Figure 1

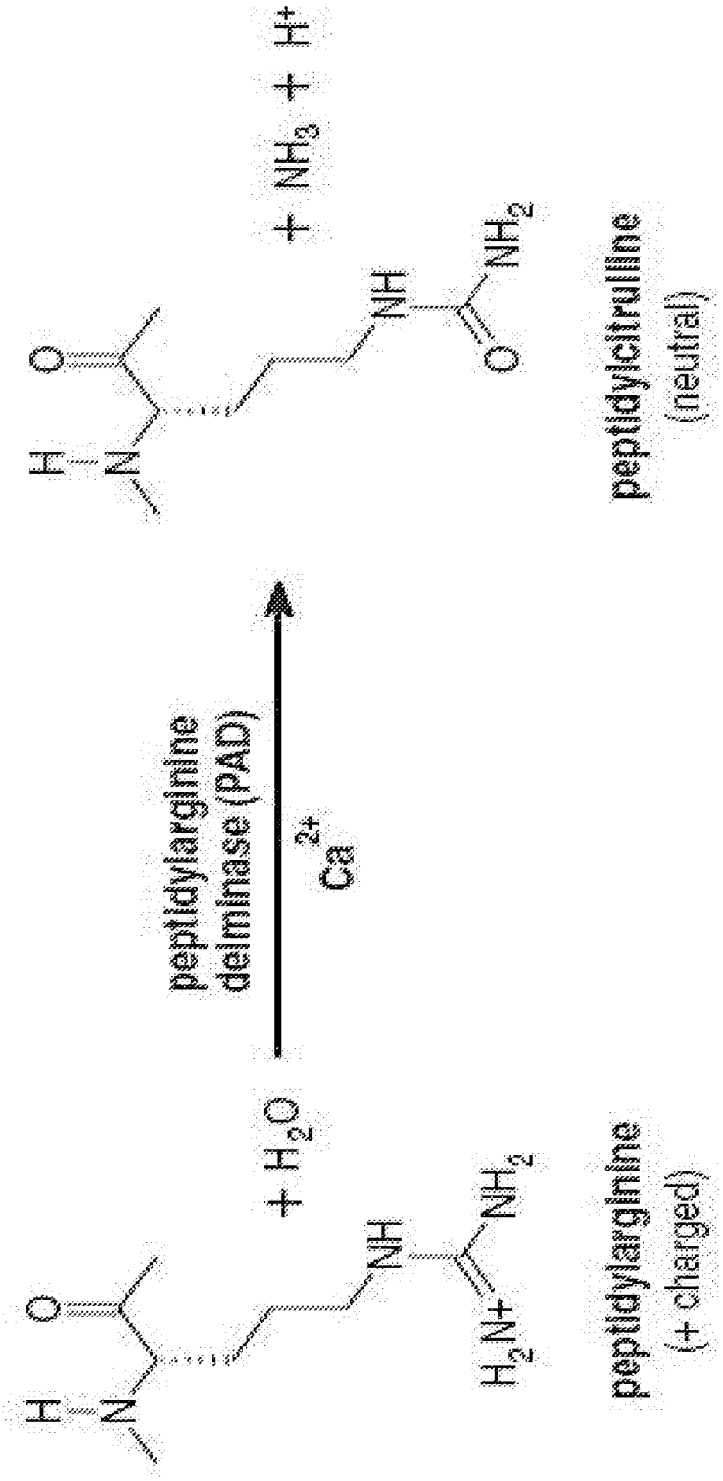

peptidylarginine
deiminase (PAD)
$Ca^{2+}$
$+ H_2O$
$+ NH_3 + H^+$
peptidylarginine
(+ charged)
peptidylcitrulline
(neutral)

Figure 2

```
        10         20         30         40         50         60
MSTRSVSSSS YRRMFGGPGT ASRPSSSRSY VTTSTRTYSL GSALRPSTSR SLYASSPGGV

        70         80         90        100        110        120
YATRSSAVRL RSSVPGVRLL QDSVDFSLAD AINTEFKNTR TNEKVELQEL NDRFANYIDK

       130        140        150        160        170        180
VRFLEQQNKI LLAELEQLKG QGKSRLGDLY EEEMRELRRQ VDQLTNDKAR VEVERDNLAE

       190        200        210        220        230        240
DIMRLREKLQ EEMLQREEAE NTLQSFRQDV DNASLARLDL ERKVESLQEE IAFLKKLHEE

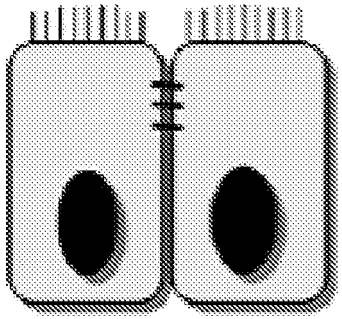
       250        260        270        280        290        300
EIQELQAQIQ EQHVQIDVDV SKPDLTAALR DVRQQYESVA AKNLQEAEEW YKSKFADLSE

       310        320        330        340        350        360
AANRNNDALR QAKQESTEYR RQVQSLTCEV DALKGTNESL ERQMREMEEN FAVEAANYQD

       370        380        390        400        410        420
TIGRLQDEIQ NMKEEMARHL REYQDLLNVK MALDIEIATY RKLLEGEESR ISLPLPNFSS

       430        440        450        460
LNLRETNLDS LPLVDTHSKR TLLIKTVETR DGQVINETSQ HHDDLE
```

Figure 3



EMT

MET



**Epithelial phenotype**

Cell polarization

Multiple cell-to-cell contacts

Cytokeratins

E-cadherin

Plakoglobin

**Mesenchymal phenotype**

Fibroblast-like morphology

Motility

Invasiveness

N-cadherin

Vimentin

Fibronectin

Matrix metalloproteases (MMPs)

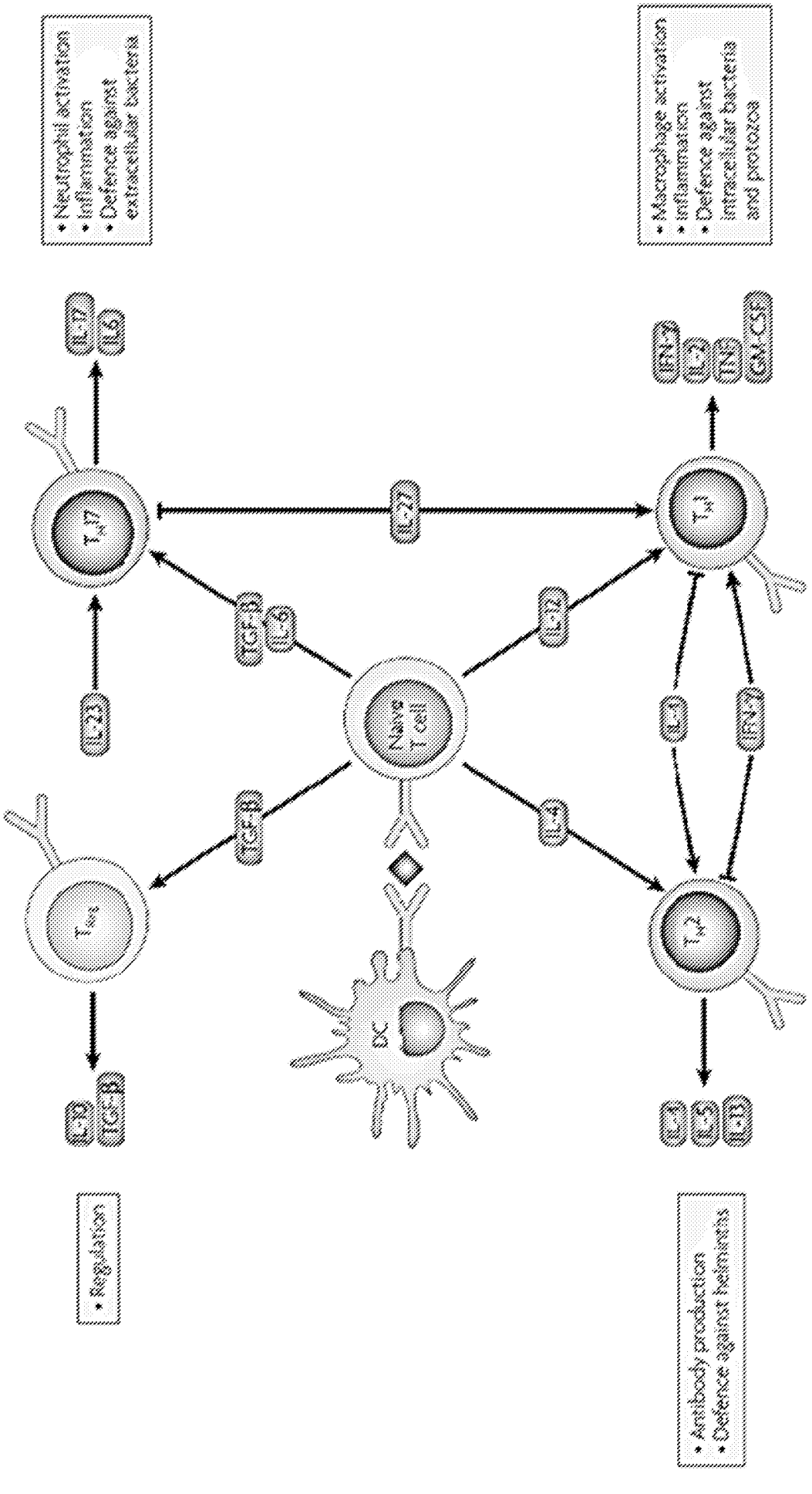



Figure 4

SUBSTITUTE SHEET (RULE 26)

Figure 5

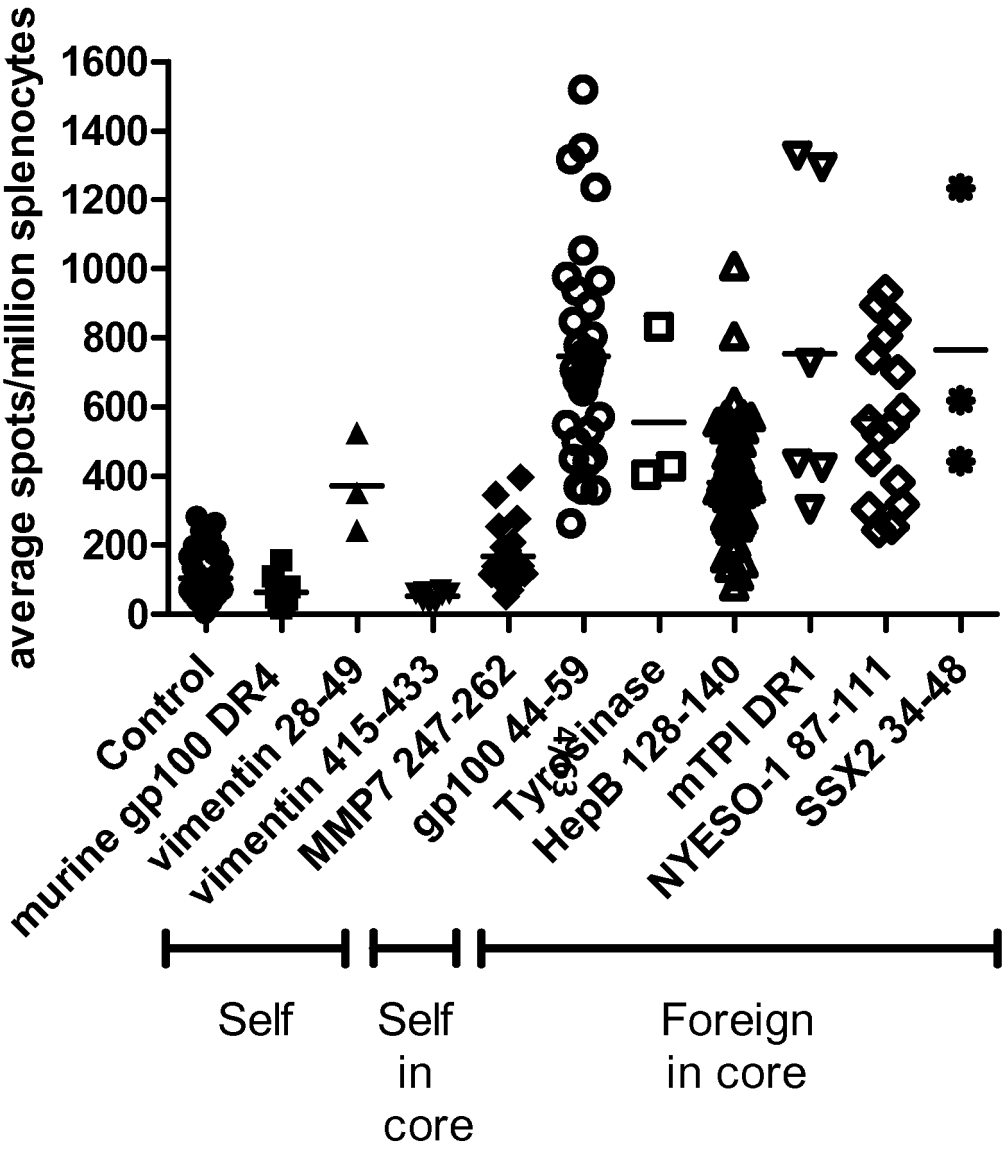
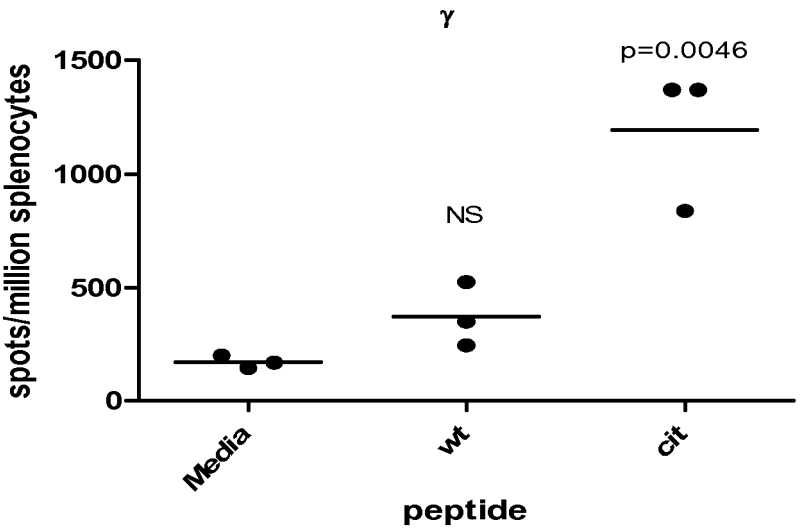
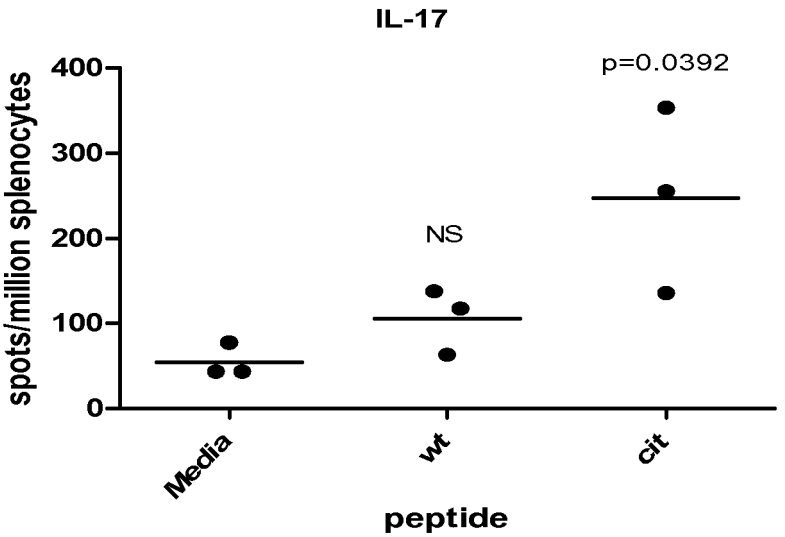

average spots/million splenocytes
1600
1400
1200
1000
800
600
400
200
0
Control
murine gp100 DR4
vimentin 28-49
vimentin 415-433
MMP7 247-262
gp100 44-59
Tyrosinase
HepB 128-140
mTPI DR1
NYESO-1 87-111
SSX2 34-48
Self
Self in core
Foreign in core

Figure 6

(i)




(ii)




(iii)

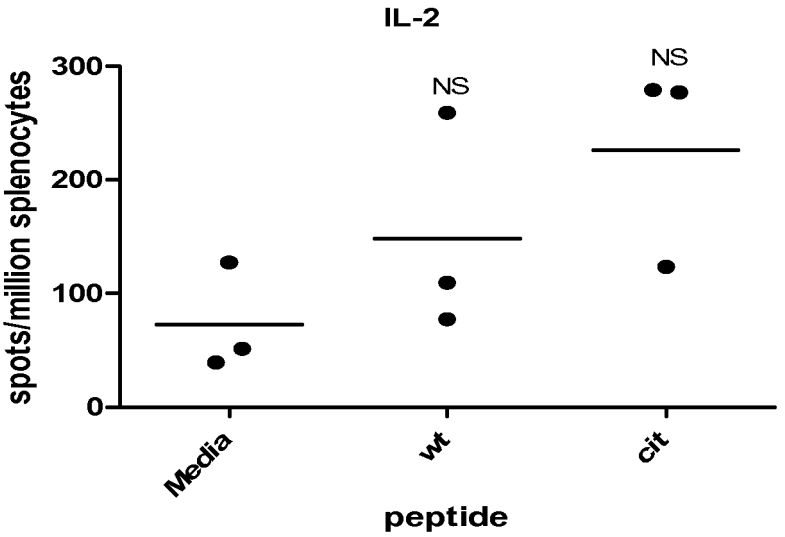
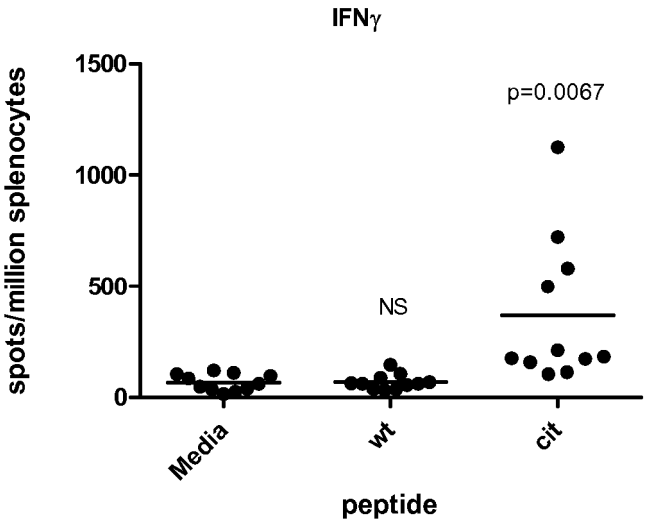
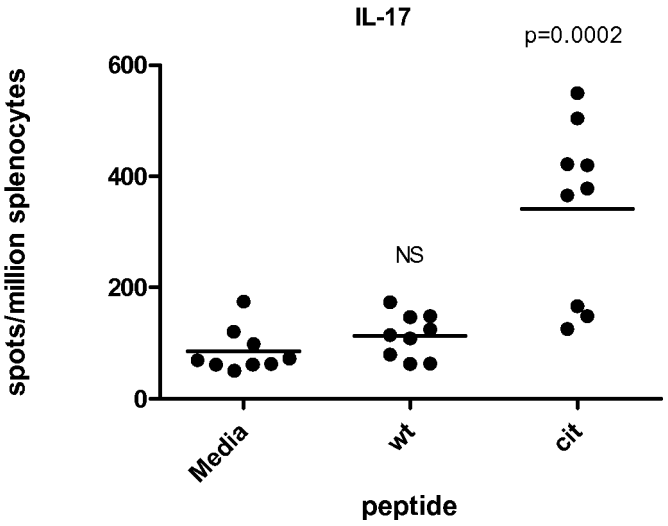


Figure 7

(i)




(ii)




(iii)

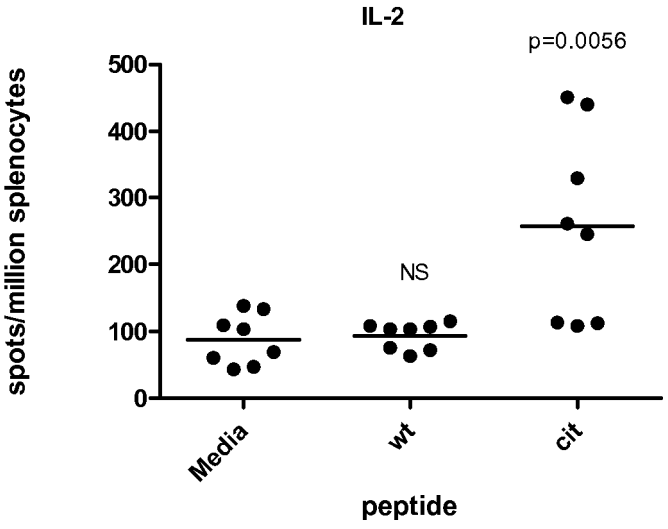
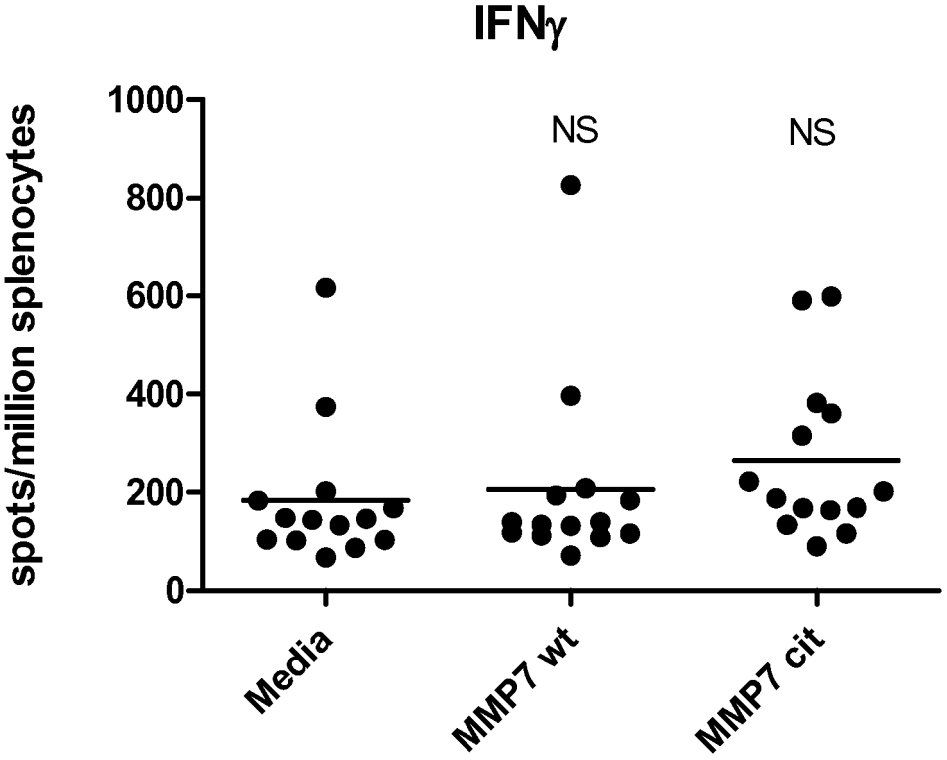


Figure 8

(i)


IFNγ
spots/million splenocytes
1000
800
600
400
200
0
NS
NS
Media
MMP7 wt
MMP7 cit

(ii)

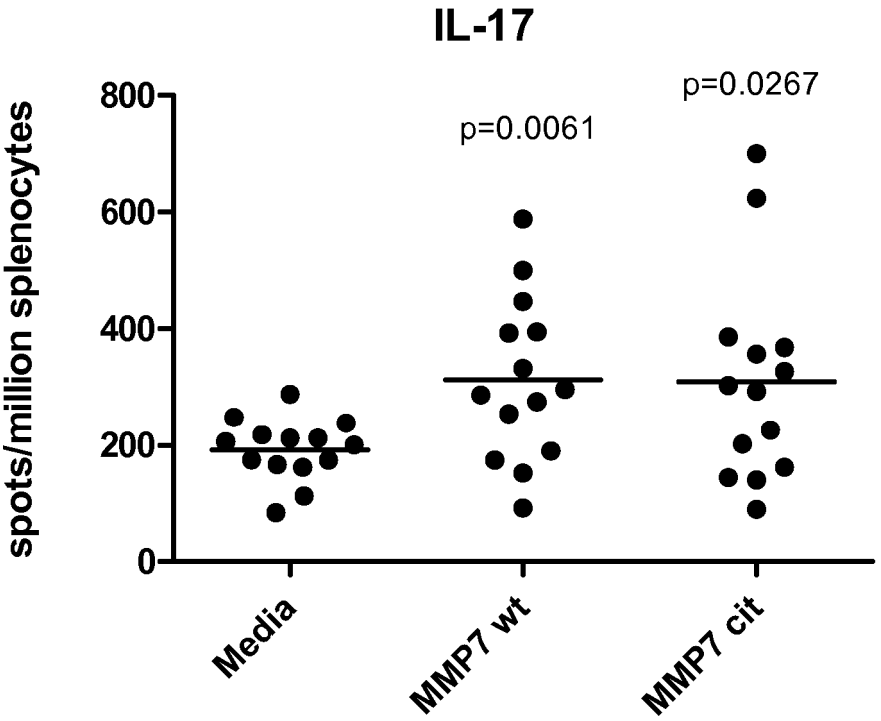
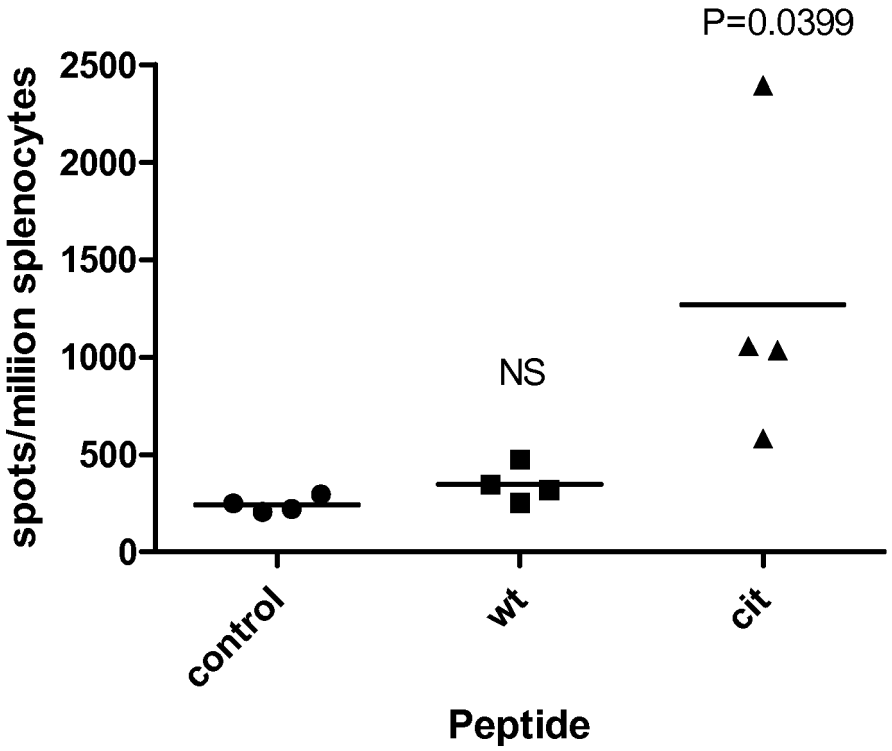

IL-17
spots/million splenocytes
800
600
400
200
0
p=0.0061
p=0.0267
Media
MMP7 wt
MMP7 cit

Figure 9

(i)


IFNγ
P=0.0399
spots/million splenocytes
2500
2000
1500
1000
500
0
NS
control
wt
cit
Peptide

(ii)

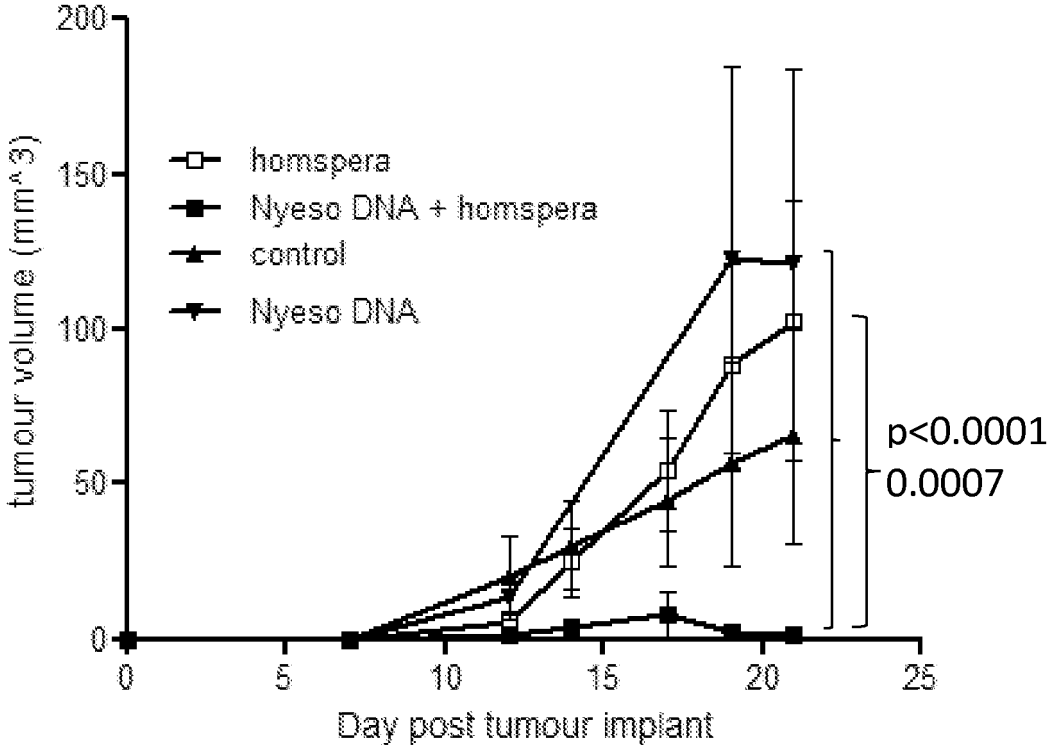

200
150
100
50
0
tumour volume (mm^3)
homspera
Nyeso DNA + homspera
control
Nyeso DNA
p<0.0001
0.0007
0
5
10
15
20
25
Day post tumour implant

Figure 10

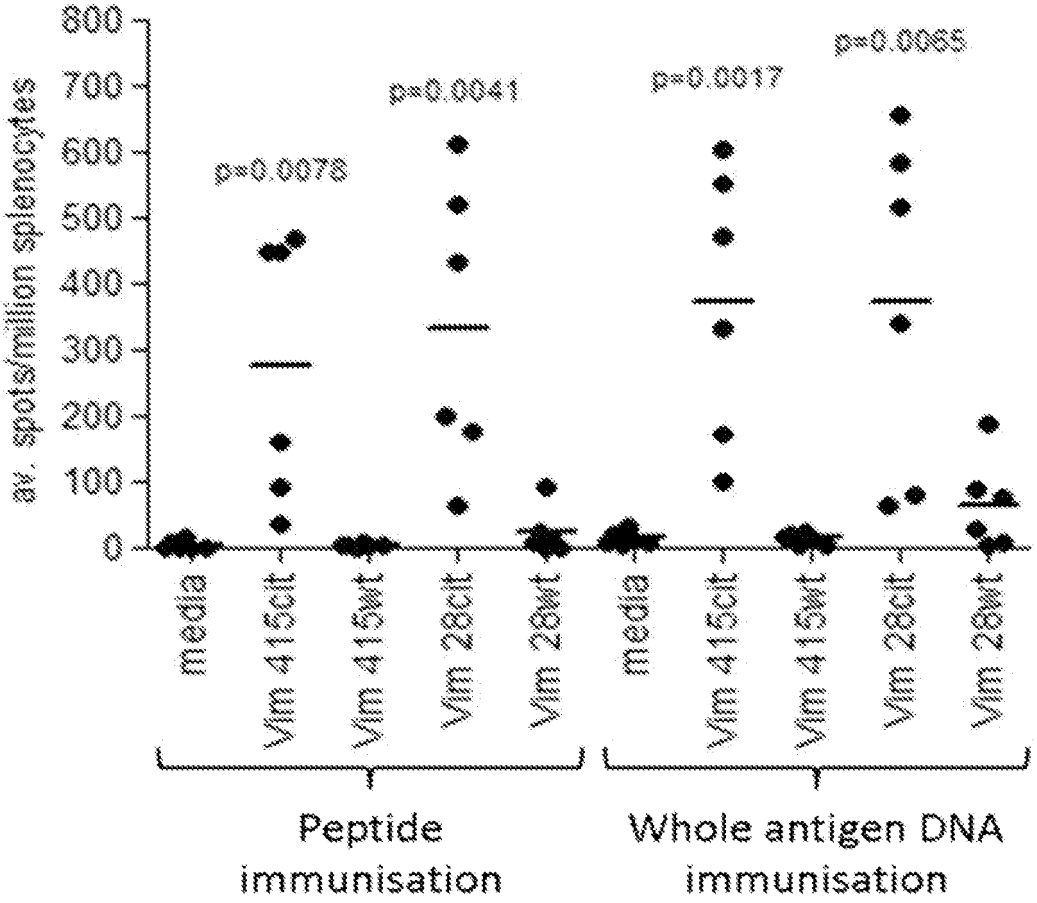
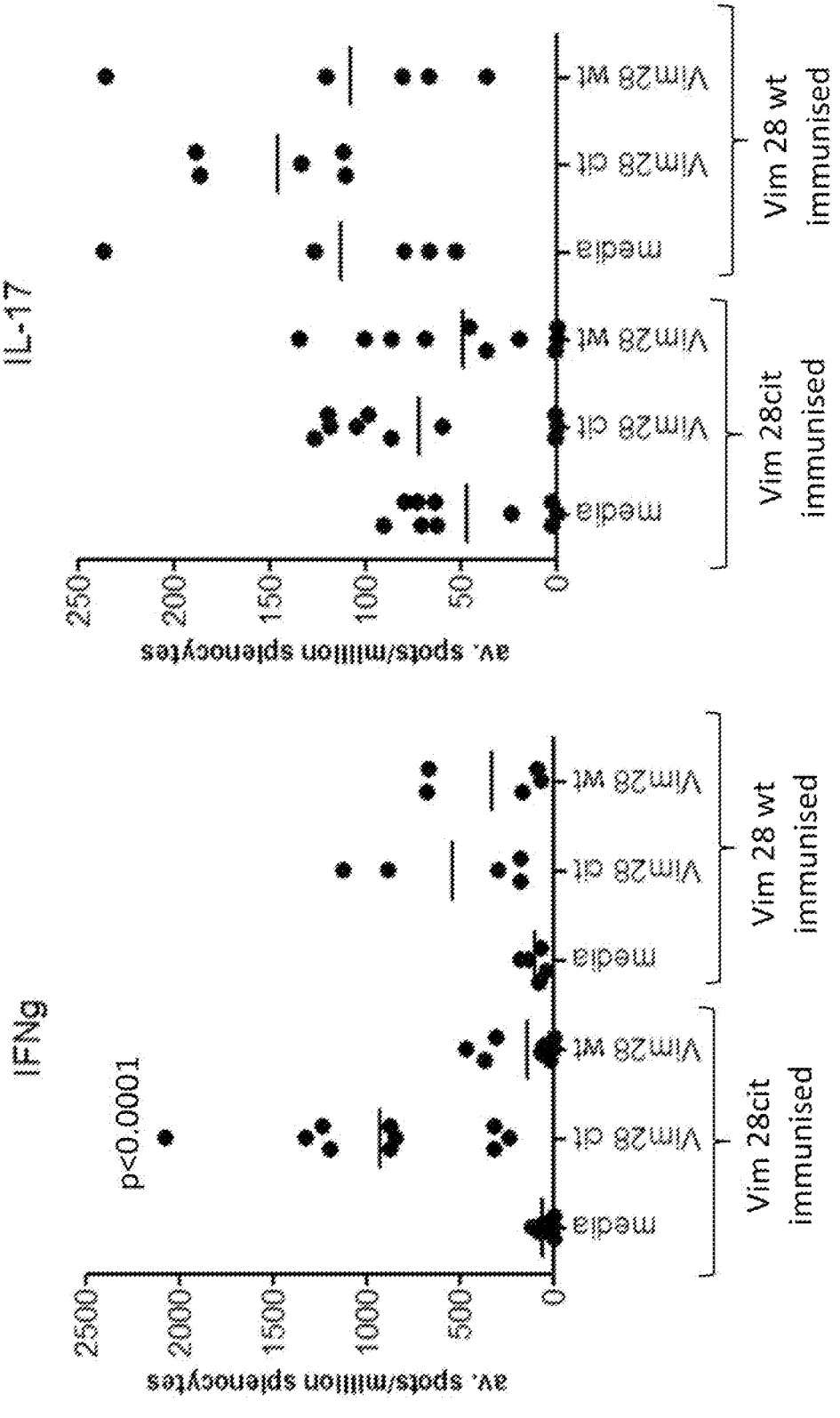

av. spots/million splenocytes
800
700
600
500
400
300
200
100
0
p=0.0078
p=0.0041
p=0.0017
p=0.0065
media
Vim 415cit
Vim 415wt
Vim 28cit
Vim 28wt
media
Vim 415cit
Vim 415wt
Vim 28cit
Vim 28wt
Peptide immunisation
Whole antigen DNA immunisation

Figure 11
(a)
(i)




SUBSTITUTE SHEET (RULE 26)

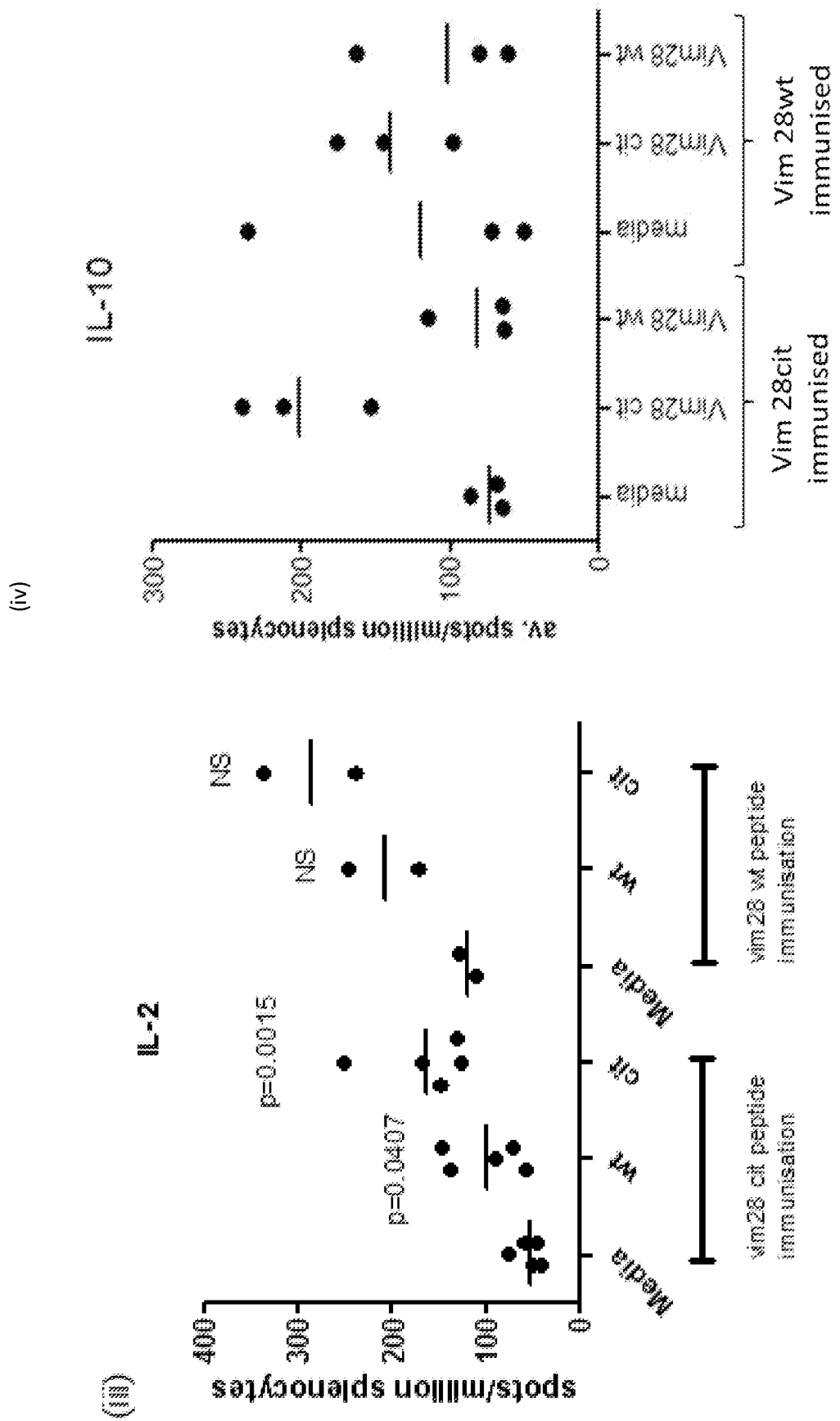



Figure 11 contd

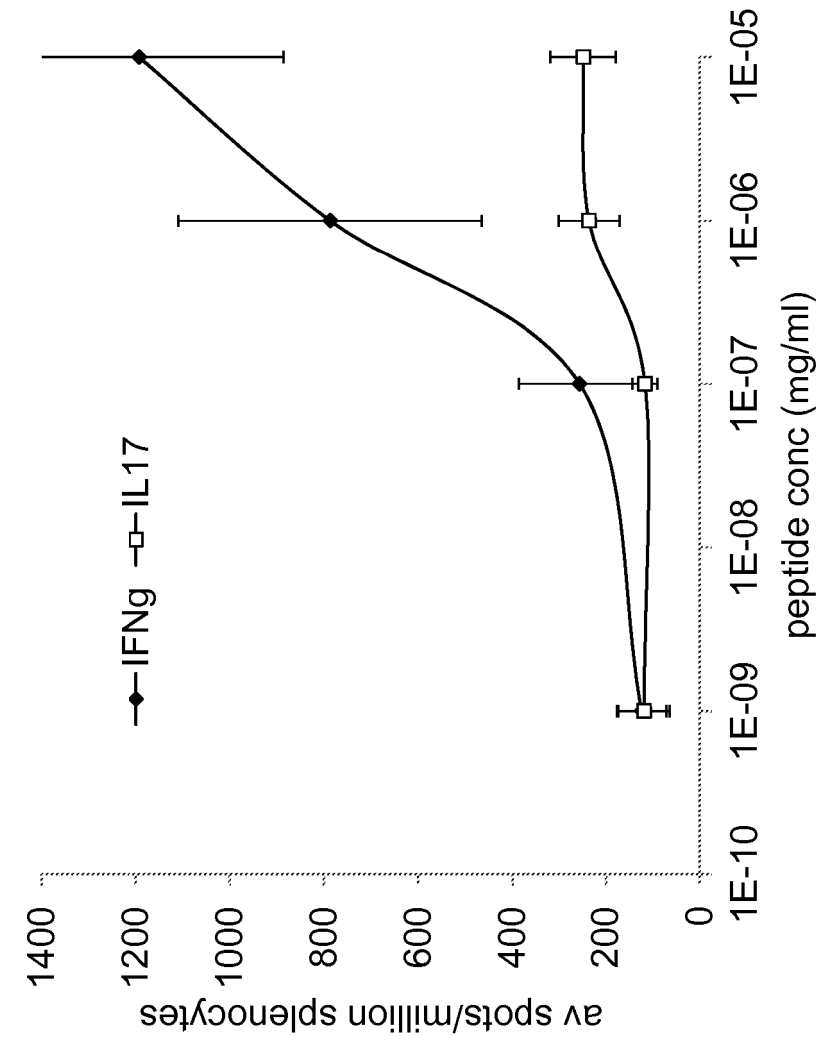



Figure 11 contd
(b)

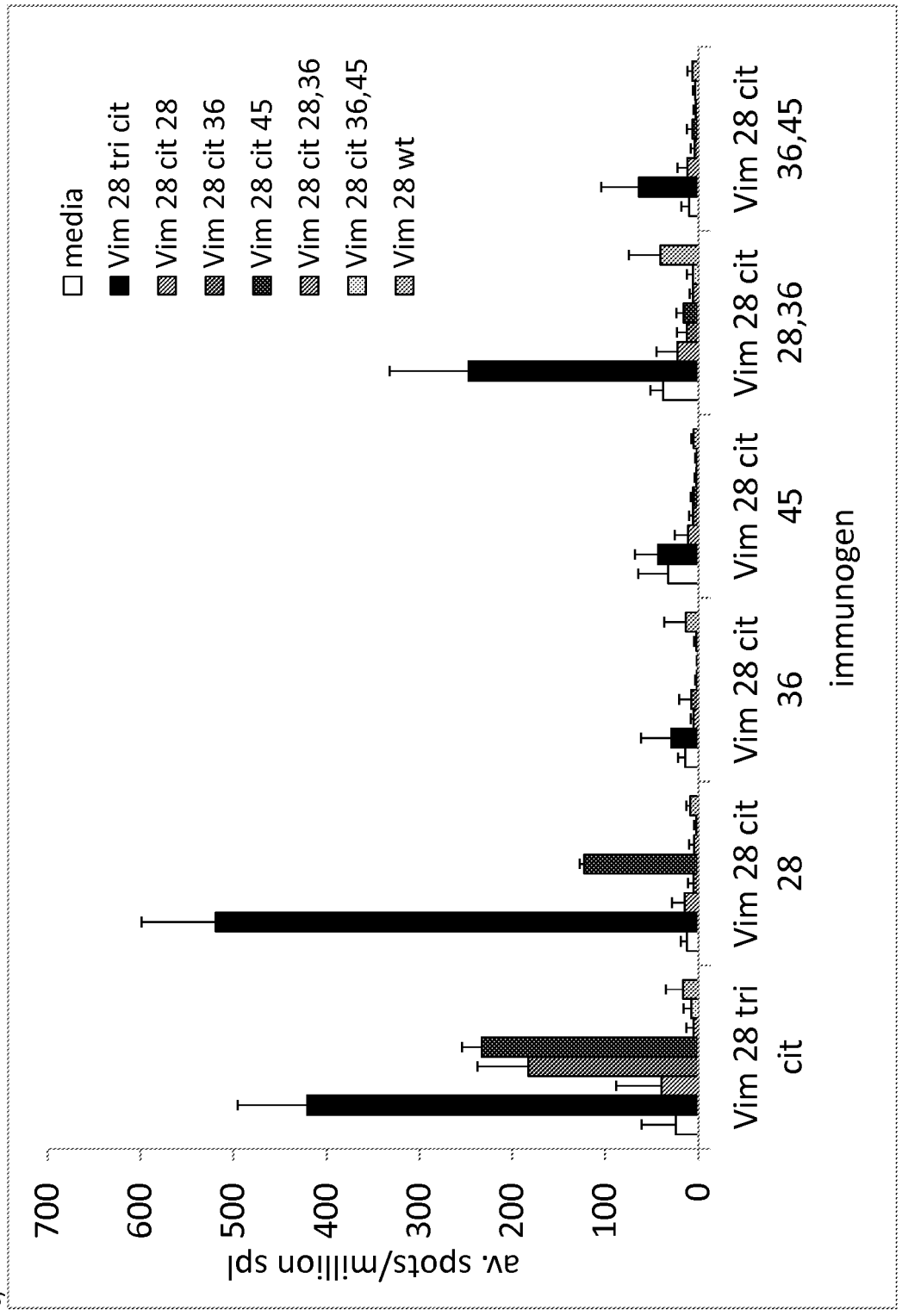



Figure 11 contd

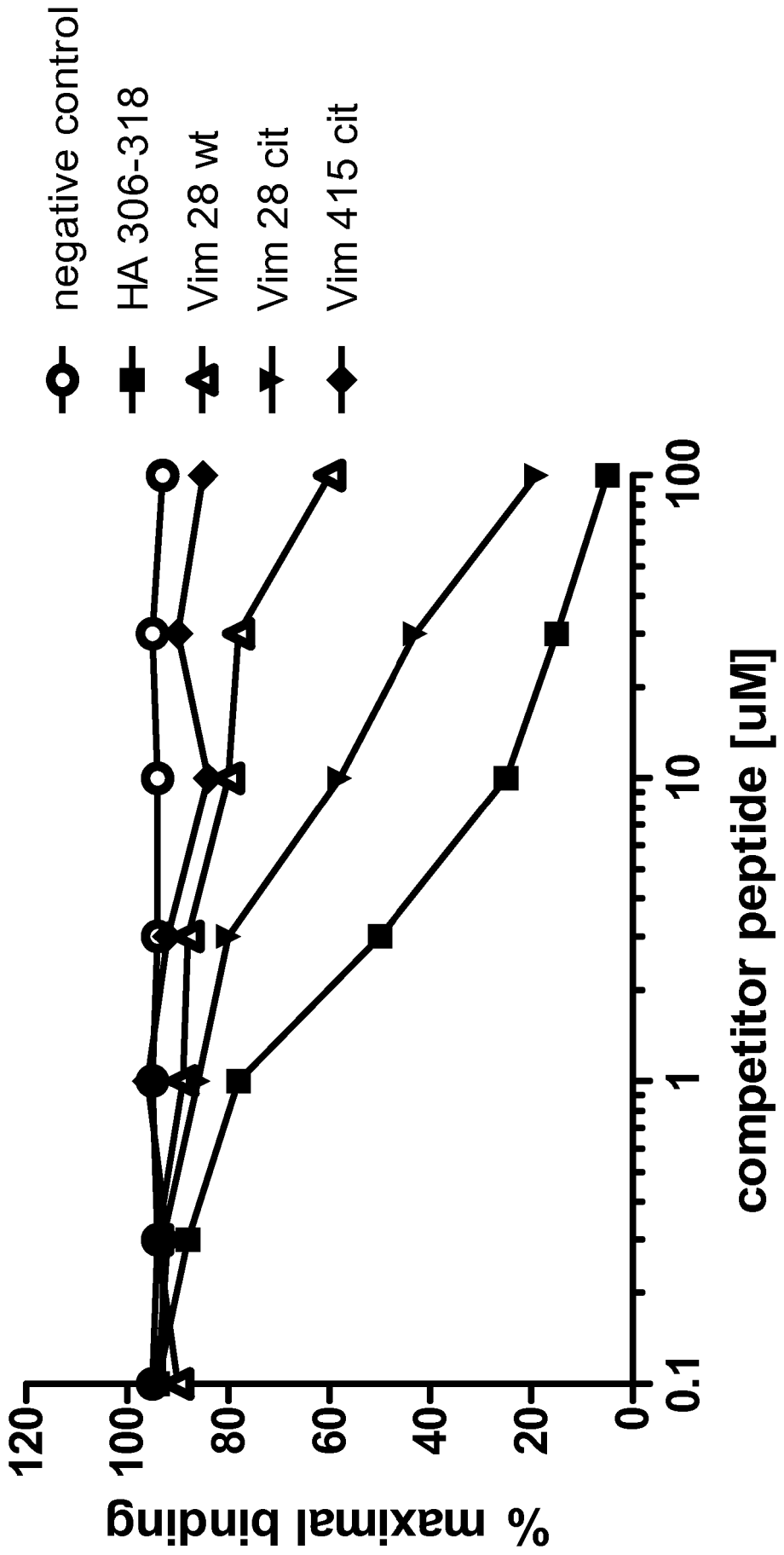


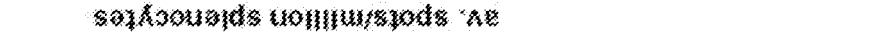

Figure 12

SUBSTITUTE SHEET (RULE 26)

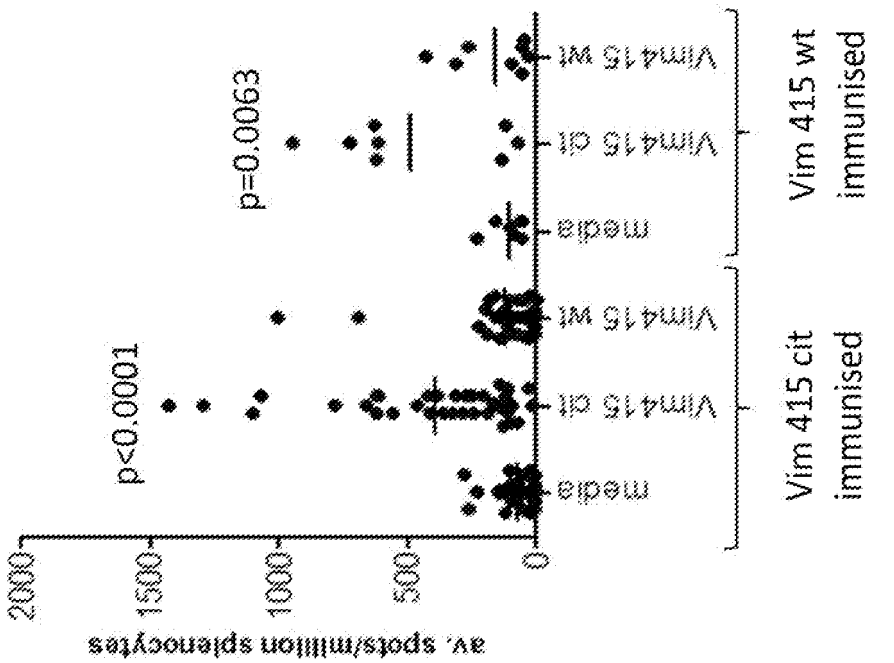
Figure 13

(a)

(i)




(ii)



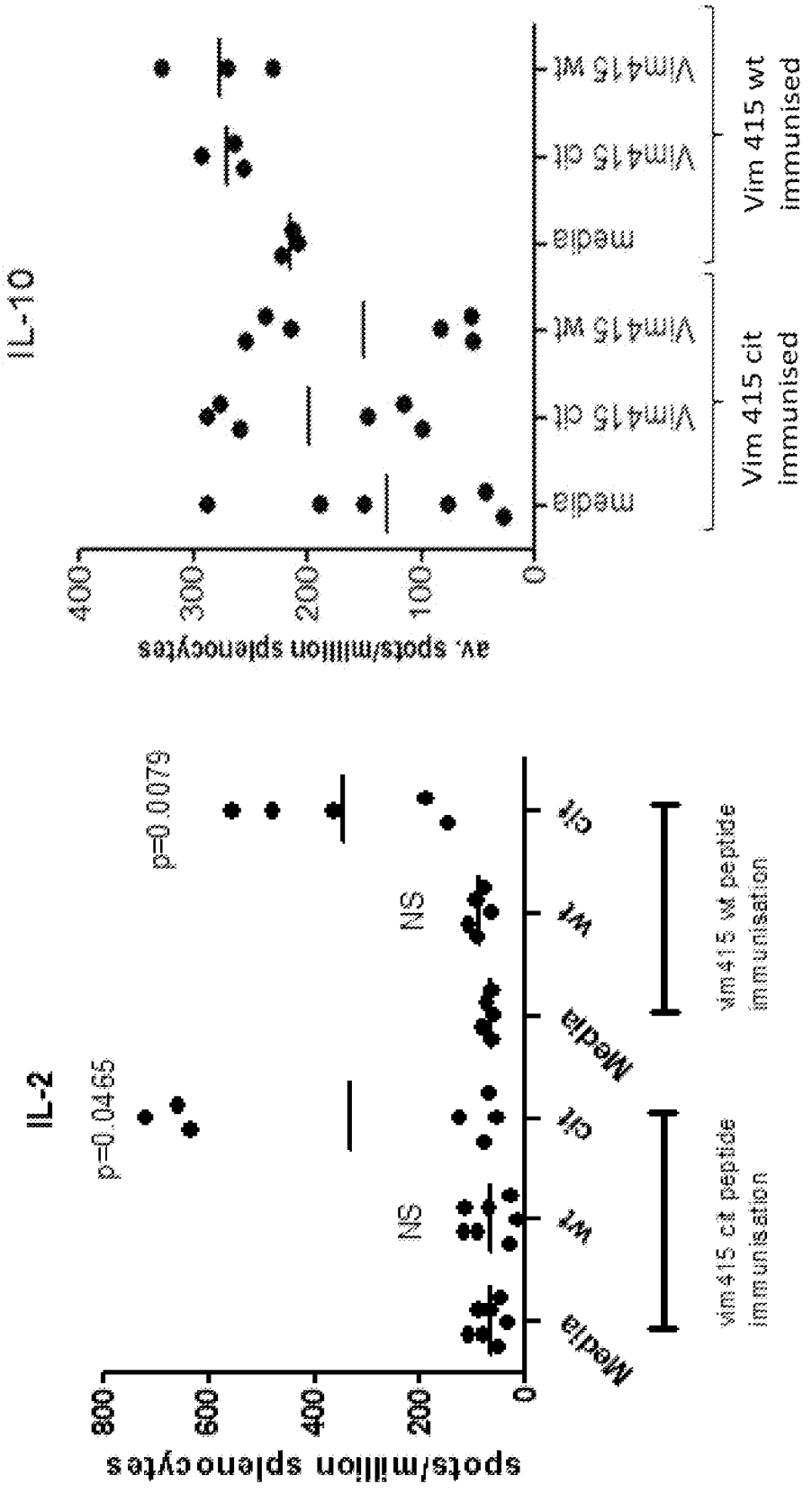



Figure 13 contd

(b)

SUBSTITUTE SHEET (RULE 26)

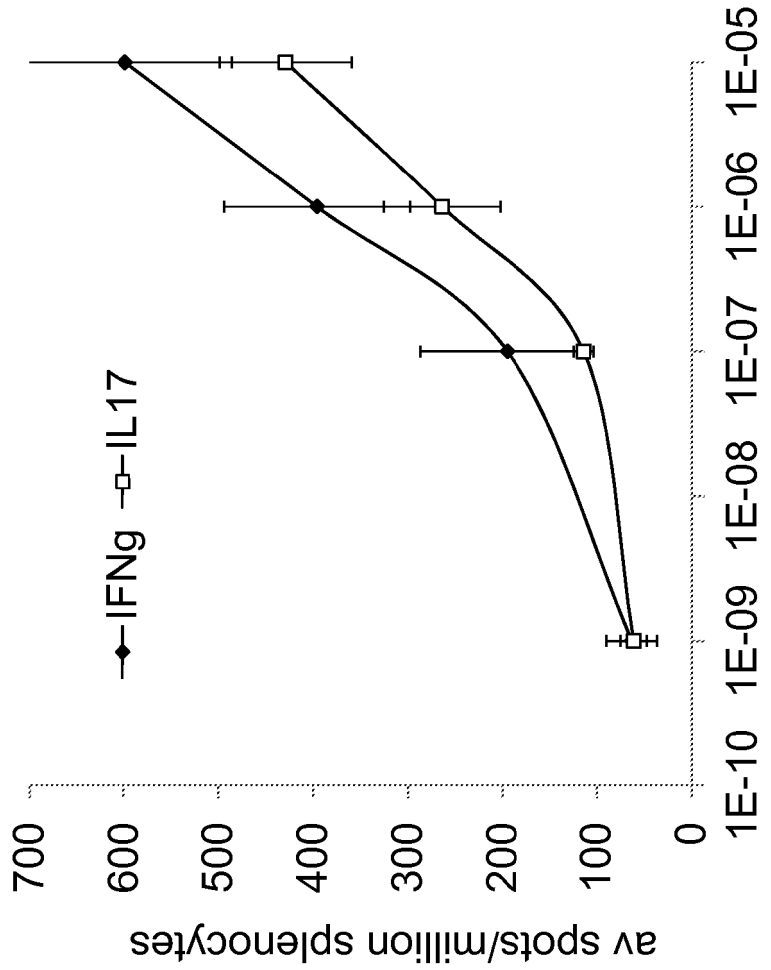
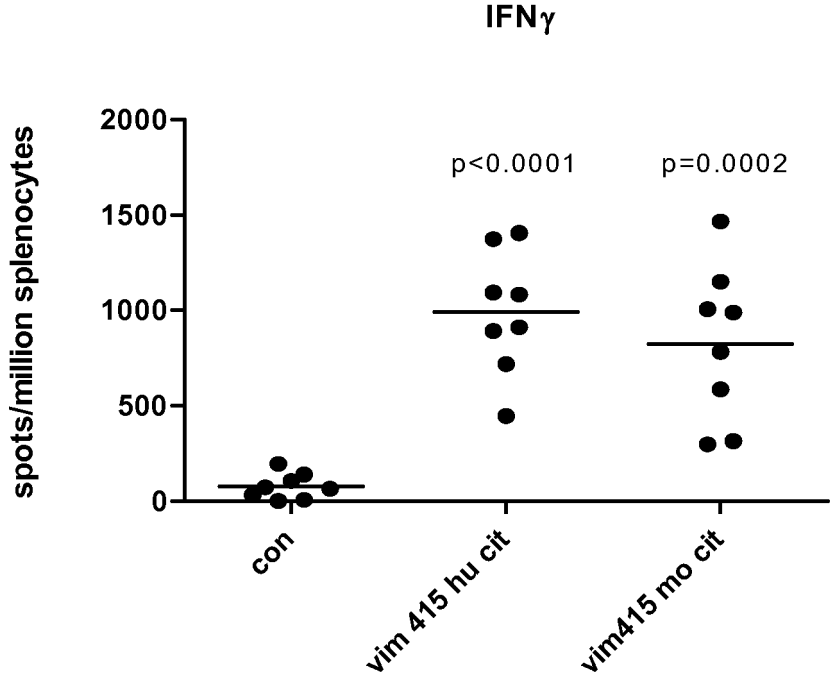

IFNg
IL17
av spots/million splenocytes
700
600
500
400
300
200
100
0
1E-10
1E-09
1E-08
1E-07
1E-06
1E-05
peptide conc (mg/ml)

Figure 14

(i)




(ii)

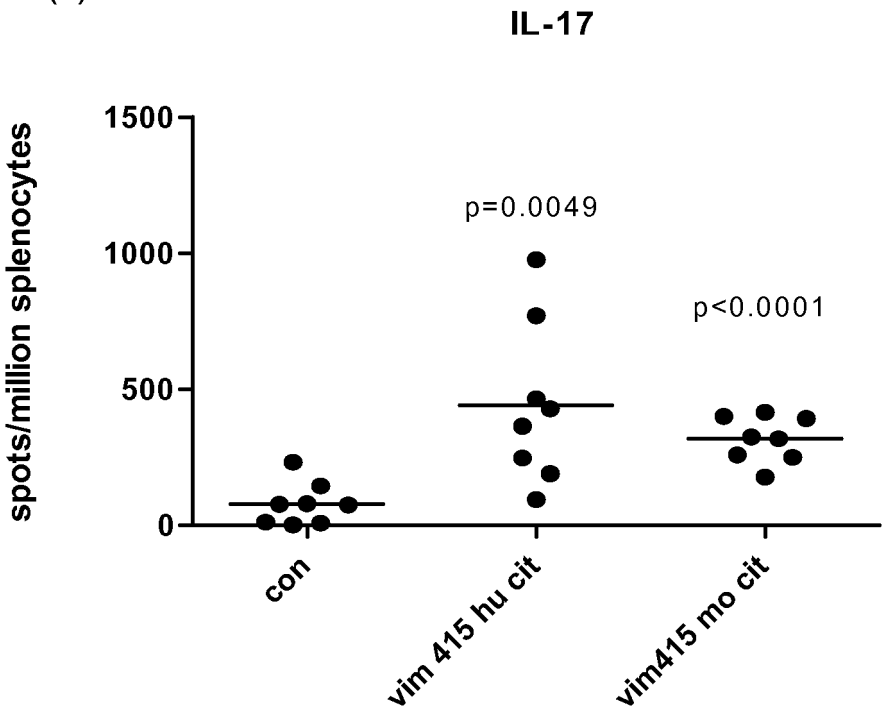
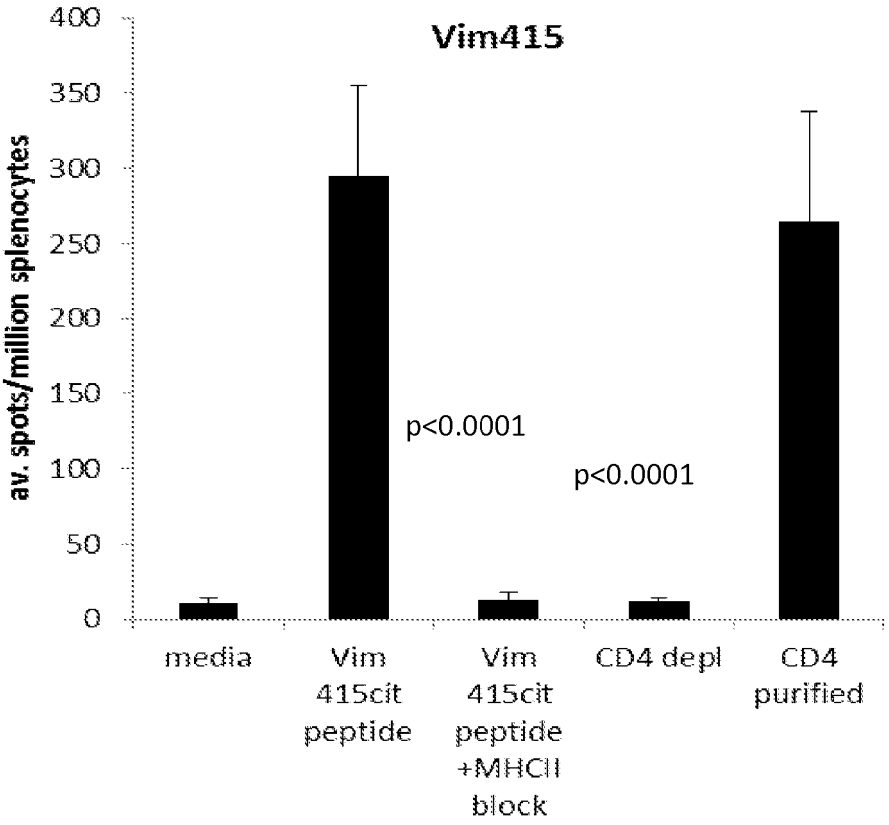


Figure 15

a)


Vim415
av. spots/million splenocytes
400
350
300
250
200
150
100
50
0
p<0.0001
p<0.0001
media
Vim 415cit peptide
Vim 415cit peptide +MHCII block
CD4 depl
CD4 purified

b)

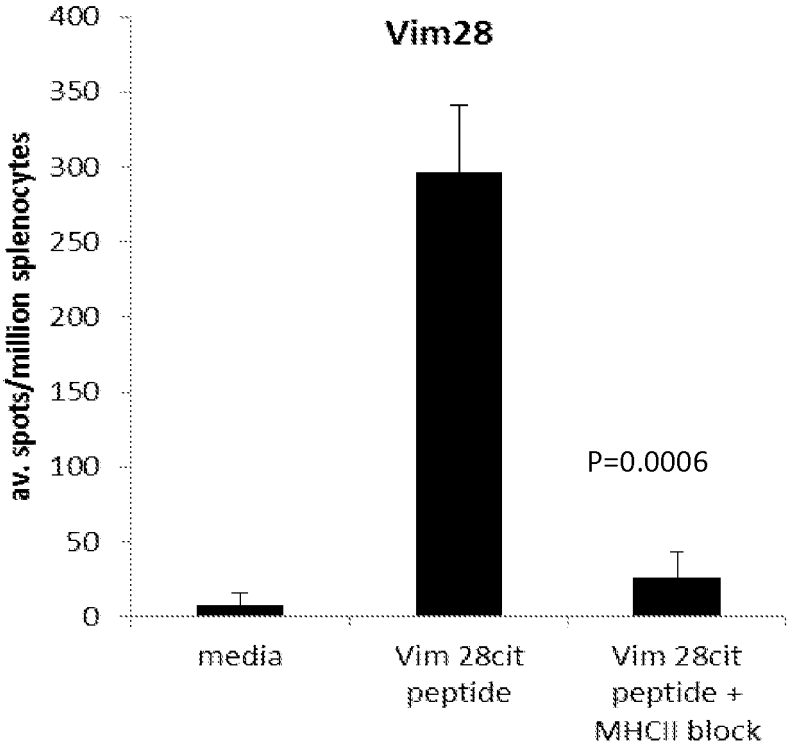
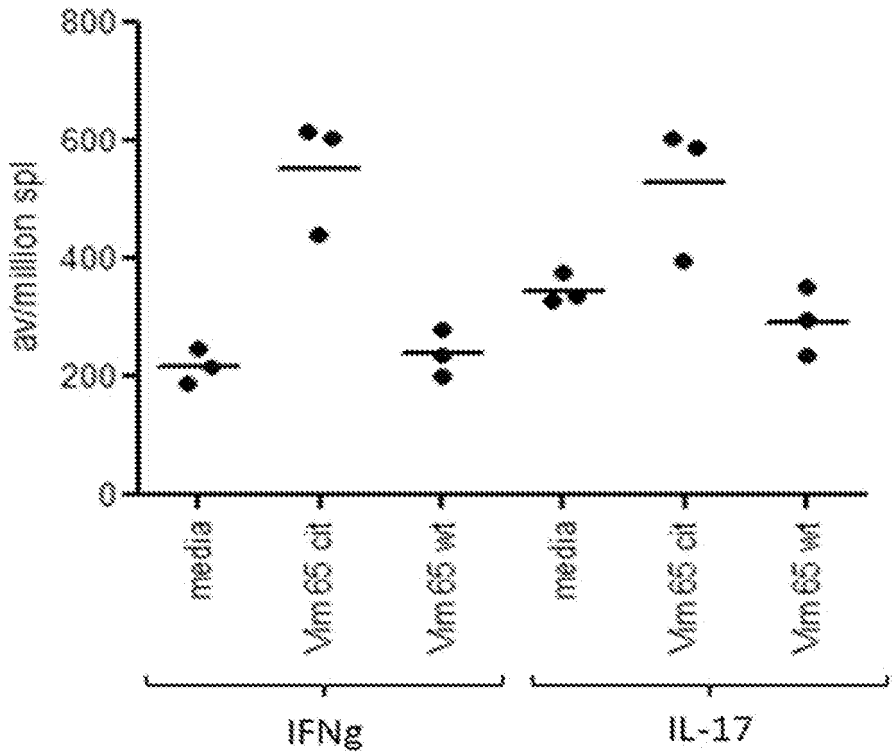

Vim28
av. spots/million splenocytes
400
350
300
250
200
150
100
50
0
P=0.0006
media
Vim 28cit peptide
Vim 28cit peptide + MHCII block

Figure 16

a)


800
600
400
200
0
av/million spl
media
Vm 65 cit
Vm 65 wt
media
Vm 65 cit
Vm 65 wt
IFNg
IL-17

b)

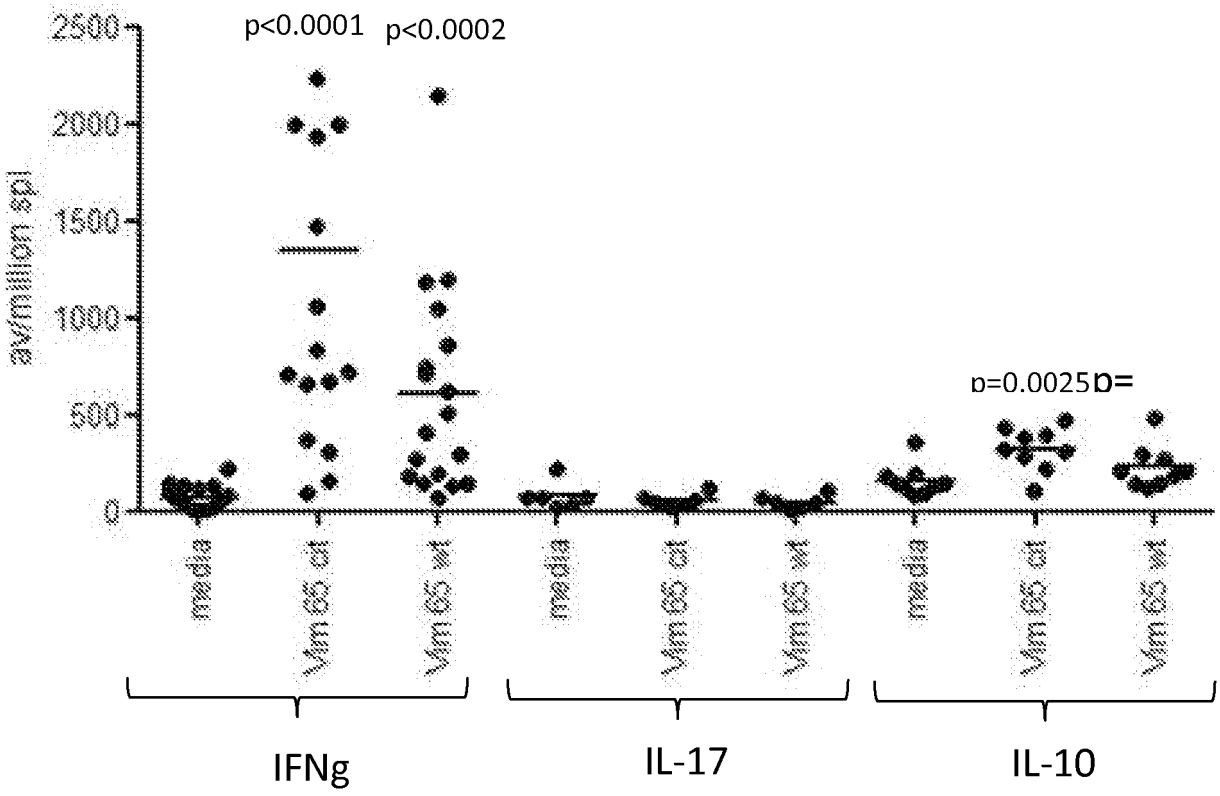

2500
2000
1500
1000
500
0
av/million spl
p<0.0001
p<0.0002
p=0.0025
media
Vm 65 cit
Vm 65 wt
media
Vm 65 cit
Vm 65 wt
media
Vm 65 cit
Vm 65 wt
IFNg
IL-17
IL-10

Figure 16 contd

c)

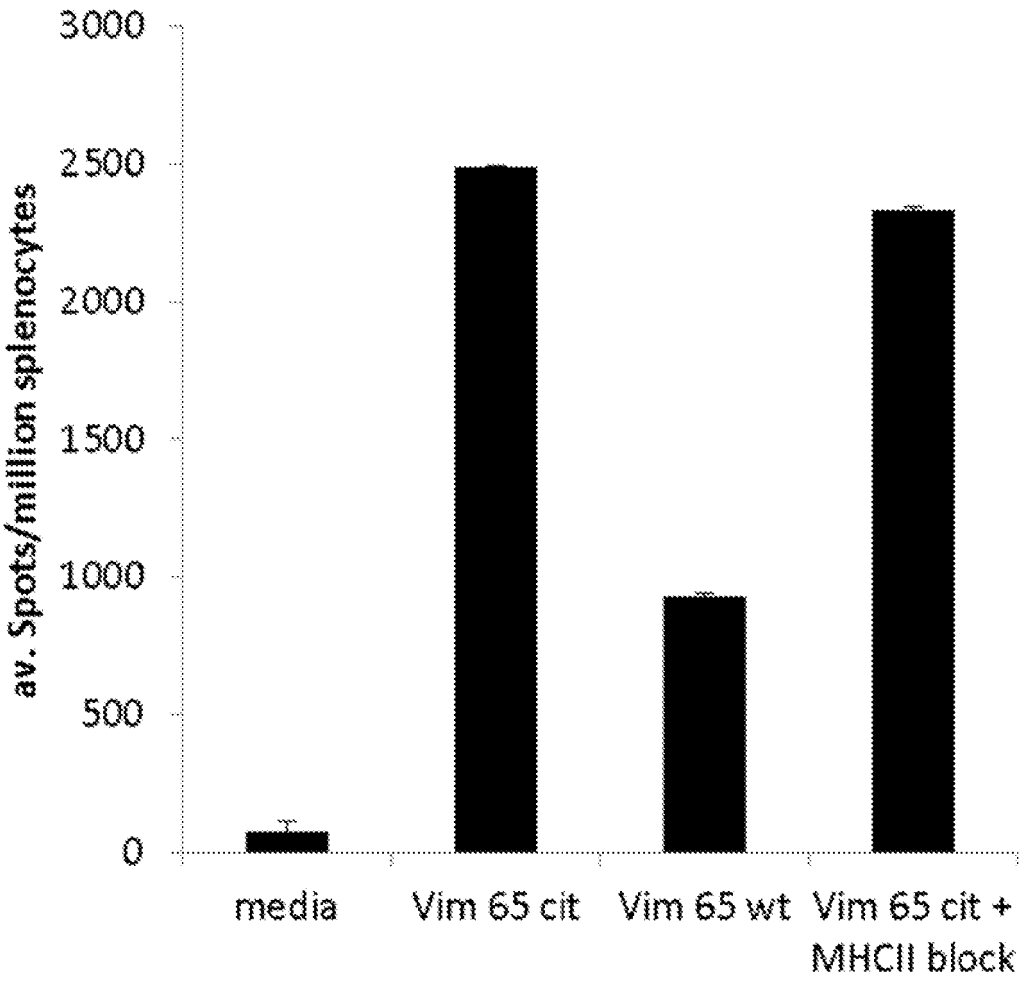


Figure 16 contd



d)

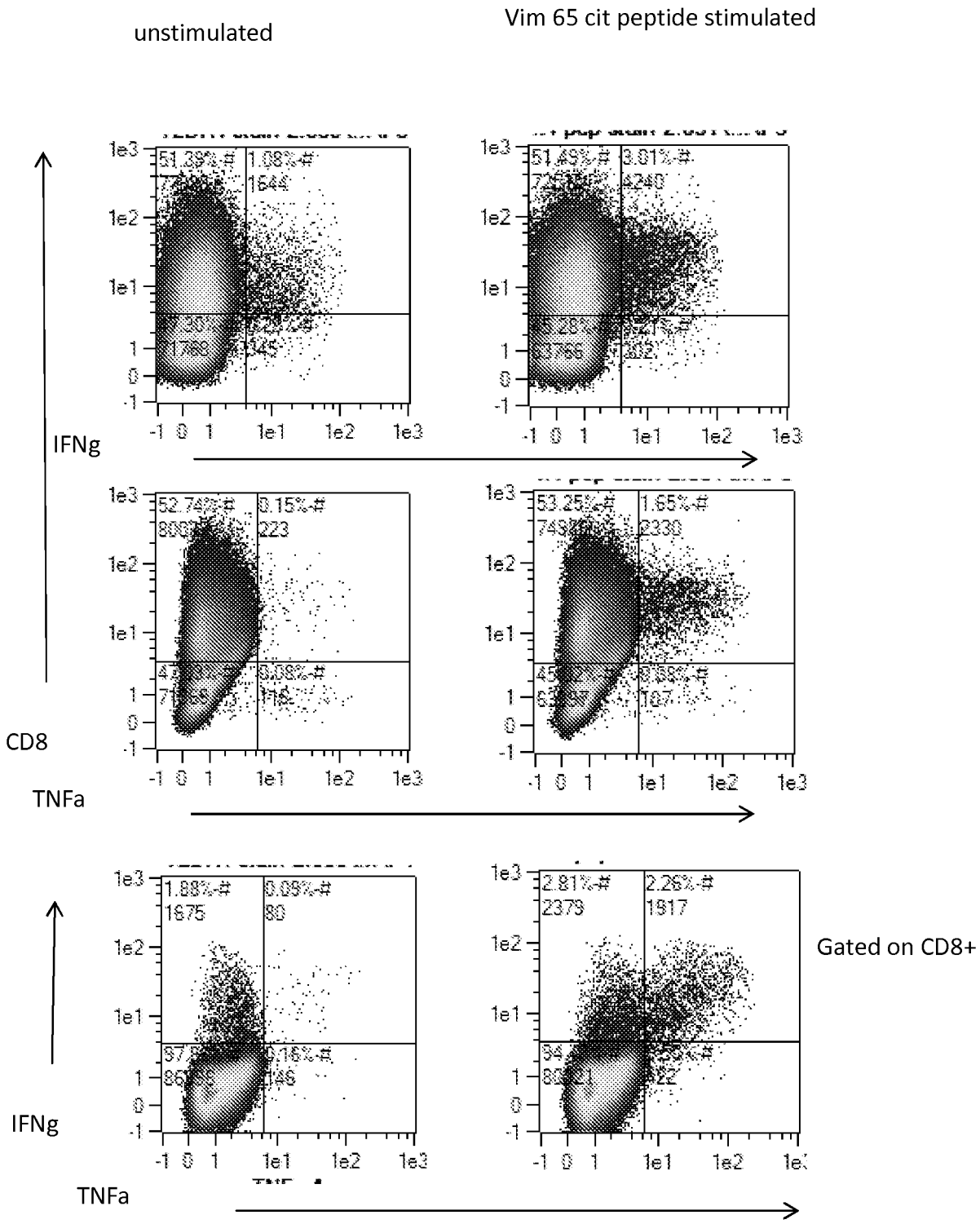
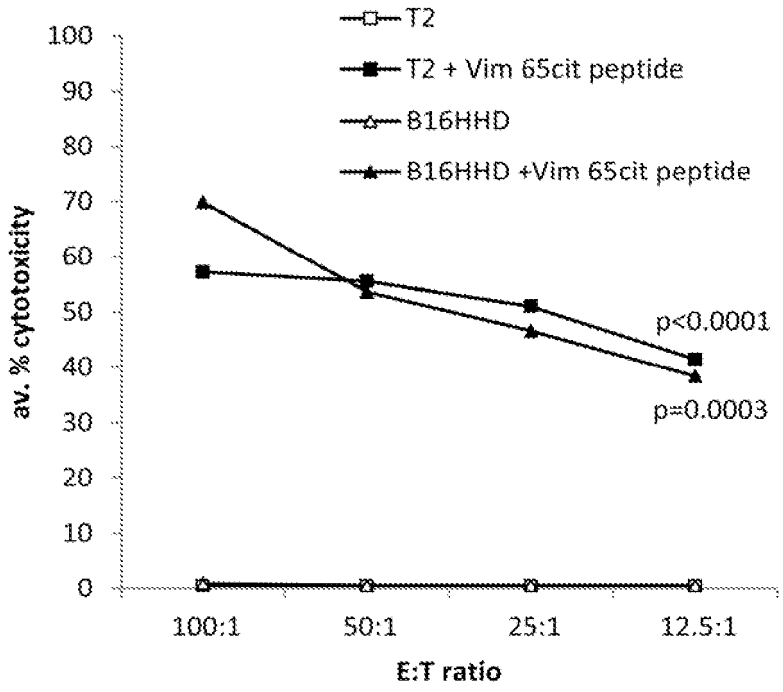


Figure 16 contd

e)




f)

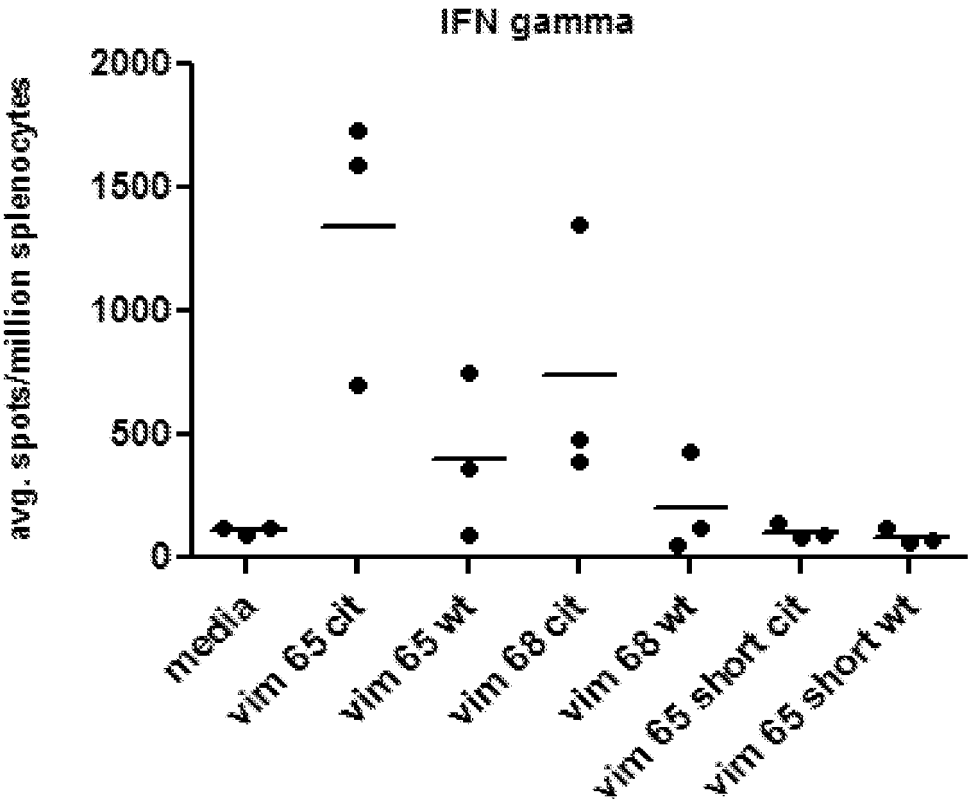


Figure 16 contd

g)

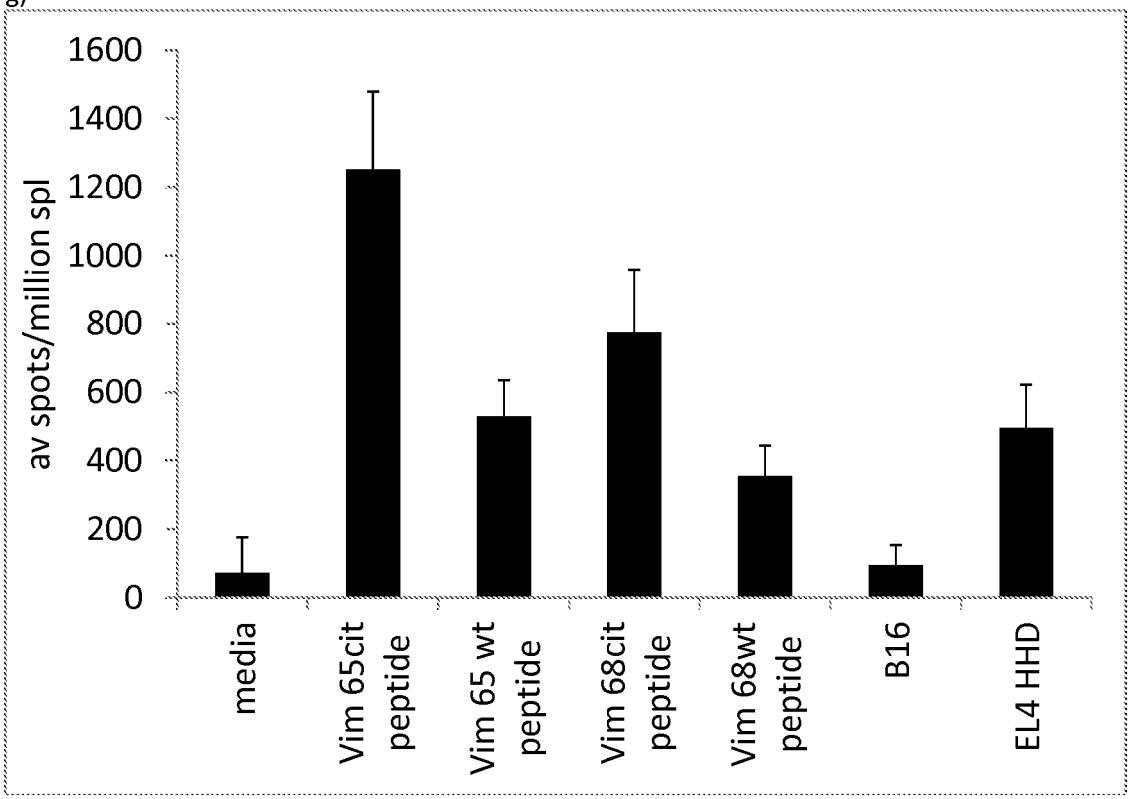
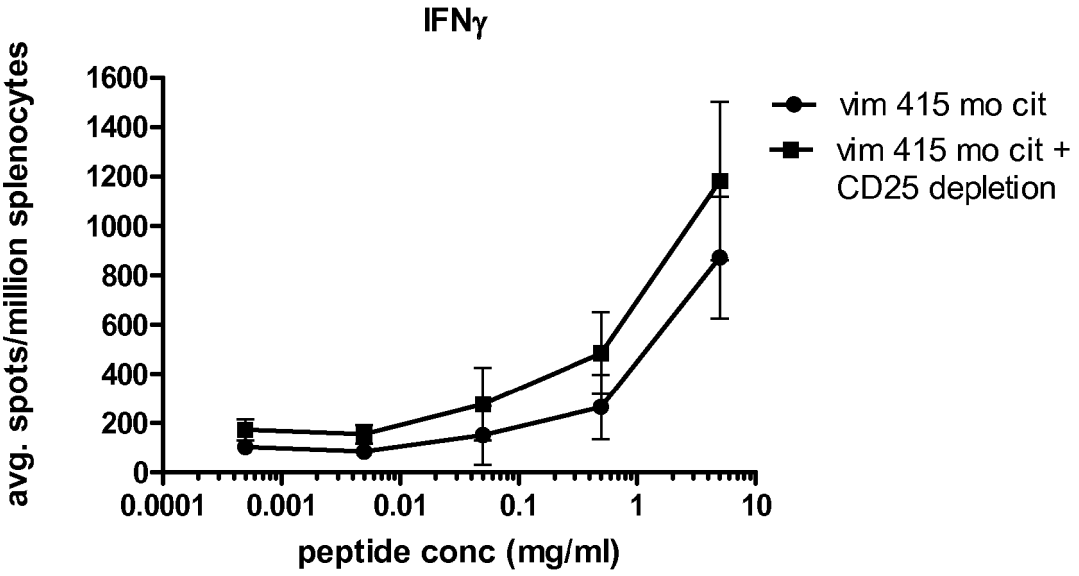



Figure 17



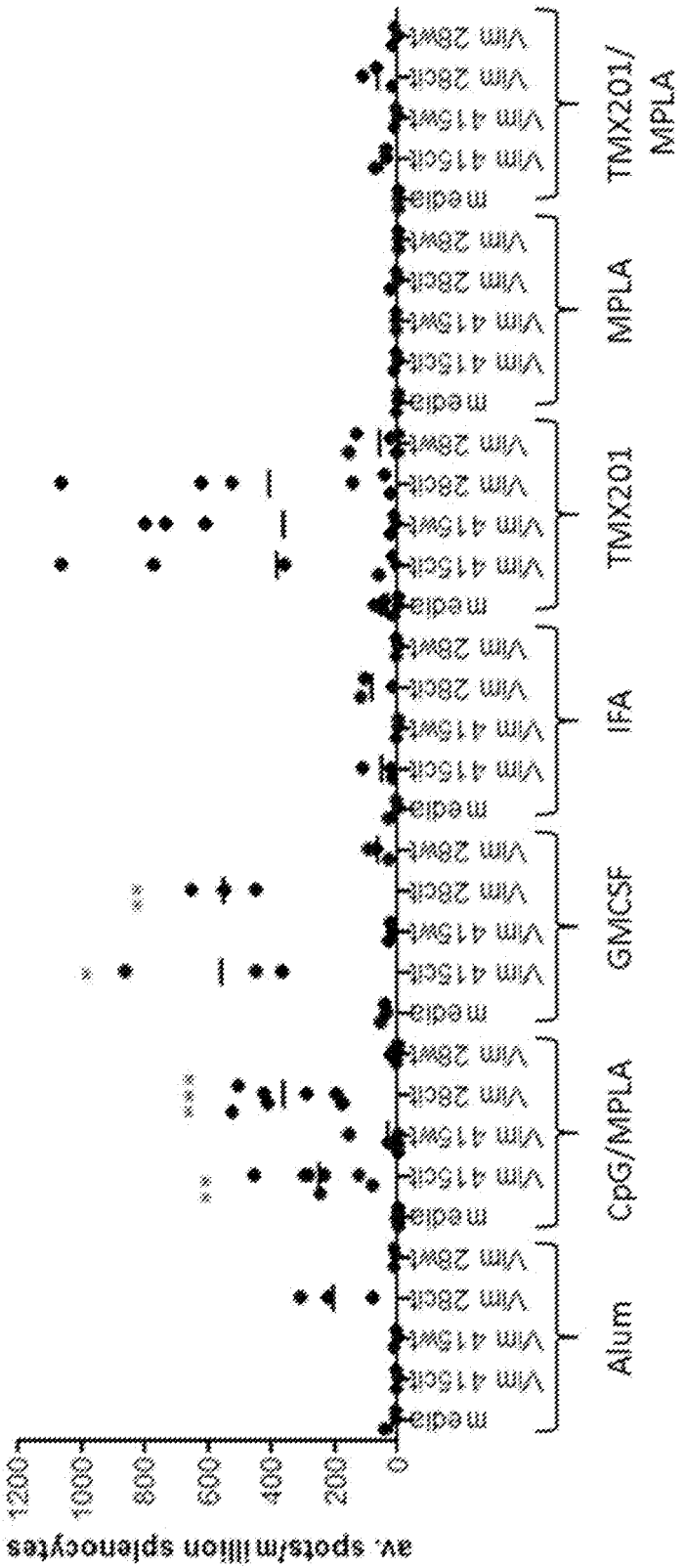



Figure 18
*p<0.05, **p<0.001, ***p<0.0001

(i)

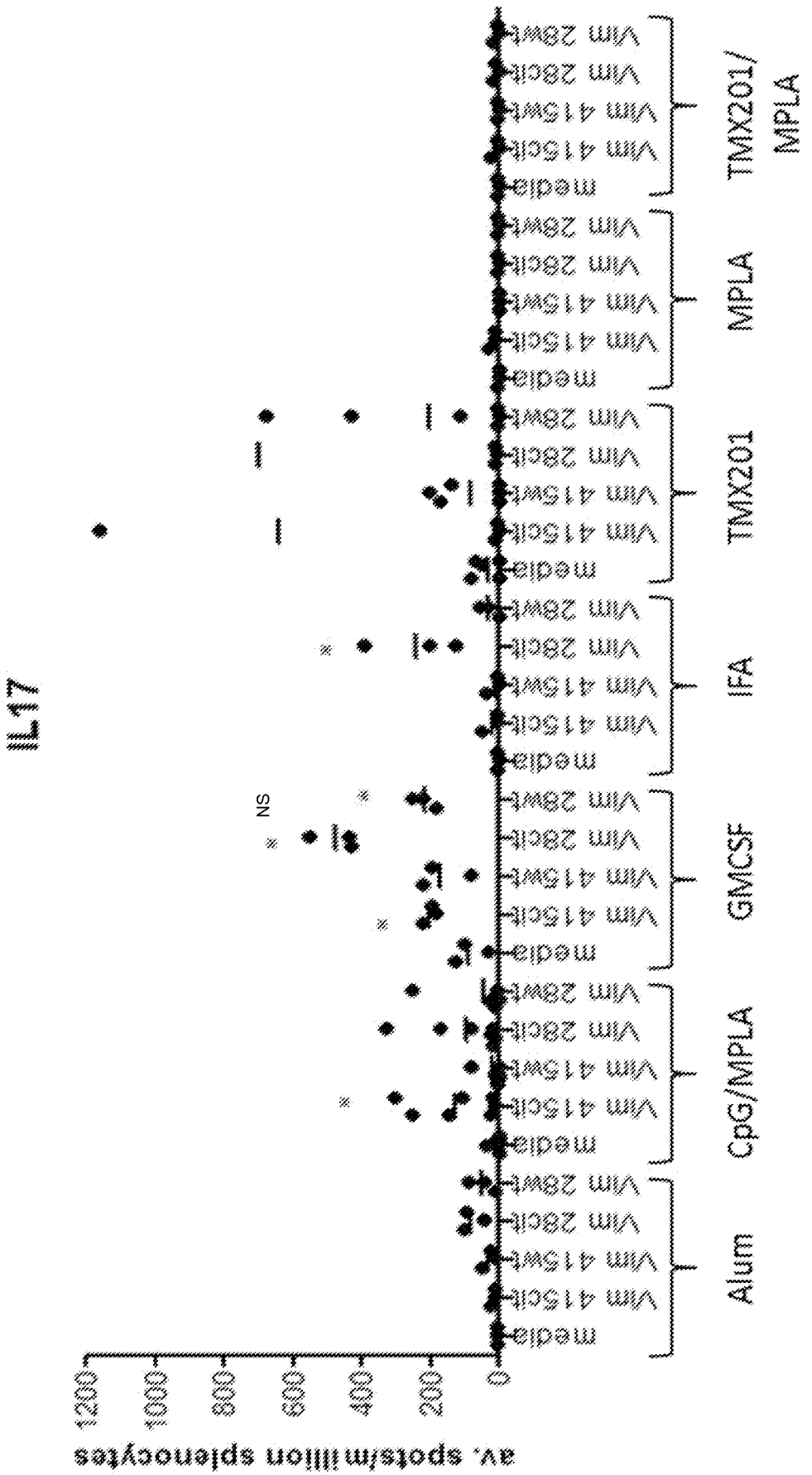



Figure 18 contd
(ii)

SUBSTITUTE SHEET (RULE 26)

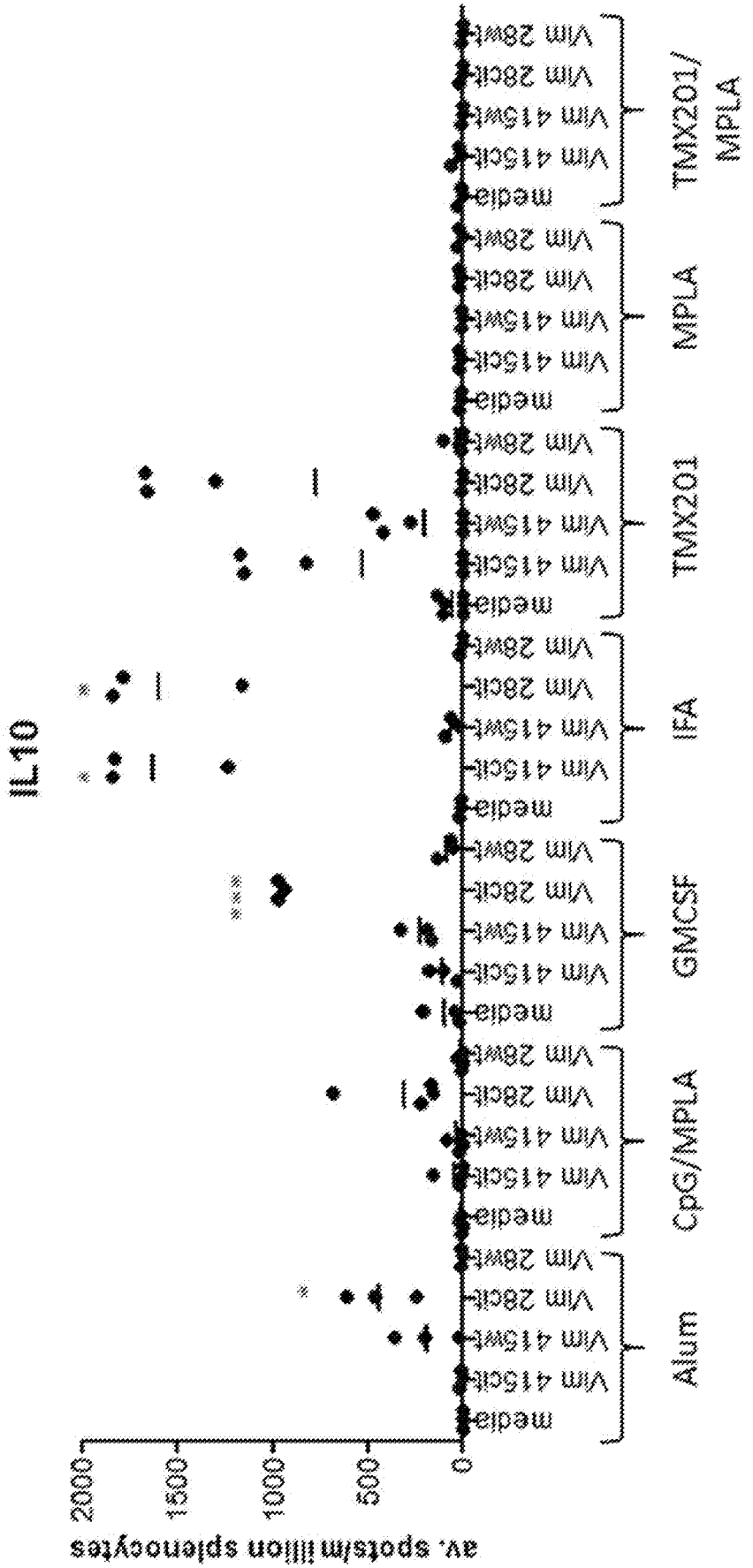


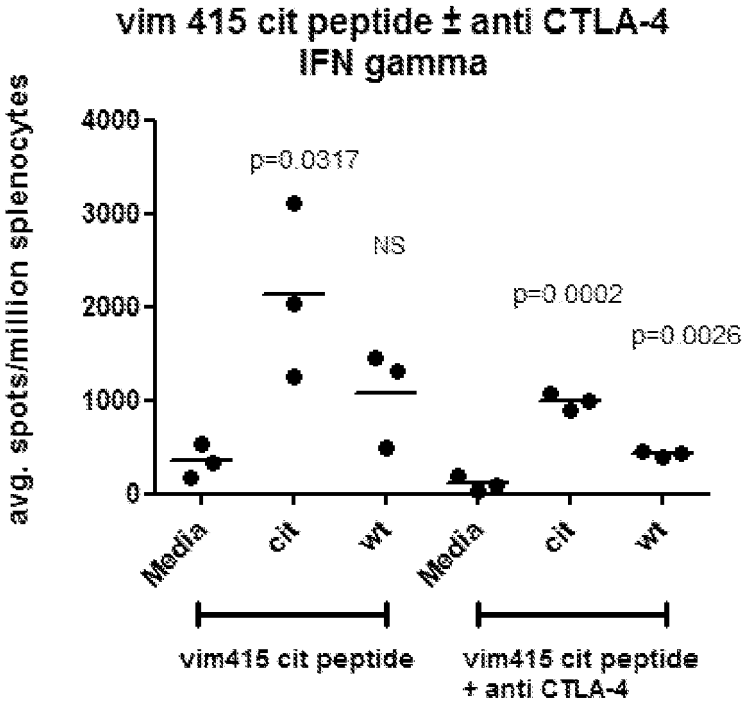

Figure 18 contd

(iii)

SUBSTITUTE SHEET (RULE 26)

Figure 19

(i)




(ii)

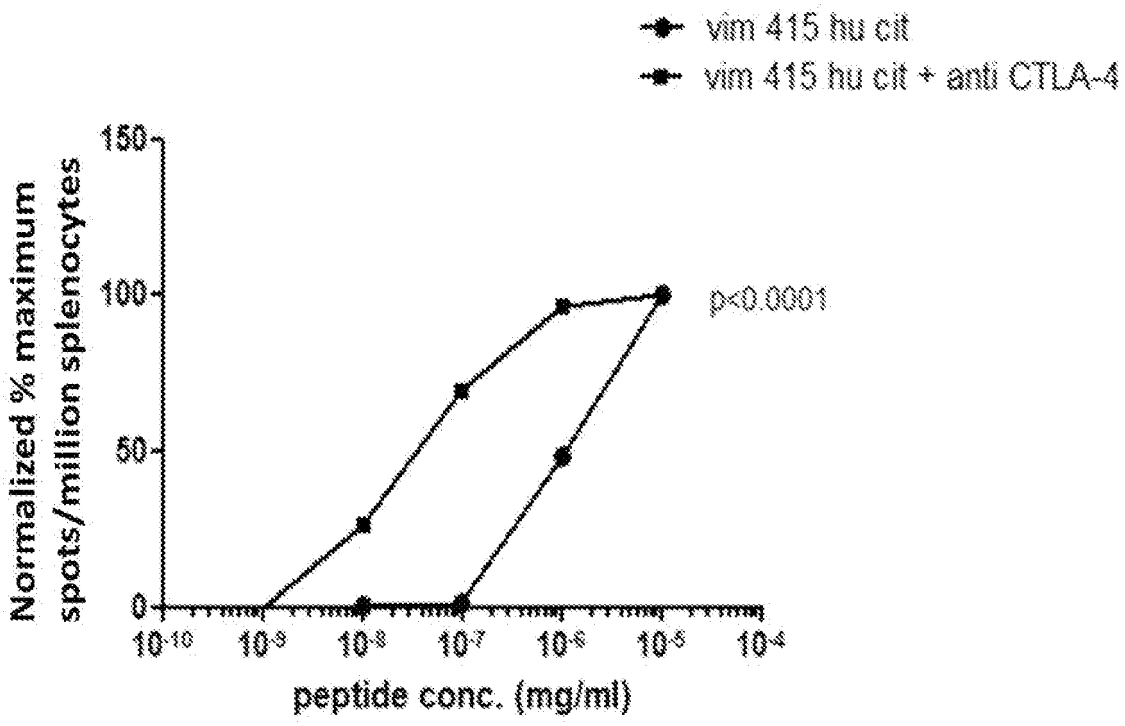


Figure 20

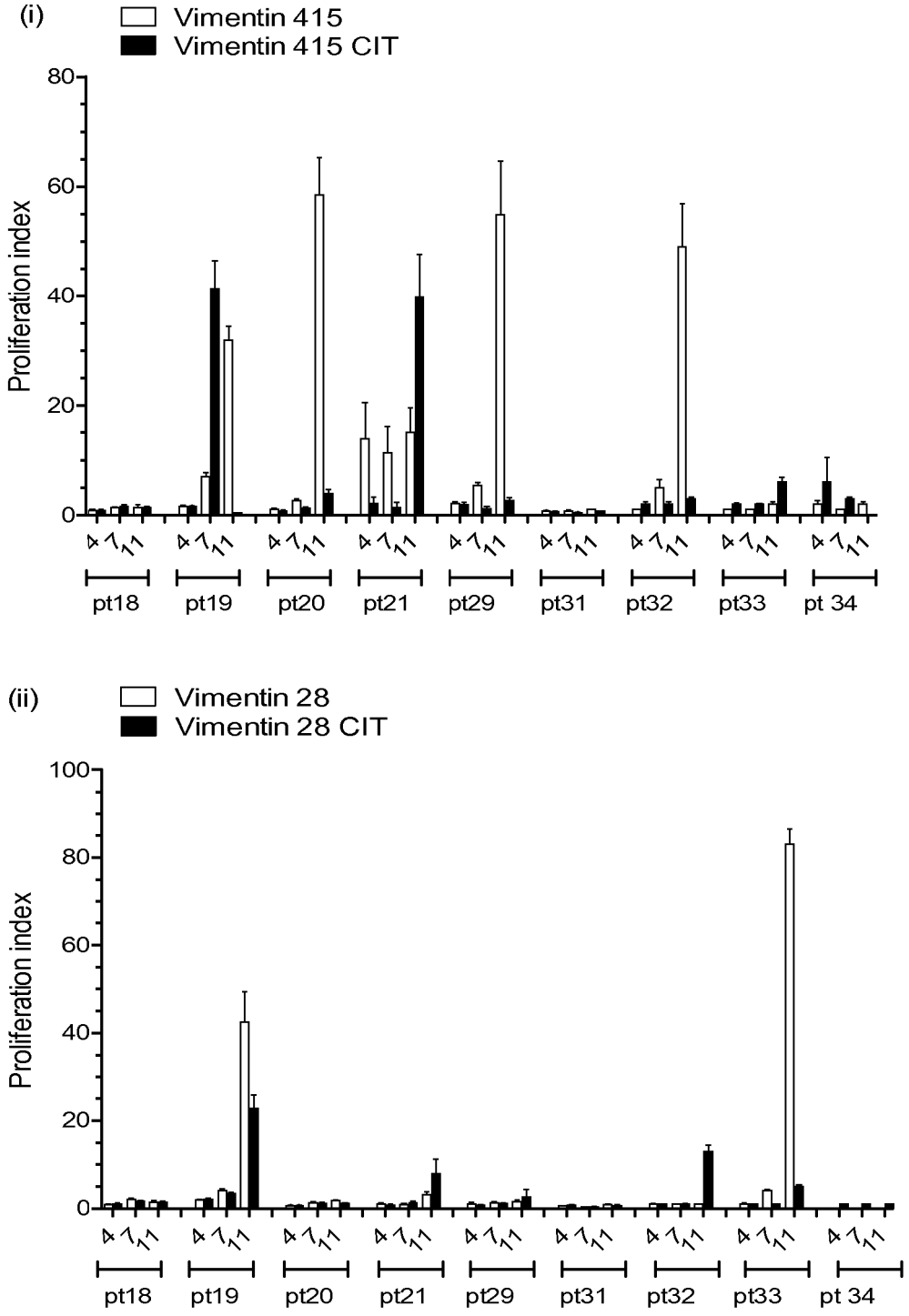
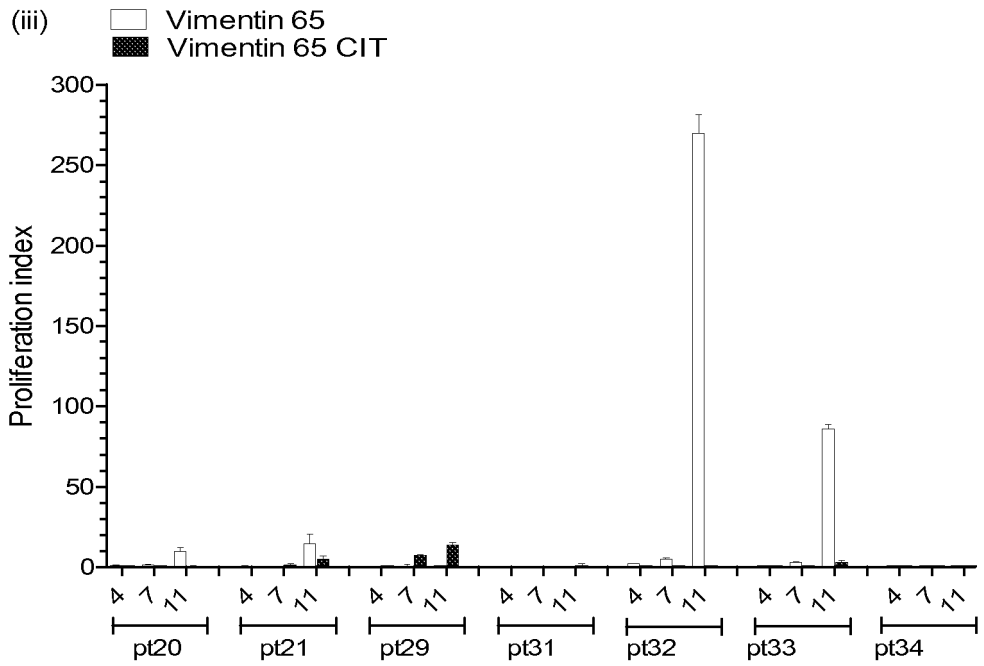

(i)
Vimentin 415
Vimentin 415 CIT
Proliferation index
0
20
40
60
80
4
7
11
pt18
pt19
pt20
pt21
pt29
pt31
pt32
pt33
pt 34
(ii)
Vimentin 28
Vimentin 28 CIT
Proliferation index
0
20
40
60
80
100
4
7
11
pt18
pt19
pt20
pt21
pt29
pt31
pt32
pt33
pt 34

Figure 20 cont



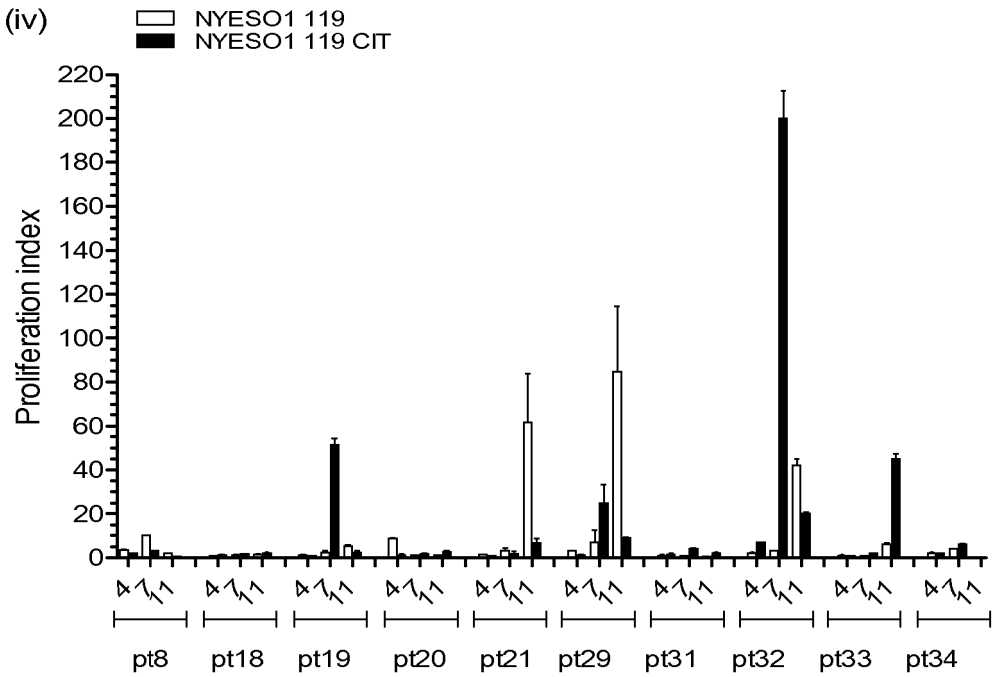
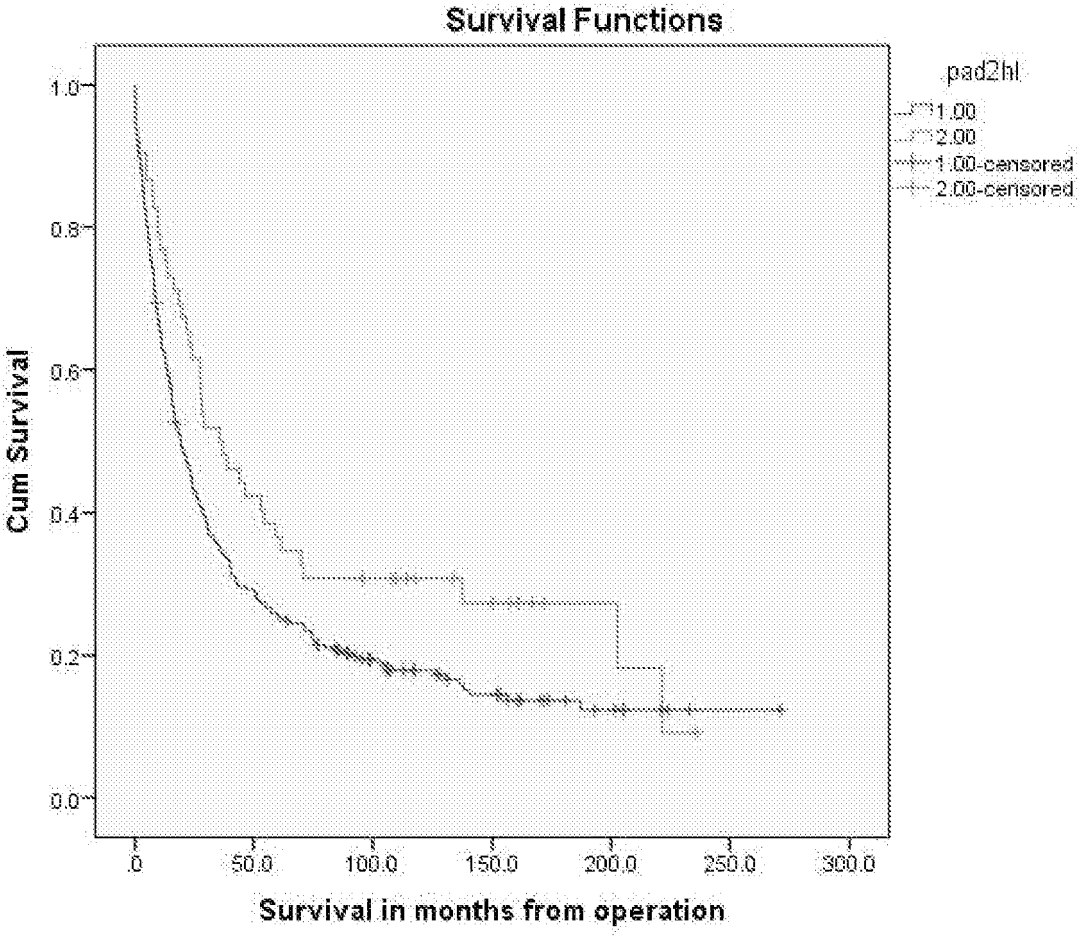



Figure 21kaplan Meier Survival of patients whose tumours express PAD or HMGB1

a) Ovarian tumours expressing PAD2

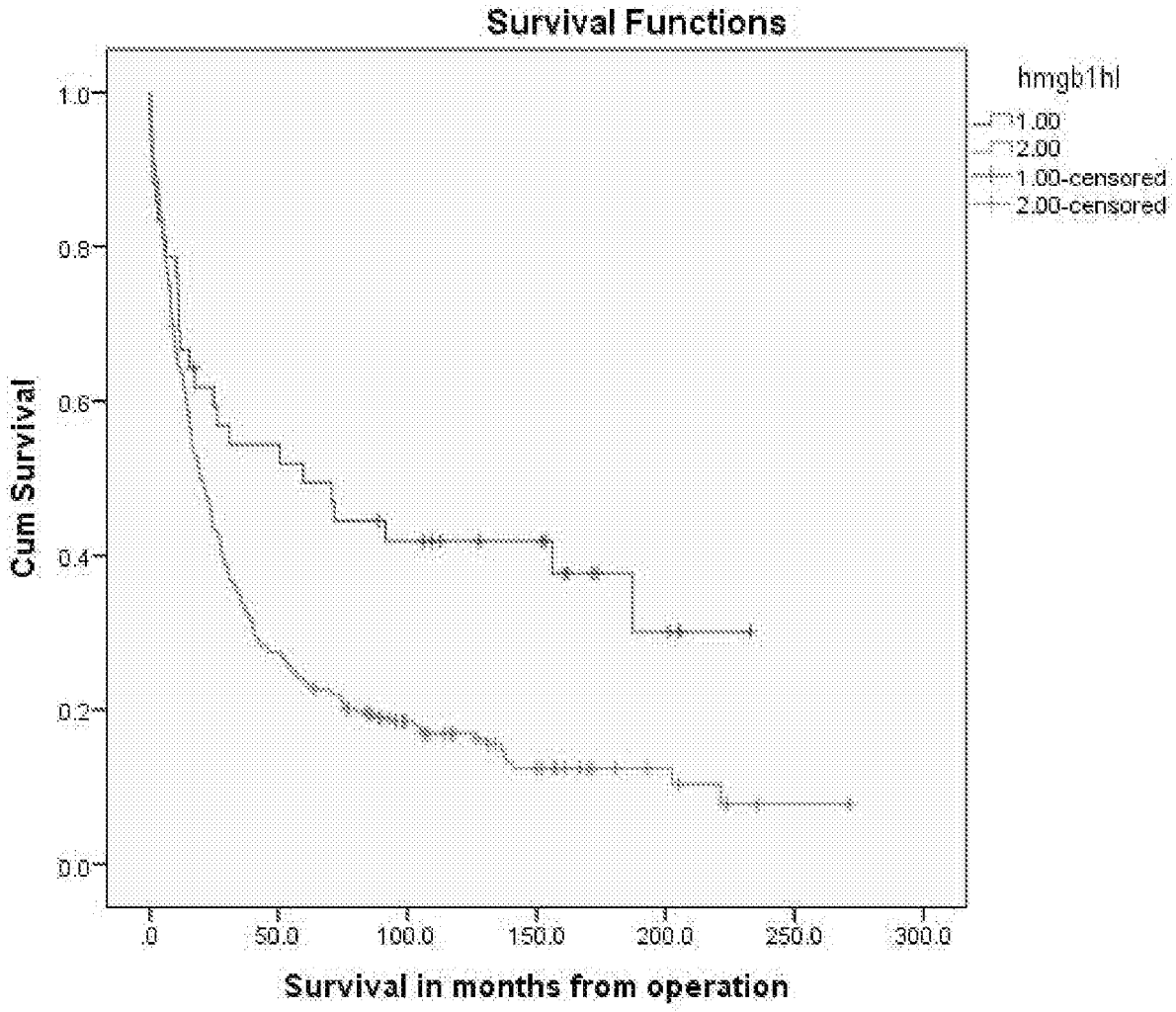



**Overall Comparisons**

| | Chi-Square | df | Sig. |
|---|---|---|---|
| Log Rank (Mantel-Cox) | 4.570 | 1 | .033 |

Test of equality of survival distributions for the different levels of pad2hl.

Figure 21 contd
b) Ovarian tumours expressing HMGB1



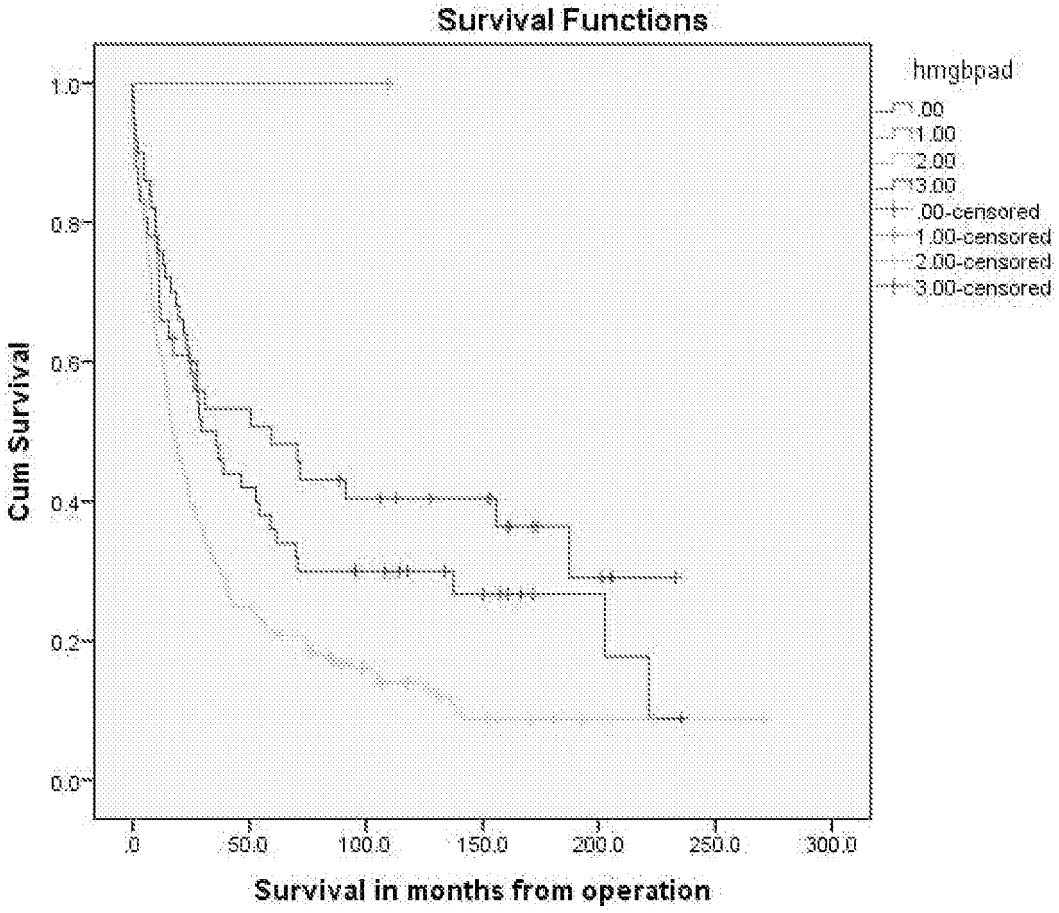

**Overall Comparisons**

| | Chi-Square | df | Sig. |
|---|---|---|---|
| Log Rank (Mantel-Cox) | 9.642 | 1 | .002 |

Test of equality of survival distributions for the different levels of hmgb1hl.

Figure 21 contd

c) ovarian tumours expressing PAD2 and HMGB1 ( 0 denotes no expression, 1 only HMGB1, 2-only PAD2 and 3 both.



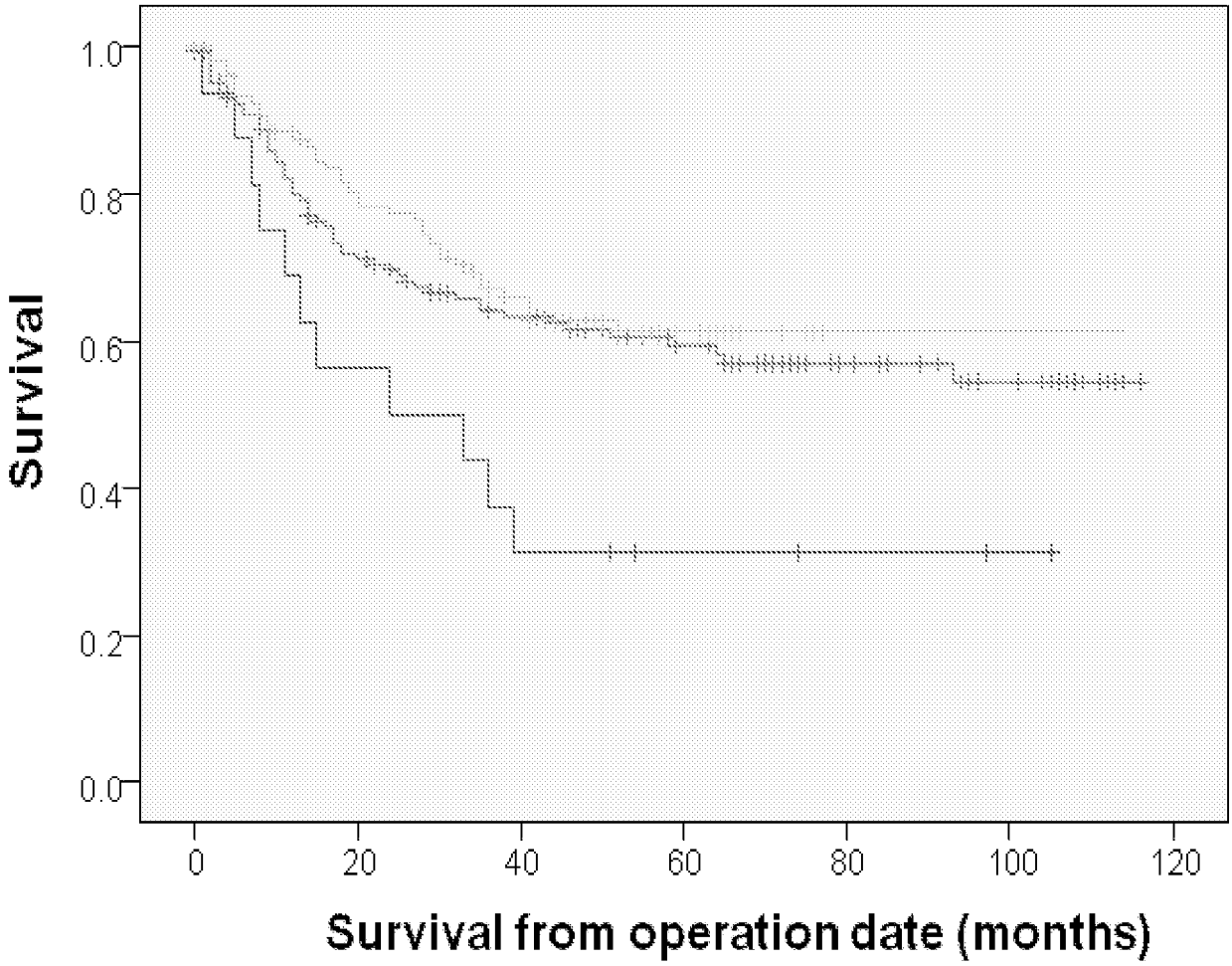

**Overall Comparisons**

| | Chi-Square | df | Sig. |
|---|---|---|---|
| Log Rank (Mantel-Cox) | 17.217 | 3 | .001 |

Test of equality of survival distributions for the different levels of hmgbpad.

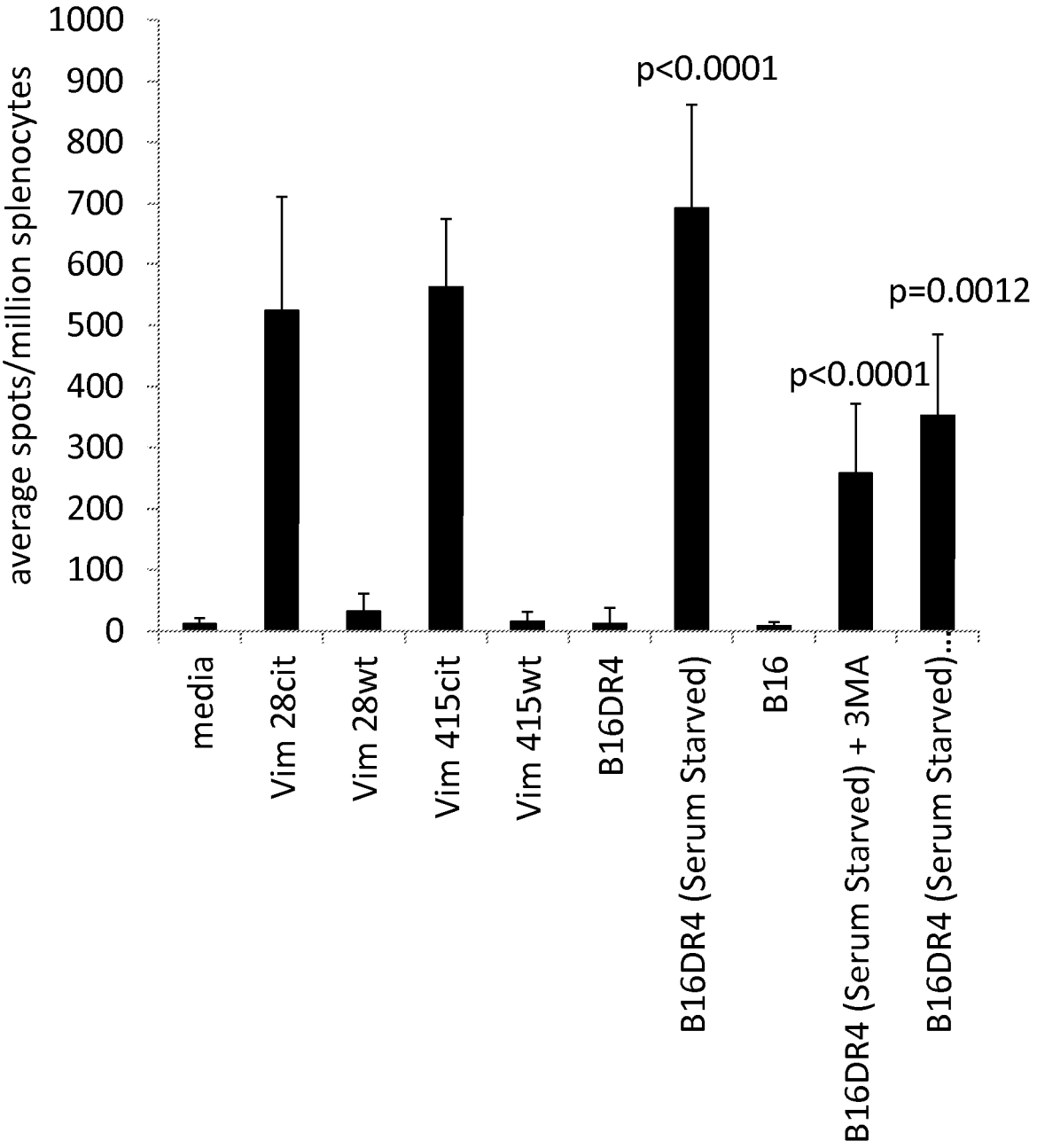
Figure 21 contd

d) colorectal cancer patients expressing PAD4




| | Chi-Square | df | Sig. |
|---|---|---|---|
| Log Rank (Mantel-Cox) | **6.871** | 2 | .032 |

Figure 22
(a)




SUBSTITUTE SHEET (RULE 26)

Figure 22 contd (b)

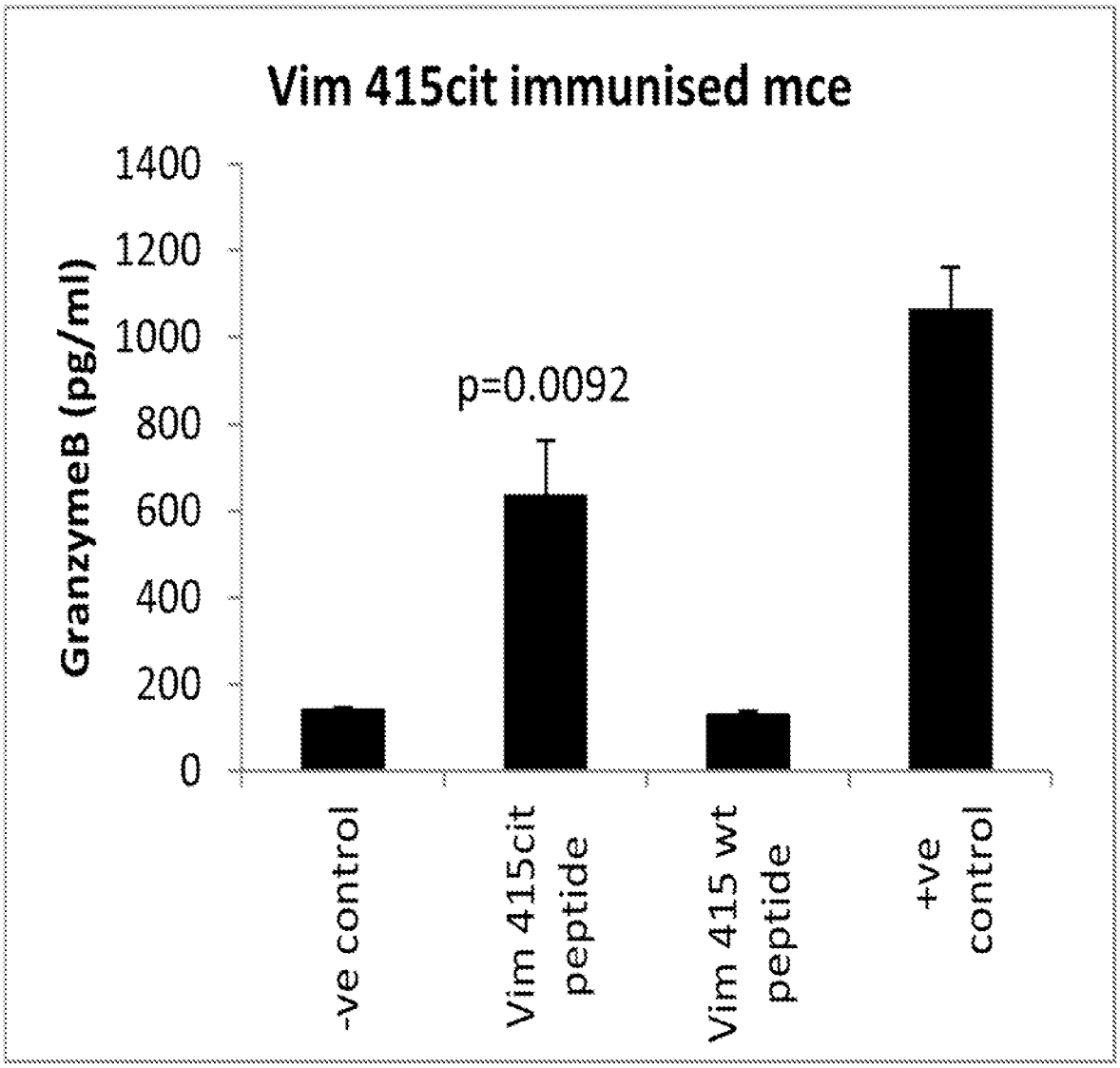
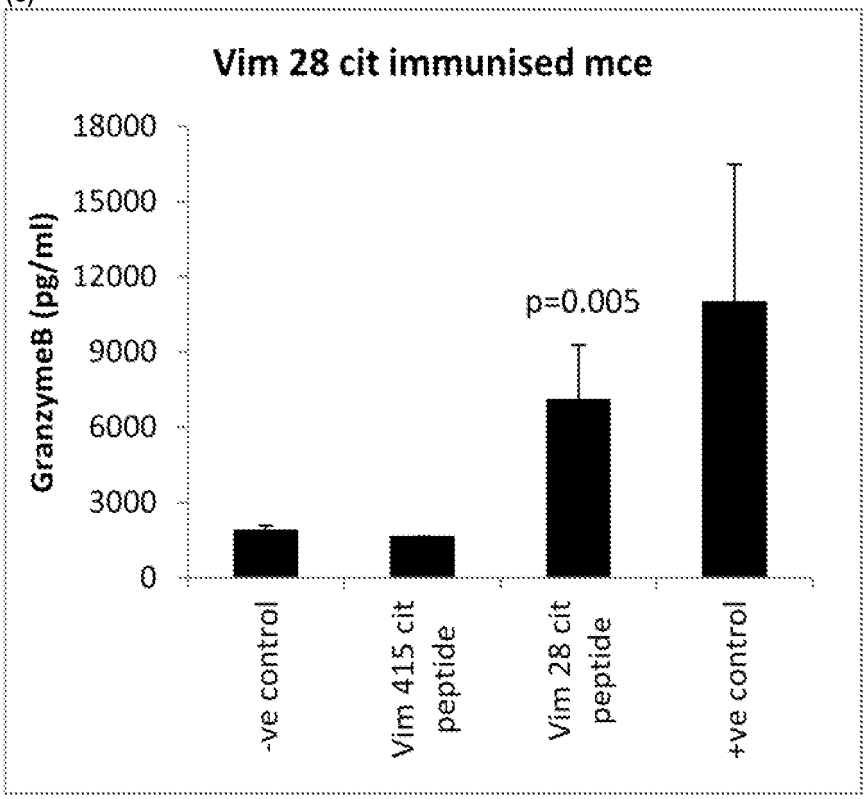


Figure 22 contd

(c)




(d)

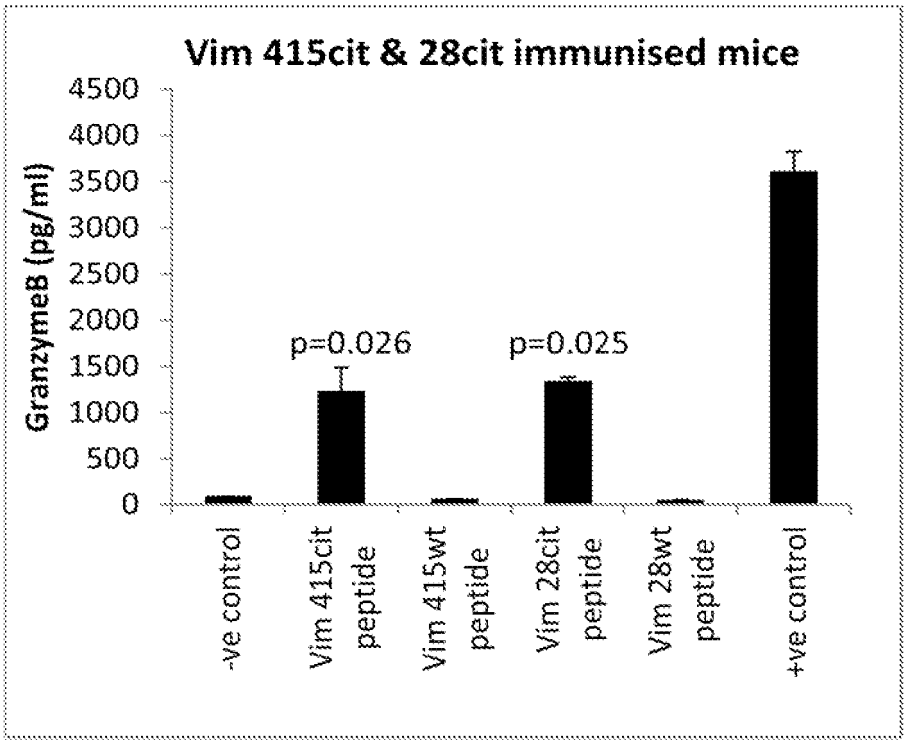
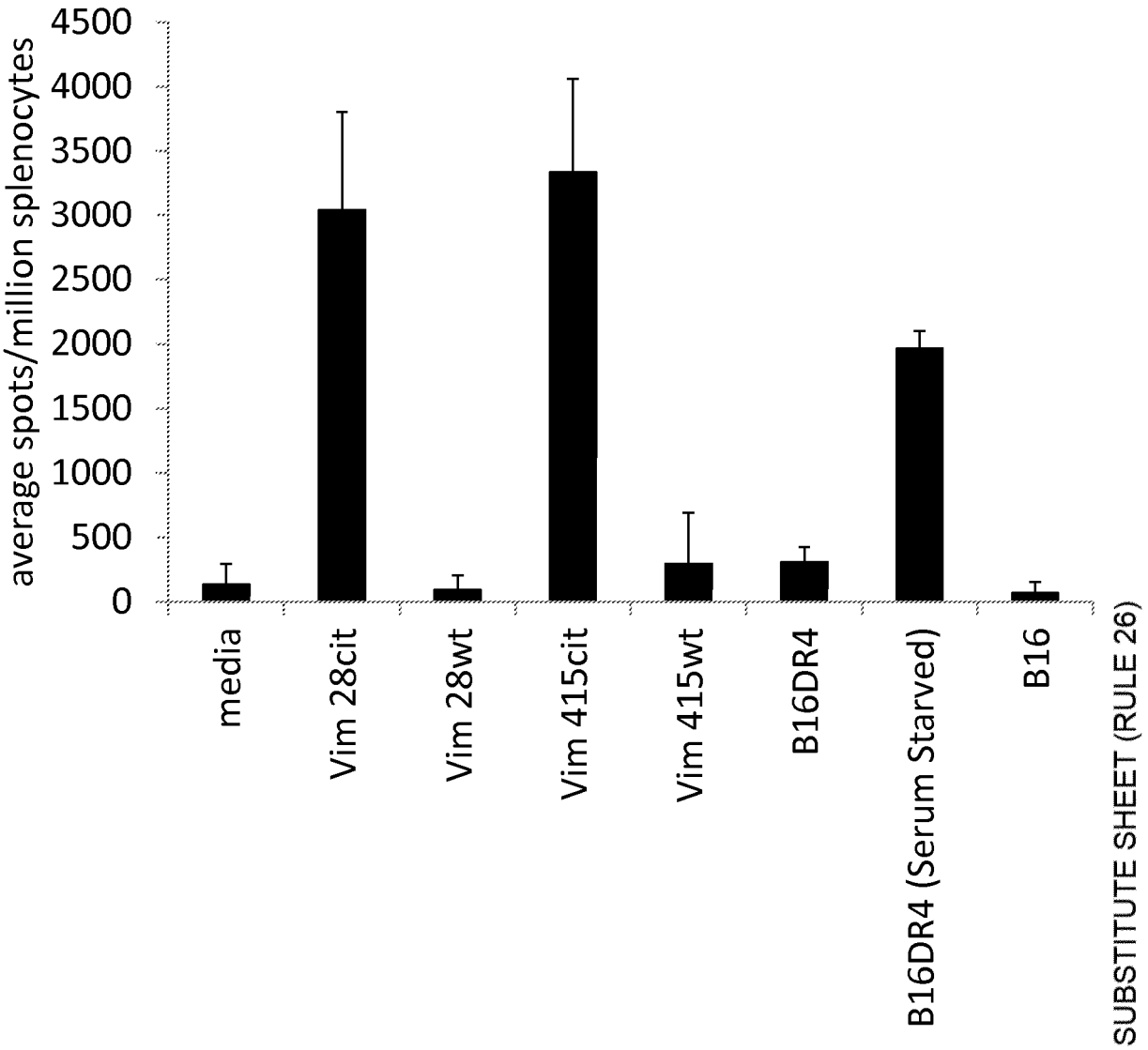


Figure 22 contd

(e)

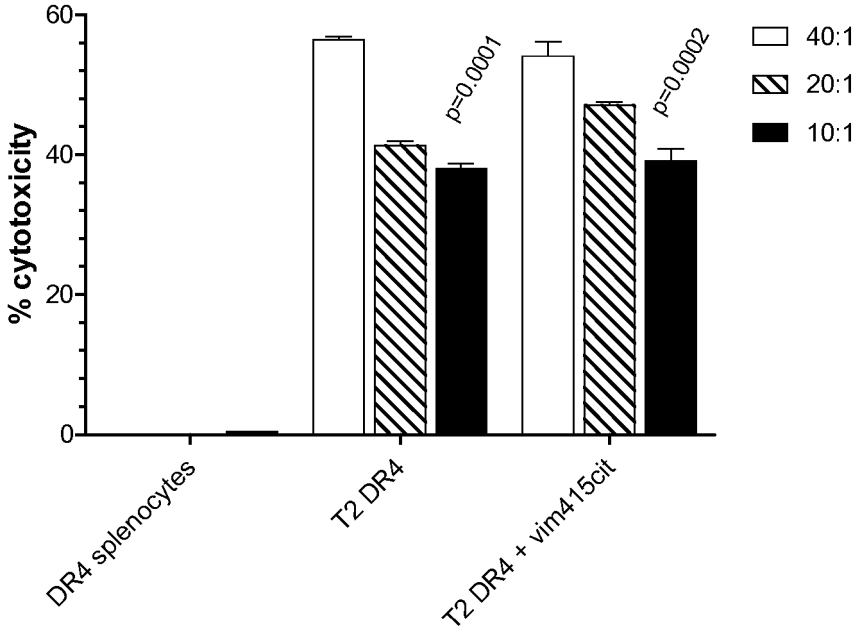



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Figure 23

(a)

(i) Vim 415 cit




(ii) Vim 28 cit

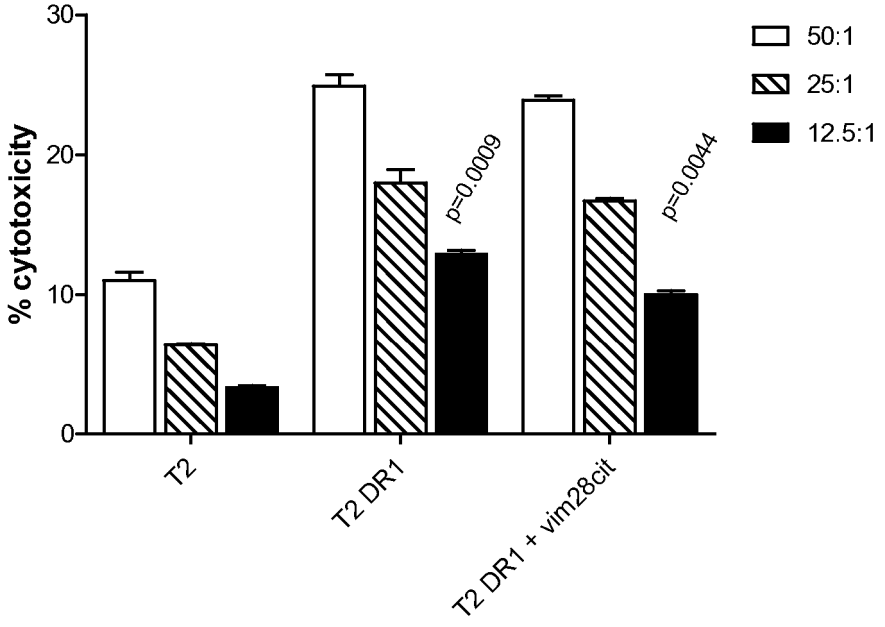
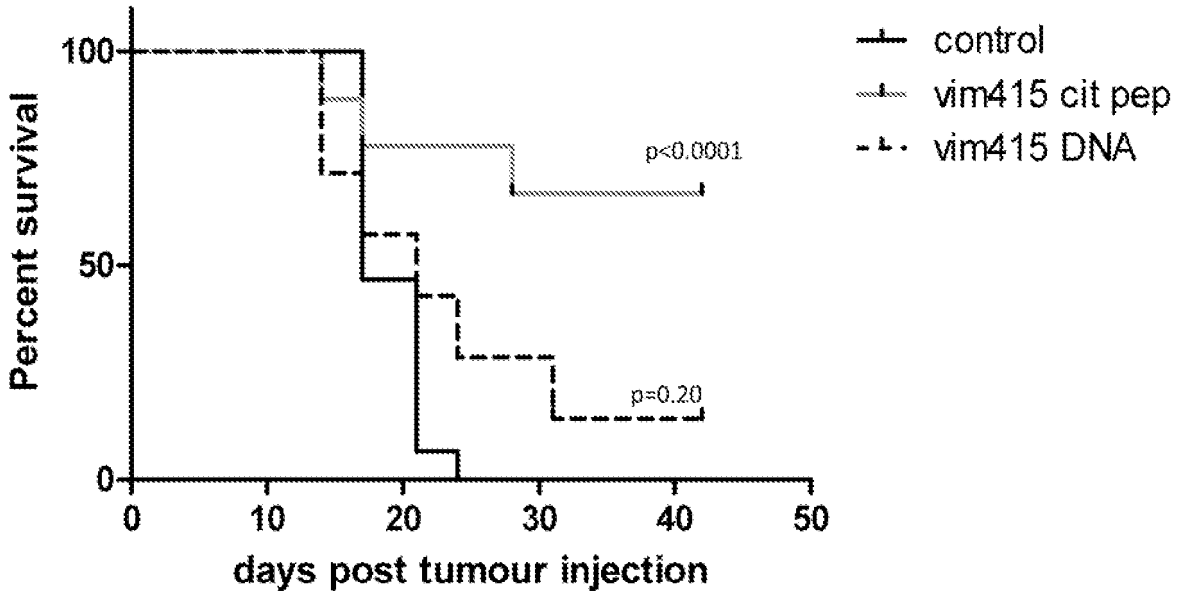


Figure 24

(a)


Percent survival
100
50
0
0
10
20
30
40
50
days post tumour injection
p<0.0001
p=0.20
control
vim415 cit pep
vim415 DNA

(b)

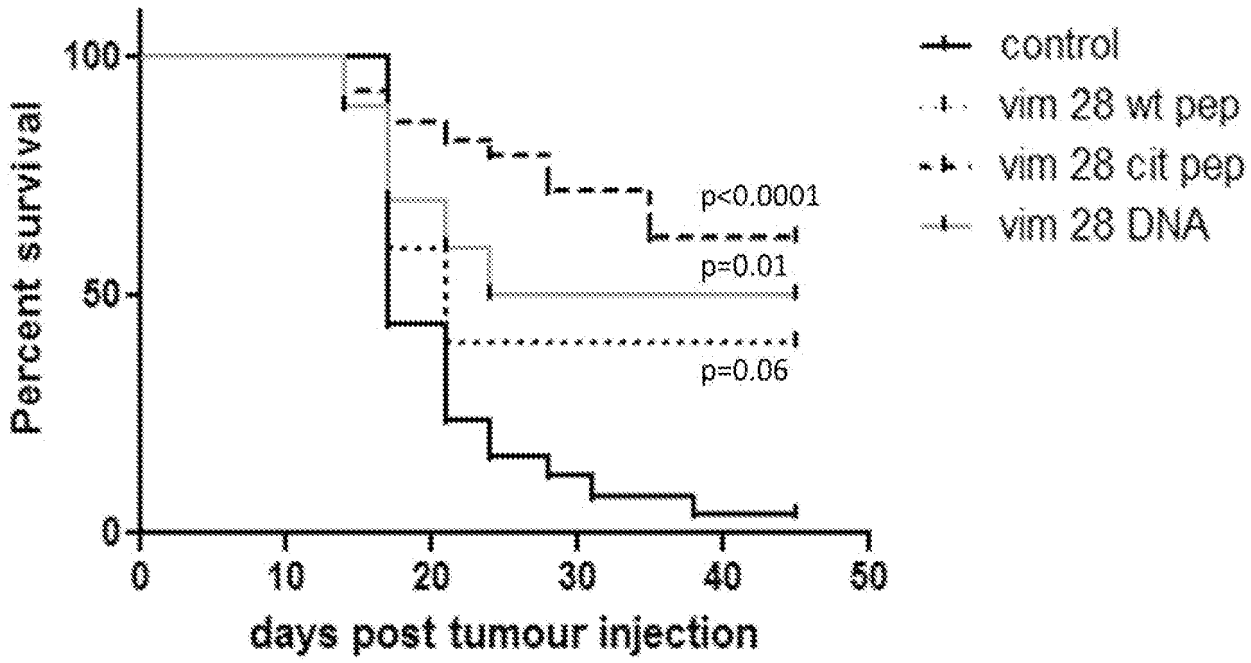
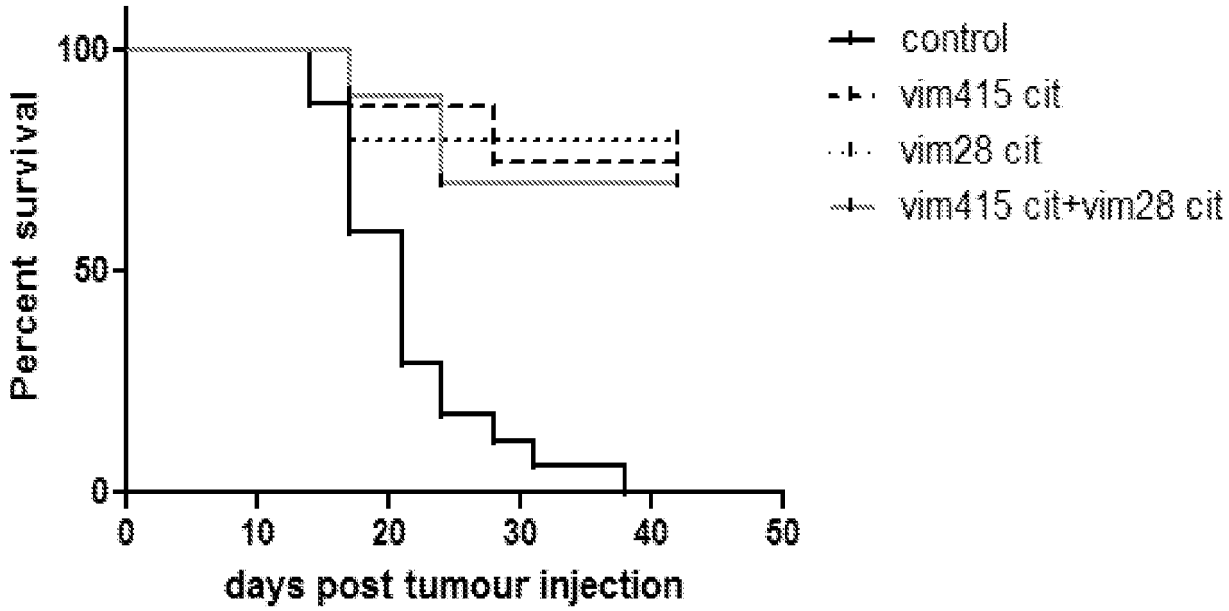

Percent survival
100
50
0
0
10
20
30
40
50
days post tumour injection
p<0.0001
p=0.01
p=0.06
control
vim 28 wt pep
vim 28 cit pep
vim 28 DNA

Figure 24 contd

(c)




(d)

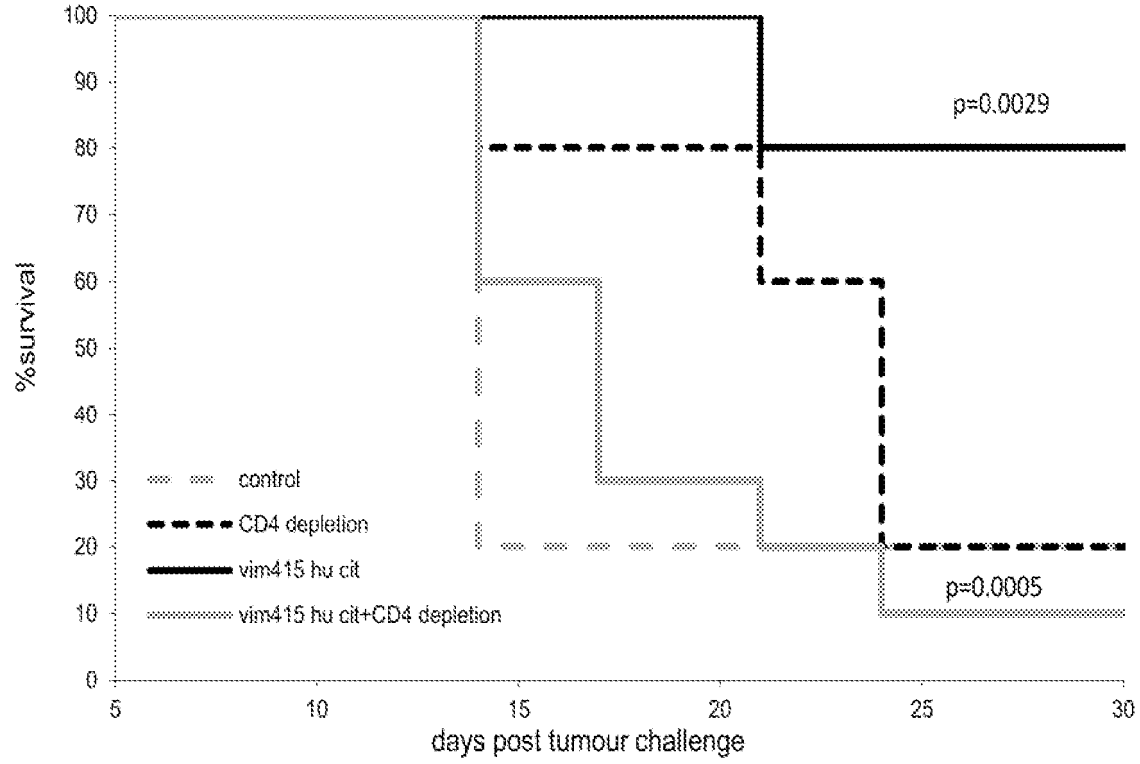


Figure 24 contd

(e)

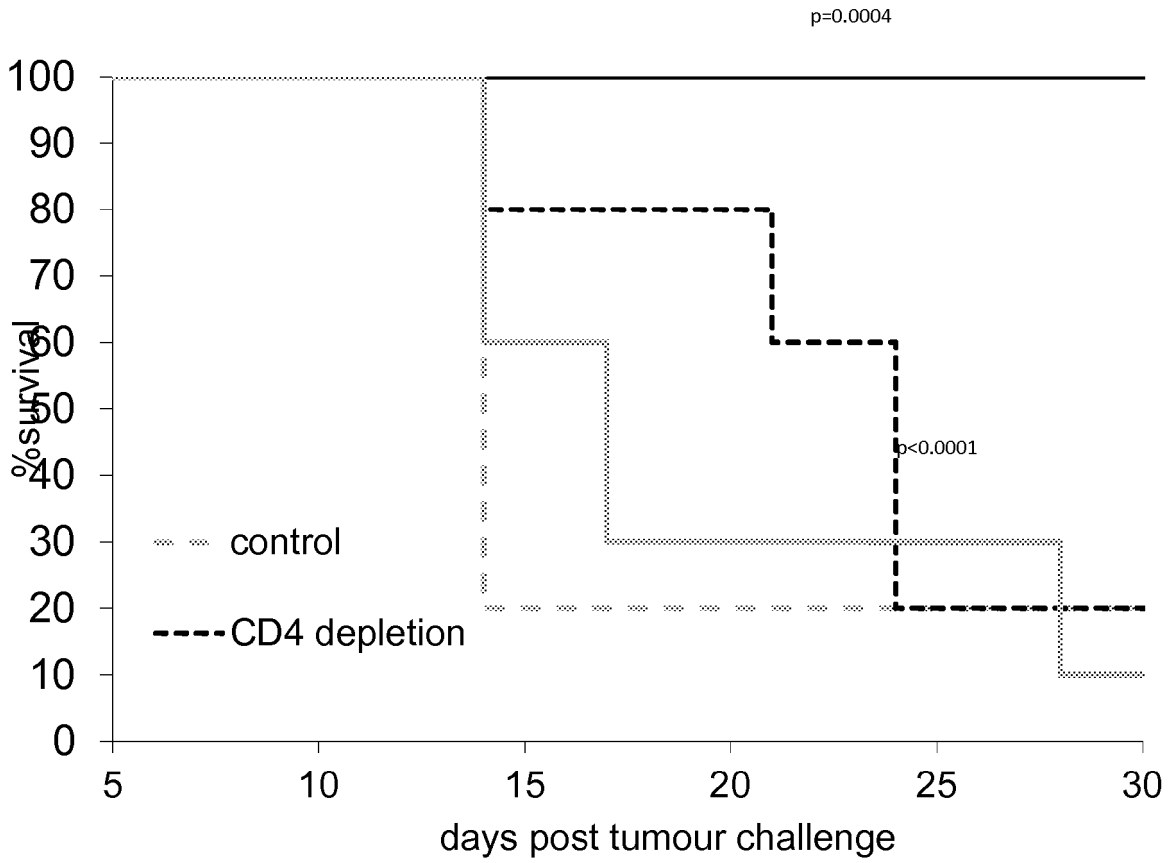
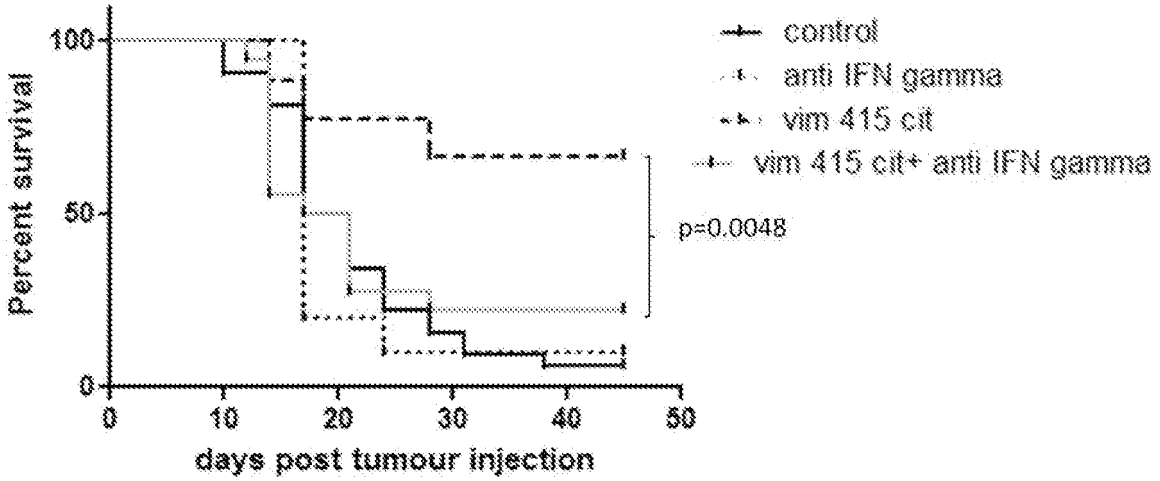


Figure 25

a)


Percent survival
100
50
0
0
10
20
30
40
50
days post tumour injection
control
anti IFN gamma
vim 415 cit
vim 415 cit+ anti IFN gamma
p=0.0048

b)

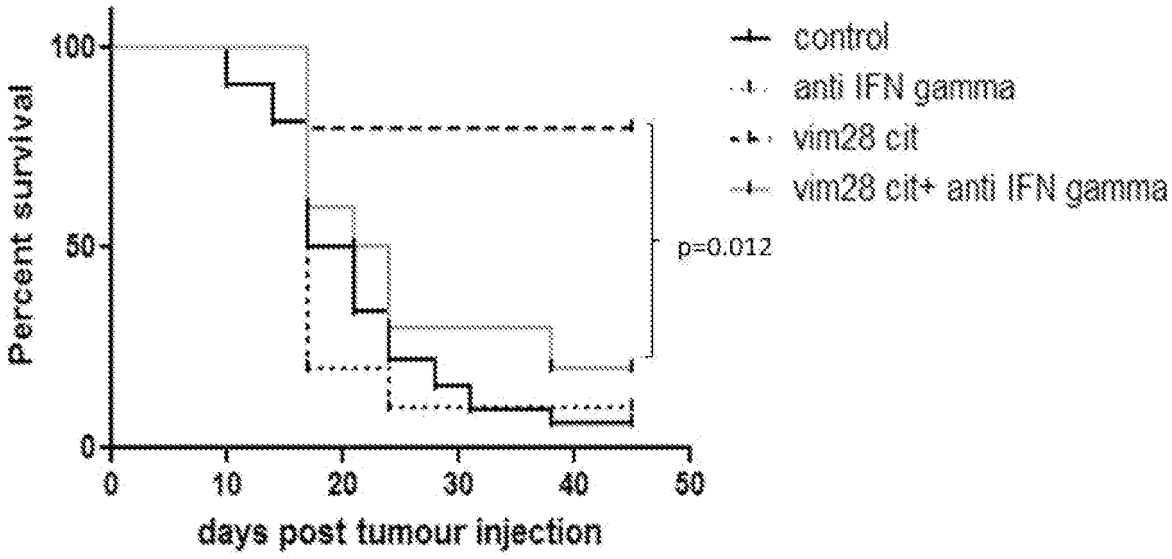
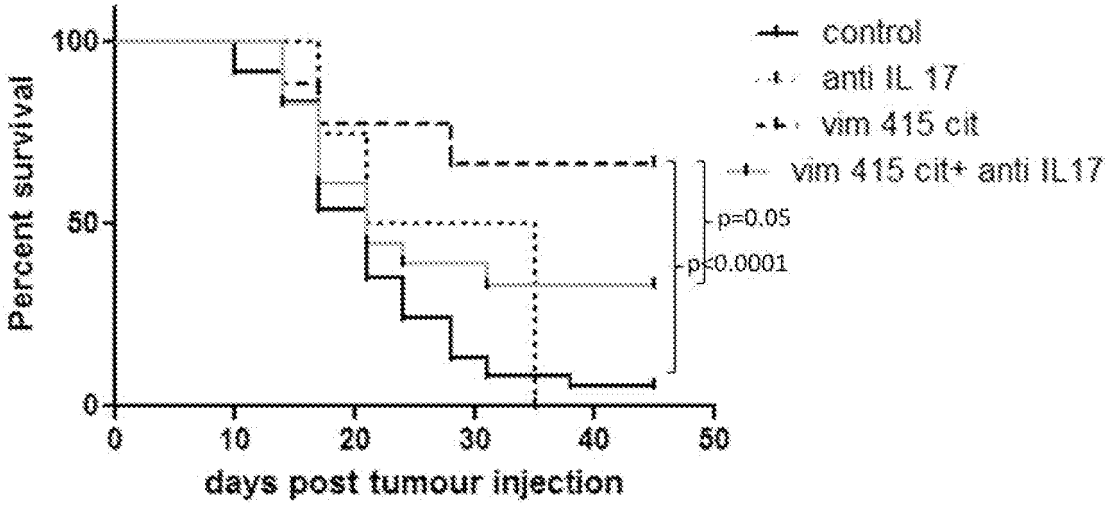

Percent survival
100
50
0
0
10
20
30
40
50
days post tumour injection
control
anti IFN gamma
vim28 cit
vim28 cit+ anti IFN gamma
p=0.012

Figure 25 contd

c)




d)

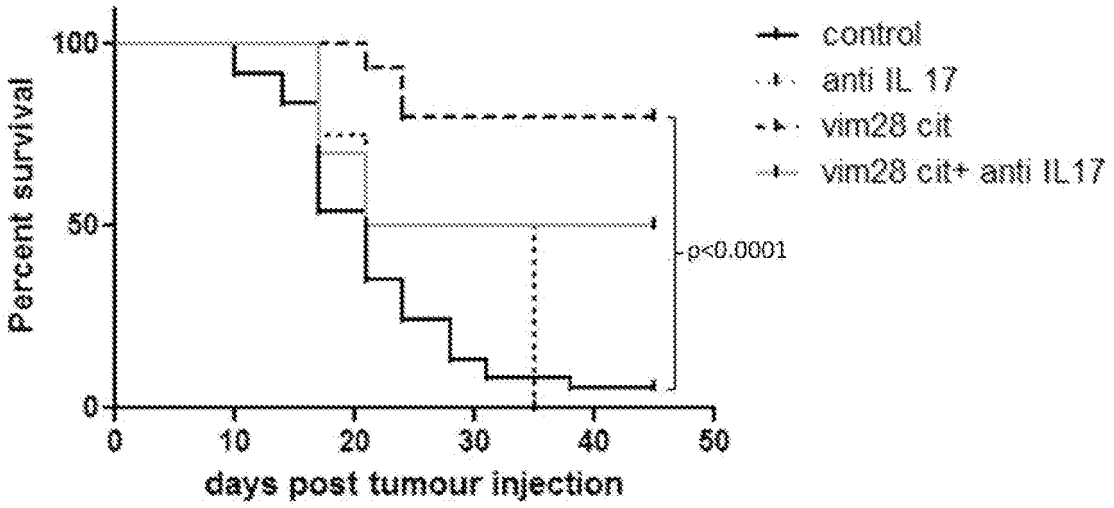
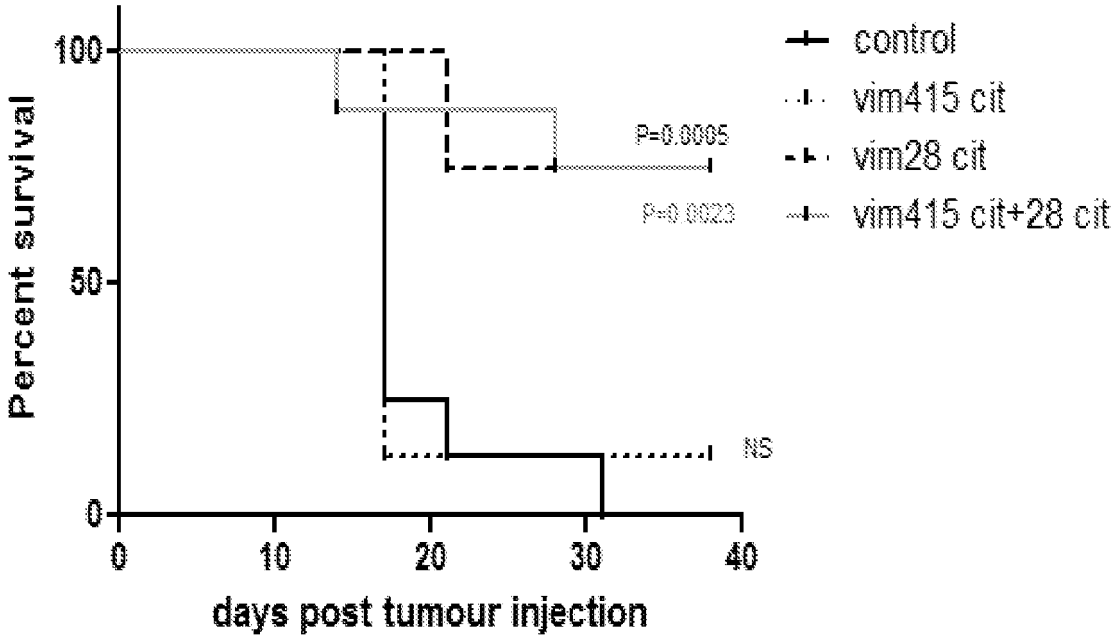


Figure 26

a)


100
50
0
Percent survival
0
10
20
30
40
days post tumour injection
control
vim415 cit
vim28 cit
vim415 cit+28 cit
P=0.0005
P=0.0023
NS

b)

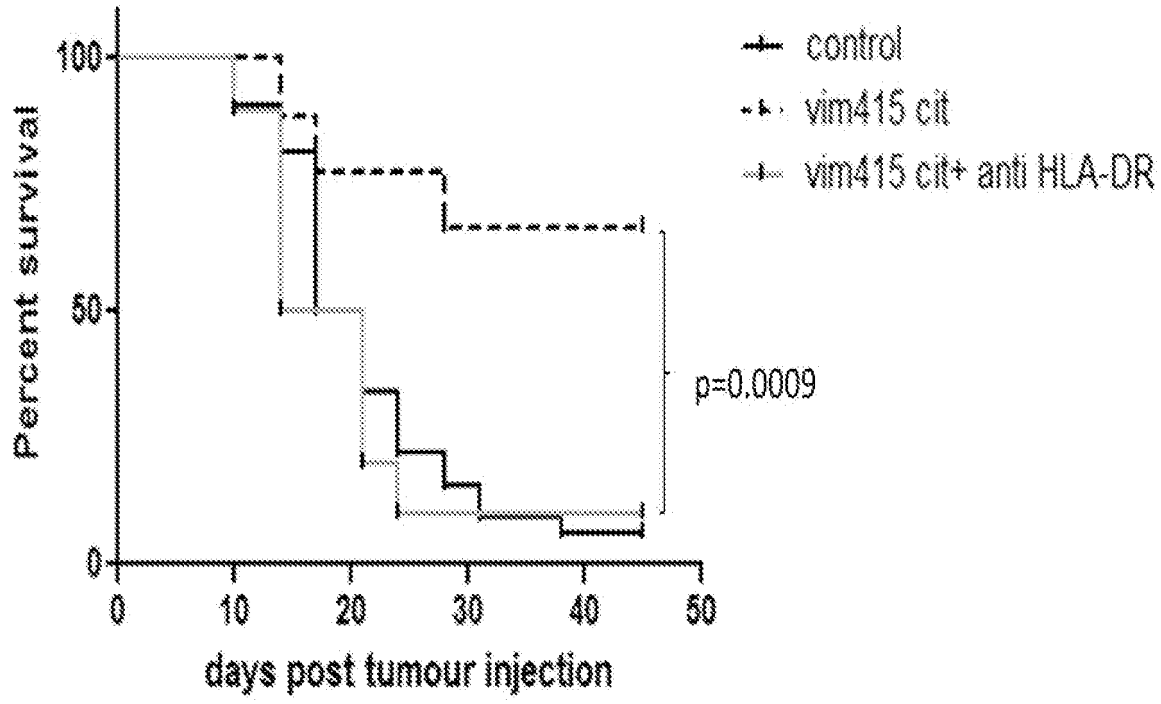
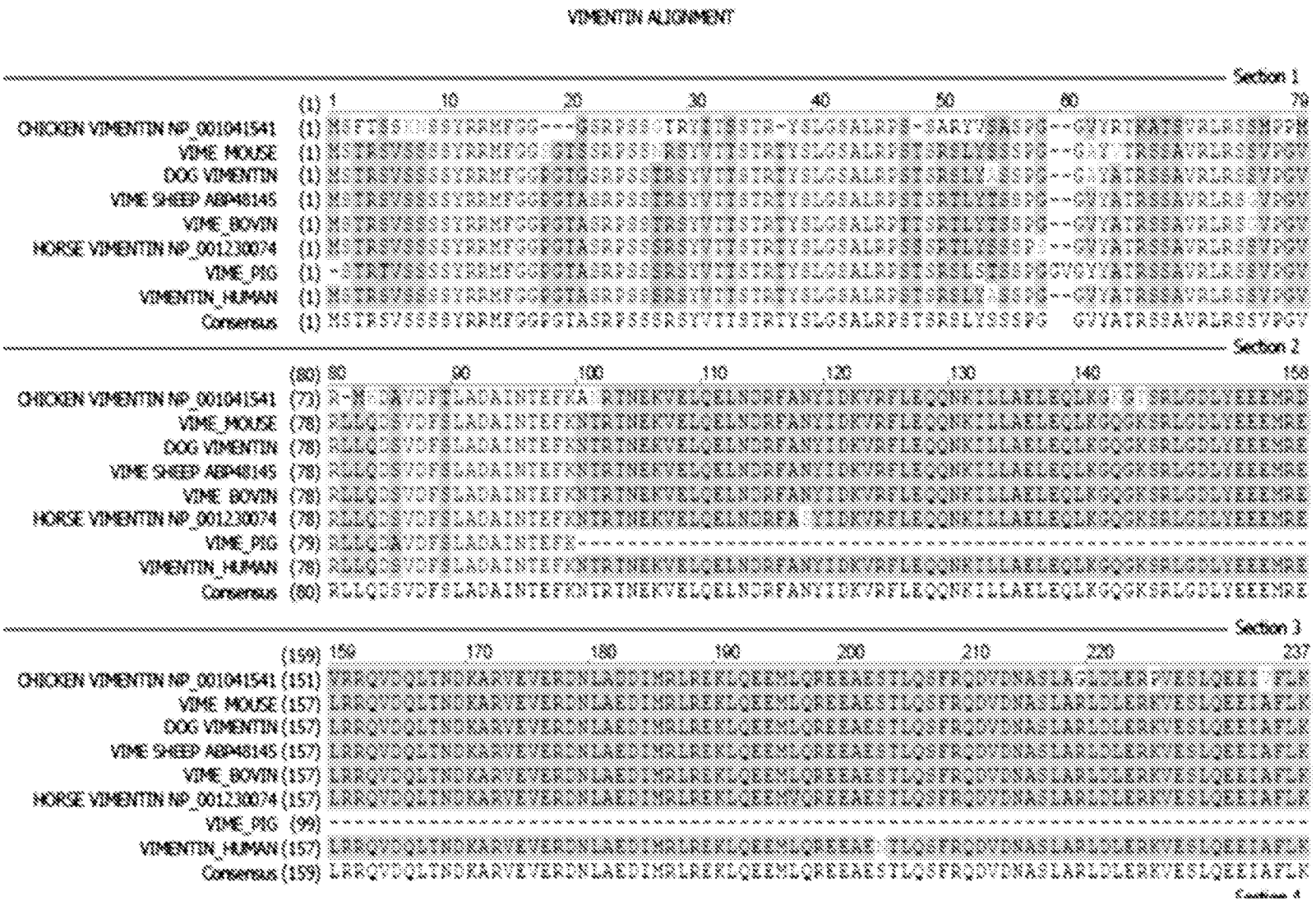

100
50
0
Percent survival
0
10
20
30
40
50
days post tumour injection
control
vim415 cit
vim415 cit+ anti HLA-DR
p=0.0009

Figure 27


VIMENTIN ALIGNMENT
Section 1
Section 2
Section 3
CHICKEN VIMENTIN NP_001041541
VIME_MOUSE
DOG VIMENTIN
VIME SHEEP ABP48145
VIME_BOVIN
HORSE VIMENTIN NP_001230074
VIME_PIG
VIMENTIN_HUMAN
Consensus

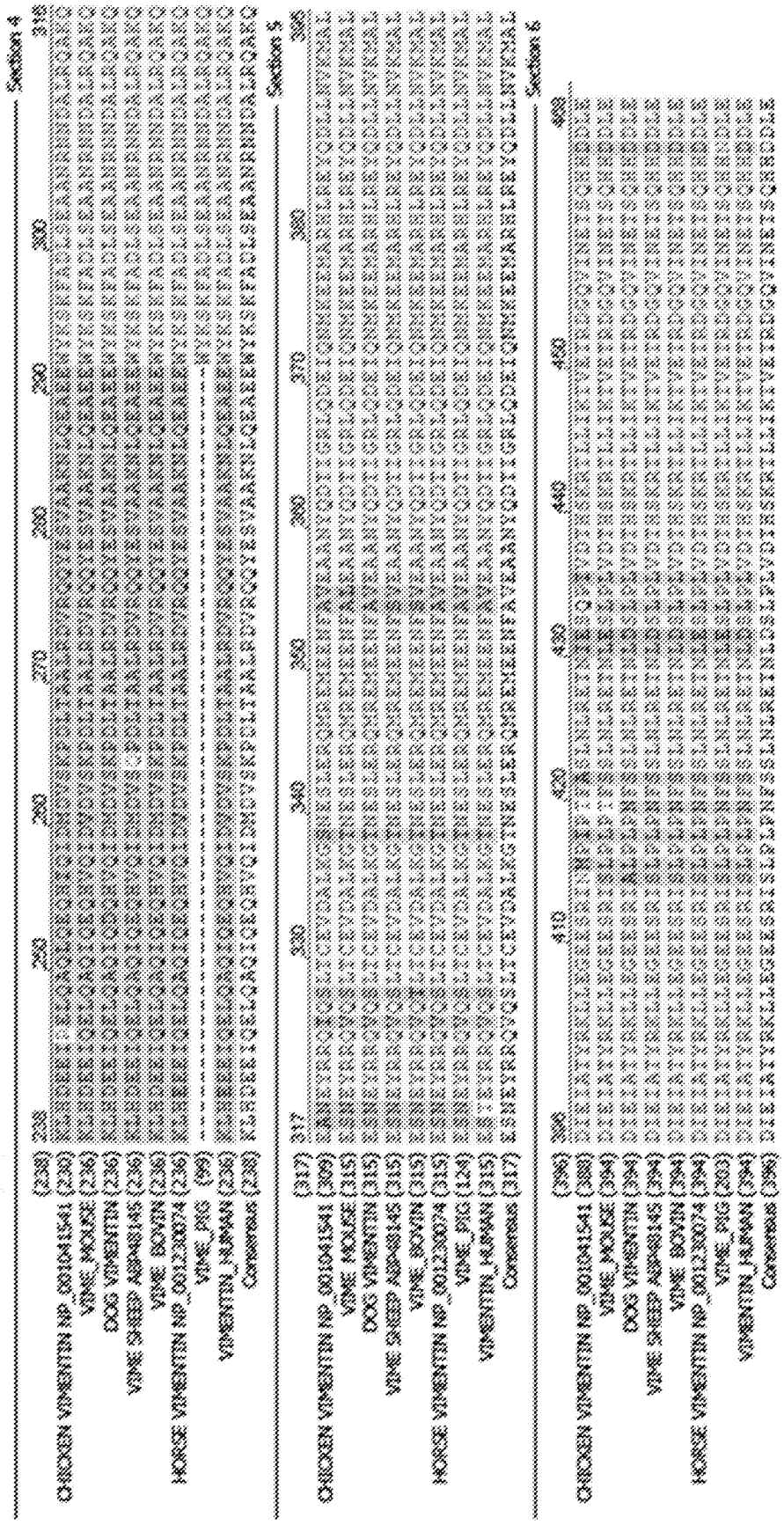
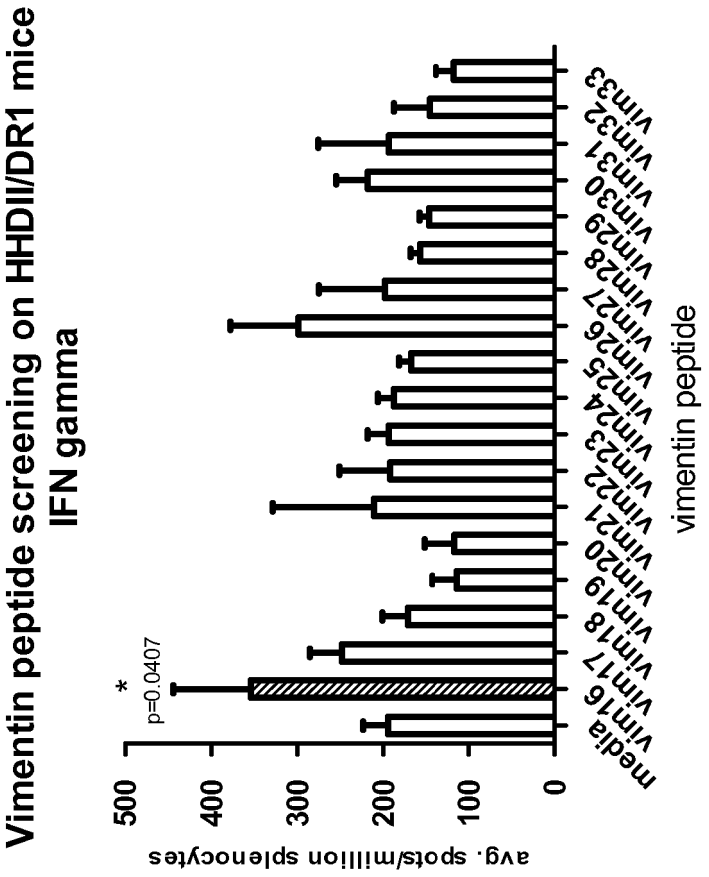
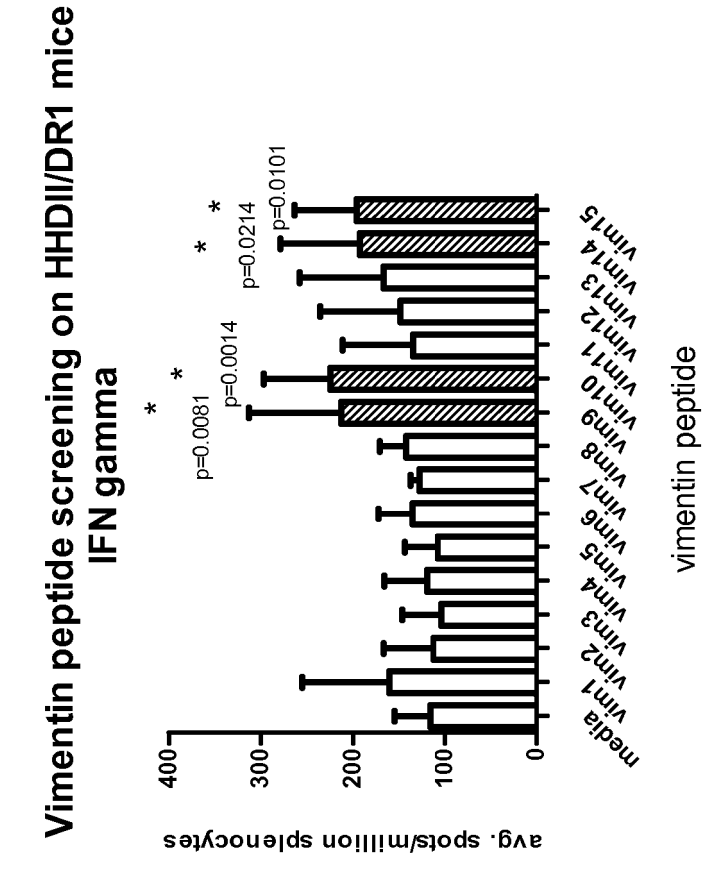


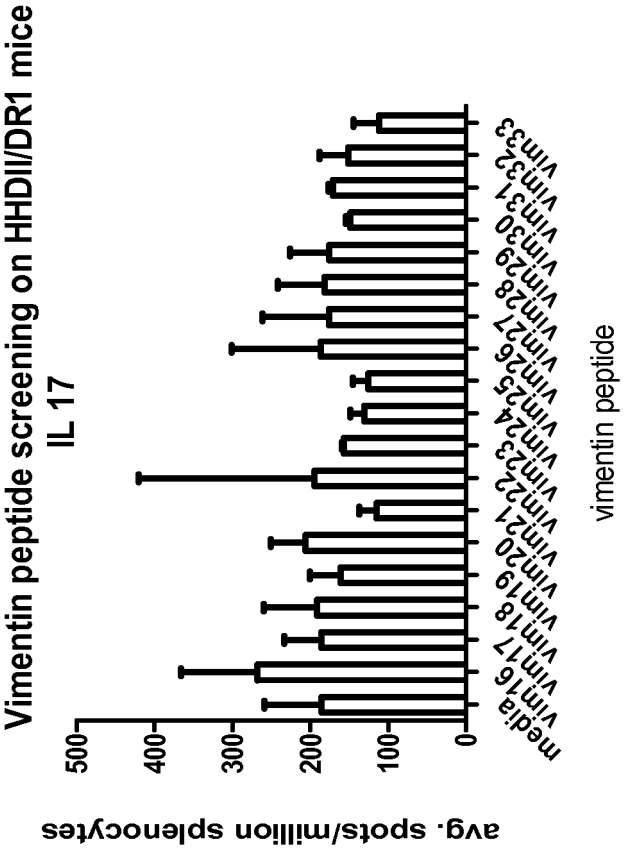
Fig 27 contd

Figure 28 Vimentin

a) HLA-DR1





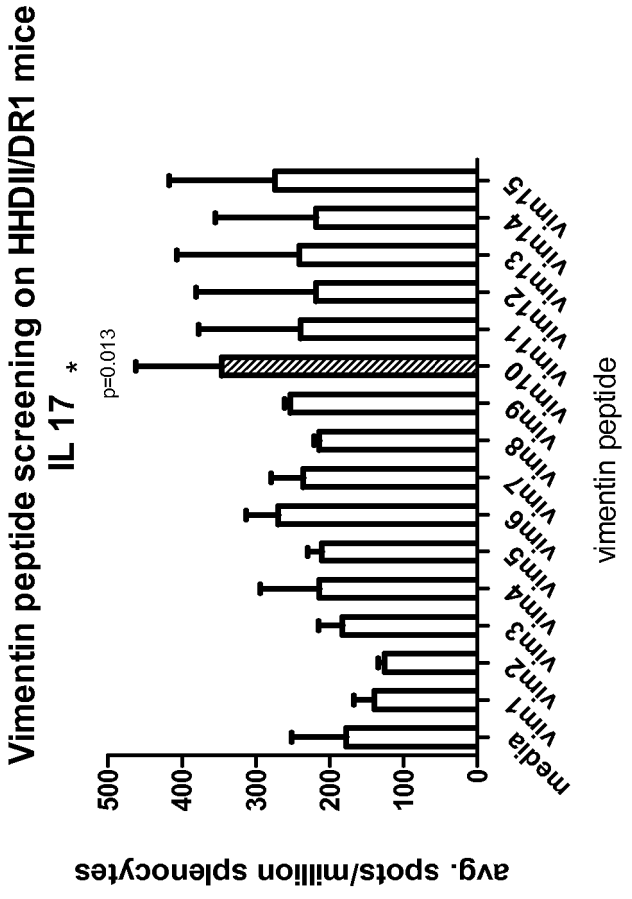
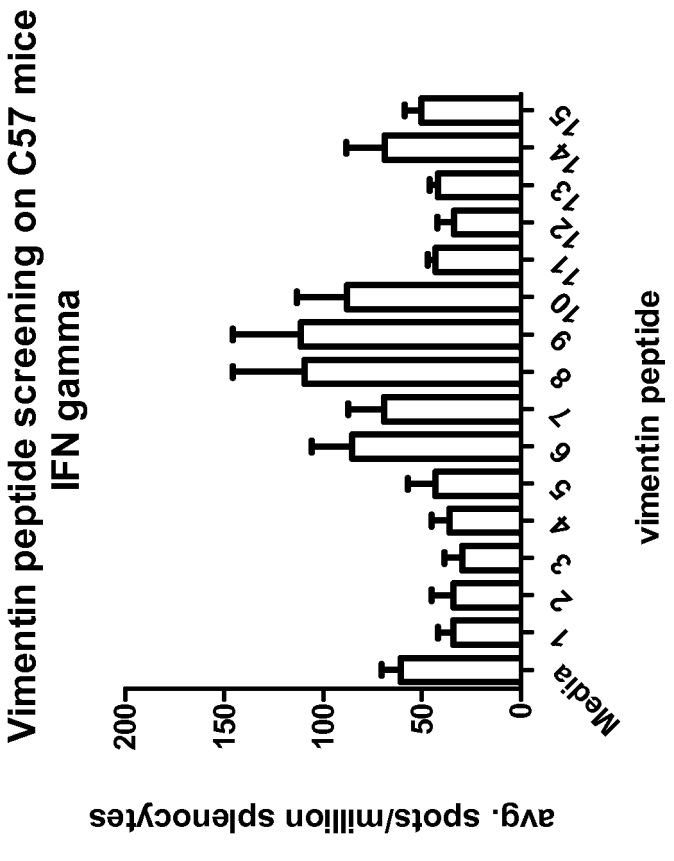
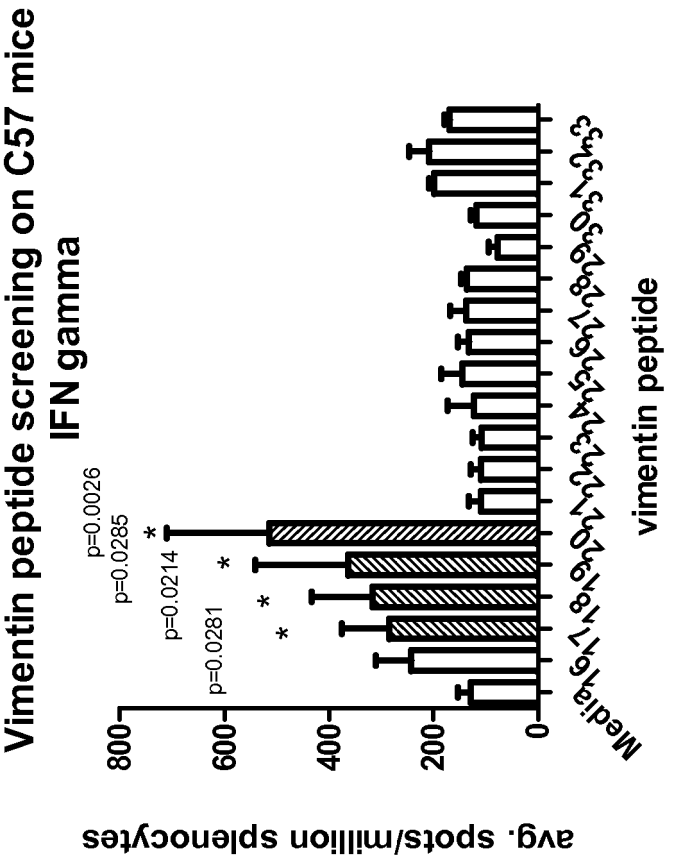



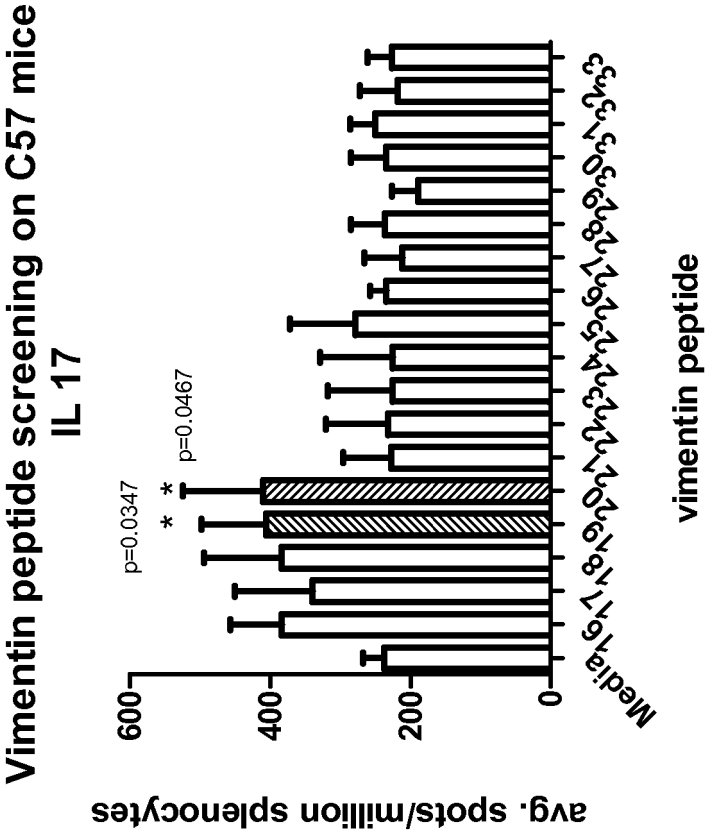

Figure 28 contd

Figure 28 contd

b) C57Bl





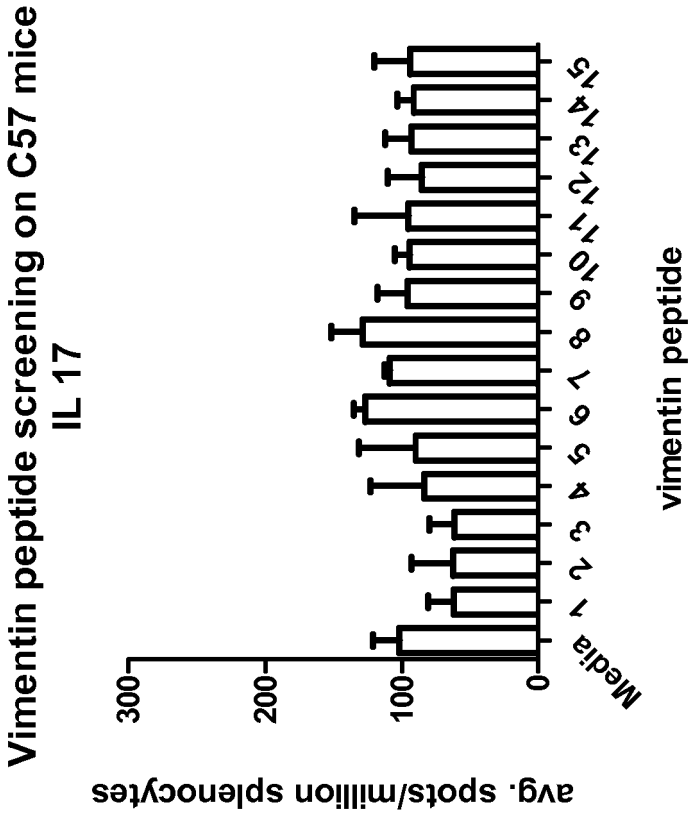




Figure 28 contd

Figure 28 contd

c)

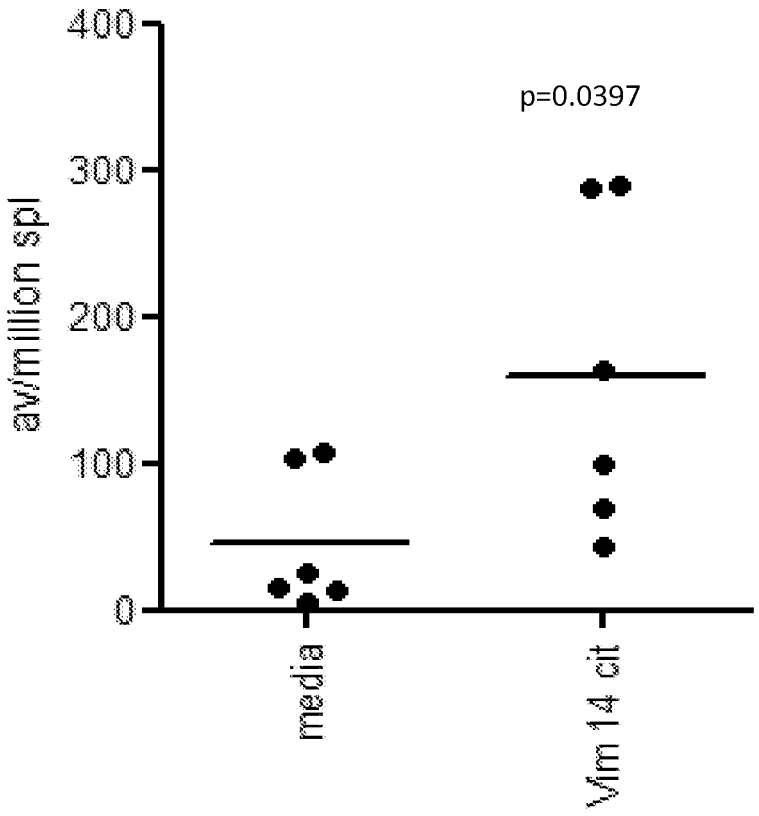


Figure 29

a) HLA -DR1 mice.

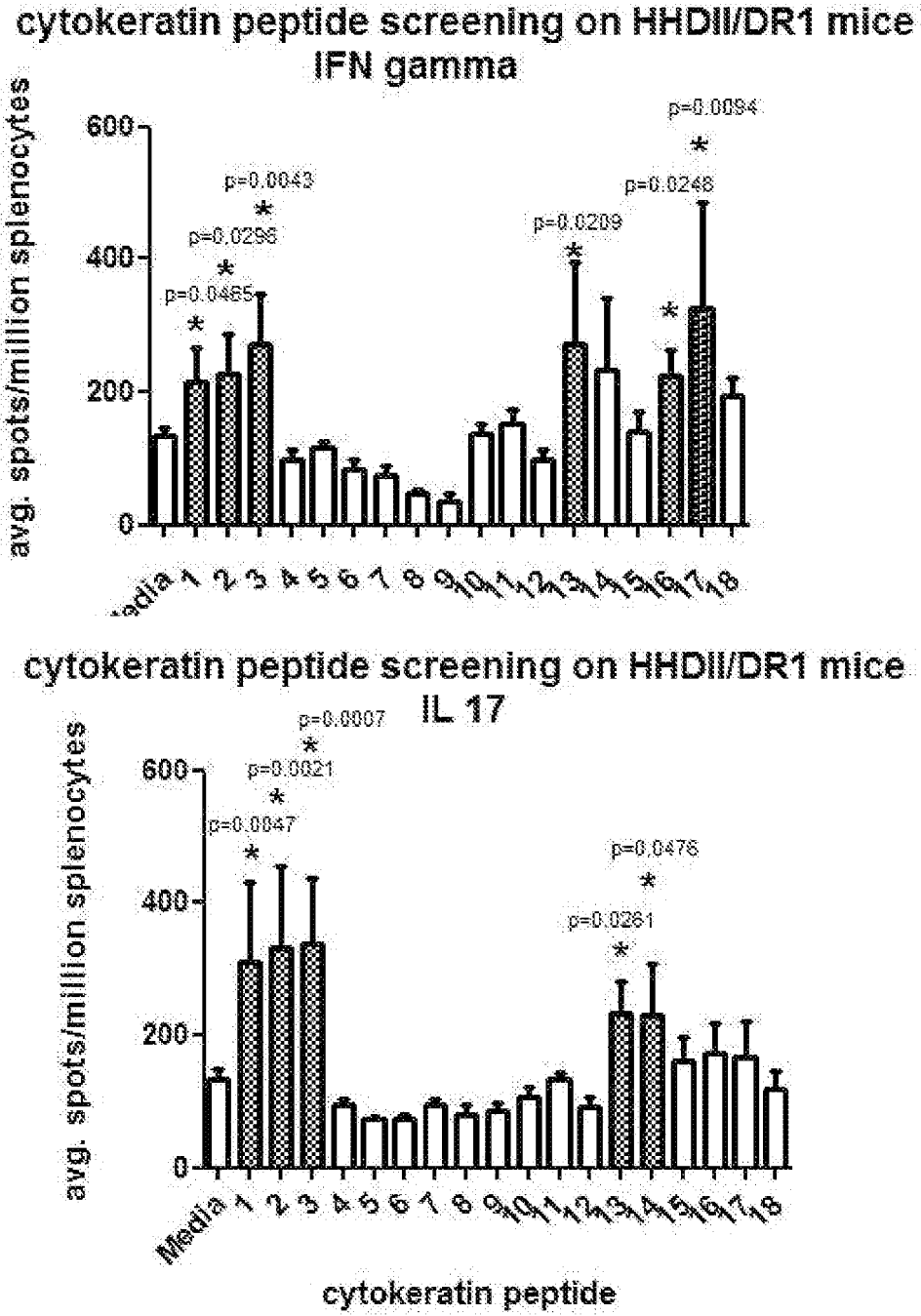
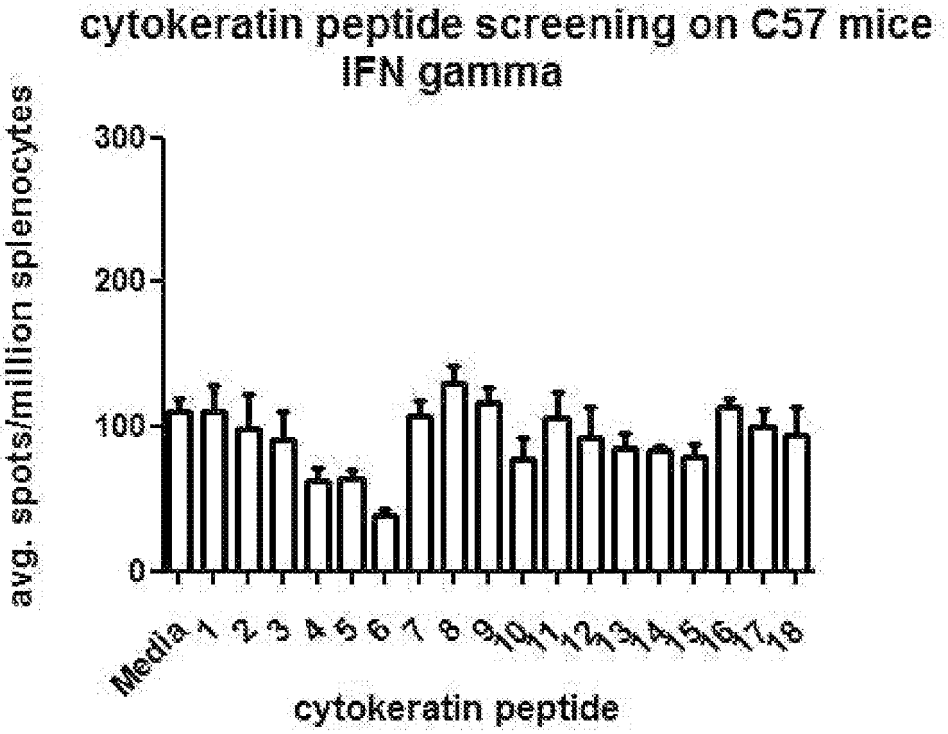


Figure 29 contd



b) C57Bl mice



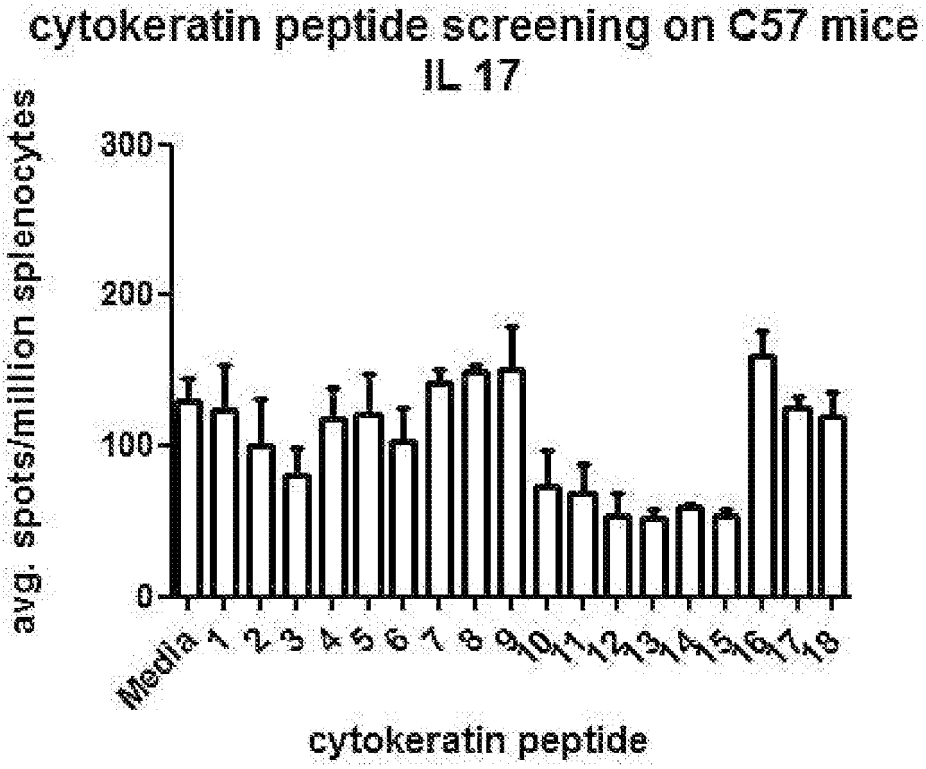



Figure 30

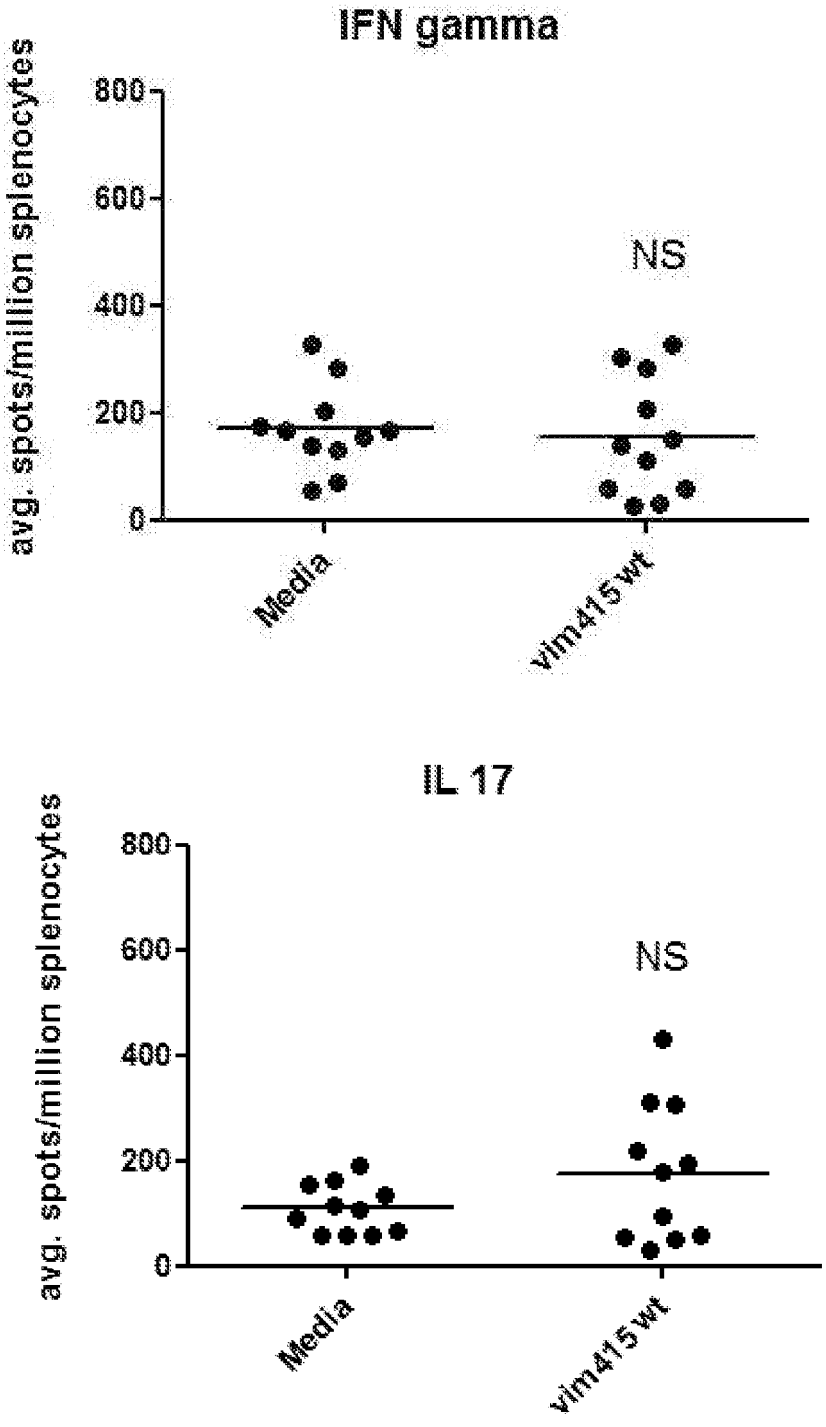

IFN gamma
avg. spots/million splenocytes
800
600
400
200
0
NS
Media
vim415wt
IL 17
avg. spots/million splenocytes
800
600
400
200
0
NS
Media
vim415wt

Figure 30 cont

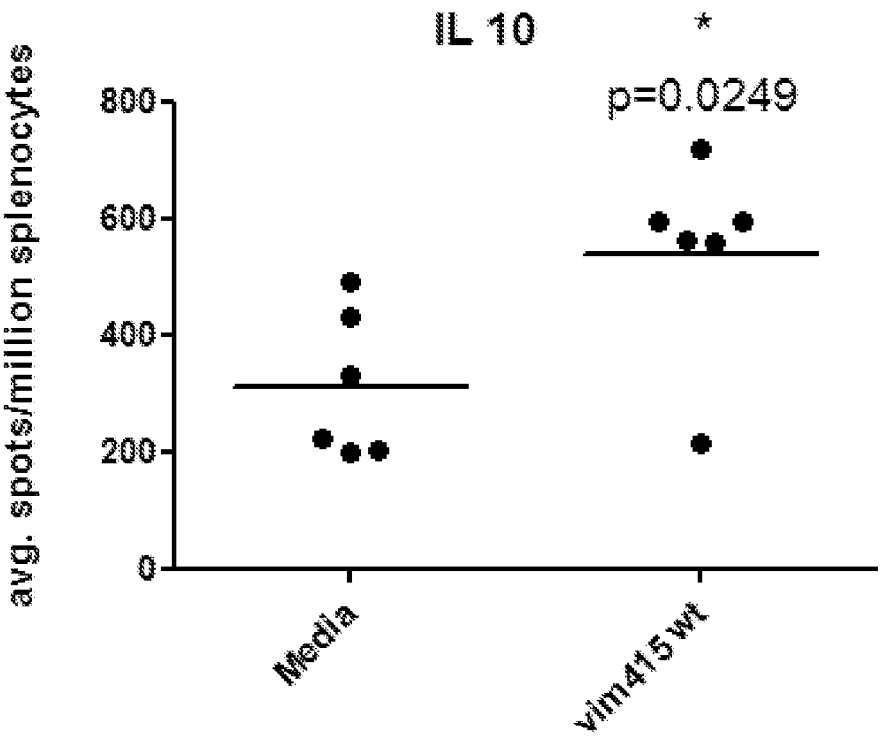



Figure 31

a)

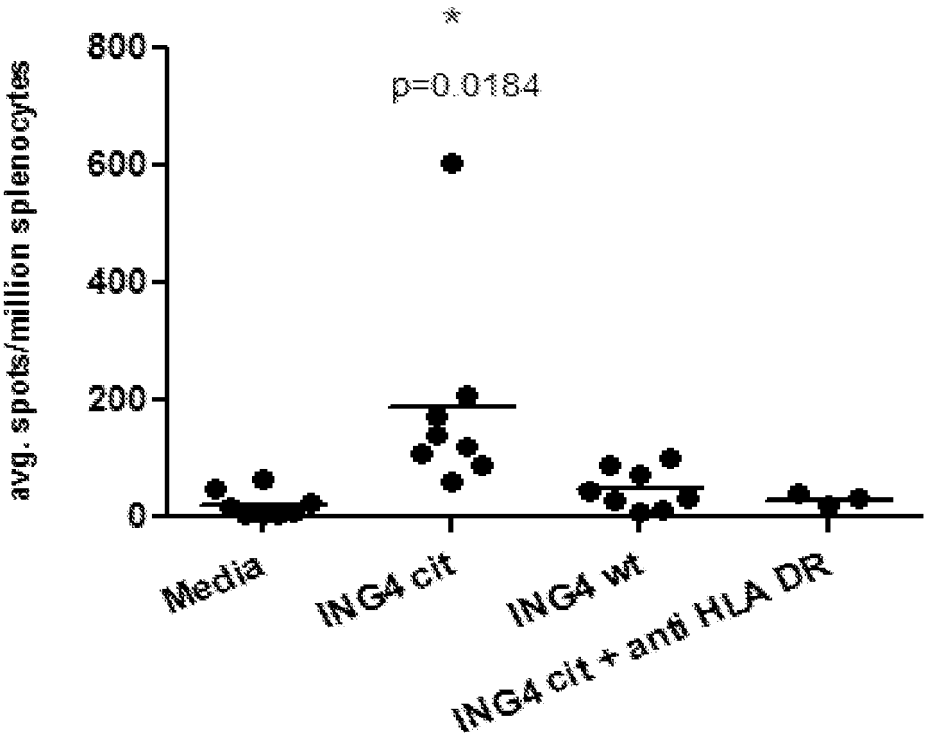


Figure 32



| | Uniprot accession number |
|---|---|
| NYESO-1 | P78358 |
| MMP7 | P09237 |
| Cytokeratin 18 | P05783 |
| Cytokeratin 8 | P05787 |
| Cytokeratin 19 | P08727 |
| Cartilage intermediate layer protein (CILP) 1<br><br>2 | O75339<br>Q8IUL8 |
| ING4 | Q9UNL4 |
| P53 | P04637 |
| PAD4 | Q9UM07 |
| Vimentin | P08670 |
| Adolase B<br>C<br>A | P05062<br>P09972<br>P04075 |
| PGK1 | P00558 |
| BiP | P11021 |
| Calreticulin | P27797 |
| HSP90α | P07900 |
| HSP80β | P08238 |
| Hsp60 | P10809 |
| GSK3β | P49841 |
| Far upstream element binding protein 1<br><br>3 | Q96AE4<br>Q96I24 |
| Asporin | Q9BXN1 |
| Cathepsin D | P07339 |
| Human Beta actin | P60709 |
| Albumin | P02768 |
| G Histamine H3 receptor | Q9Y5N1 |

Figure 32 contd

| | Uniprot accession number |
|---|---|
| H1<br>H2 | P35367<br>P25021 |
| ALDH2 | P05091 |
| Protein disulphide isomerase ER60 precursor (PDIA3) | P30101 |
| F- actin capping protein alpha 1 subunit | P52907 |
| Heparin binding protein | P20160 |
| Nucleophosmin B23 | P06748 |
| P300 coactivator? | Q09472 |
| Aggrecan | P16112 |
| Glucose related protein | Q9Y4L1 |
| CXCL-12 | P48061 |
| CXCL-8 | P10145 |
| CXCL-10 | P02778 |
| alpha-enolase | P06733 |
| myelin basic protein | P02686 |
| Antithrombin | P01008 |
| Elongation factor 1alpha | P68104 |
| Adenylcyclase associated protein | Q01518 |
| Histone H1- H1.0 | P07305 |
| Histone H1- H1.1 | Q02539 |
| Histone H1- H1.2 | P16403 |
| Histone H1- H1.3 | P16402 |
| Histone H1- H1.4 | P10412 |
| Histone H1- H1.5 | P16401 |
| Histone H1-H1t | P22492 |
| Histone H1- H1FNT | Q75WM6 |
| Histone H1-H1oo | Q8IZA3 |
| Histone H1-H1x | Q92522 |
| Histone H2A- type 1 | P0C0S8 |
| Histone H2A -type 3 | Q7L7L0 |
| Histone H2A- type 2-A | Q6FI13 |

Figure 32 contd

| | Uniprot accession number |
|---|---|
| Histone H2A- type 2-B | Q8IUE6 |
| Histone H2A -type 2-C | Q16777 |
| Histone H2B -type 1-A | Q96A08 |
| Histone H2B -type 1-B | P33778 |
| Histone H2B -type 1-C/E/F/G/I | P62807 |
| Histone H2B -type 1-H | Q93079 |
| Histone H2B -type 1-M | Q99879 |
| Histone H2B -type 1-L | Q99880 |
| Histone H2B -type 1-N | Q99877 |
| Histone H2B -type 1-O | P23527 |
| Histone H2B -type 1-J | P06899 |
| Histone H2B -type 1-D | P58876 |
| Histone H2B -type 1-K | O60814 |
| Putative histone H2B type 2-C | Q6DN03 |
| Putative histone H2B type 2-D | Q6DRA6 |
| Histone H2B -type 2-E | Q16778 |
| Histone H2B -type 2-F | Q5QNW6 |
| Histone H2B type 3-B | Q8N257 |
| Histone H2B type F-S | P57053 |
| Histone H2B type F-M | P0C1H6 |
| Histone H2B type W-T | Q7Z2G1 |
| Histone H3-H3.1 | P68431 |
| Histone H3-H3.2 | Q71DI3 |
| Histone H3-H3.3 | P84243 |
| Histone H4 | P62805 |

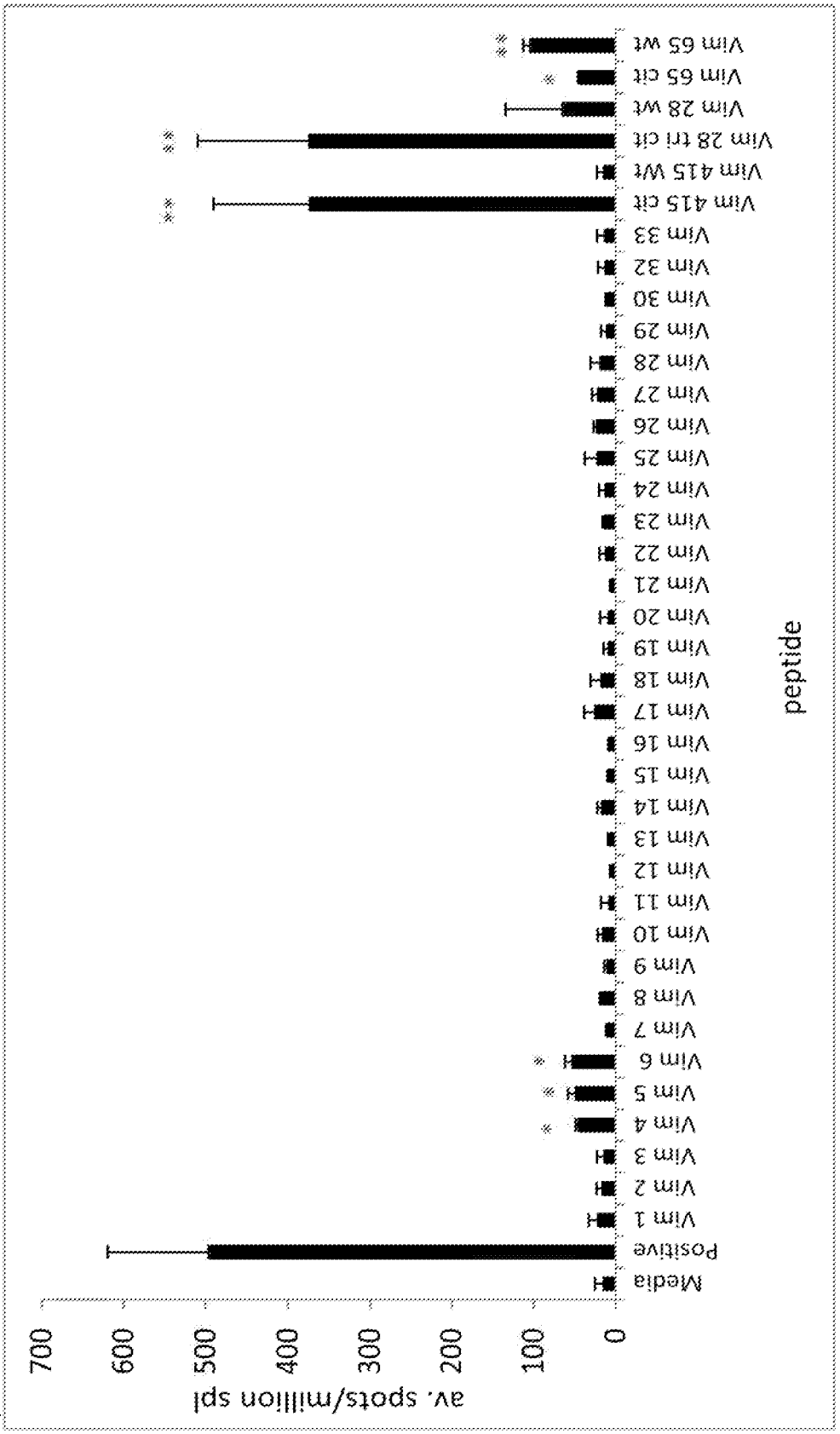



Figure 33 a)

SUBSTITUTE SHEET (RULE 26)

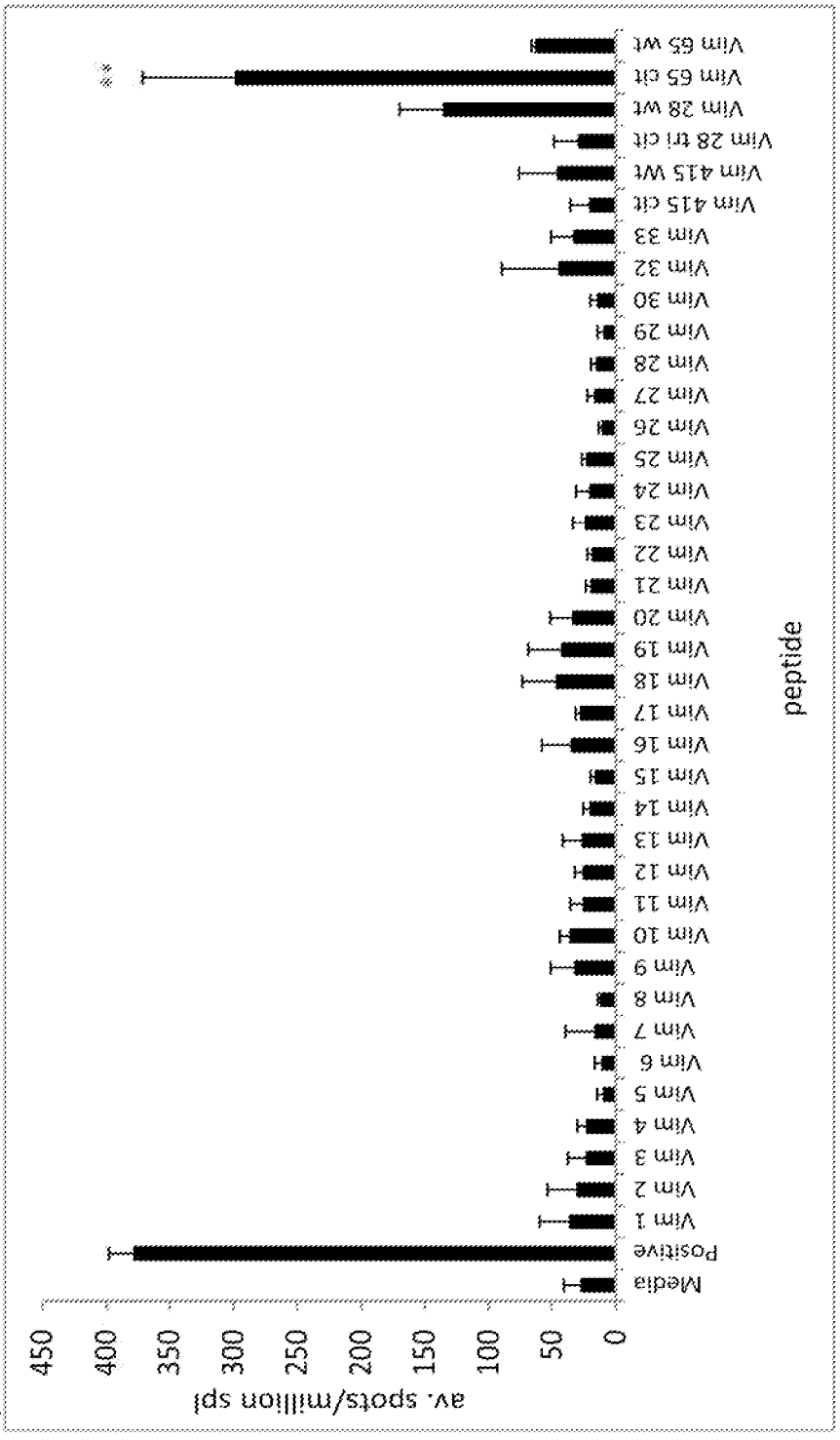



Figure 33 contd
b)

*p<0.05, ** p<0.005, *** p<0.0001

SUBSTITUTE SHEET (RULE 26)

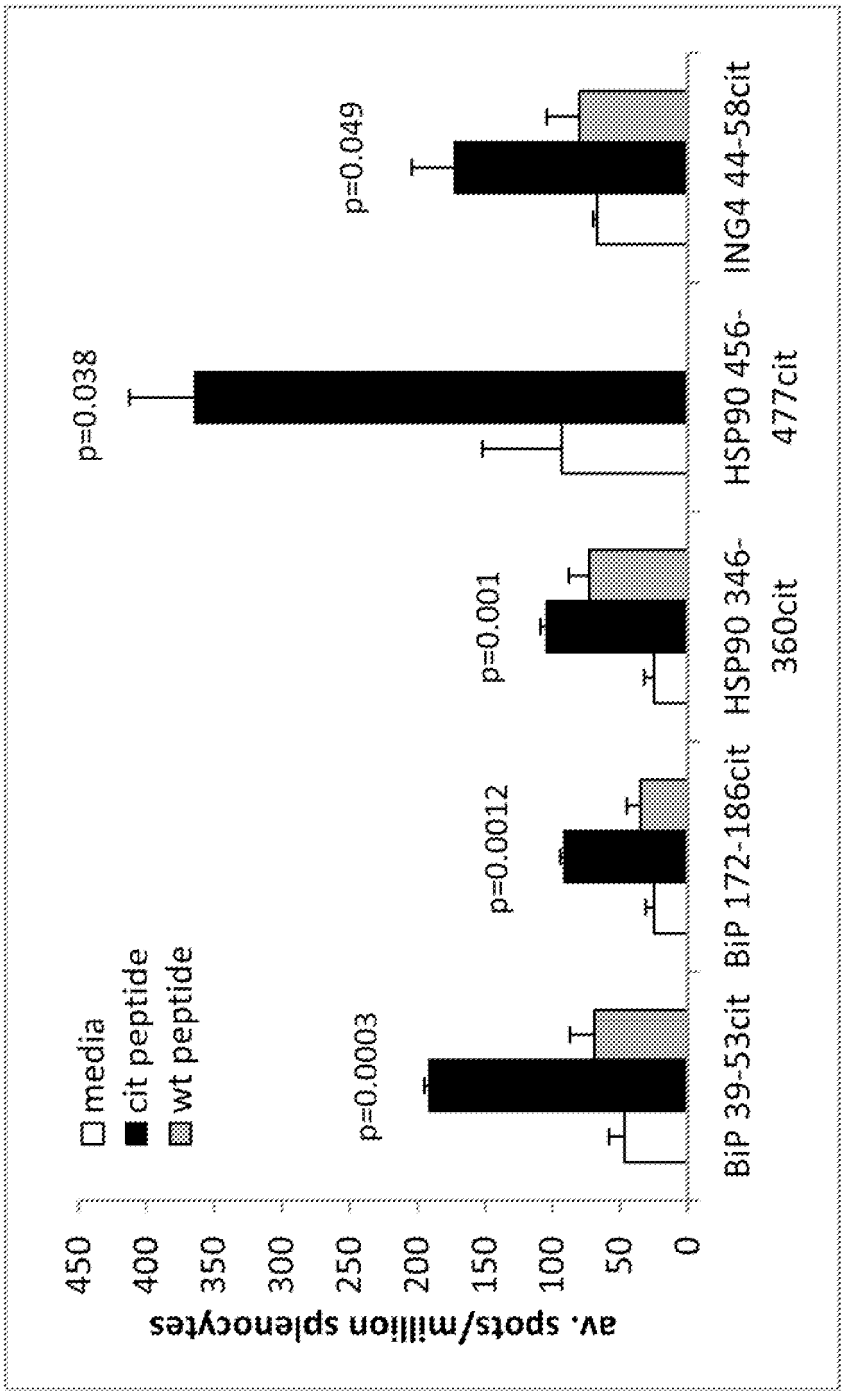

av. spots/million splenocytes
450
400
350
300
250
200
150
100
50
0
media
cit peptide
wt peptide
p=0.0003
p=0.0012
p=0.001
p=0.038
p=0.049
BiP 39-53cit
BiP 172-186cit
HSP90 346-360cit
HSP90 456-477cit
ING4 44-58cit

Figure 34