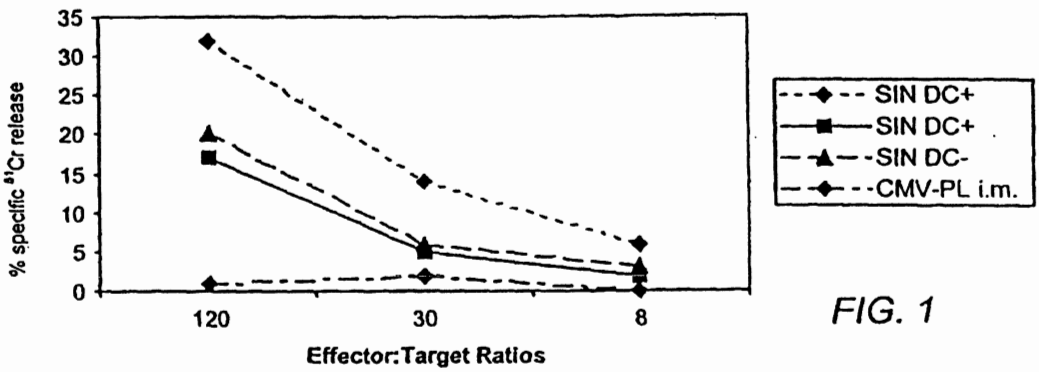

35
30
25
20
15
10
5
0
% specific ^{51}Cr release
120
30
8
Effector:Target Ratios
SIN DC+
SIN DC+
SIN DC-
CMV-PL i.m.

FIG. 1

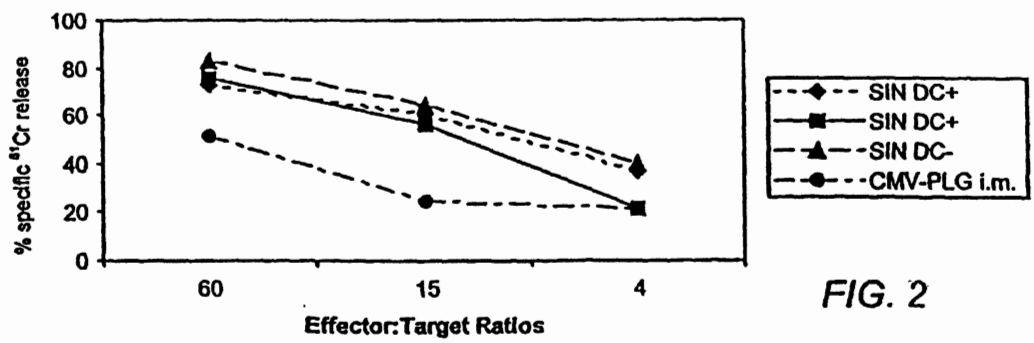

100
80
60
40
20
0
% specific ^{51}Cr release
60
15
4
Effector:Target Ratios
SIN DC+
SIN DC+
SIN DC-
CMV-PLG i.m.

FIG. 2

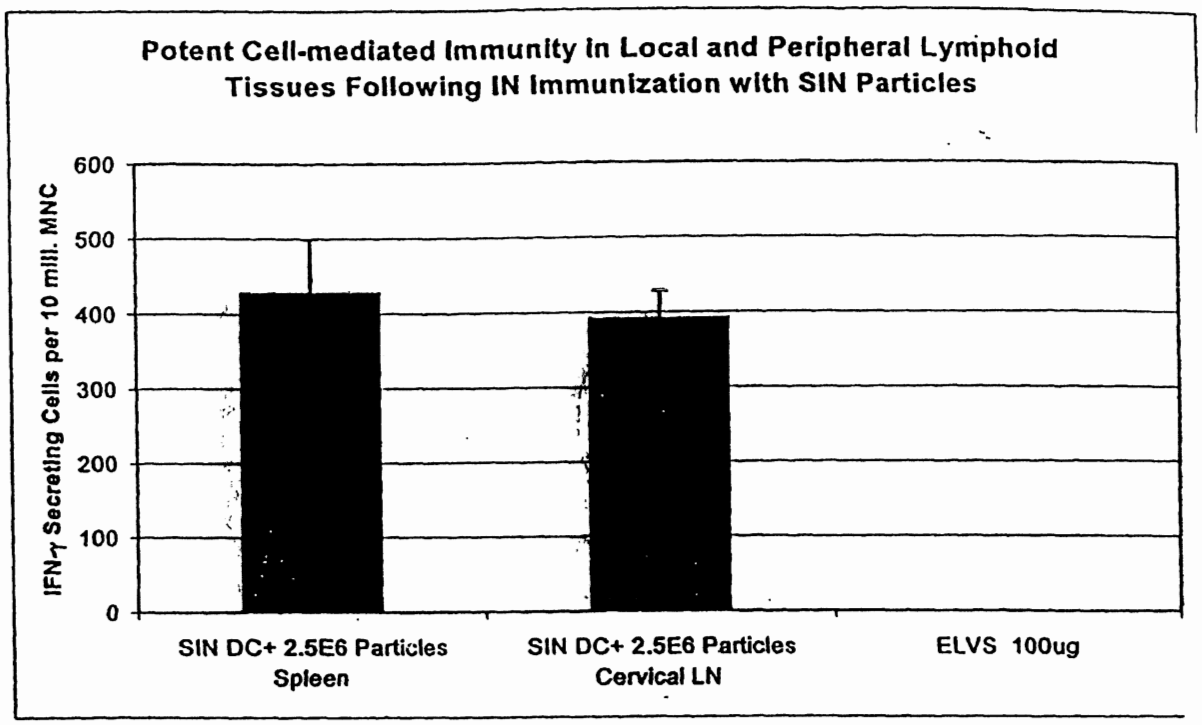

Potent Cell-mediated Immunity in Local and Peripheral Lymphoid Tissues Following IN Immunization with SIN Particles
IFN-γ Secreting Cells per 10 mill. MNC
600
500
400
300
200
100
0
SIN DC+ 2.5E6 Particles Spleen
SIN DC+ 2.5E6 Particles Cervical LN
ELVS 100ug

FIG. 3

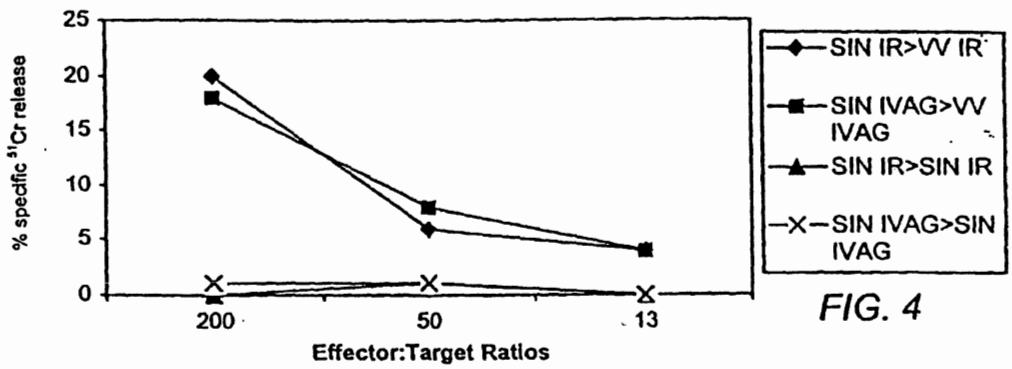

25
20
15
10
5
0
% specific ^{51}Cr release
200
50
13
Effector:Target Ratios
SIN IR>VV IR
SIN IVAG>VV IVAG
SIN IR>SIN IR
SIN IVAG>SIN IVAG

FIG. 4

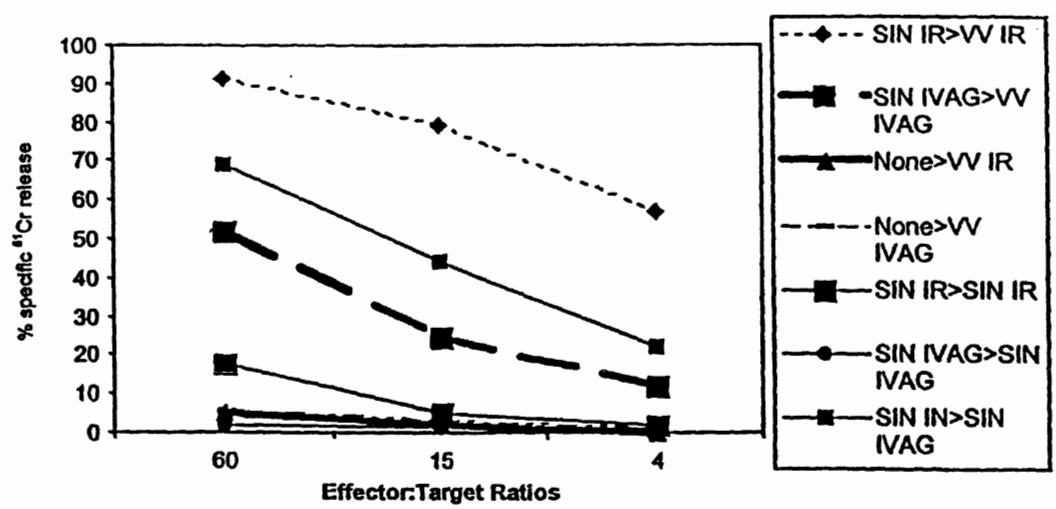

100
90
80
70
60
50
40
30
20
10
0
% specific ^{51}Cr release
60
15
4
Effector:Target Ratios
SIN IR>VV IR
SIN IVAG>VV IVAG
None>VV IR
None>VV IVAG
SIN IR>SIN IR
SIN IVAG>SIN IVAG
SIN IN>SIN IVAG

FIG. 5

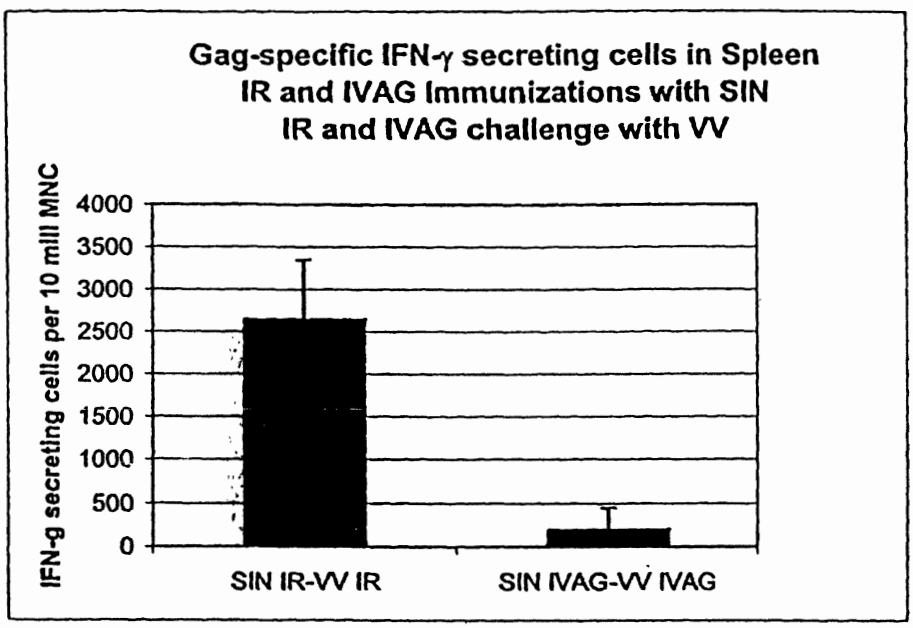

Gag-specific IFN-γ secreting cells in Spleen
IR and IVAG Immunizations with SIN
IR and IVAG challenge with VV
IFN-g secreting cells per 10 mill MNC
4000
3500
3000
2500
2000
1500
1000
500
0
SIN IR-VV IR
SIN IVAG-VV IVAG

FIG. 6

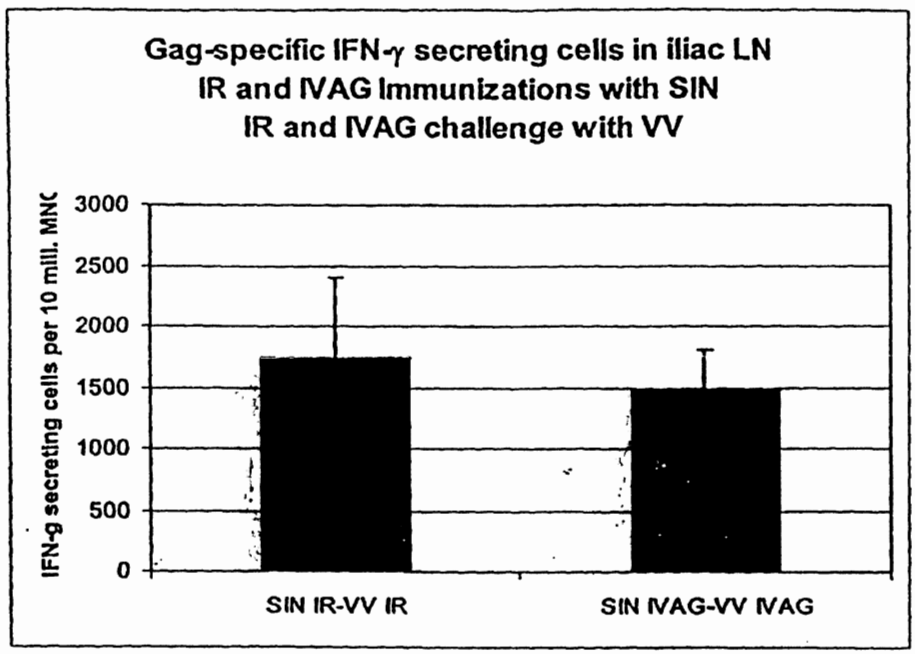

Gag-specific IFN-γ secreting cells in iliac LN
IR and IVAG Immunizations with SIN
IR and IVAG challenge with VV
IFN-g secreting cells per 10 mill. MNC
3000
2500
2000
1500
1000
500
0
SIN IR-VV IR
SIN IVAG-VV IVAG

FIG. 7

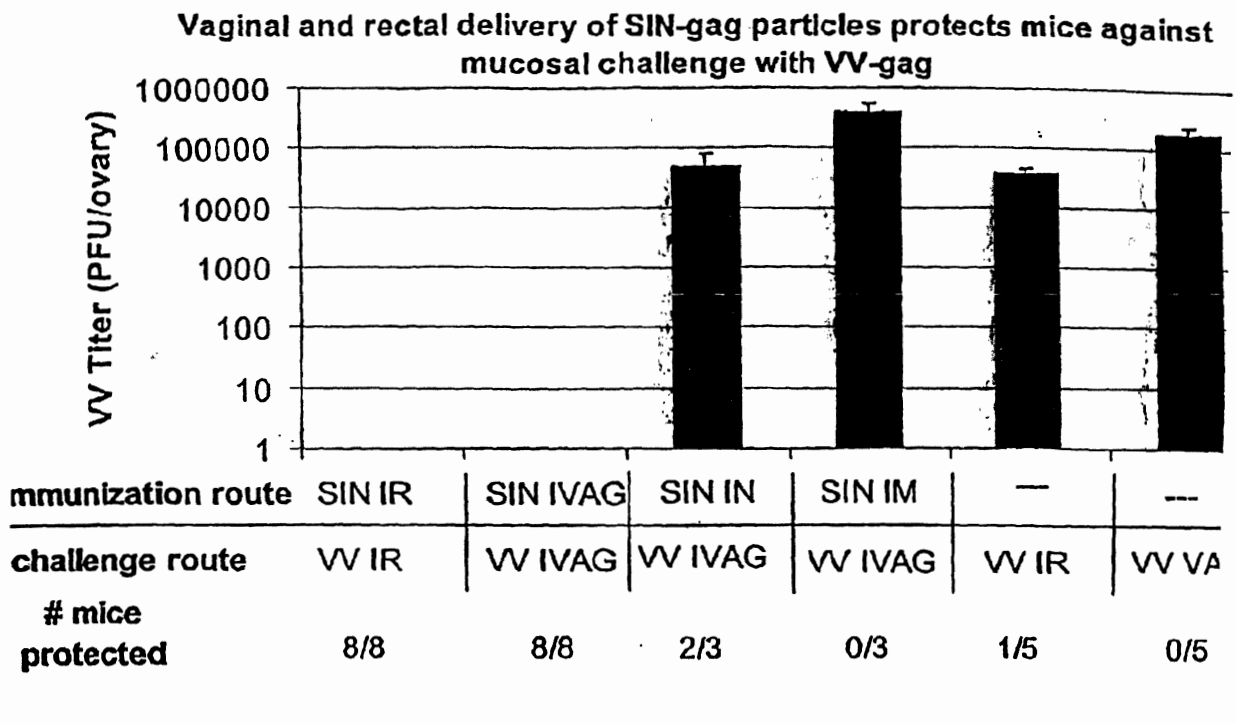

Vaginal and rectal delivery of SIN-gag particles protects mice against mucosal challenge with VV-gag
VV Titer (PFU/ovary)
1000000
100000
10000
1000
100
10
1
mmunization route
SIN IR
SIN IVAG
SIN IN
SIN IM
—
---
challenge route
VV IR
VV IVAG
VV IVAG
VV IVAG
VV IR
VV VA
mice protected
8/8
8/8
2/3
0/3
1/5
0/5

FIG. 8

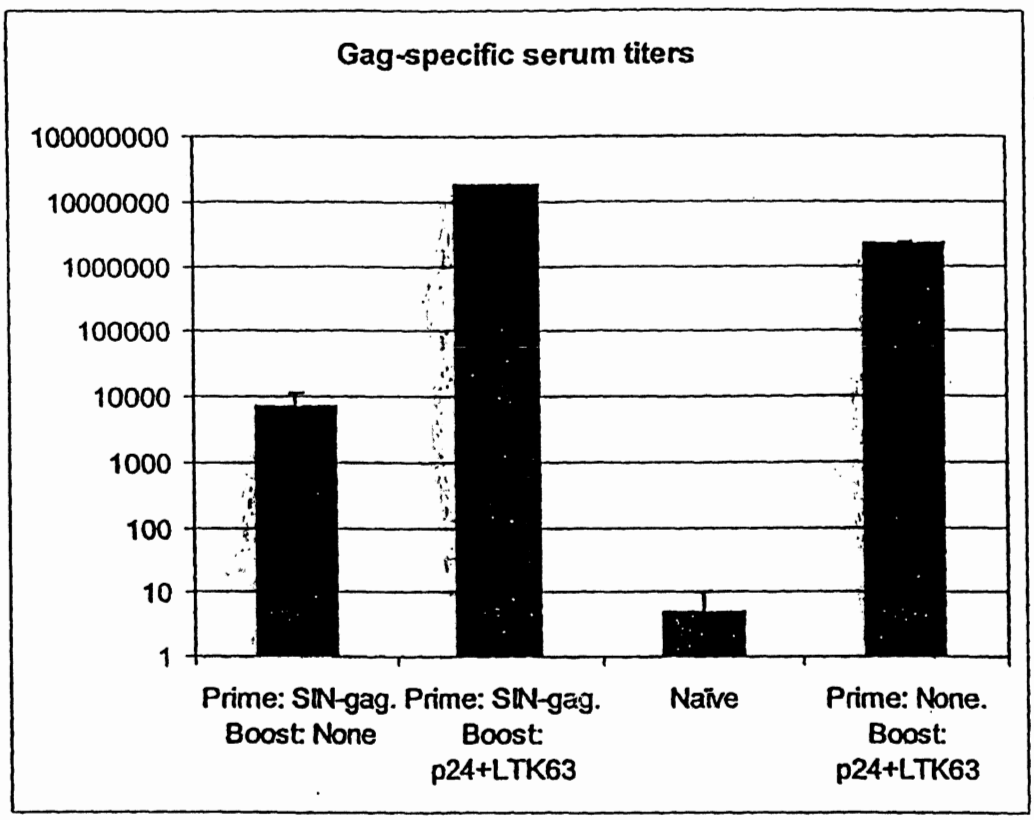

Gag-specific serum titers
100000000
10000000
1000000
100000
10000
1000
100
10
1
Prime: SIN-gag. Boost: None
Prime: SIN-gag. Boost: p24+LTK63
Naïve
Prime: None. Boost: p24+LTK63

FIG. 9

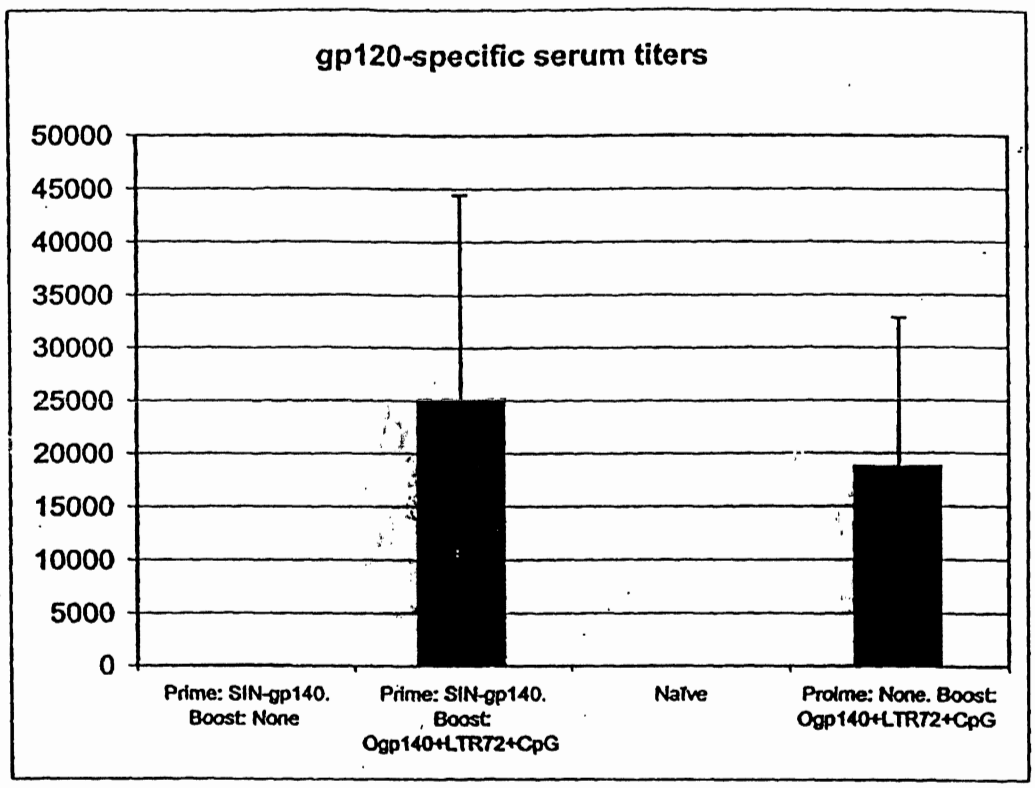

gp120-specific serum titers
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
Prime: SIN-gp140. Boost: None
Prime: SIN-gp140. Boost: Ogp140+LTR72+CpG
Naïve
Prolme: None. Boost: Ogp140+LTR72+CpG

FIG. 10

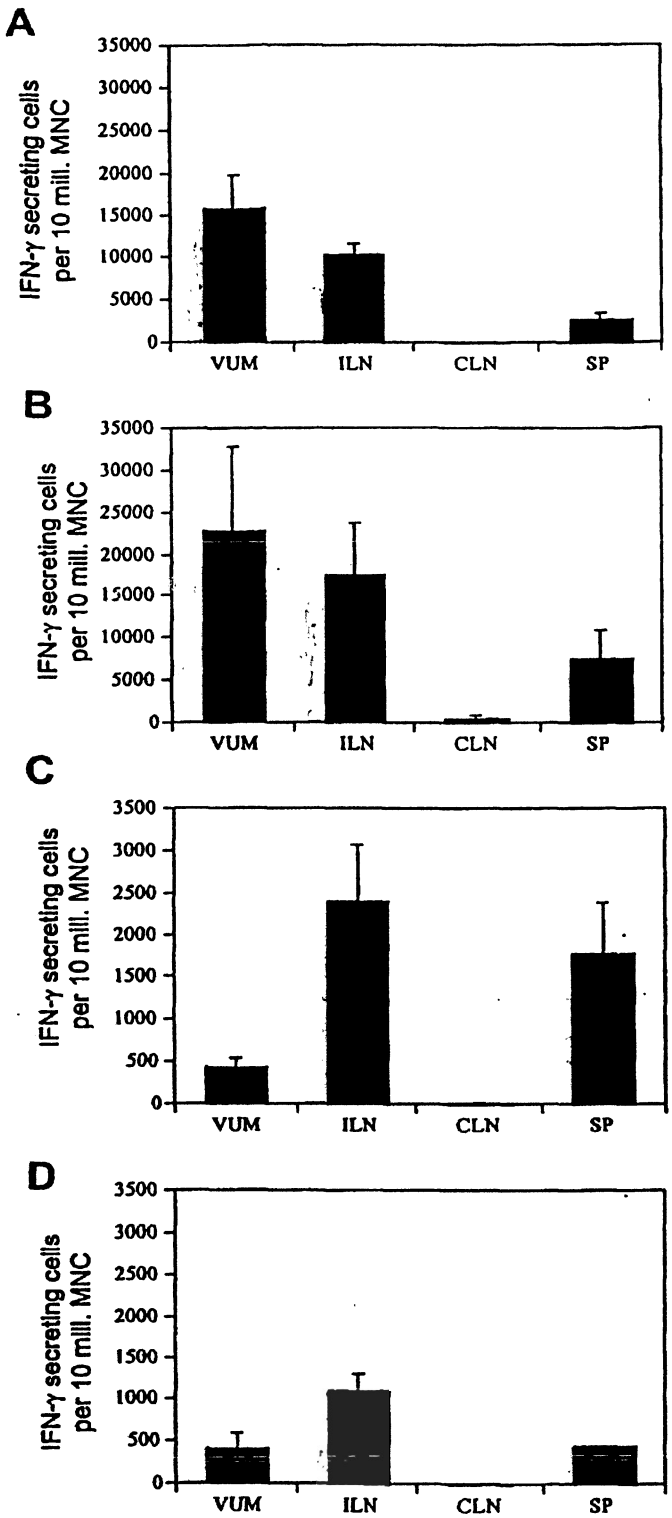

A
IFN-γ secreting cells per 10 mill. MNC
35000
30000
25000
20000
15000
10000
5000
0
VUM
ILN
CLN
SP
B
IFN-γ secreting cells per 10 mill. MNC
35000
30000
25000
20000
15000
10000
5000
0
VUM
ILN
CLN
SP
C
IFN-γ secreting cells per 10 mill. MNC
3500
3000
2500
2000
1500
1000
500
0
VUM
ILN
CLN
SP
D
IFN-γ secreting cells per 10 mill. MNC
3500
3000
2500
2000
1500
1000
500
0
VUM
ILN
CLN
SP

Figure 11

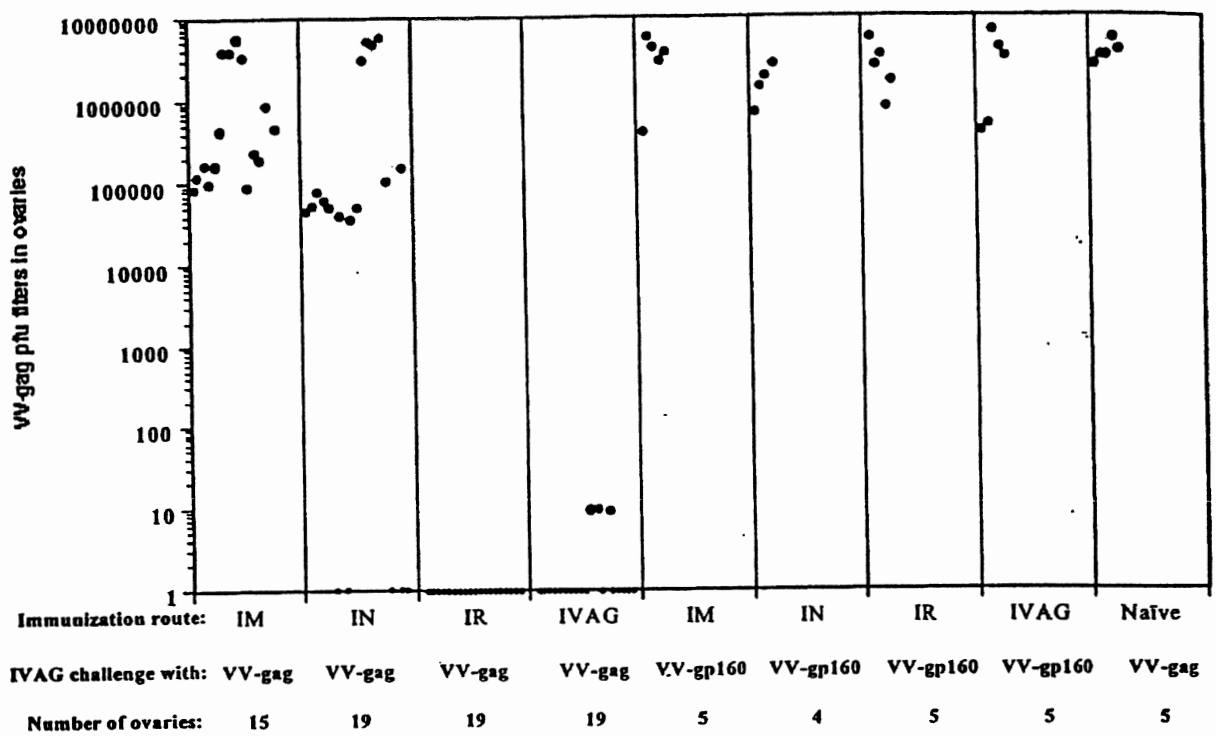
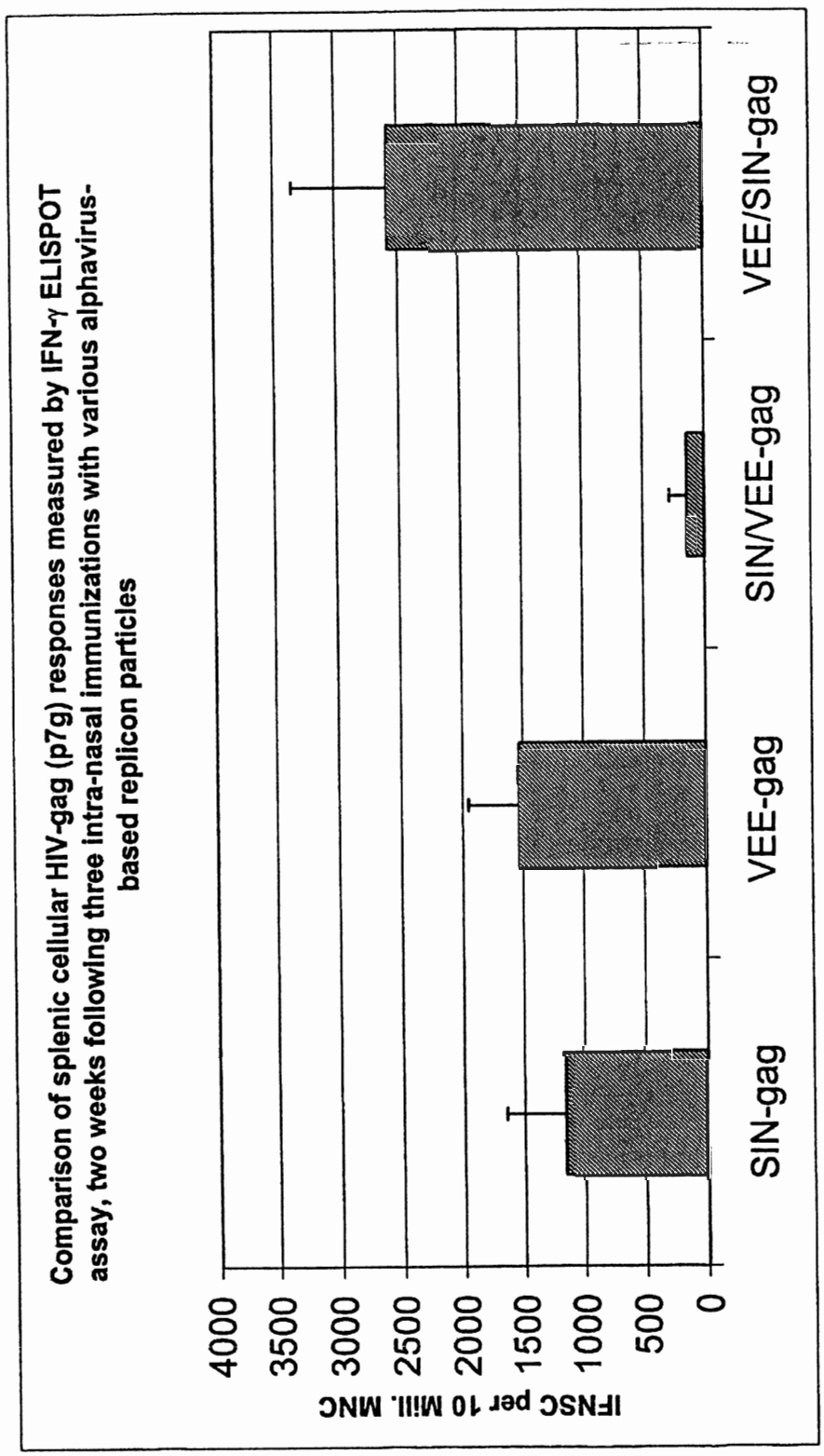

10000000
1000000
100000
10000
1000
100
10
1
VV-gag pfu titers in ovaries
Immunization route: IM IN IR IVAG IM IN IR IVAG Naïve
IVAG challenge with: VV-gag VV-gag VV-gag VV-gag VV-gp160 VV-gp160 VV-gp160 VV-gp160 VV-gag
Number of ovaries: 15 19 19 19 5 4 5 5 5

Figure 12

FIGURE 13


Comparison of splenic cellular HIV-gag (p7g) responses measured by IFN-γ ELISPOT assay, two weeks following three intra-nasal immunizations with various alphavirus-based replicon particles
IFNSC per 10 Mill. MNC
4000
3500
3000
2500
2000
1500
1000
500
0
SIN-gag
VEE-gag
SIN/VEE-gag
VEE/SIN-gag