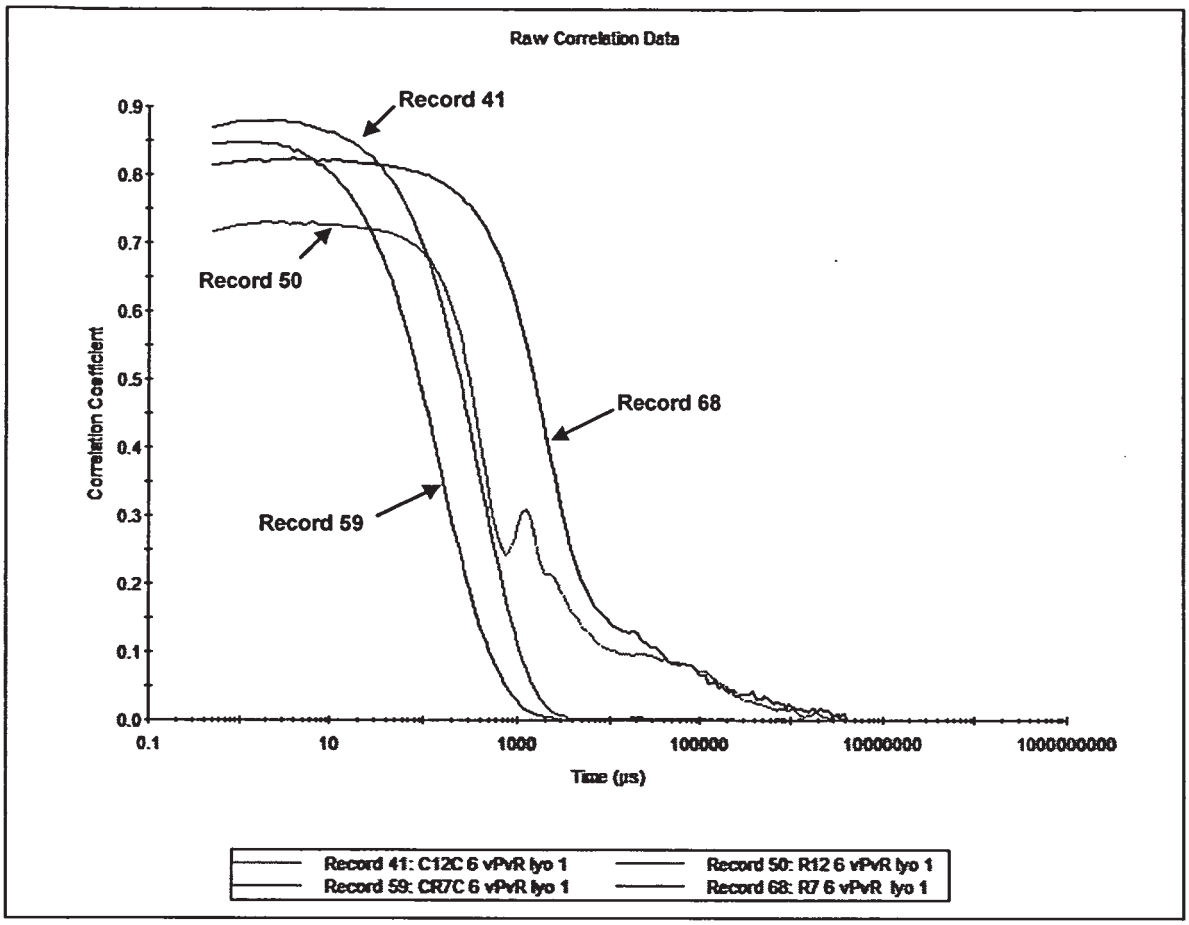
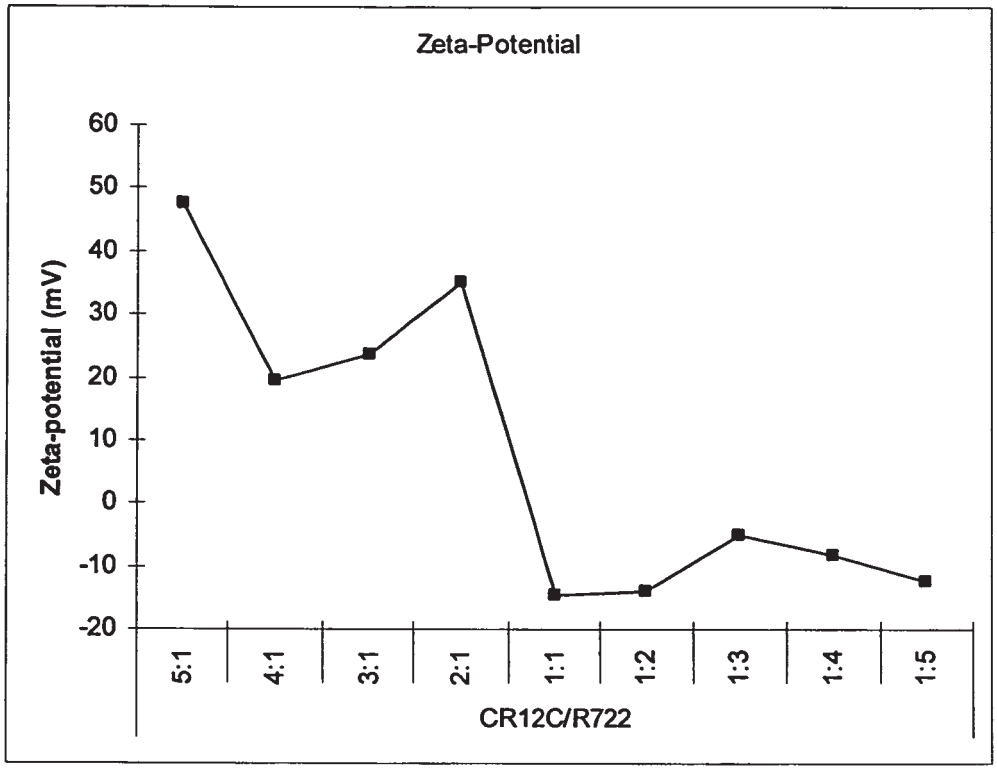

Raw Correlation Data
Record 41
Record 50
Record 68
Record 59
Correlation Coefficient
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0.1
10
1000
100000
10000000
1000000000
Time (µs)
Record 41: C12C 6 vPvR lyo 1
Record 59: CR7C 6 vPvR lyo 1
Record 50: R12 6 vPvR lyo 1
Record 68: R7 6 vPvR lyo 1

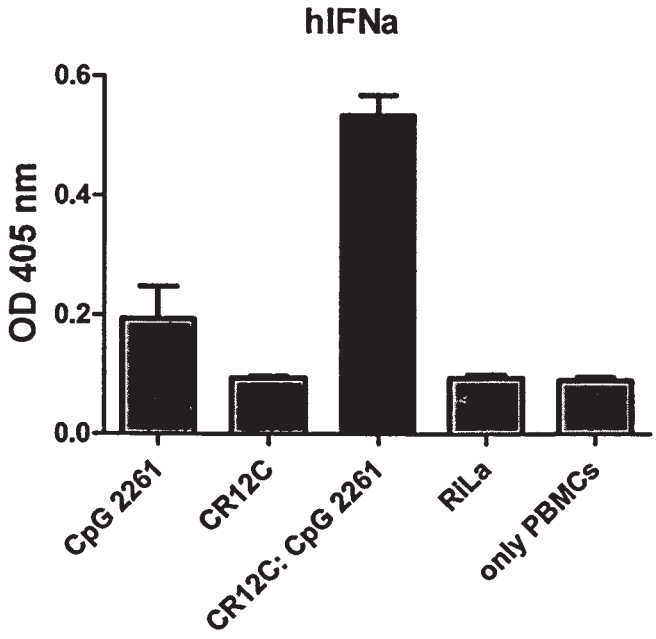
Fig. 1



Cationic component/nucleic acid	Ratio (w/w)	ZP mV
$CR_{12}C$/R722	5:1	47,5
$CR_{12}C$/R722	4:1	19,6
$CR_{12}C$/R722	3:1	23,8
$CR_{12}C$/R722	2:1	35
$CR_{12}C$/R722	1:1	-14,5
$CR_{12}C$/R722	1:2	-14
$CR_{12}C$/R722	1:3	-5,16
$CR_{12}C$/R722	1:4	-8,07
$CR_{12}C$/R722	1:5	-12,4

Fig. 2

A


hIFNa
OD 405 nm
0.6
0.4
0.2
0.0
CpG 2261
CR12C
CR12C: CpG 2261
RiLa
only PBMCs

B

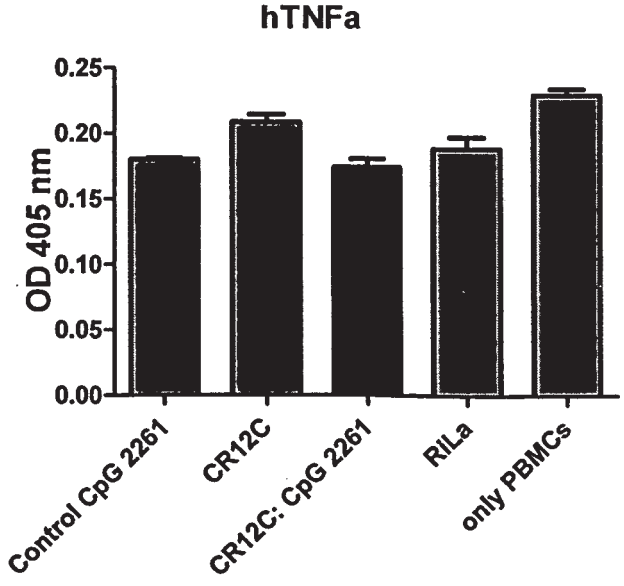
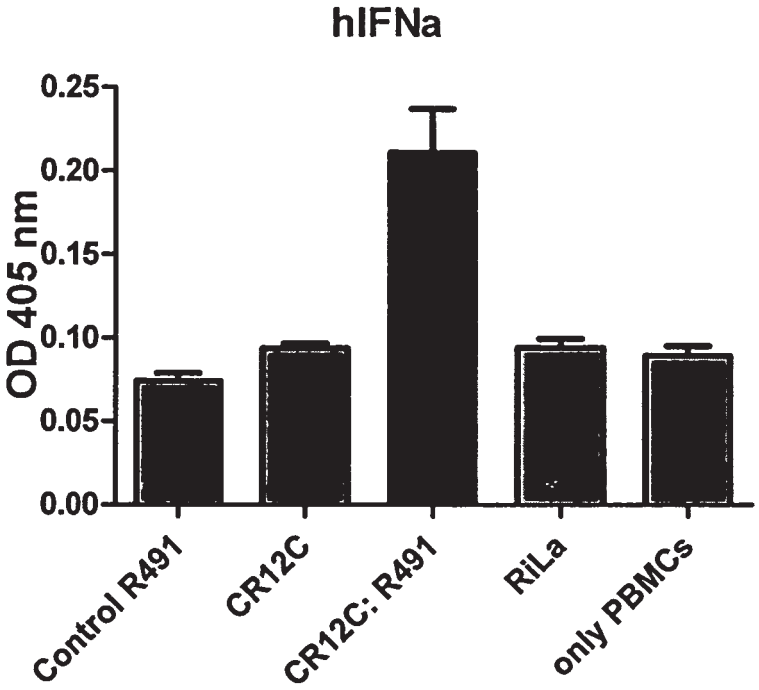

hTNFa
OD 405 nm
0.25
0.20
0.15
0.10
0.05
0.00
Control CpG 2261
CR12C
CR12C: CpG 2261
RiLa
only PBMCs

Fig. 3

A


hIFNa
OD 405 nm
0.25
0.20
0.15
0.10
0.05
0.00
Control R491
CR12C
CR12C: R491
RiLa
only PBMCs

B

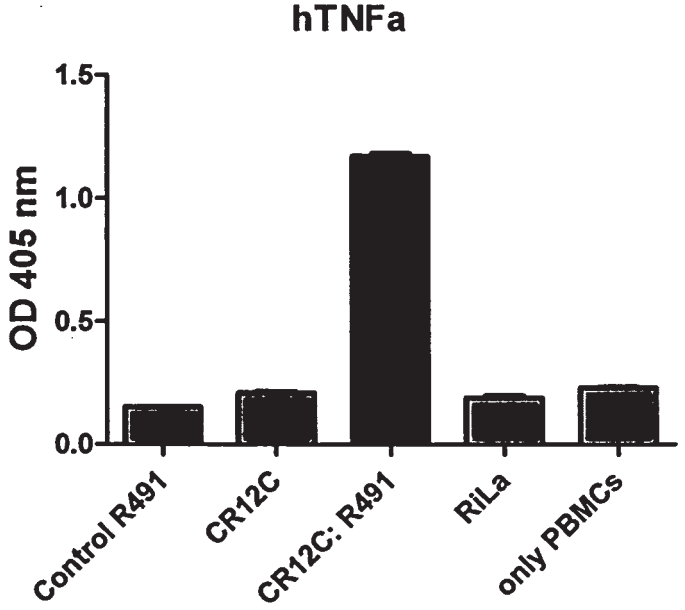
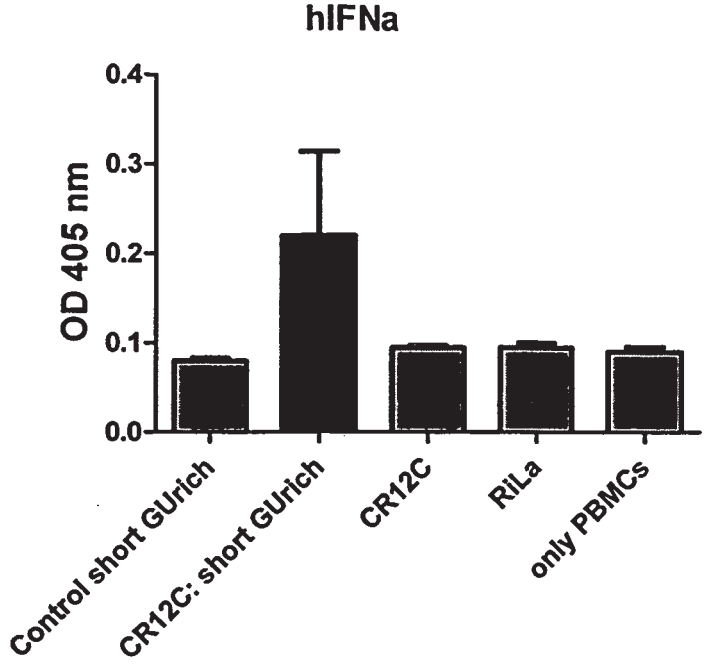

hTNFa
OD 405 nm
1.5
1.0
0.5
0.0
Control R491
CR12C
CR12C: R491
RiLa
only PBMCs

Fig. 4

A


hIFNa
OD 405 nm
0.4
0.3
0.2
0.1
0.0
Control short GUrich
CR12C: short GUrich
CR12C
RiLa
only PBMCs

B

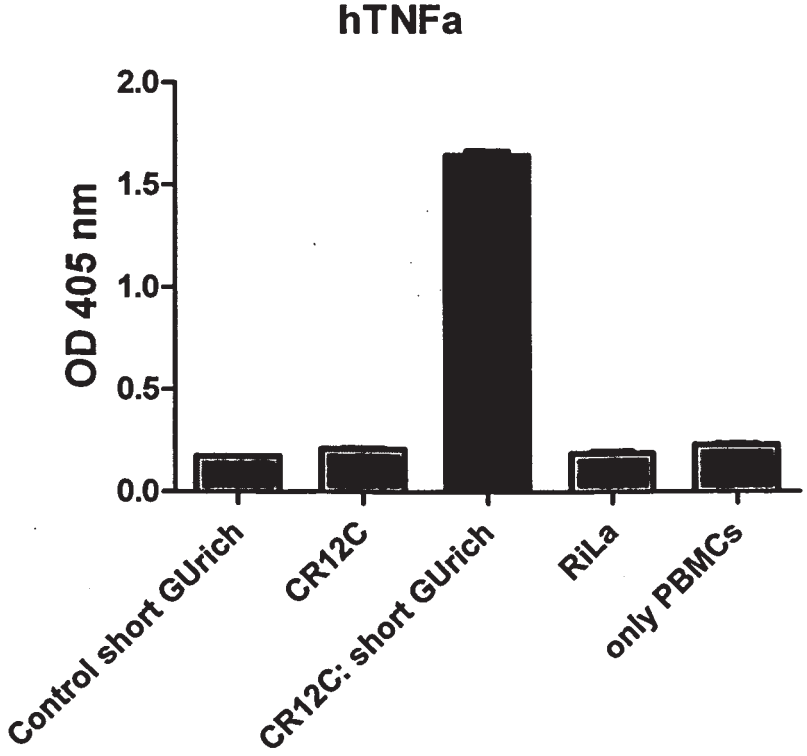
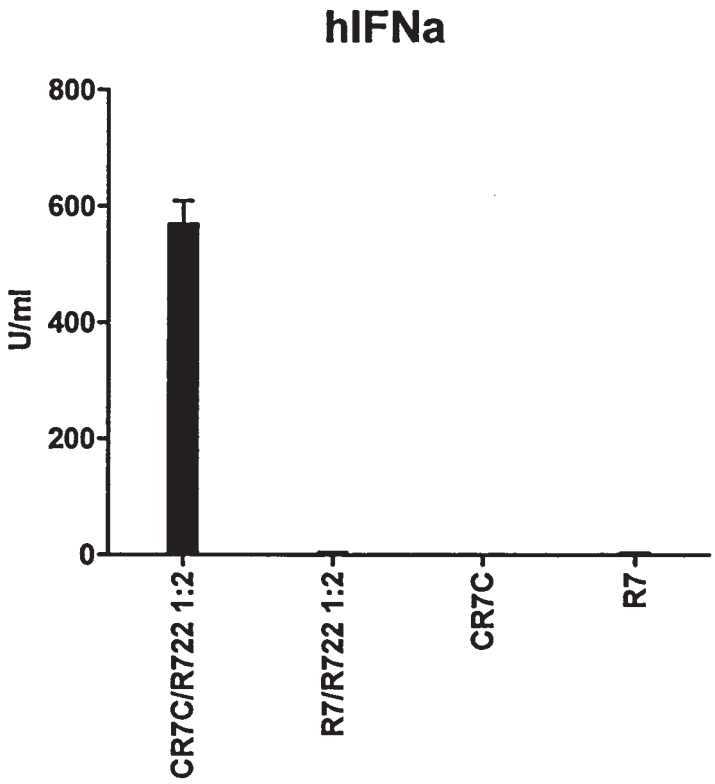

hTNFa
OD 405 nm
2.0
1.5
1.0
0.5
0.0
Control short GUrich
CR12C
CR12C: short GUrich
RiLa
only PBMCs

Fig. 5

A


hIFNa
800
600
400
200
0
U/ml
CR7C/R722 1:2
R7/R722 1:2
CR7C
R7

B

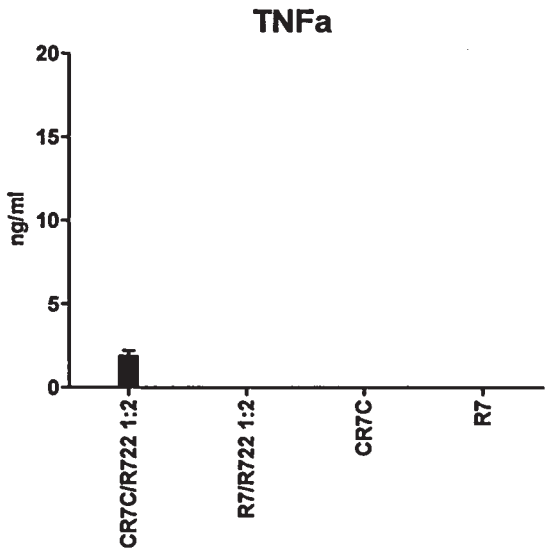
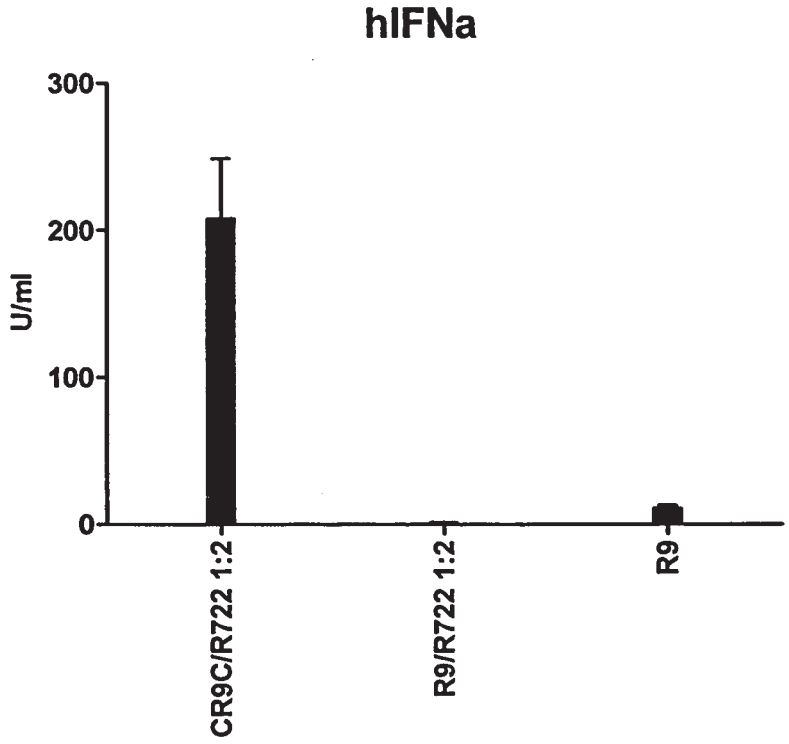

TNFa
20
15
10
5
0
ng/ml
CR7C/R722 1:2
R7/R722 1:2
CR7C
R7

Fig. 6

A


hIFNa
300
200
100
0
U/ml
CR9C/R722 1:2
R9/R722 1:2
R9

B

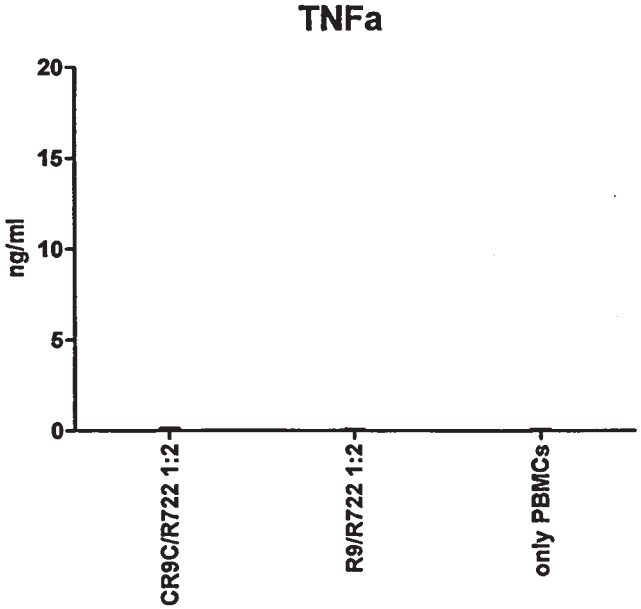
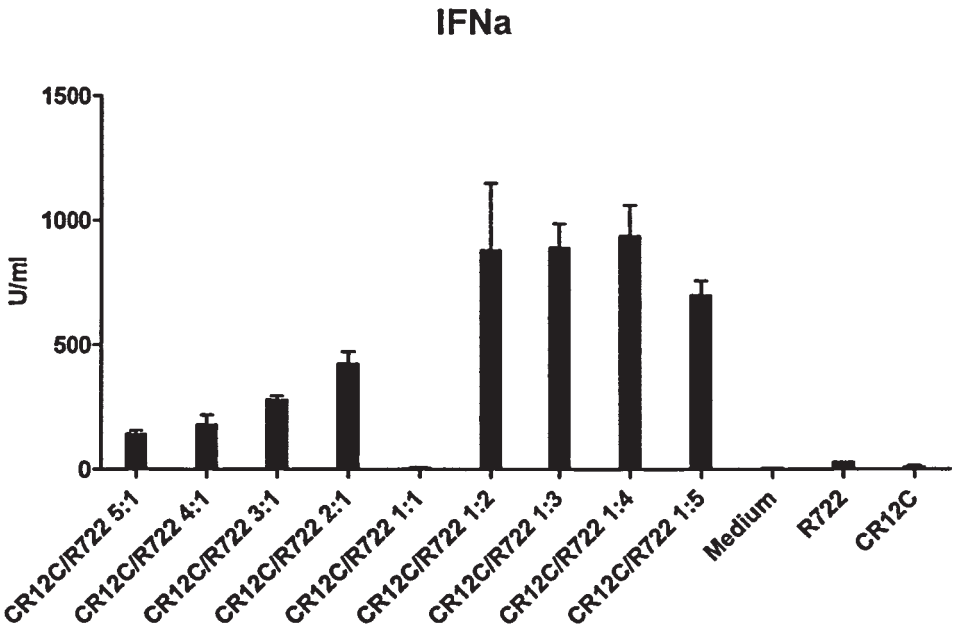

TNFa
20
15
10
5
0
ng/ml
CR9C/R722 1:2
R9/R722 1:2
only PBMCs

Fig. 7

A


IFNa
1500
1000
500
0
U/ml
CR12C/R722 5:1
CR12C/R722 4:1
CR12C/R722 3:1
CR12C/R722 2:1
CR12C/R722 1:1
CR12C/R722 1:2
CR12C/R722 1:3
CR12C/R722 1:4
CR12C/R722 1:5
Medium
R722
CR12C

B

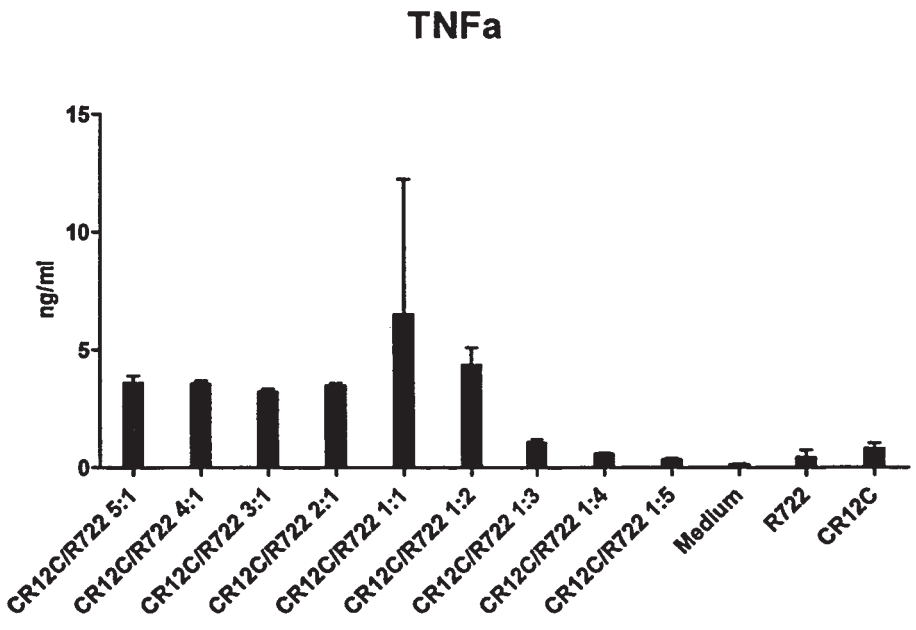
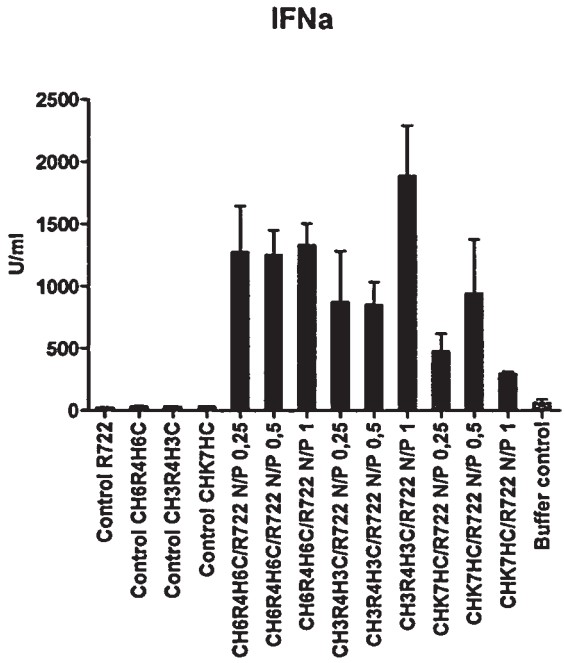

TNFa
15
10
5
0
ng/ml
CR12C/R722 5:1
CR12C/R722 4:1
CR12C/R722 3:1
CR12C/R722 2:1
CR12C/R722 1:1
CR12C/R722 1:2
CR12C/R722 1:3
CR12C/R722 1:4
CR12C/R722 1:5
Medium
R722
CR12C

Fig. 8

A


IFNa
U/ml
2500
2000
1500
1000
500
0
Control R722
Control CH6R4H6C
Control CH3R4H3C
Control CHK7HC
CH6R4H6C/R722 N/P 0,25
CH6R4H6C/R722 N/P 0,5
CH6R4H6C/R722 N/P 1
CH3R4H3C/R722 N/P 0,25
CH3R4H3C/R722 N/P 0,5
CH3R4H3C/R722 N/P 1
CHK7HC/R722 N/P 0,25
CHK7HC/R722 N/P 0,5
CHK7HC/R722 N/P 1
Buffer control

B

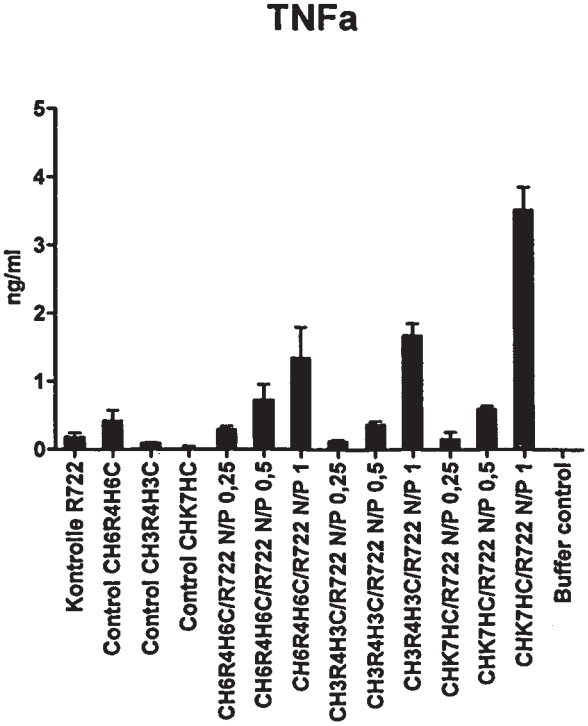

TNFa
ng/ml
5
4
3
2
1
0
Kontrolle R722
Control CH6R4H6C
Control CH3R4H3C
Control CHK7HC
CH6R4H6C/R722 N/P 0,25
CH6R4H6C/R722 N/P 0,5
CH6R4H6C/R722 N/P 1
CH3R4H3C/R722 N/P 0,25
CH3R4H3C/R722 N/P 0,5
CH3R4H3C/R722 N/P 1
CHK7HC/R722 N/P 0,25
CHK7HC/R722 N/P 0,5
CHK7HC/R722 N/P 1
Buffer control

Fig. 9

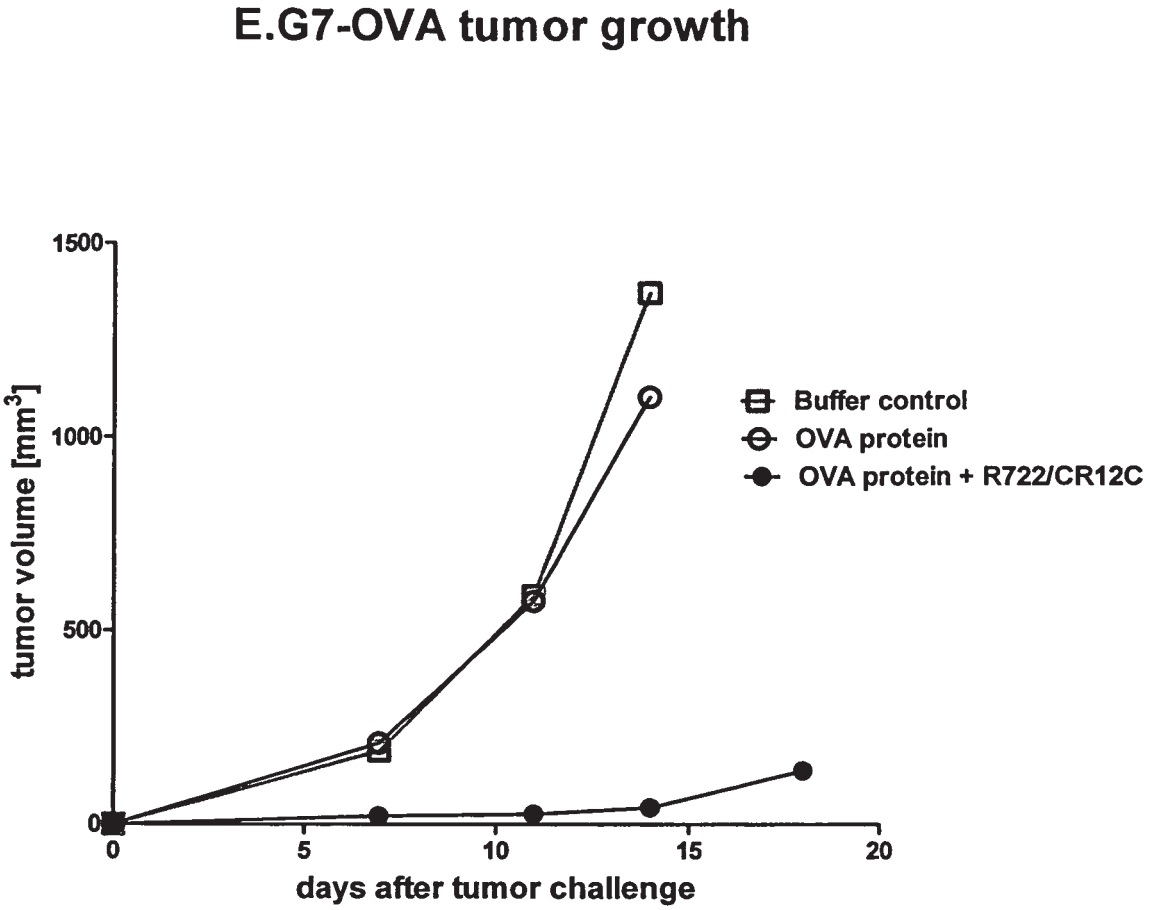

E.G7-OVA tumor growth
1500
1000
500
0
tumor volume [mm3]
0
5
10
15
20
days after tumor challenge
Buffer control
OVA protein
OVA protein + R722/CR12C

Fig. 10

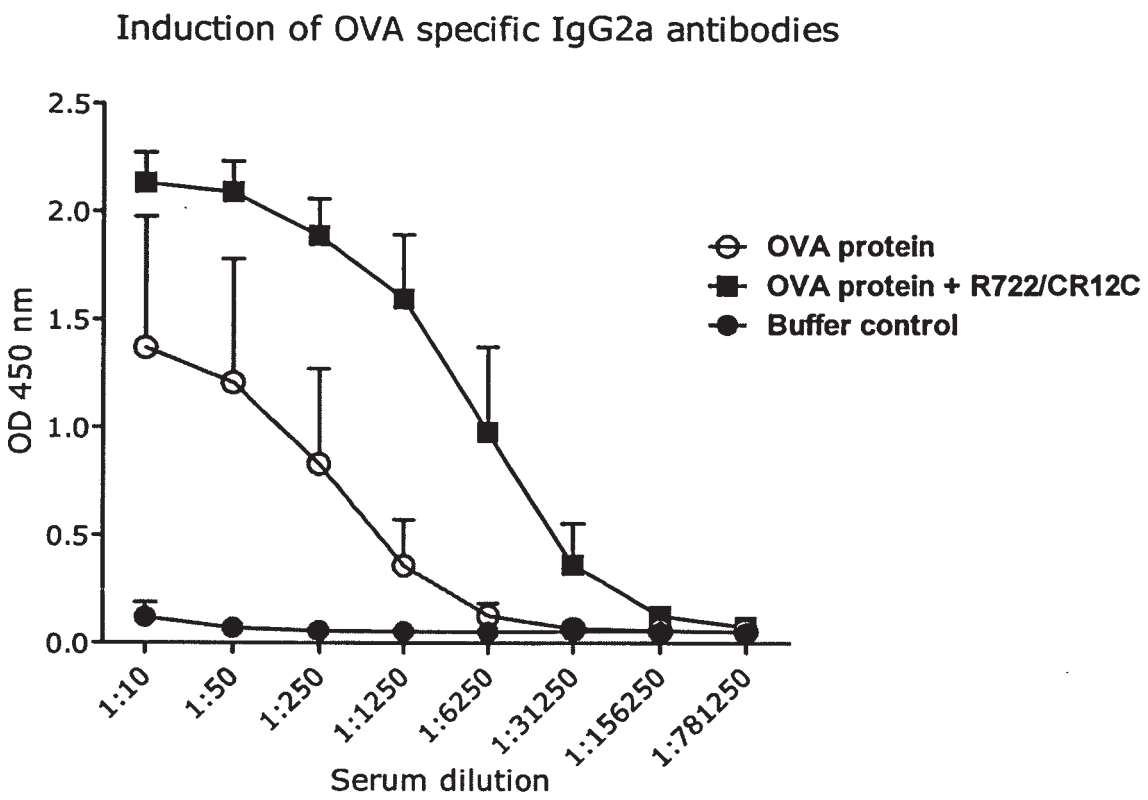

Induction of OVA specific IgG2a antibodies
OD 450 nm
2.5
2.0
1.5
1.0
0.5
0.0
1:10
1:50
1:250
1:1250
1:6250
1:31250
1:156250
1:781250
Serum dilution
OVA protein
OVA protein + R722/CR12C
Buffer control

Fig. 11

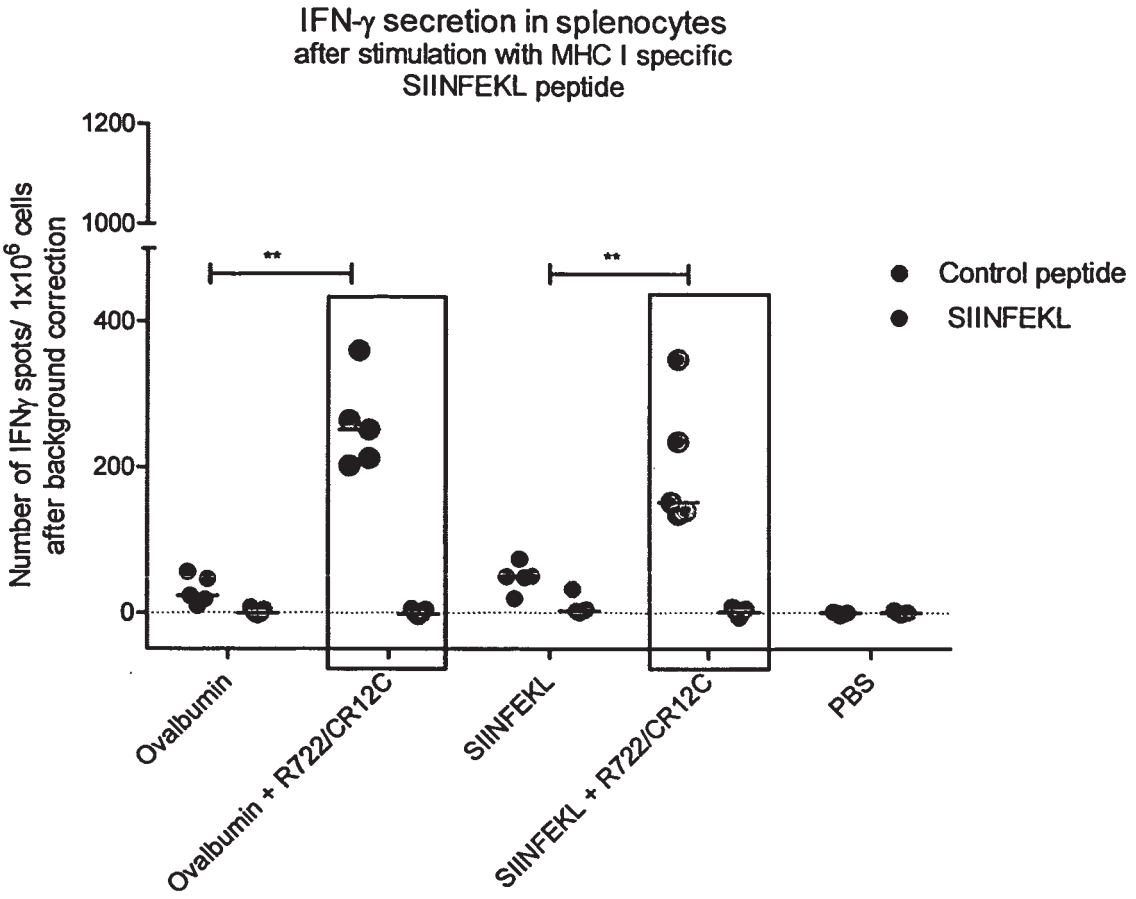

IFN-γ secretion in splenocytes
after stimulation with MHC I specific
SIINFEKL peptide
Number of IFNγ spots/ 1x10^6 cells
after background correction
1200
1000
400
200
0
**
**
Control peptide
SIINFEKL
Ovalbumin
Ovalbumin + R722/CR12C
SIINFEKL
SIINFEKL + R722/CR12C
PBS

Fig. 12

Induction of total IgG antibodies after vaccination with Rabipur

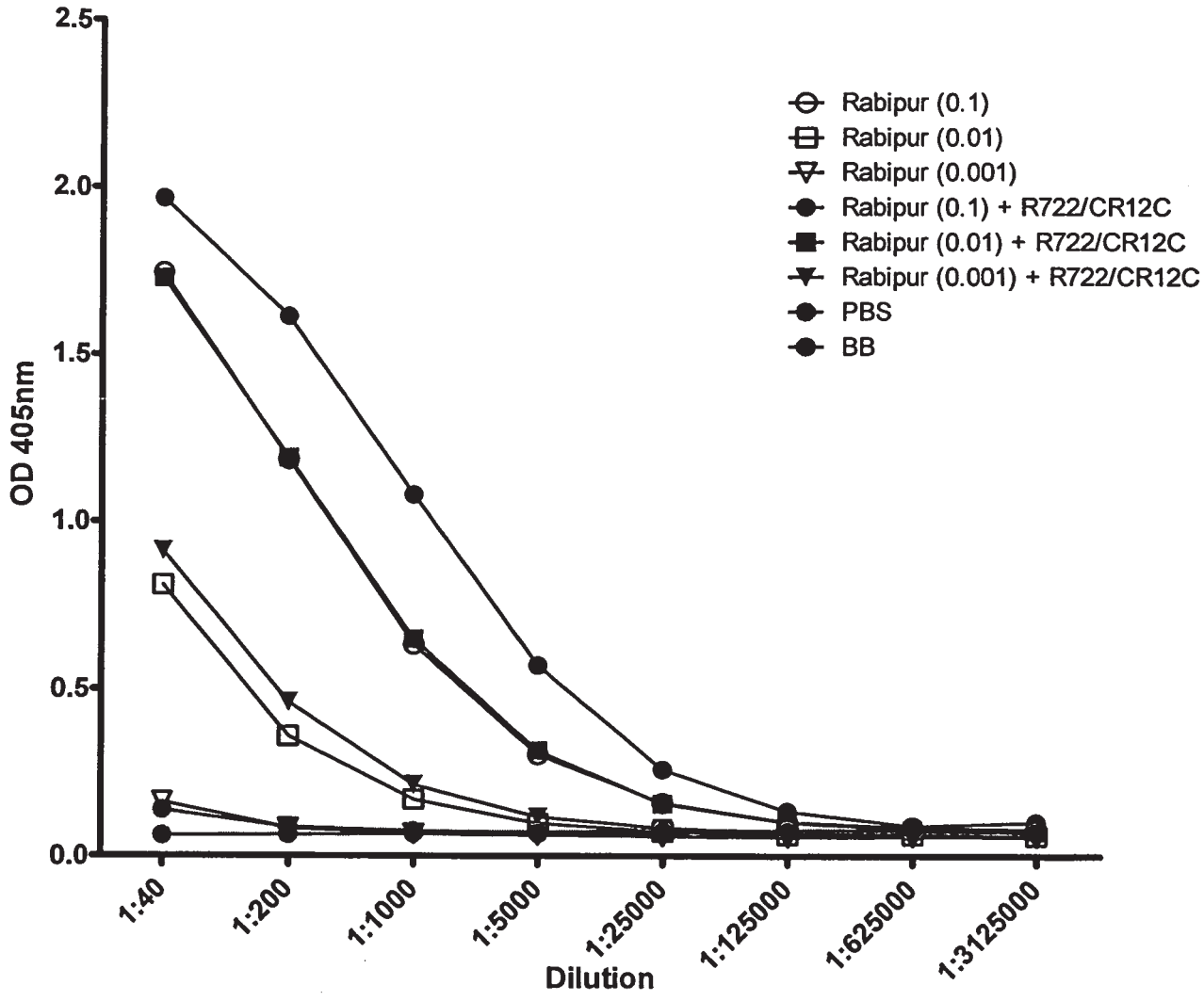


Fig. 13

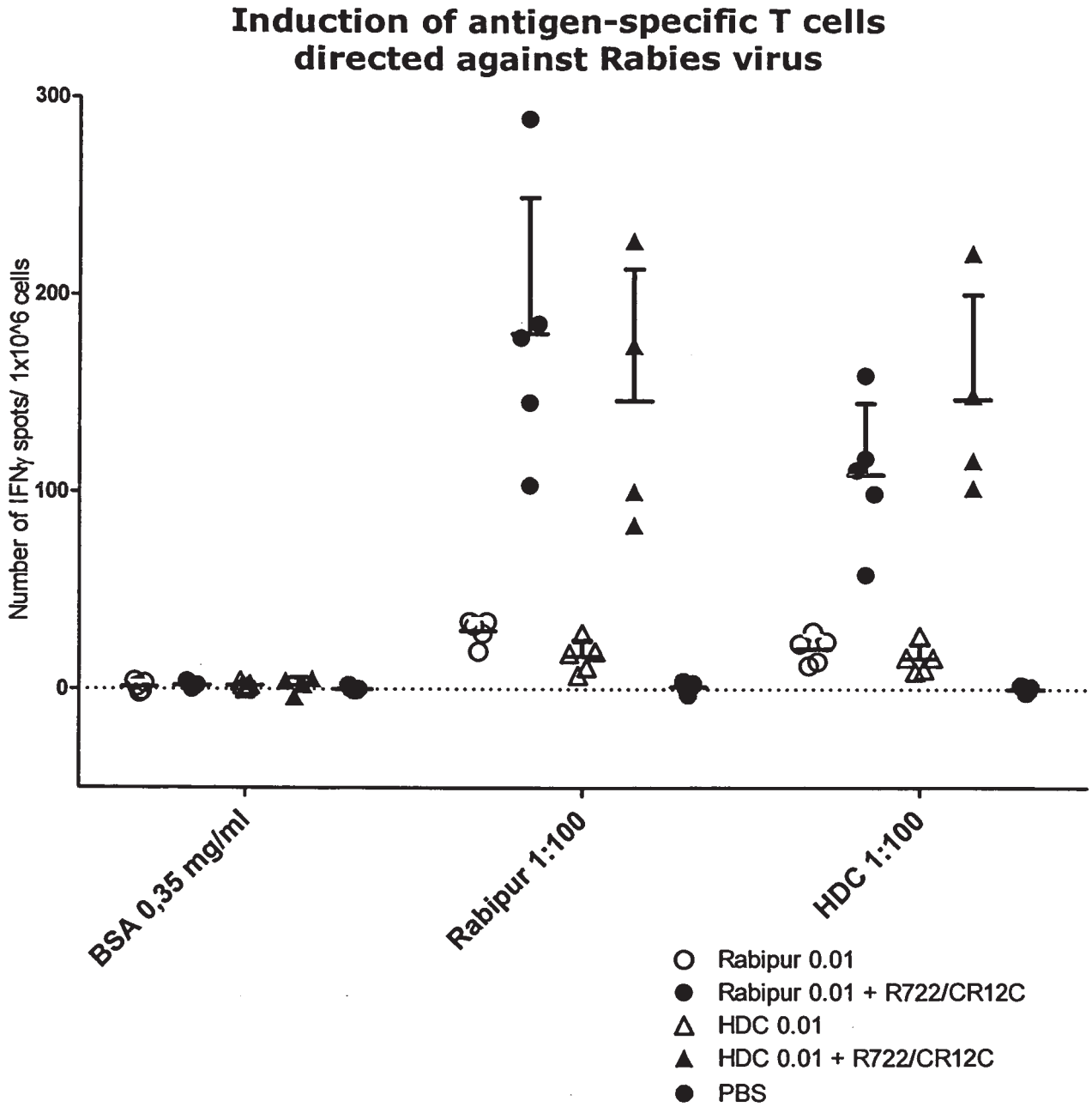

Induction of antigen-specific T cells
directed against Rabies virus
Number of IFNγ spots/ 1x10^6 cells
300
200
100
0
BSA 0,35 mg/ml
Rabipur 1:100
HDC 1:100
Rabipur 0.01
Rabipur 0.01 + R722/CR12C
HDC 0.01
HDC 0.01 + R722/CR12C
PBS

Fig. 14

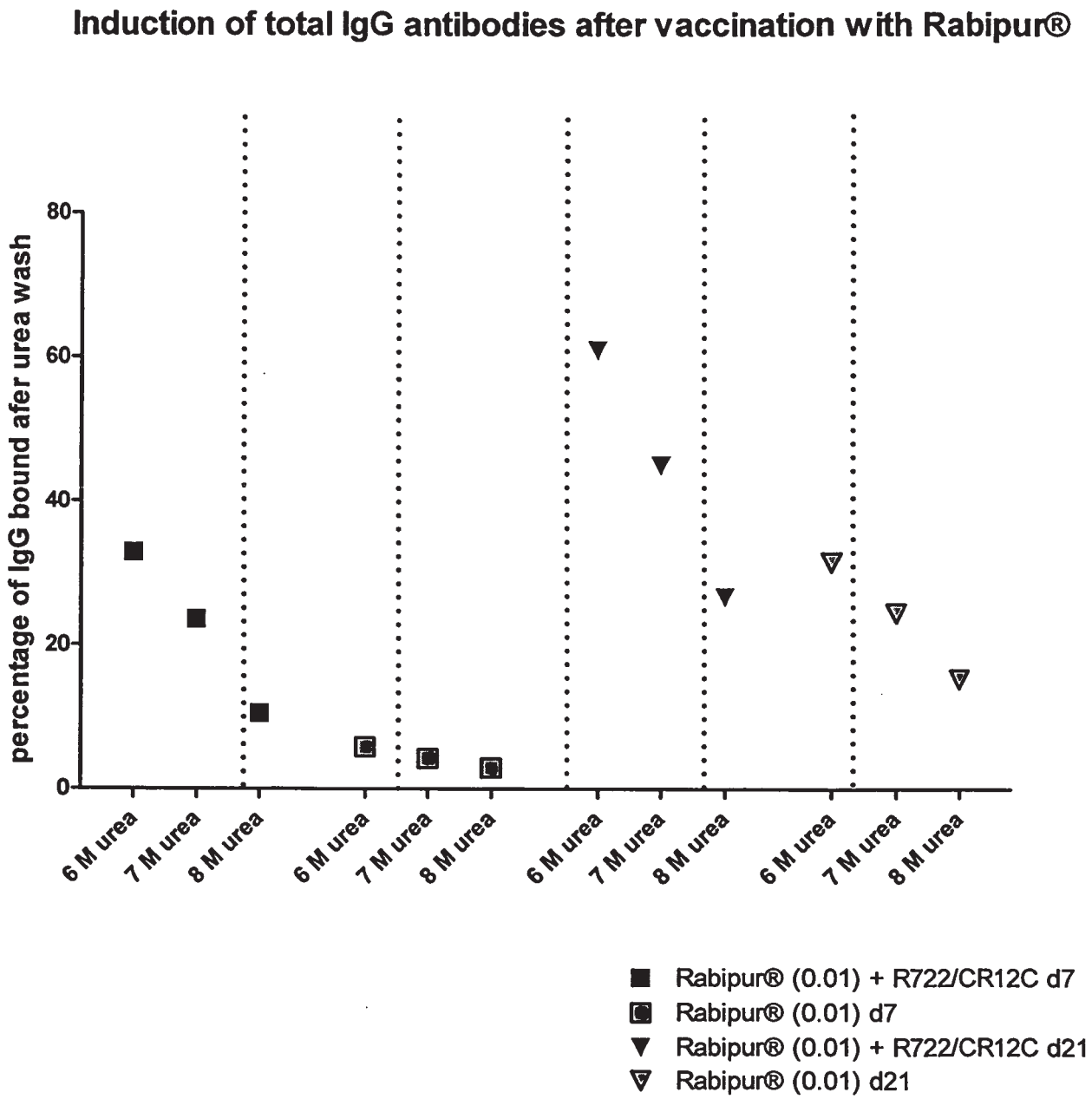

Induction of total IgG antibodies after vaccination with Rabipur®
percentage of IgG bound afer urea wash
80
60
40
20
0
6 M urea
7 M urea
8 M urea
6 M urea
7 M urea
8 M urea
6 M urea
7 M urea
8 M urea
6 M urea
7 M urea
8 M urea
Rabipur® (0.01) + R722/CR12C d7
Rabipur® (0.01) d7
Rabipur® (0.01) + R722/CR12C d21
Rabipur® (0.01) d21

Fig. 15

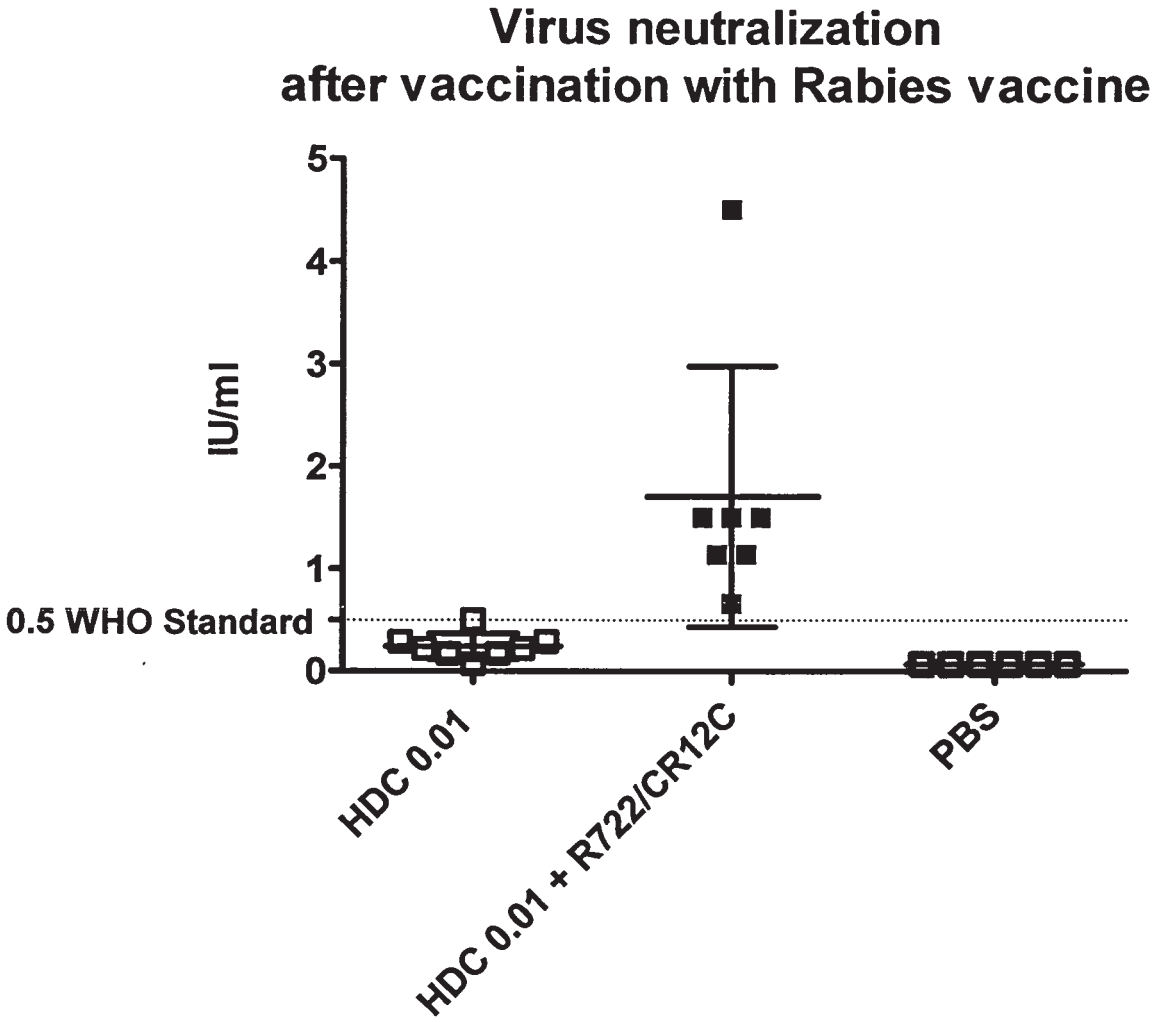

Virus neutralization
after vaccination with Rabies vaccine
IU/ml
5
4
3
2
1
0
0.5 WHO Standard
HDC 0.01
HDC 0.01 + R722/CR12C
PBS

Fig. 16

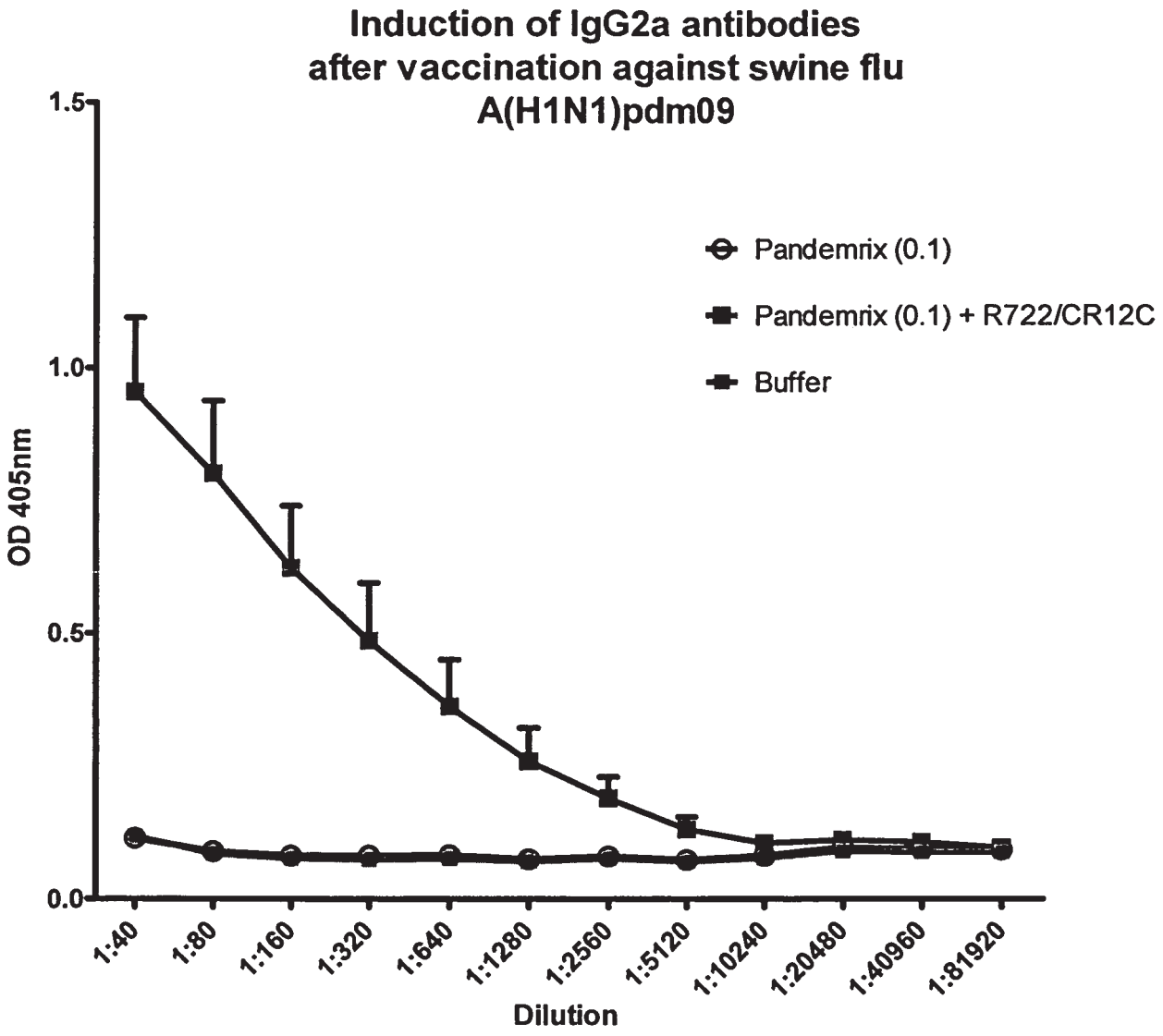

Induction of IgG2a antibodies
after vaccination against swine flu
A(H1N1)pdm09
Pandemrix (0.1)
Pandemrix (0.1) + R722/CR12C
Buffer
OD 405nm
1.5
1.0
0.5
0.0
1:40
1:80
1:160
1:320
1:640
1:1280
1:2560
1:5120
1:10240
1:20480
1:40960
1:81920
Dilution

Fig. 17

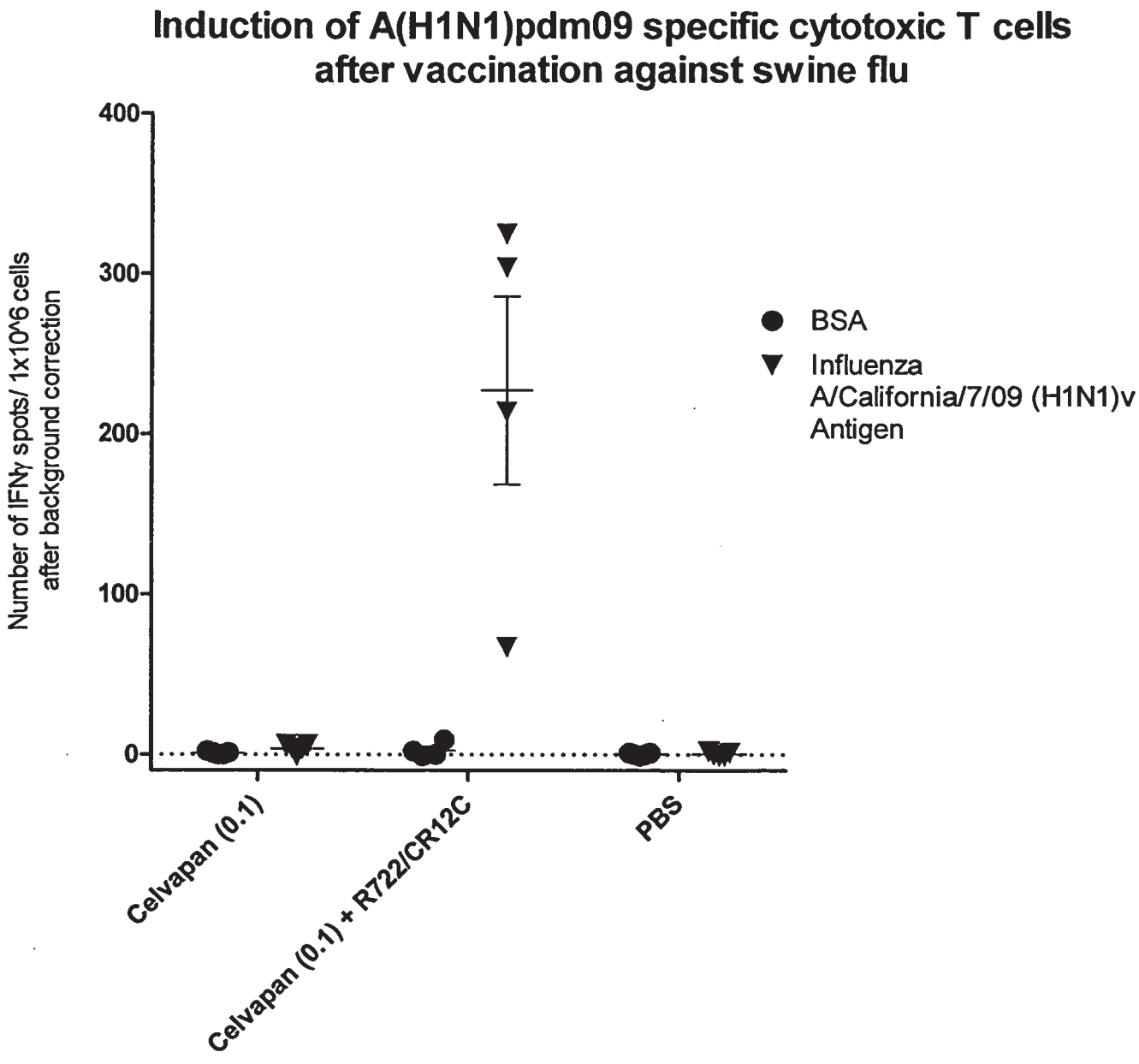

Induction of A(H1N1)pdm09 specific cytotoxic T cells after vaccination against swine flu
Number of IFNγ spots/ 1x10^6 cells after background correction
400
300
200
100
0
BSA
Influenza A/California/7/09 (H1N1)v Antigen
Celvapan (0.1)
Celvapan (0.1) + R722/CR12C
PBS

Fig. 18

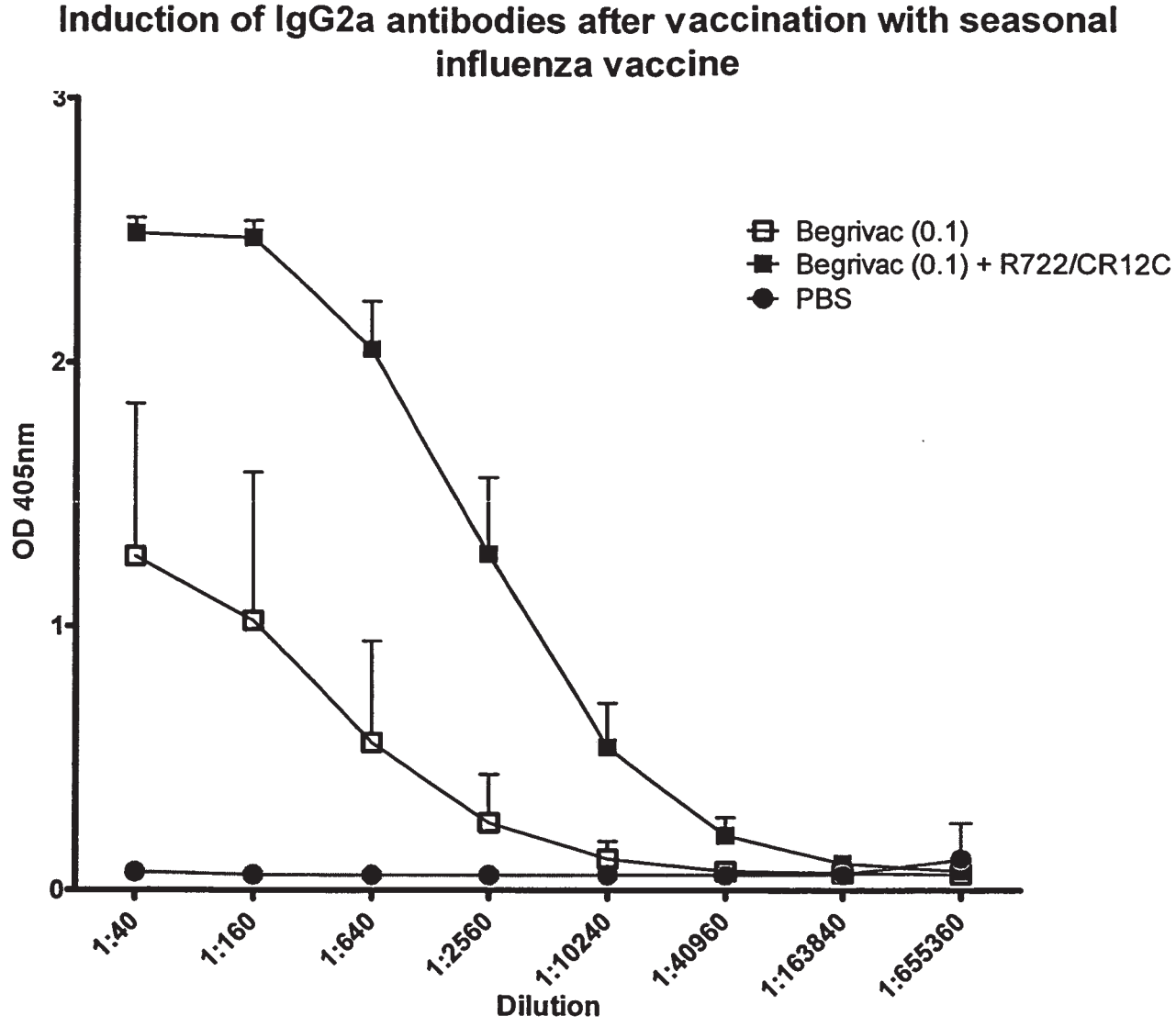

Induction of IgG2a antibodies after vaccination with seasonal influenza vaccine
OD 405nm
3
2
1
0
Begrivac (0.1)
Begrivac (0.1) + R722/CR12C
PBS
1:40
1:160
1:640
1:2560
1:10240
1:40960
1:163840
1:655360
Dilution

Fig. 19

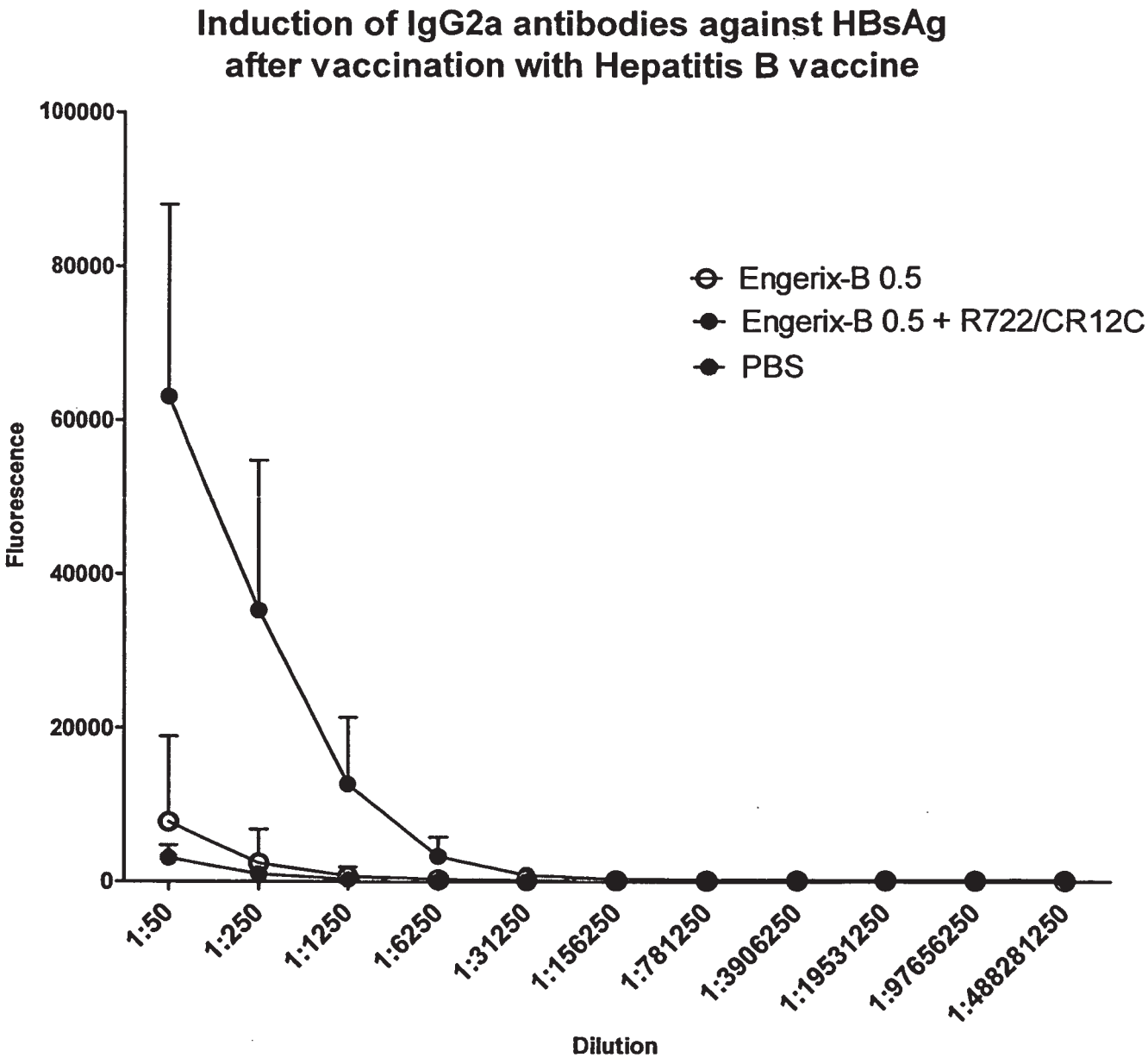

Induction of IgG2a antibodies against HBsAg
after vaccination with Hepatitis B vaccine
100000
80000
60000
40000
20000
0
Fluorescence
Engerix-B 0.5
Engerix-B 0.5 + R722/CR12C
PBS
1:50
1:250
1:1250
1:6250
1:31250
1:156250
1:781250
1:3906250
1:19531250
1:97656250
1:488281250
Dilution

Fig. 20

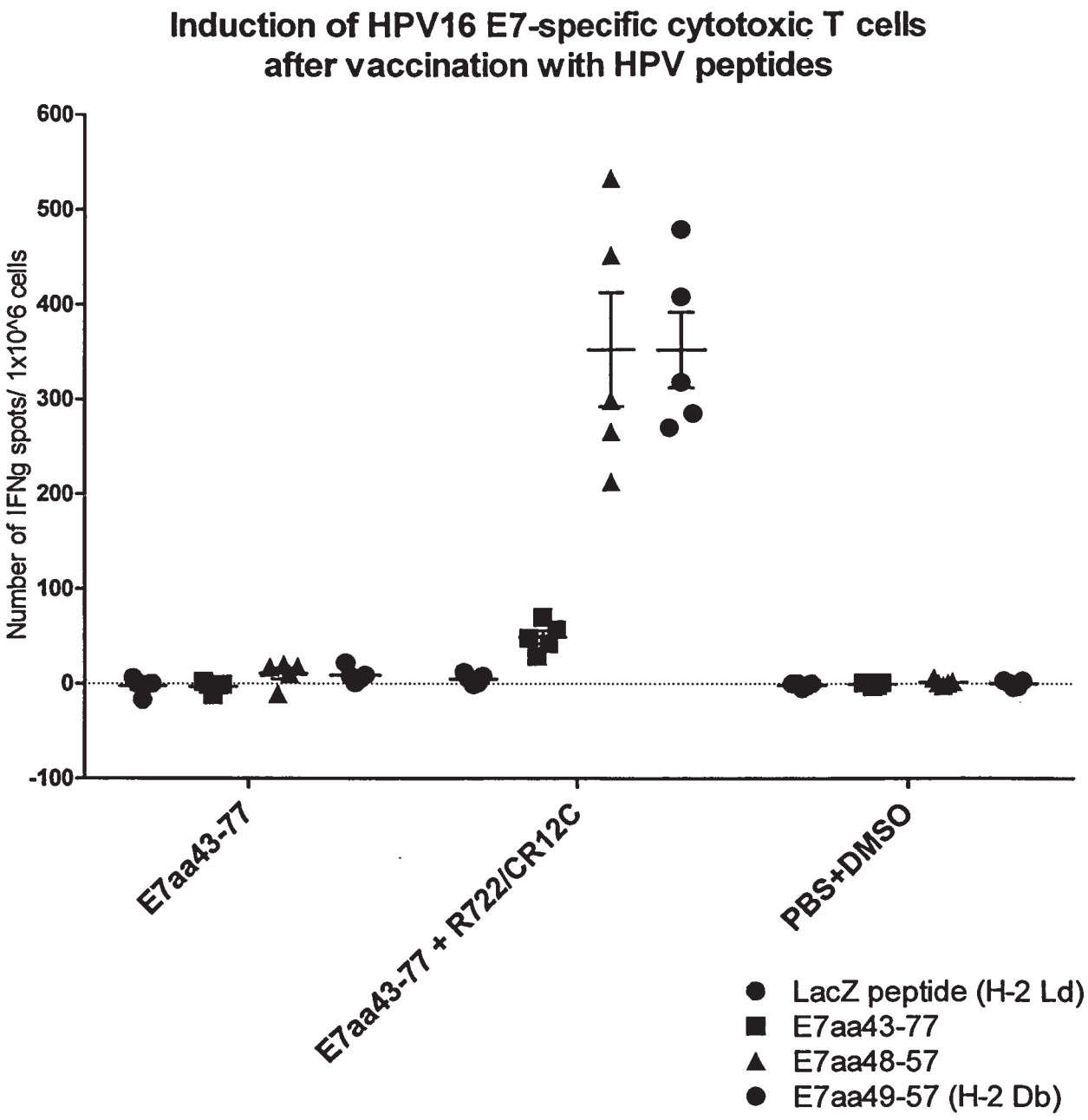

Induction of HPV16 E7-specific cytotoxic T cells
after vaccination with HPV peptides
Number of IFNg spots/ 1x10^6 cells
600
500
400
300
200
100
0
-100
E7aa43-77
E7aa43-77 + R722/CR12C
PBS+DMSO
LacZ peptide (H-2 Ld)
E7aa43-77
E7aa48-57
E7aa49-57 (H-2 Db)

Fig. 21

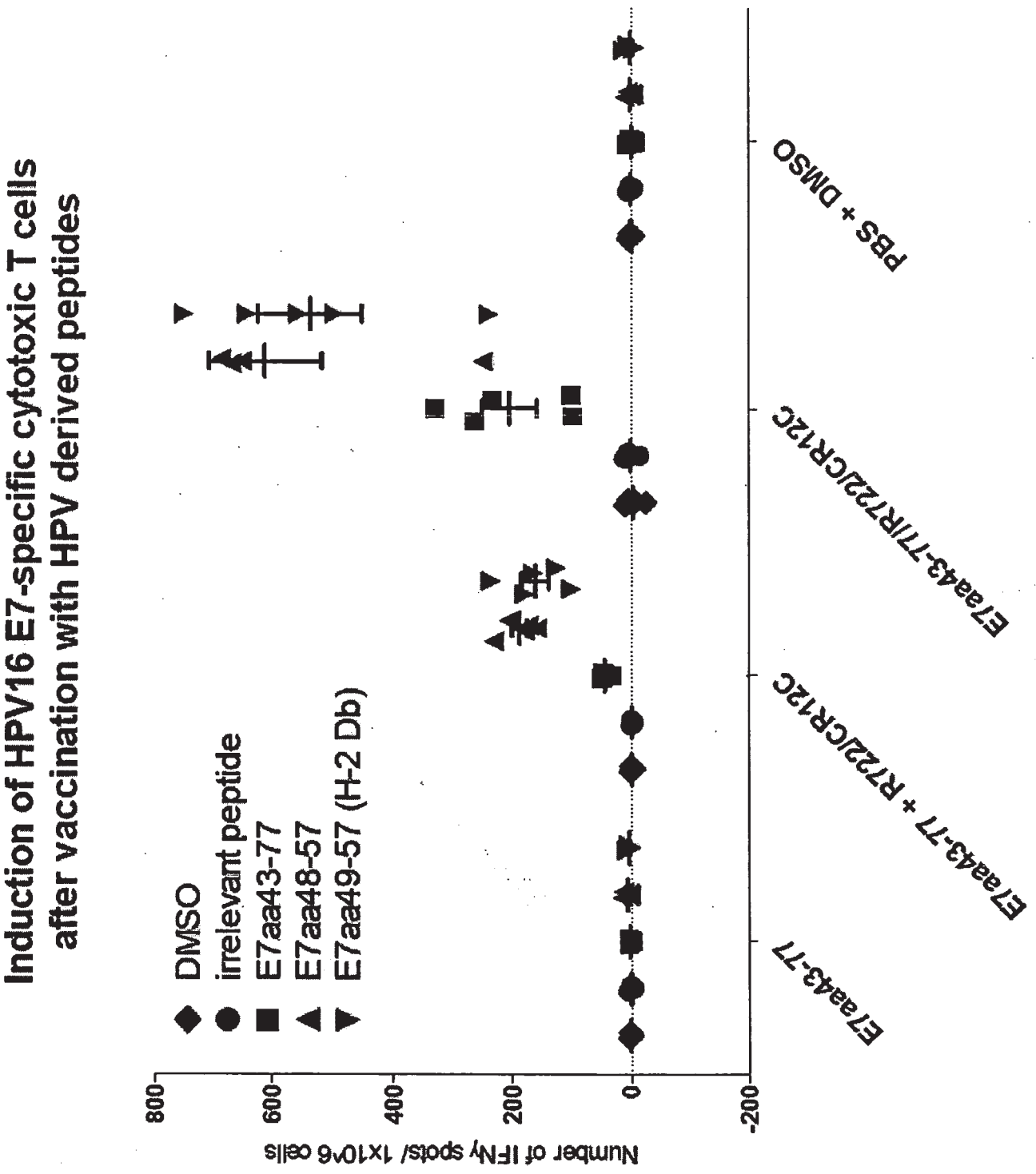

Induction of HPV16 E7-specific cytotoxic T cells
after vaccination with HPV derived peptides
DMSO
irrelevant peptide
E7aa43-77
E7aa48-57
E7aa49-57 (H-2 Db)
Number of IFNγ spots/ 1X10^6 cells
800
600
400
200
0
-200
E7aa43-77
E7aa43-77 + R72ΔCR12C
E7aa43-77/R72ΔCR12C
PBS + DMSO

Fig. 22

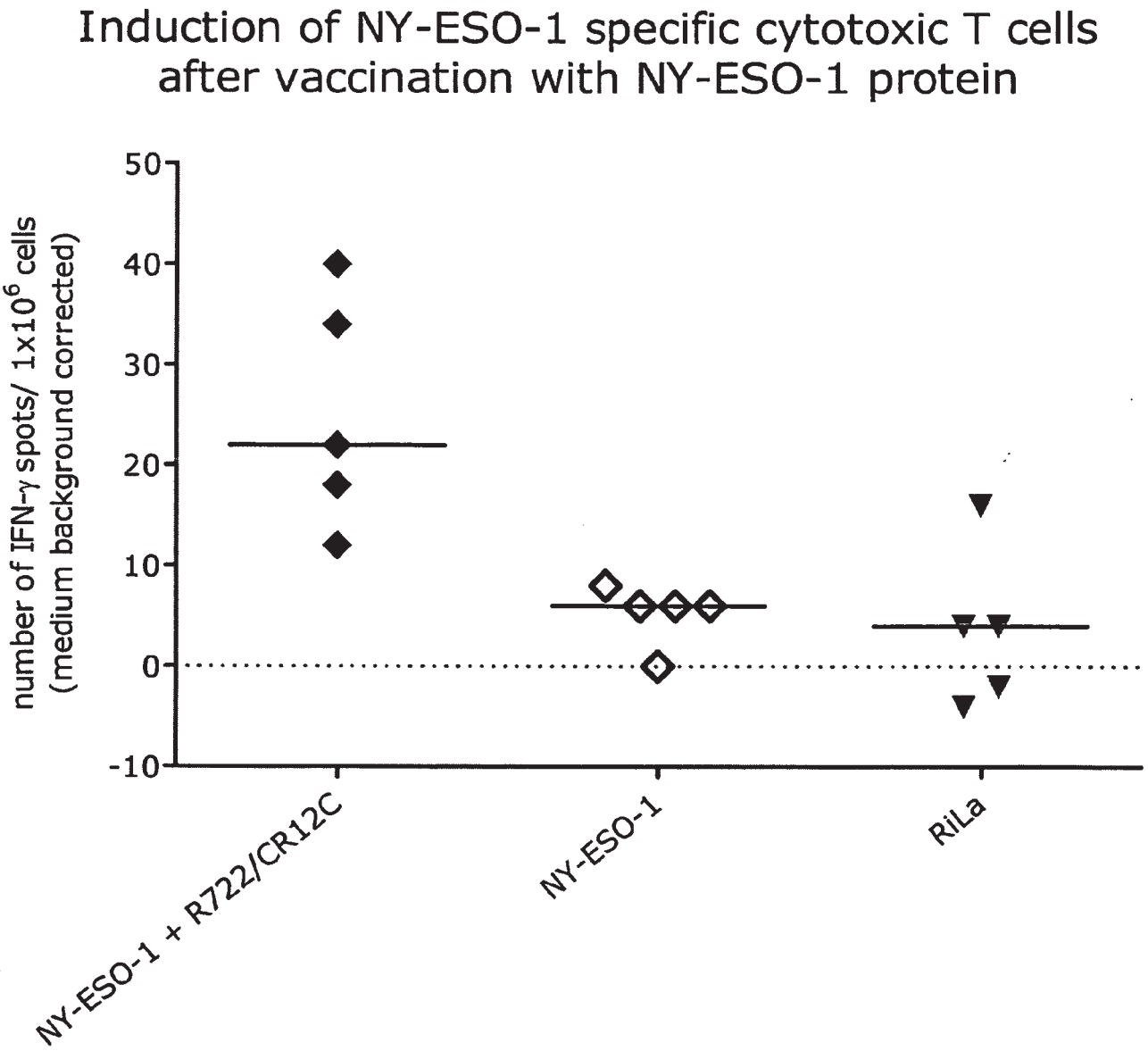

Induction of NY-ESO-1 specific cytotoxic T cells after vaccination with NY-ESO-1 protein
number of IFN-γ spots/ 1x10^6 cells (medium background corrected)
50
40
30
20
10
0
-10
NY-ESO-1 + R722/CR12C
NY-ESO-1
RiLa

Fig. 23

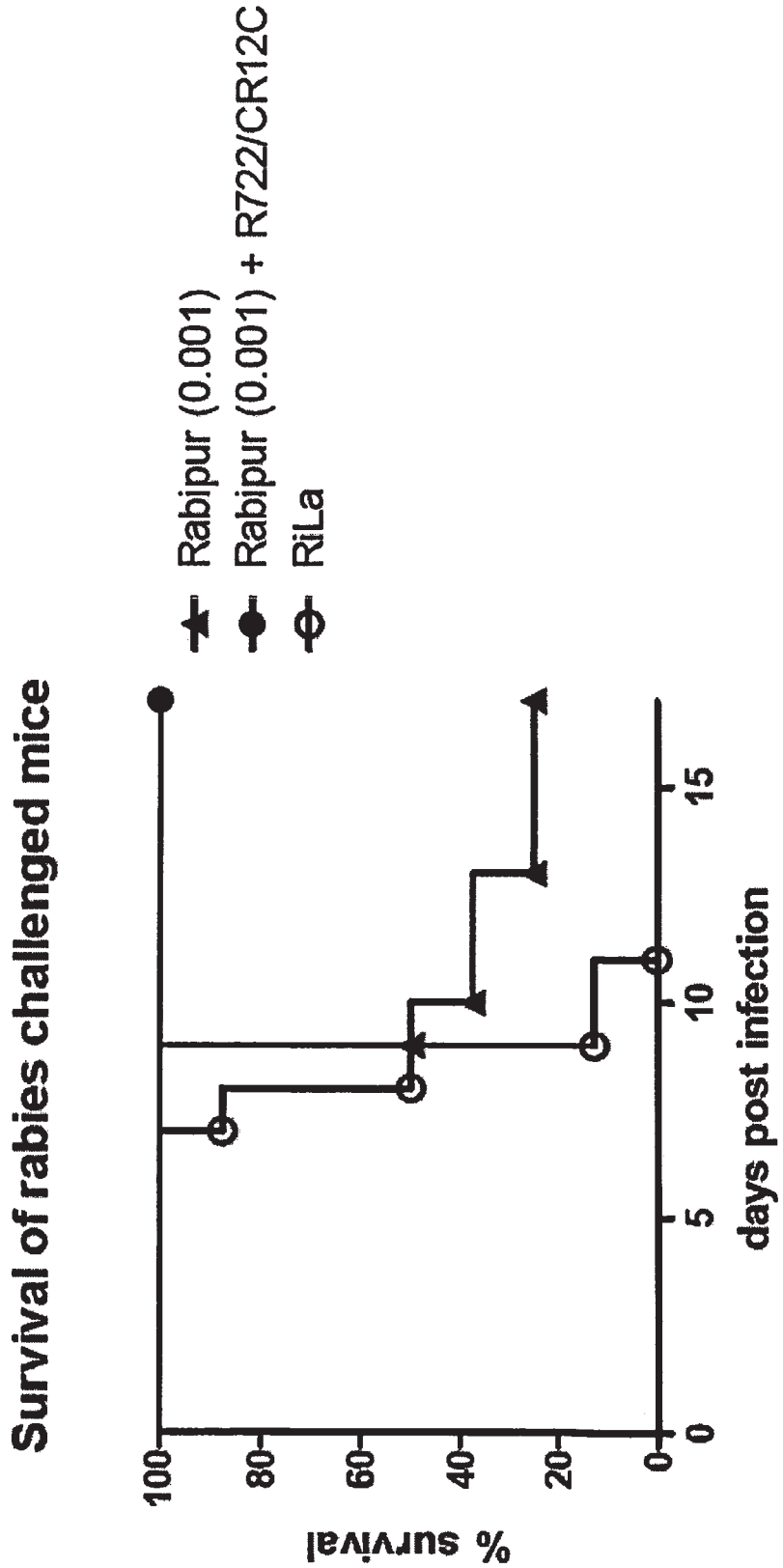
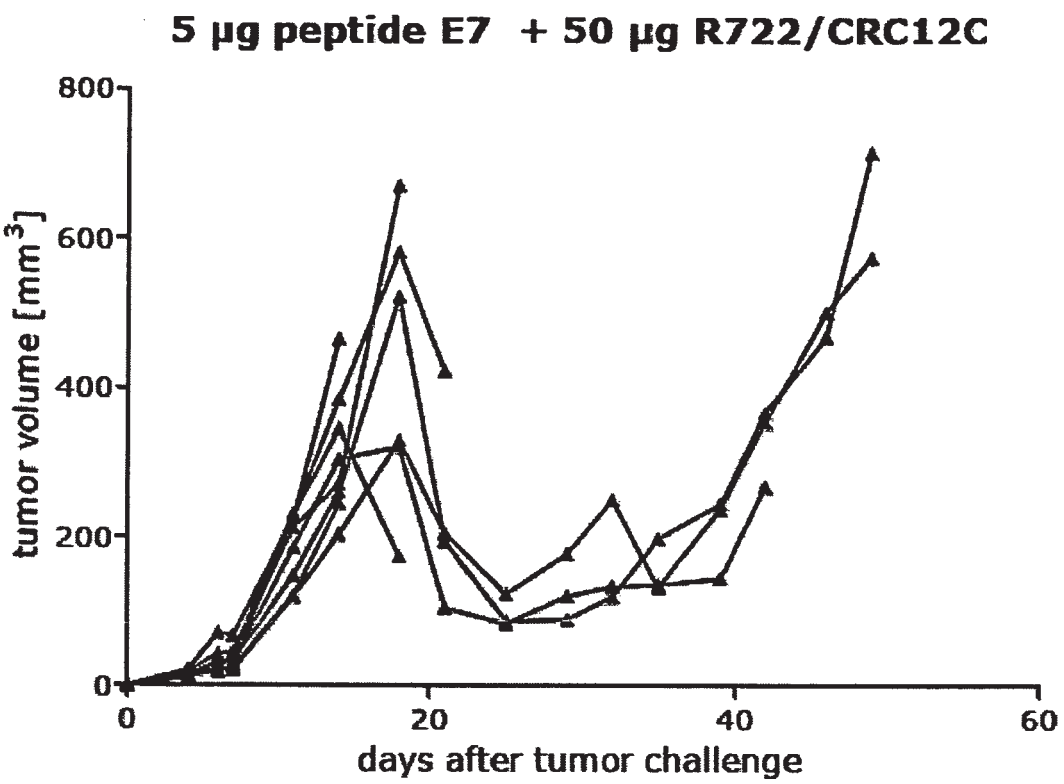

Survival of rabies challenged mice
Rabipur (0.001)
Rabipur (0.001) + R722/CR12C
RiLa
% survival
100
80
60
40
20
0
0
5
10
15
days post infection

Fig. 24

A


5 µg peptide E7 + 50 µg R722/CRC12C
tumor volume [mm3]
800
600
400
200
0
0
20
40
60
days after tumor challenge

B

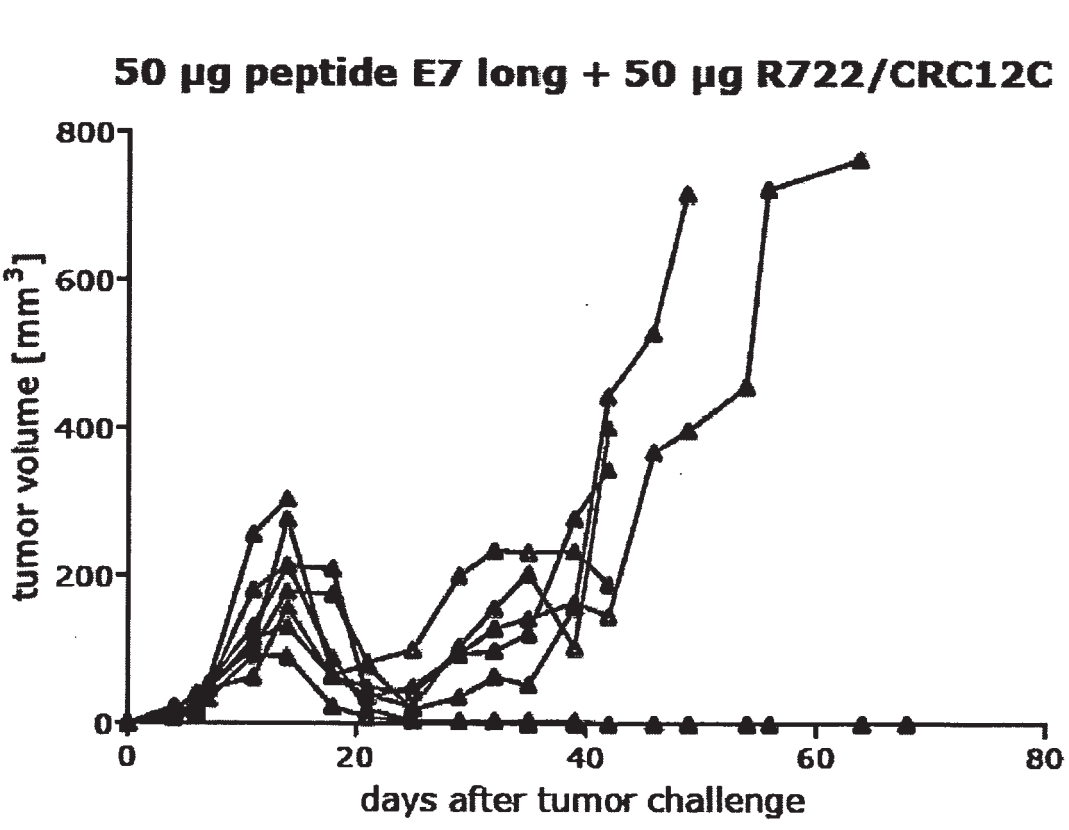

50 µg peptide E7 long + 50 µg R722/CRC12C
tumor volume [mm3]
800
600
400
200
0
0
20
40
60
80
days after tumor challenge

Fig. 25

C

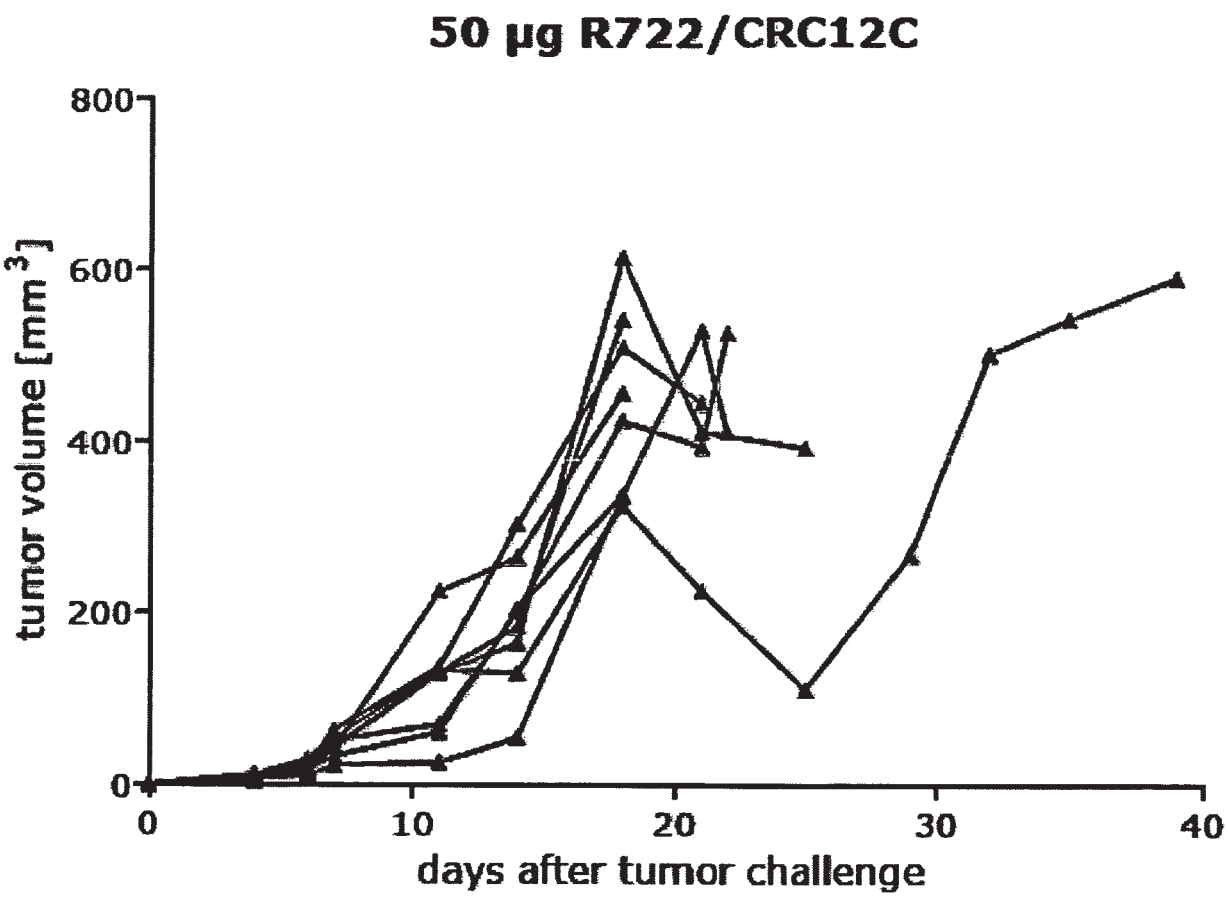

50 µg R722/CRC12C
800
600
400
200
0
tumor volume [mm3]
0
10
20
30
40
days after tumor challenge

Fig. 25

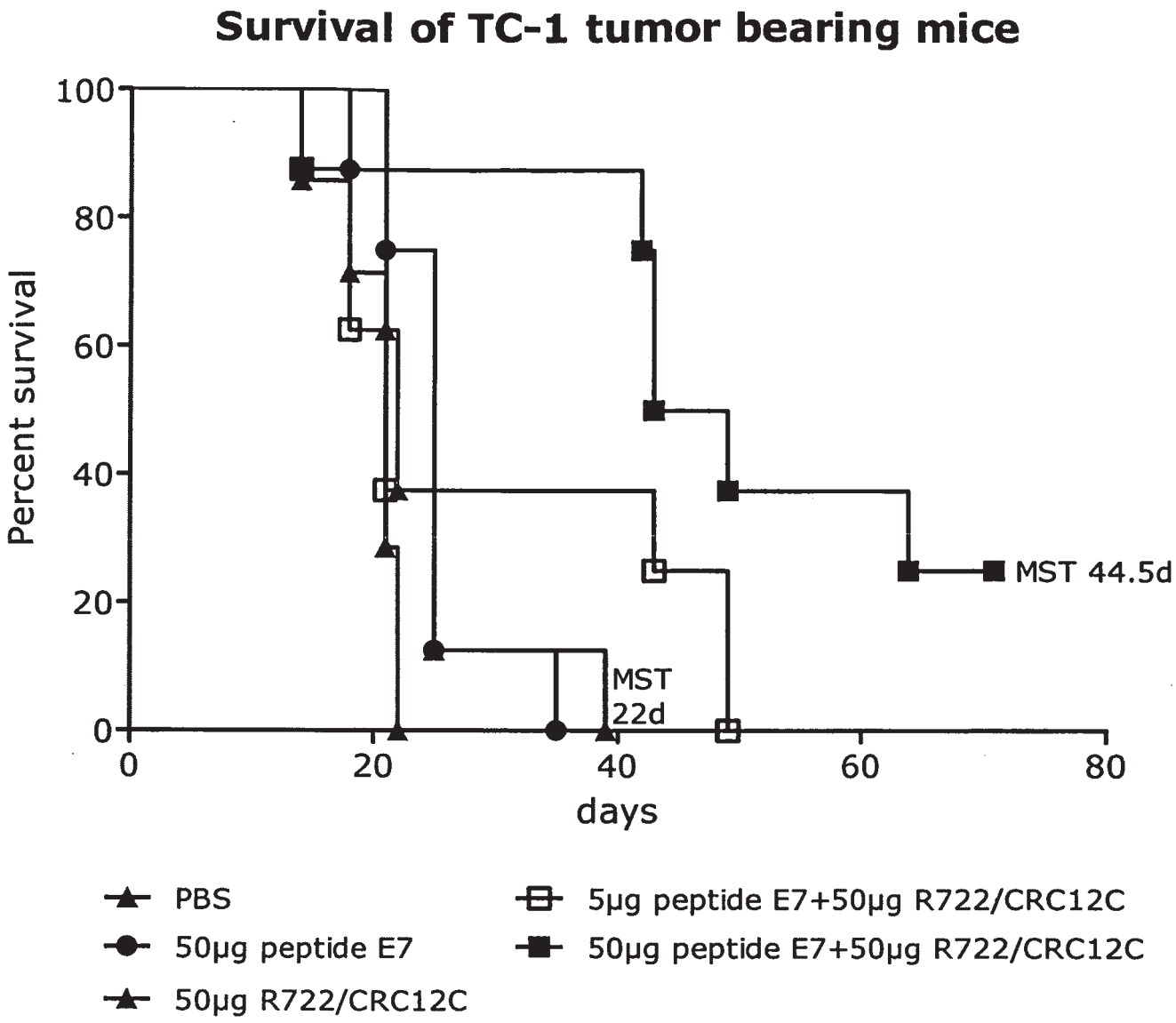

Survival of TC-1 tumor bearing mice
Percent survival
100
80
60
40
20
0
0
20
40
60
80
days
MST 44.5d
MST
22d
PBS
50µg peptide E7
50µg R722/CRC12C
5µg peptide E7+50µg R722/CRC12C
50µg peptide E7+50µg R722/CRC12C

Fig. 26

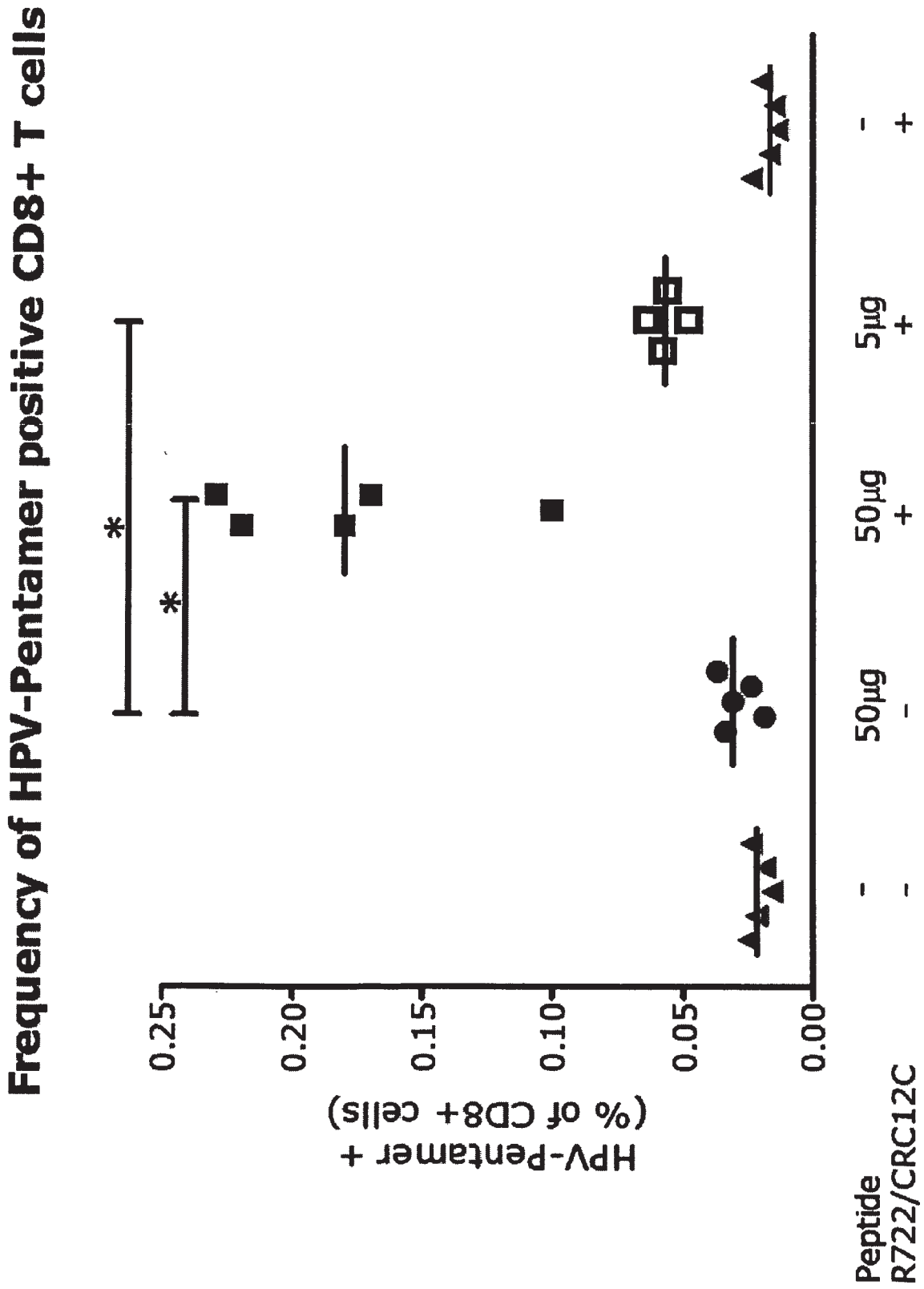

Frequency of HPV-Pentamer positive CD8+ T cells
HPV-Pentamer +
(% of CD8+ cells)
0.25
0.20
0.15
0.10
0.05
0.00
*
*
Peptide
R722/CRC12C
-
-
50µg
-
50µg
+
5µg
+
-
+

Fig. 27

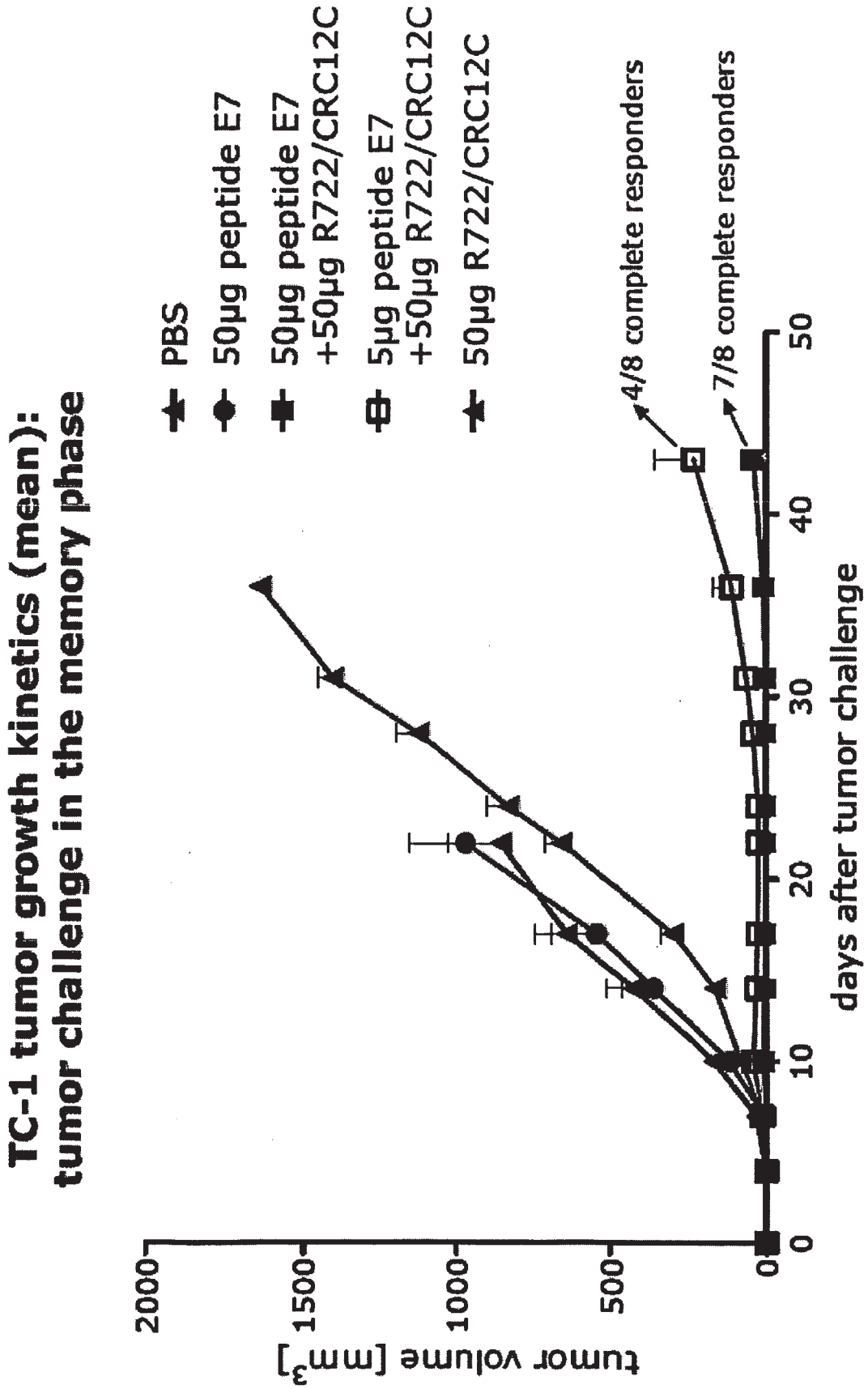

TC-1 tumor growth kinetics (mean):
tumor challenge in the memory phase
PBS
50µg peptide E7
50µg peptide E7 +50µg R722/CRC12C
5µg peptide E7 +50µg R722/CRC12C
50µg R722/CRC12C
4/8 complete responders
7/8 complete responders
tumor volume [mm³]
2000
1500
1000
500
0
0
10
20
30
40
50
days after tumor challenge

Fig. 28

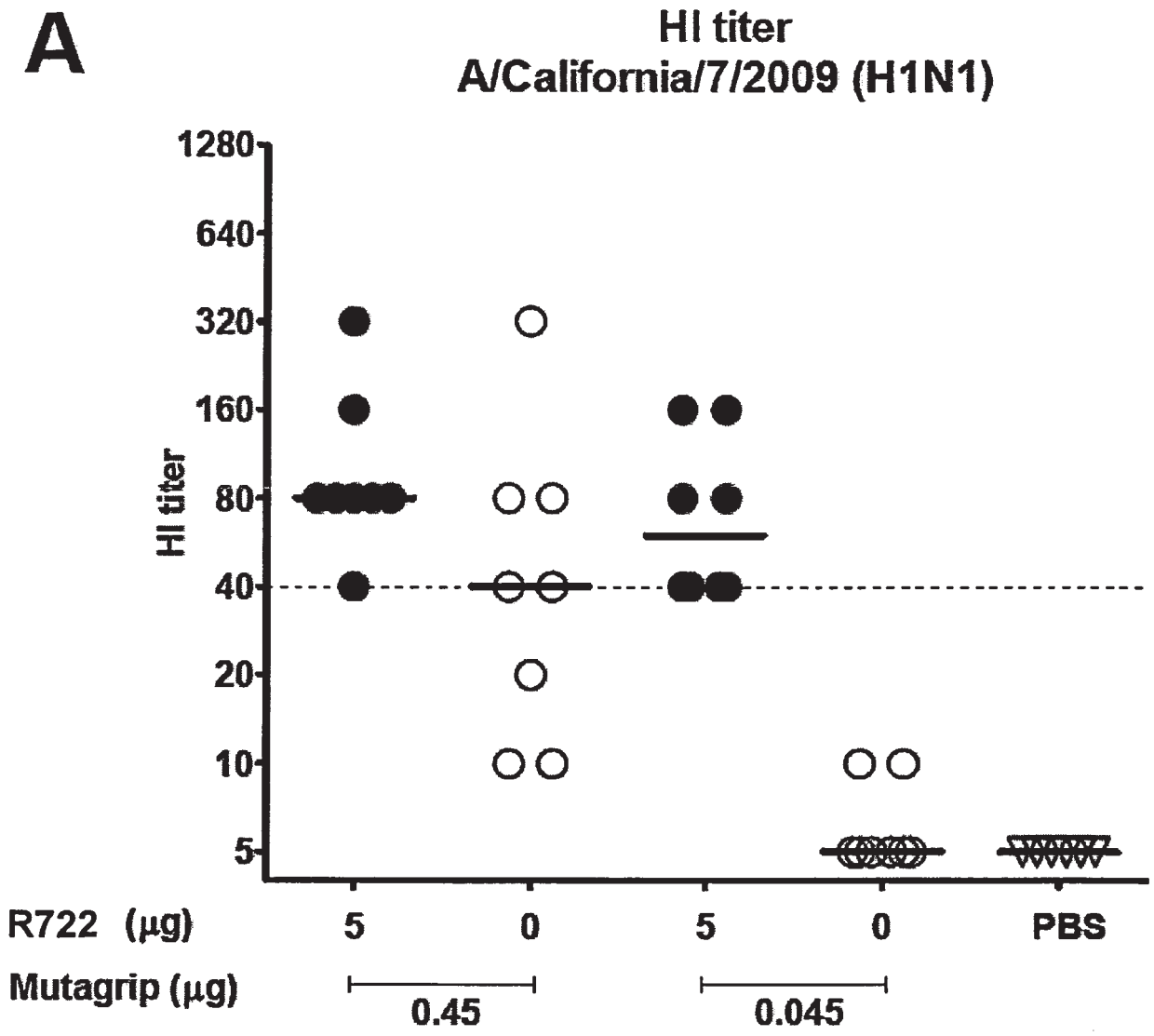

A
HI titer
A/California/7/2009 (H1N1)
HI titer
1280
640
320
160
80
40
20
10
5
R722 (µg)
5
0
5
0
PBS
Mutagrip (µg)
0.45
0.045

Fig. 29

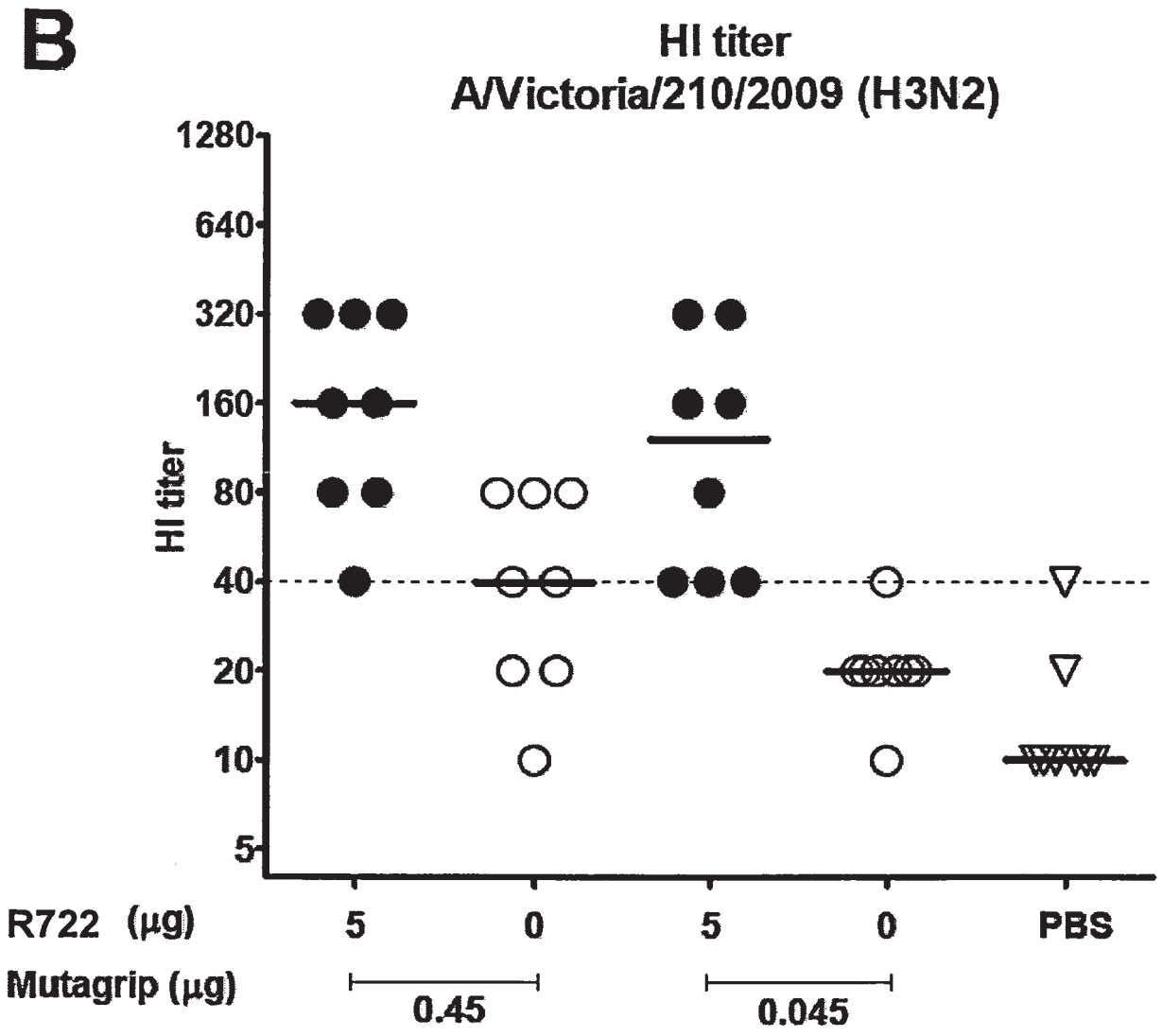

B
HI titer
A/Victoria/210/2009 (H3N2)
HI titer
1280
640
320
160
80
40
20
10
5
R722 (µg)
5
0
5
0
PBS
Mutagrip (µg)
0.45
0.045

Fig. 29

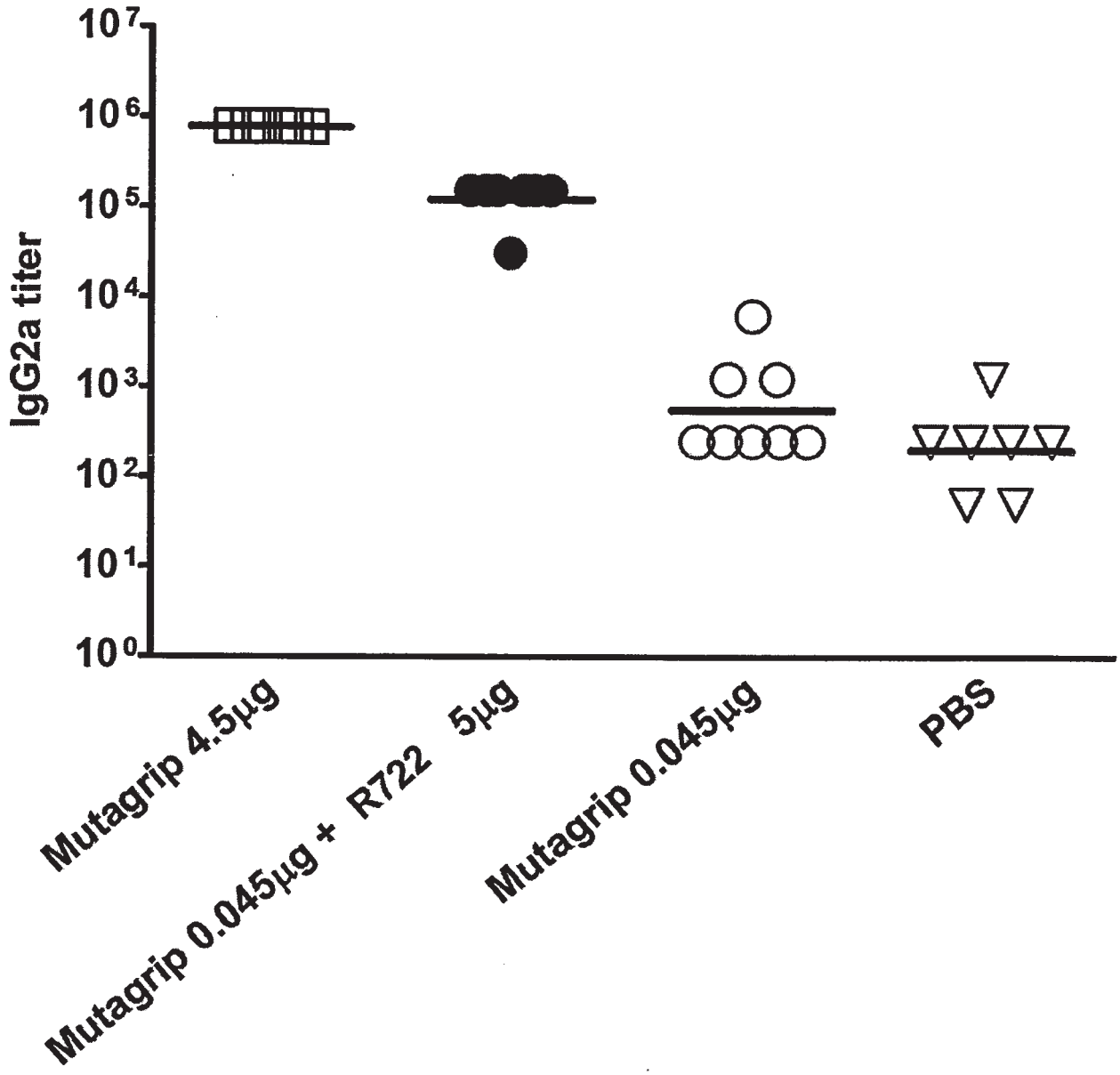

IgG2a titer
10^7
10^6
10^5
10^4
10^3
10^2
10^1
10^0
Mutagrip 4.5µg
Mutagrip 0.045µg + R722
5µg
Mutagrip 0.045µg
PBS

Fig. 30