGCAETDEDHAHWLEA
49	Zika NS3 [481-500]	DEDHAHWLEARMLLDNIYLQ
50	Zika NS3 [491-510]	RMLLDNIYLQDGLIASLYRP
51	Zika NS3 [501-520]	DGLIASLYRPEADKVA AIEG
52	Zika NS3 [511-530]	EADKVA AIEGEFKLRTEQRK
53	Zika NS3 [521-540]	EFKLRTEQRKTFVELMKRGD
54	Zika NS3 [531-550]	TFVELMKRGDLPVWLAYQVA
55	Zika NS3 [541-560]	LPVWLAYQVASAGITYTDRR
56	Zika NS3 [551-570]	SAGITYTDRRWCFDGTNNNT
57	Zika NS3 [561-580]	WCFDGTNNNTIMEDSVPAEV
58	Zika NS3 [571-590]	IMEDSVPAEVWTRHGEKRVL
59	Zika NS3 [581-600]	WTRHGEKRVLKPRWMDARVC
60	Zika NS3 [591-610]	KPRWMDARVCS DHAALKSFK
61	Zika NS3 [598-617]	RVCS DHAALKSFK EFAAGKR

ZIKV NS5 (10AA OVERLAP)

PEPTIDE NO.	peptide name	peptide sequence
1	Zika NS5 [1-20]	GGGTGETLGEKWKARLNQMS
2	Zika NS5 [11-30]	KWKARLNQMSALEFYKKS
3	Zika NS5 [21-40]	ALEFYKKS GITEVCREEA
4	Zika NS5 [31-50]	GITEVCREEARRALKDGVAT
5	Zika NS5 [41-60]	RRALKDGVATGGHAVSRGSA
6	Zika NS5 [51-70]	GGHAVSRGSAKLRWLVERGY
7	Zika NS5 [61-80]	KLRWLVERGYLQPYGKVIDL
8	Zika NS5 [71-90]	LQPYGKVIDLGCGRGGWSYY
9	Zika NS5 [81-100]	GCGRGGWSYYAATIRKVQEV
10	Zika NS5 [91-110]	AATIRKVQEVKGYTKGGPGH
11	Zika NS5 [101-120]	KGYTKGGPGHEEPVLVQSYG
12	Zika NS5 [111-130]	EELVQSYGWNIVRLKSGV
13	Zika NS5 [121-140]	WNIVRLKSGVDVFMMAEPC
14	Zika NS5 [131-150]	DVFMMAEPCDTLLCDIGES
15	Zika NS5 [141-160]	DTLLCDIGESSSSPEVEEAR
16	Zika NS5 [151-170]	SSSPEVEEARTLRVLSMVG
17	Zika NS5 [161-180]	TLRVLSMVGDWLEKRPAGFC
18	Zika NS5 [171-190]	WLEKRPAGFCIKVLCPYTST
19	Zika NS5 [181-200]	IKVLCPYTSTMMETLERLQR
20	Zika NS5 [191-210]	MMETLERLQRRYGGGLVRVP
21	Zika NS5 [201-220]	RYGGGLVRVPLSRNSTHEMY
22	Zika NS5 [211-230]	LSRNSTHEMYWVSGAKSNTI
23	Zika NS5 [221-240]	WVSGAKSNTIKSVSTTSQLL
24	Zika NS5 [231-250]	KSVSTTSQLLLGRMDGPRRP
25	Zika NS5 [241-260]	LGRMDGPRRPVKYEEDVNLG
26	Zika NS5 [251-270]	VKYEEDVNLGSGTRAVVSCA
27	Zika NS5 [261-280]	SGTRAVVSCAEAPNMKIIGN
28	Zika NS5 [271-290]	EAPNMKIIGNRIERIRSEHA
29	Zika NS5 [281-300]	RIERIRSEHAETWFFDENHP
30	Zika NS5 [291-310]	ETWFFDENHPYRTWAYHGSY
31	Zika NS5 [301-320]	YRTWAYHGSYEAPTQGSASS
32	Zika NS5 [311-330]	EAPTQGSASSLINGVVRLLS
33	Zika NS5 [321-340]	LINGVVRLLSKPWDVVTGVT
34	Zika NS5 [331-350]	KPWDVVTGVTGIAMTDTTPY
35	Zika NS5 [341-360]	GIAMTDTTPYQQRVFKEKV
36	Zika NS5 [351-370]	QQRVFKEKVDTRVPDPQEG
37	Zika NS5 [361-380]	DTRVPDPQEGTRQVMSMVSS
38	Zika NS5 [371-390]	TRQVMSMVSSWLWELGKHK
39	Zika NS5 [381-400]	WLWELGKHKRPRVCTKEEF
40	Zika NS5 [391-410]	RPRVCTKEEFINKVRSNAAL
41	Zika NS5 [401-420]	INKVRSNAALGAIFEEKEW

42	Zika NS5 [411-430]	G A I F E E E K E W K T A V E A V N D P
43	Zika NS5 [421-440]	K T A V E A V N D P R F W A L V D K E R
44	Zika NS5 [431-450]	R F W A L V D K E R E H H L R G E C Q S
45	Zika NS5 [441-460]	E H H L R G E C Q S C V Y N M M G K R E
46	Zika NS5 [451-470]	C V Y N M M G K R E K K Q G E F G K A K
47	Zika NS5 [461-480]	K K Q G E F G K A K G S R A I W Y M W L
48	Zika NS5 [471-490]	G S R A I W Y M W L G A R F L E F E A L
49	Zika NS5 [481-500]	G A R F L E F E A L G F L N E D H W M G
50	Zika NS5 [491-510]	G F L N E D H W M G R E N S G G G V E G
51	Zika NS5 [501-520]	R E N S G G G V E G L G L Q R L G Y V L
52	Zika NS5 [511-530]	L G L Q R L G Y V L E E M S R I P G G R
53	Zika NS5 [521-540]	E E M S R I P G G R M Y A D D T A G W D
54	Zika NS5 [531-550]	M Y A D D T A G W D T R I S R F D L E N
55	Zika NS5 [541-560]	T R I S R F D L E N E A L I T N Q M E K
56	Zika NS5 [551-570]	E A L I T N Q M E K G H R A L A L A I I
57	Zika NS5 [561-580]	G H R A L A L A I I K Y T Y Q N K V V K
58	Zika NS5 [571-590]	K Y T Y Q N K V V K V L R P A E K G K T
59	Zika NS5 [581-600]	V L R P A E K G K T V M D I I S R Q D Q
60	Zika NS5 [591-610]	V M D I I S R Q D Q R G S G Q V V T Y A
61	Zika NS5 [601-620]	R G S G Q V V T Y A L N T F T N L V V Q
62	Zika NS5 [611-630]	L N T F T N L V V Q L I R N M E A E E V
63	Zika NS5 [621-640]	L I R N M E A E E V L E M Q D L W L L R
64	Zika NS5 [631-650]	L E M Q D L W L L R R S E K V T N W L Q
65	Zika NS5 [641-660]	R S E K V T N W L Q S N G W D R L K R M
66	Zika NS5 [651-670]	S N G W D R L K R M A V S G D D C V V K
67	Zika NS5 [661-680]	A V S G D D C V V K P I D D R F A H A L
68	Zika NS5 [671-690]	P I D D R F A H A L R F L N D M G K V R
69	Zika NS5 [681-700]	R F L N D M G K V R K D T Q E W K P S T
70	Zika NS5 [691-710]	K D T Q E W K P S T G W D N W E E V P F
71	Zika NS5 [701-720]	G W D N W E E V P F C S H H F N K L H L
72	Zika NS5 [711-730]	C S H H F N K L H L K D G R S I V V P C
73	Zika NS5 [721-740]	K D G R S I V V P C R H Q D E L I G R A
74	Zika NS5 [731-750]	R H Q D E L I G R A R V S P G A G W S I
75	Zika NS5 [741-760]	R V S P G A G W S I R E T A C L A K S Y
76	Zika NS5 [751-770]	R E T A C L A K S Y A Q M W Q L L Y F H
77	Zika NS5 [761-780]	A Q M W Q L L Y F H R R D L R L M A N A
78	Zika NS5 [771-790]	R R D L R L M A N A I C S S V P V D W V
79	Zika NS5 [781-800]	I C S S V P V D W V P T G R T T W S I H
80	Zika NS5 [791-810]	P T G R T T W S I H G K G E W M T T E D
81	Zika NS5 [801-820]	G K G E W M T T E D M L V V W N R V W I
82	Zika NS5 [811-830]	M L V V W N R V W I E E N D H M E D K T
83	Zika NS5 [821-840]	E E N D H M E D K T P V T K W T D I P Y
84	Zika NS5 [831-850]	P V T K W T D I P Y L G K R E D L W C G
85	Zika NS5 [841-860]	L G K R E D L W C G S L I G H R P R T T

86	Zika NS5 [851-870]	SLIGHRPRTTWAENIKNTVN
87	Zika NS5 [861-880]	WAENIKNTVNMVRRRIIGDEE
88	Zika NS5 [871-890]	MVRRRIIGDEEKYMDYLSTQV
89	Zika NS5 [881-900]	KYMDYLSTQVRYLGEEGSTP
90	Zika NS5 [884-903]	DYLSTQVRYLGEEGSTPGVL

ZIKV ENVELOPE PROTEIN Env (10AA OVERLAP)

PEPTIDE NO.	peptide name	peptide sequence
1	Zika ENV [1-20]	IRCIGVSNRDFVEGMSGGTW
2	Zika ENV [11-30]	FVEGMSGGTWVDVVLEHGGC
3	Zika ENV [21-40]	VDVVLEHGGCVTVMAQDKPT
4	Zika ENV [31-50]	VTVMAQDKPTVDIELVTTTV
5	Zika ENV [41-60]	VDIELVTTTVSNMAEVRSYC
6	Zika ENV [51-70]	SNMAEVRSYCYEASISDMAS
7	Zika ENV [61-80]	YEASISDMASDSRCPTQGEA
8	Zika ENV [71-90]	DSRCPTQGEAYLDKQSDTOY
9	Zika ENV [81-100]	YLDKQSDTOYVCKRTLVDGR
10	Zika ENV [91-110]	VCKRTLVDGRWGNGCGLFGK
11	Zika ENV [101-120]	WGNGCGLFGKGLVTCAKFA
12	Zika ENV [111-130]	GSLVTCAKFACSKKMTGKSI
13	Zika ENV [121-140]	CSKKMTGKSIQPENLEYRIM
14	Zika ENV [131-150]	QPENLEYRIMLSVHGSQHSG
15	Zika ENV [141-160]	LSVHGSQHSGMIVNDTGHET
16	Zika ENV [151-170]	MIVNDTGHETDENRAKVEIT
17	Zika ENV [161-180]	DENRAKVEITPNSPRAEATL
18	Zika ENV [171-190]	PNSPRAEATLGGFGSLGLDC
19	Zika ENV [181-200]	GGFGSLGLDCEPRTGLDFSD
20	Zika ENV [191-210]	EPRTGLDFSDLYYLTMNNKH
21	Zika ENV [201-220]	LYYLTMNNKHWLVHKEWFHD
22	Zika ENV [211-230]	WLVHKEWFHDIPLPWHAGAD
23	Zika ENV [221-240]	IPLPWHAGADTGTPHWNKE
24	Zika ENV [231-250]	TGTPHWNKEALVEFKDAHA
25	Zika ENV [241-260]	ALVEFKDAHAKRQTVVVLGS
26	Zika ENV [251-270]	KRQTVVVLGSQEGAVHTALA
27	Zika ENV [261-280]	QEGAVHTALAGALEAEMDGA
28	Zika ENV [271-290]	GALEAEMDGAKGRLSSGHLK
29	Zika ENV [281-300]	KGRLSSGHLKCRLKMDKLRL
30	Zika ENV [291-310]	CRLKMDKLRLKGVSYSLCTA
31	Zika ENV [301-320]	KGVSYSLCTAAFTFTKIPAE
32	Zika ENV [311-330]	AFTFTKIPAE TLHGTVTVEV
33	Zika ENV [321-340]	TLHGTVTVEVQYAGTDGPCK
34	Zika ENV [331-350]	QYAGTDGPCKVPAQMAVDMQ
35	Zika ENV [341-360]	VPAQMAVDMQTLTPVGRLIT
36	Zika ENV [351-370]	TLTPVGRLITANPVITESTE
37	Zika ENV [361-380]	ANPVITESTENSKMMLELDP
38	Zika ENV [371-390]	NSKMMLELDPPFGDSYIVIG
39	Zika ENV [381-400]	PFGDSYIVIGVGEKKITHHW
40	Zika ENV [391-410]	VGEKKITHHWHRSGSTIGKA
41	Zika ENV [401-420]	HRSGSTIGKA FEATVRGAKR

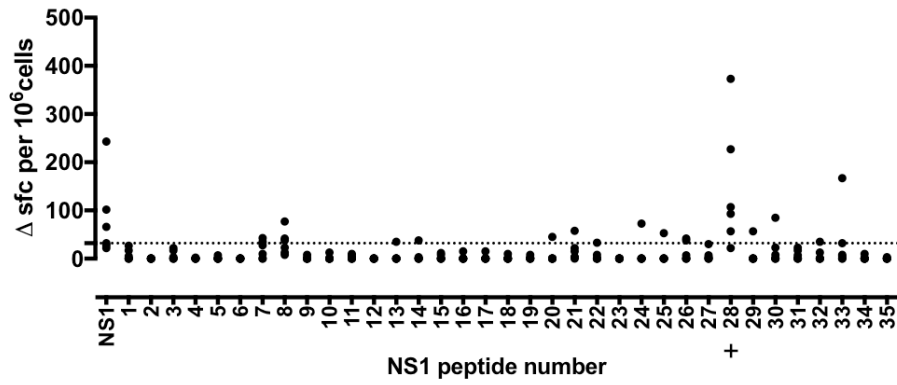
42	Zika ENV [411-430]	FEATVRGAKRMAVLGDTAWD
43	Zika ENV [421-440]	MAVLGDTAWDFGSVGGALNS
44	Zika ENV [431-450]	FGSVGGALNSLGKGIHQIFG
45	Zika ENV [441-460]	LGKGIHQIFGAAFKSLFGGM
46	Zika ENV [451-470]	AAFKSLFGGMSWFSQILIGT
47	Zika ENV [461-480]	SWFSQILIGTLLMWLGLNTK
48	Zika ENV [471-490]	LLMWLGLNTKNGSISLMCLA
49	Zika ENV [481-500]	NGSISLMCLALGGVLIFLST
50	Zika ENV [485-504]	SLMCLALGGVLIFLSTAVSA

S1 Fig. CD4 T cell epitopes to ZIKV non-structural proteins NS1, NS3 and NS5 in HLA-DR1 and HLA-DR4 transgenic mice.

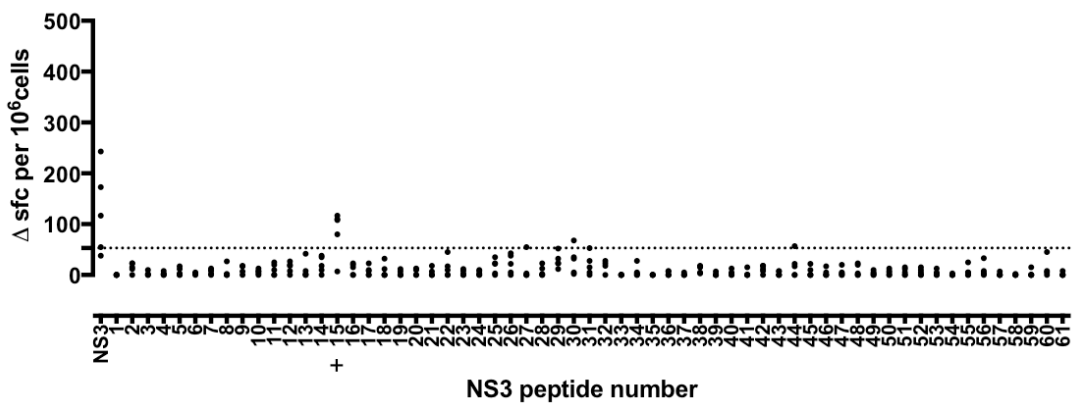
Mice transgenic for HLA-DR1 (DRB1*0101) (i) and HLA-DR4 (DRB1*0401) (ii) were footpad primed with 25 μ g of recombinant ZIKV proteins NS1 (A), NS3 (B) and NS5 (C). Ten days after immunisation, draining lymph node (DLN) cells were assayed by IFN γ ELISpot for recall responses to the immunising protein and to an overlapping panel of 20mer peptides spanning the length of each protein. Data shown are for n=6 mice per group except for (A ii) and (B i) which were n=4 and n=5 respectively. Data are plotted as number of spot forming cells (SFC) per 10^6 cells for individual mice. Responses were considered positive (+) if the response was greater than 2 SD above the mean of the response in the absence of any antigen (shown as horizontal dotted line).

HLA-DR1 (DRB1*0101)

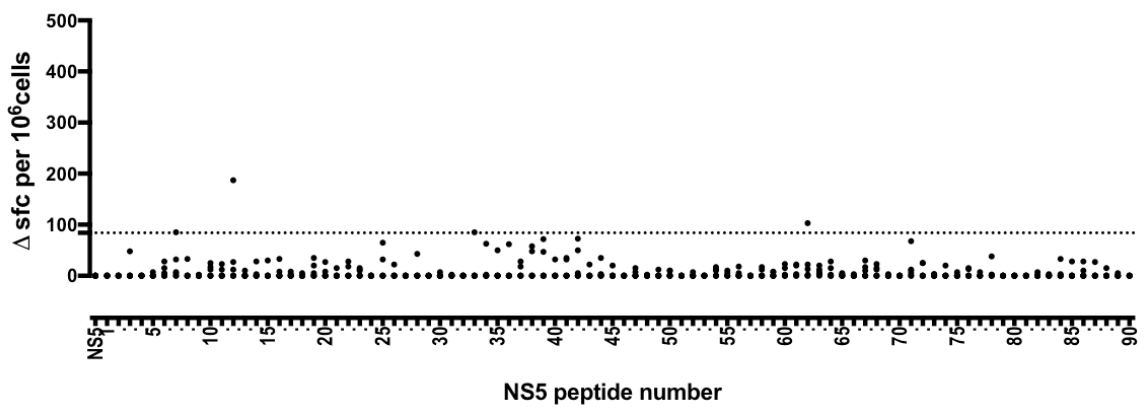
A (i)



B (i)

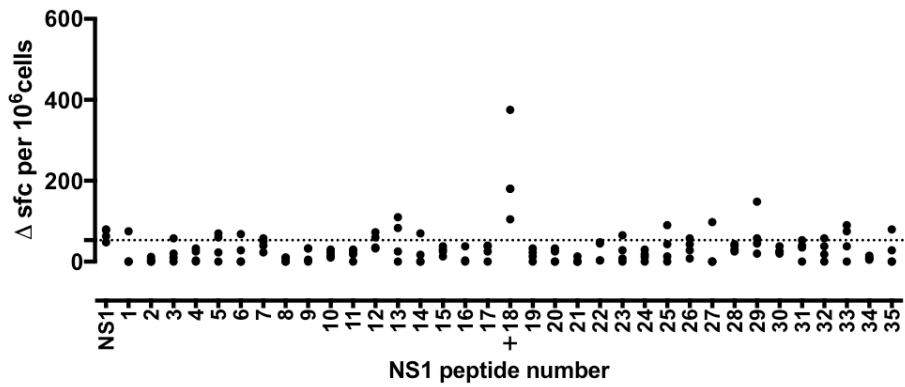


C (i)

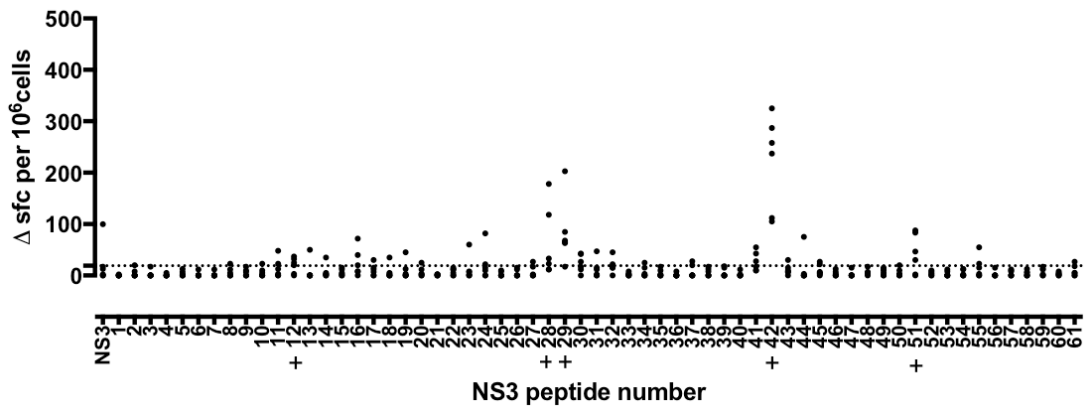


HLA-DR4 (DRB1*0401)

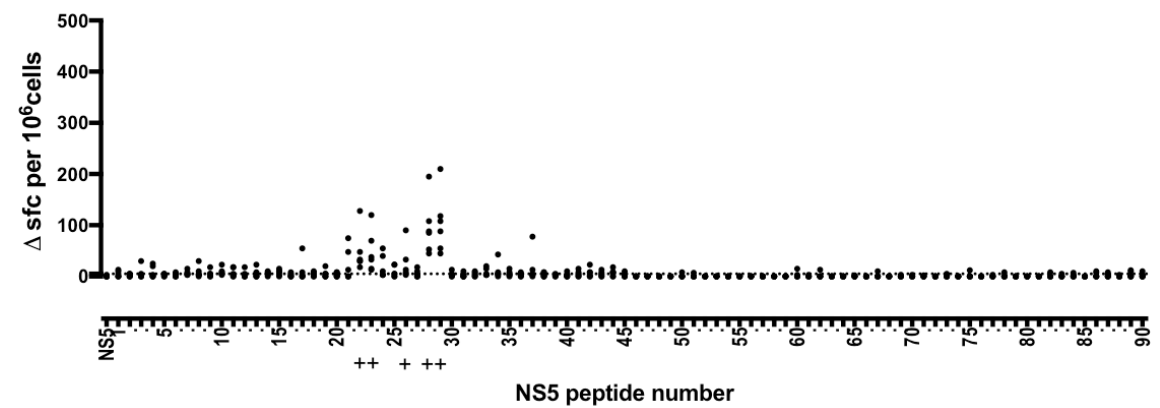
A (ii)



B (ii)



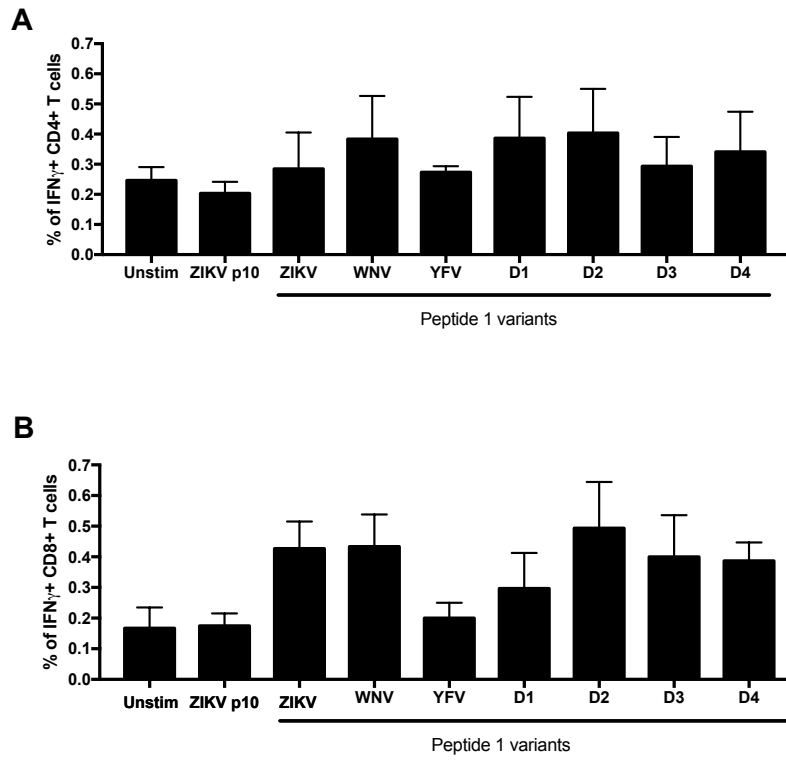
C (ii)



S2 Fig. CD4⁺ and CD8⁺ T cells respond to peptide 1 and variants of ZIKV Env

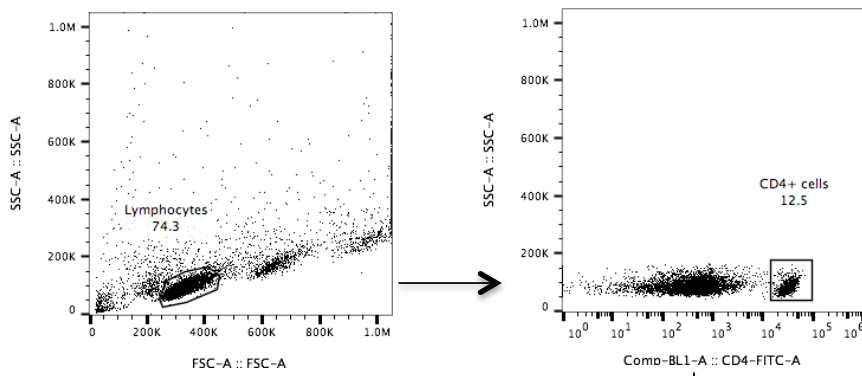
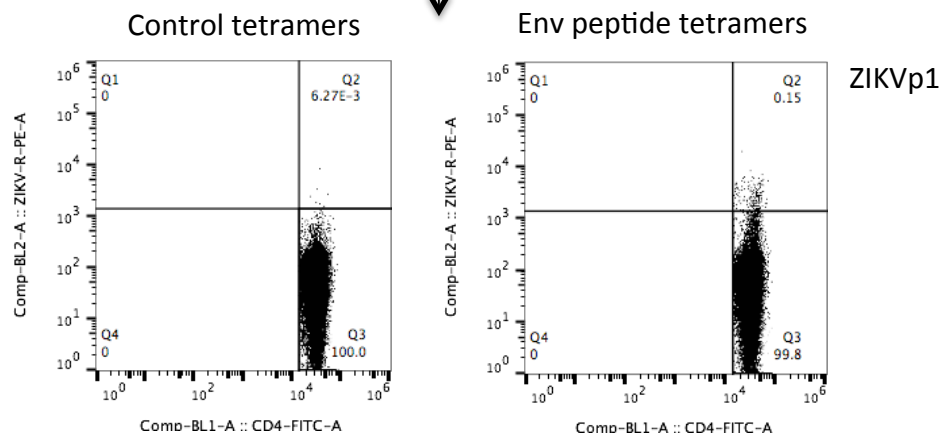
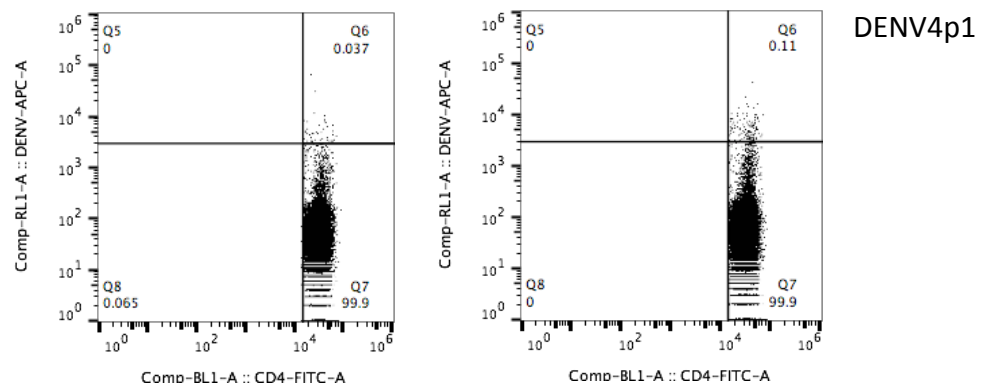
Mice transgenic for HLA-DQ8 (DQB1*0302) n=3 were primed with 25 µg of recombinant ZIKV envelope protein (Env). 11 days after immunisation, DLNs were cultured *in vitro* for 7 hours, in the presence of brefeldin A, with 25 µg/ml of Env peptide 10, Env peptide 1 or the peptide 1 variants of west Nile virus (WNV), yellow fever virus (YFV), dengue virus 1 (D1), dengue virus 2 (D2), dengue virus 3 (D3) or dengue virus 4 (D4). Cells were stained for the cell surface markers CD3, CD4 and CD8 and intracellularly for the production of IFN γ . Data are plotted as the percentage of (A) CD4⁺ T cells or (B) CD8⁺ T cells producing IFN γ . Data shown represent mean \pm SEM.

S2 Fig. CD4⁺ and CD8⁺ T cells respond to peptide 1 and variants of ZIKV Env



S3 Fig. Draining lymph node (DLN) cells from HLA-DR1 transgenic mice primed with ZIKV Env and stained with HLA class II tetramers loaded with peptide confirm the presence of ZIKV Env p1 specific T cells and demonstrate a high degree of cross-reactivity with the DENV4 p1 variant peptide at the clonal level.

HLA-DR1 (DRB1*0101) mice were primed sub-cutaneously in one hind footpad with 25µg of recombinant protein emulsified in Hunters Titermax Gold adjuvant (Sigma-Aldrich, UK). Fourteen days post immunisation, the draining popliteal lymph node was removed and disaggregated into a single-cell suspension. Cells were stained with HLA-DRB1*0101 tetramers loaded with either no peptide, ZIKV Env p1 or the DENV4 Env p1 variant followed by staining with an anti-mouse CD4 FITC antibody. (A) Samples were gated on live lymphocytes followed by CD4⁺ cells before analysis of (B) ZIKV Env p1 specific T cells, (C) DENV4 Env p1 variant specific T cells and (D) dual ZIKV Env p1 and DENV4 Env p1 specific T cells.

A**B****C****D**