FIG. 1A

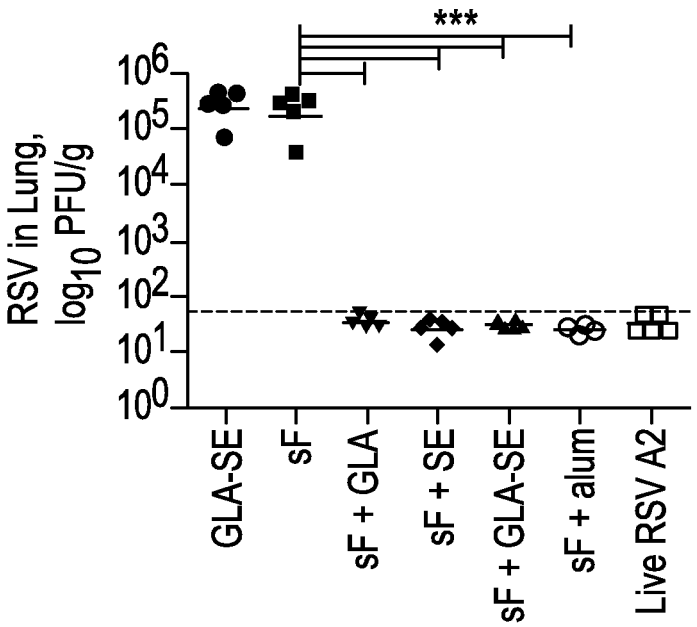

***
RSV in Lung, log10 PFU/g
10^6
10^5
10^4
10^3
10^2
10^1
10^0
GLA-SE
sF
sF + GLA
sF + SE
sF + GLA-SE
sF + alum
Live RSV A2

FIG. 1B

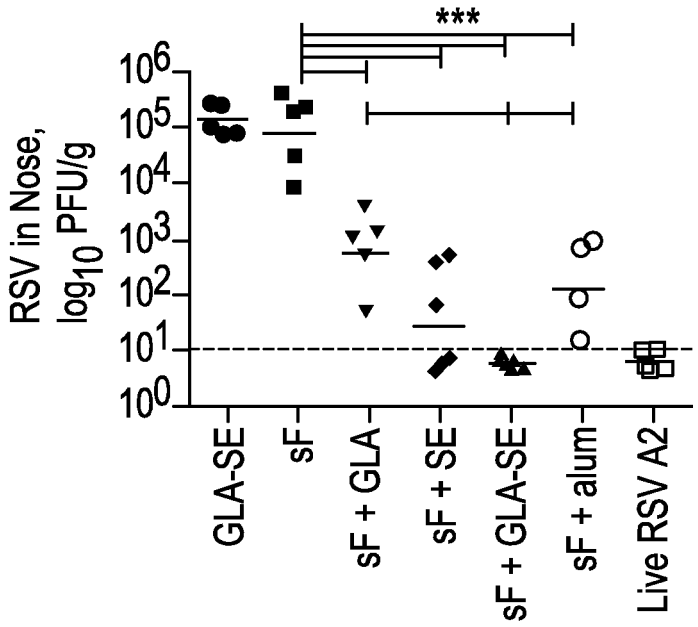

***
RSV in Nose, log10 PFU/g
10^6
10^5
10^4
10^3
10^2
10^1
10^0
GLA-SE
sF
sF + GLA
sF + SE
sF + GLA-SE
sF + alum
Live RSV A2

FIG. 1C

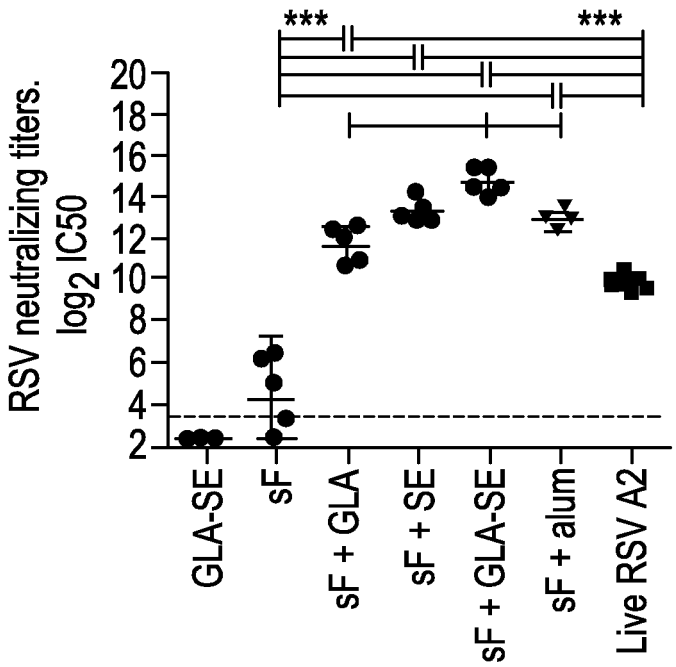

***
***
RSV neutralizing titers.
log2 IC50
20
18
16
14
12
10
8
6
4
2
GLA-SE
sF
sF + GLA
sF + SE
sF + GLA-SE
sF + alum
Live RSV A2

FIG. 1D

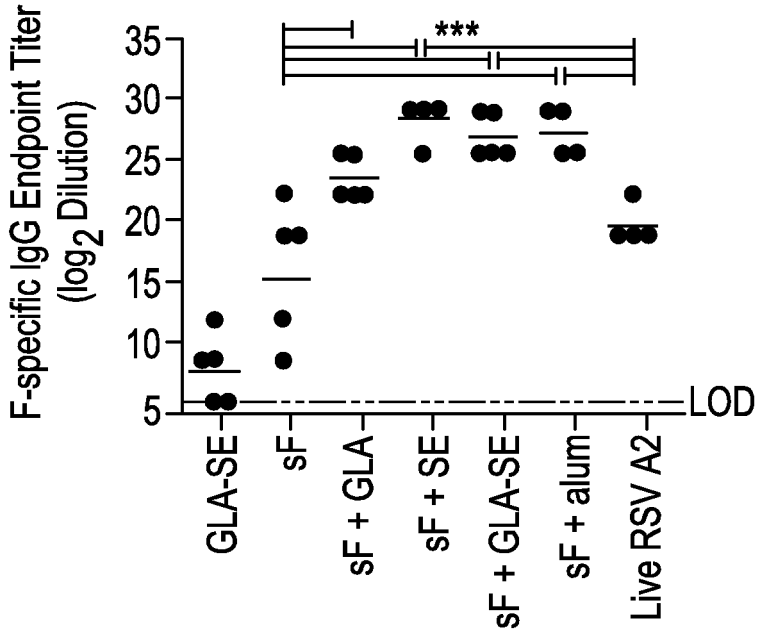

***
F-specific IgG Endpoint Titer
(log2 Dilution)
35
30
25
20
15
10
5
LOD
GLA-SE
sF
sF + GLA
sF + SE
sF + GLA-SE
sF + alum
Live RSV A2

FIG. 1E

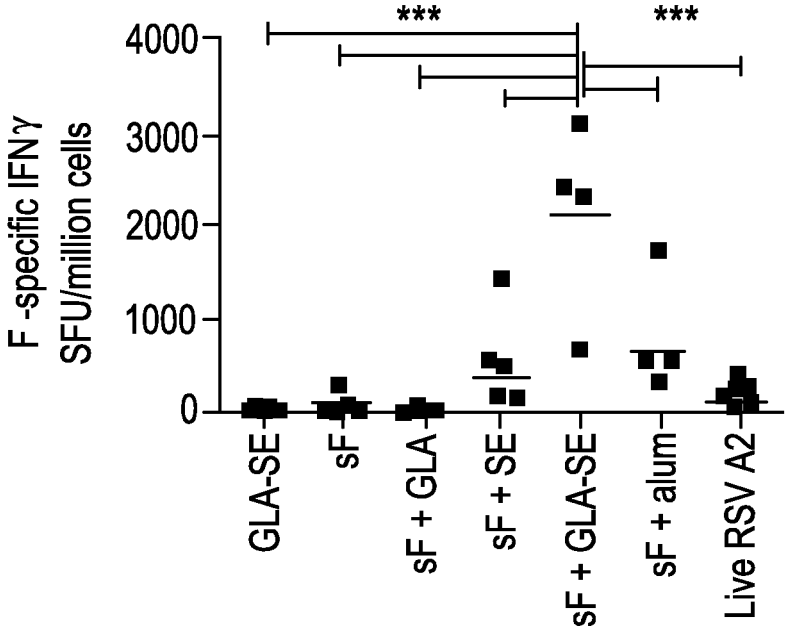

***
***
4000
3000
2000
1000
0
F -specific IFNγ
SFU/million cells
GLA-SE
sF
sF + GLA
sF + SE
sF + GLA-SE
sF + alum
Live RSV A2

FIG. 1F

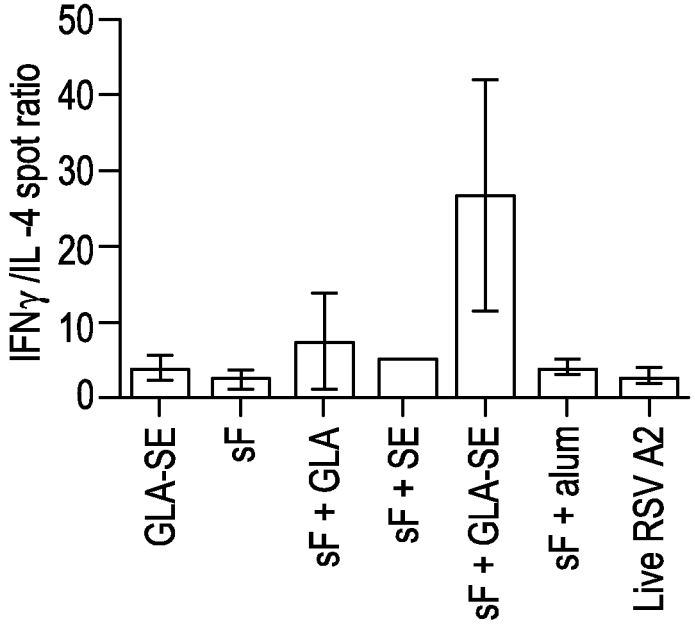

50
40
30
20
10
0
IFNγ /IL -4 spot ratio
GLA-SE
sF
sF + GLA
sF + SE
sF + GLA-SE
sF + alum
Live RSV A2

FIG. 2A

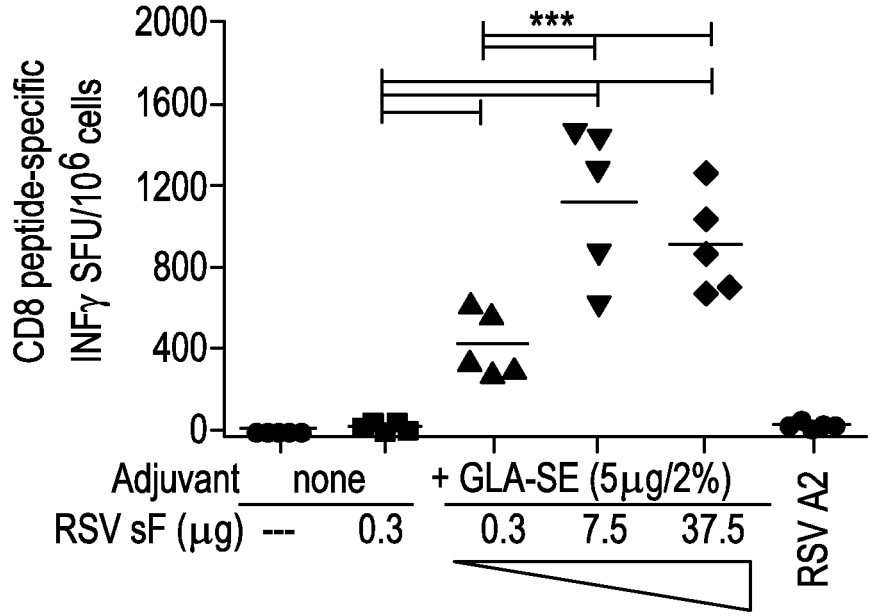

2000
1600
1200
800
400
0
CD8 peptide-specific
INFγ SFU/10^6 cells
***
Adjuvant none + GLA-SE (5μg/2%)
RSV sF (μg) --- 0.3 0.3 7.5 37.5
RSV A2

FIG. 2B

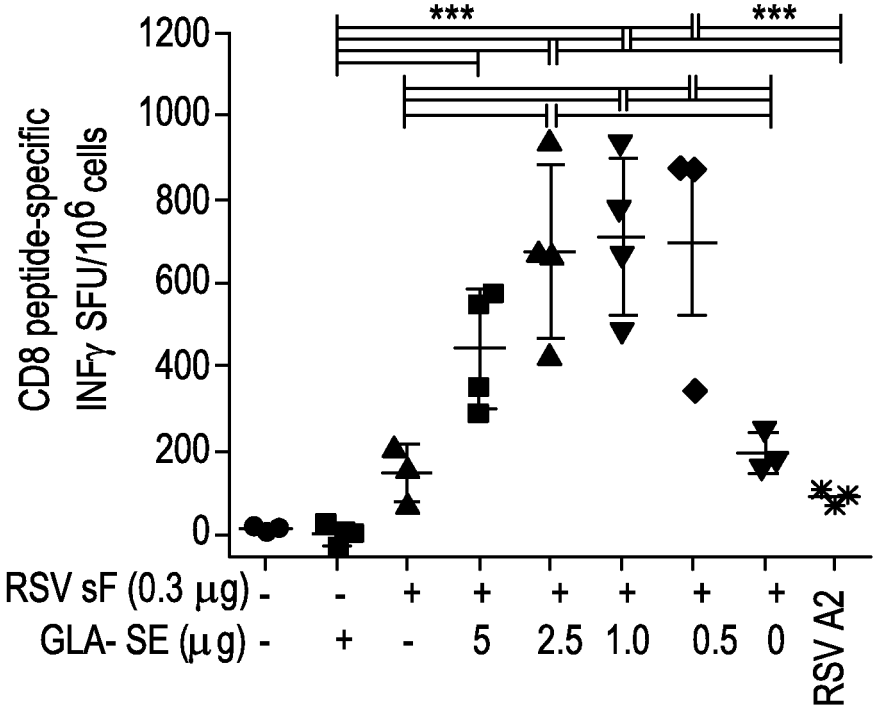

1200
1000
800
600
400
200
0
CD8 peptide-specific
INFγ SFU/10^6 cells
***
***
RSV sF (0.3 μg) - - + + + + + + RSV A2
GLA- SE (μg) - + - 5 2.5 1.0 0.5 0

FIG. 3A

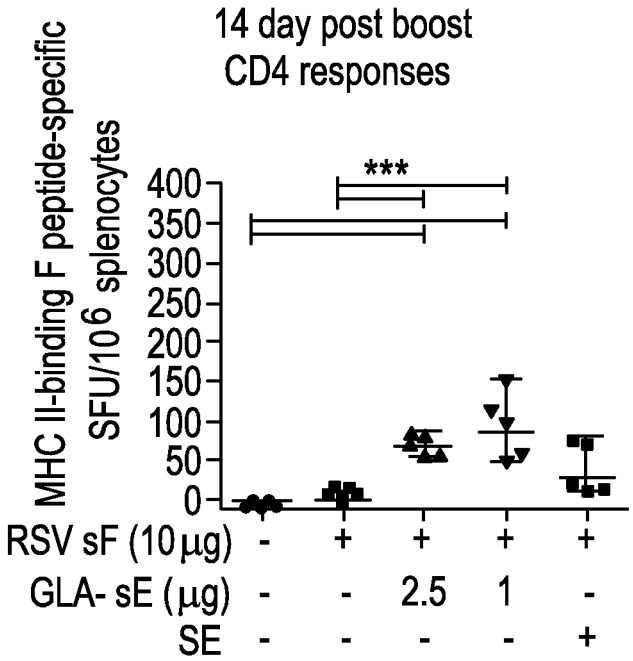


FIG. 3B

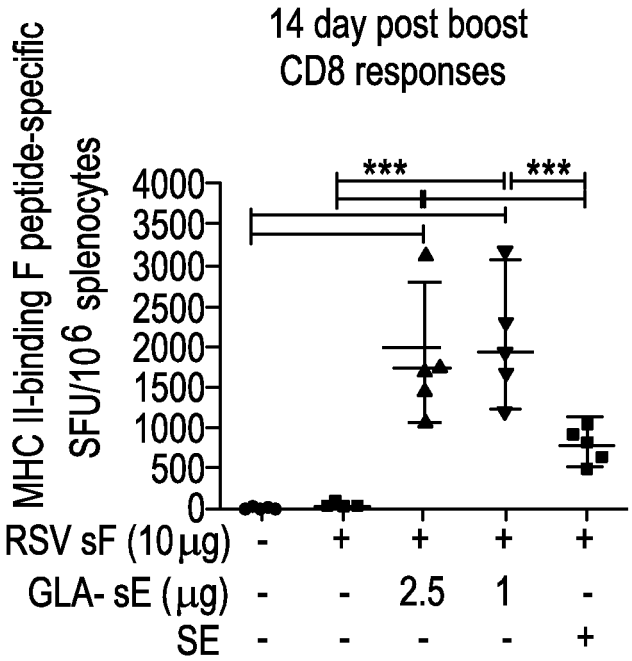


FIG. 3C

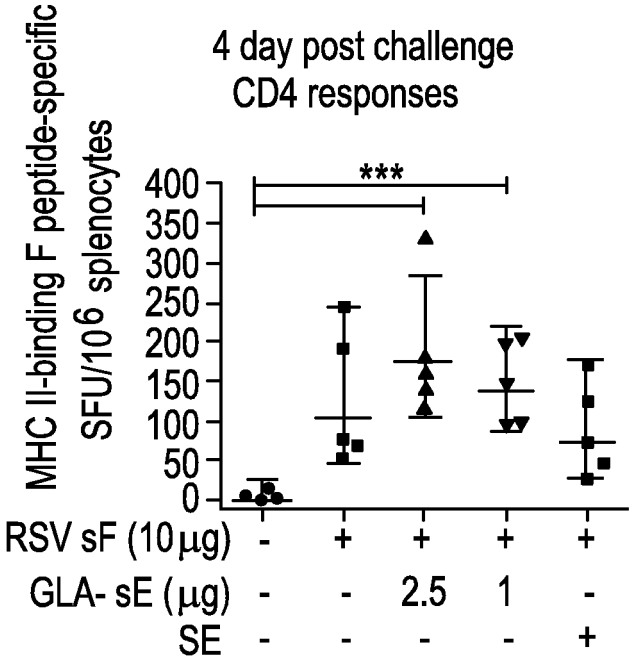


FIG. 3D

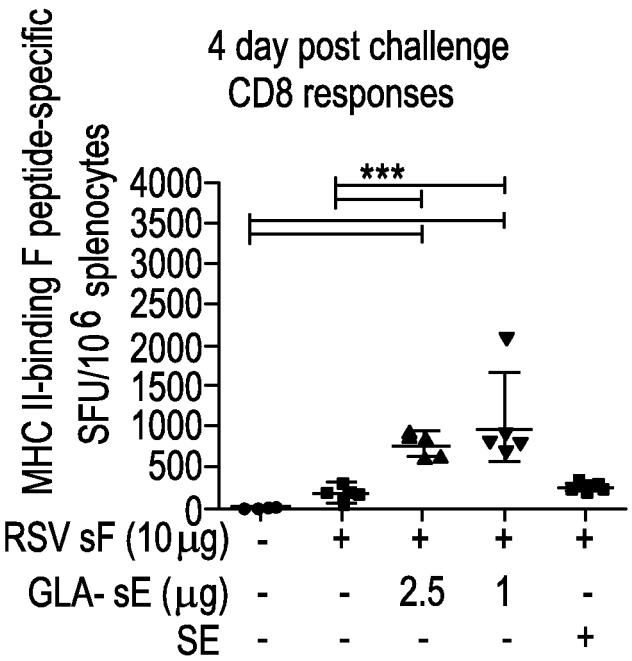


FIG. 4A

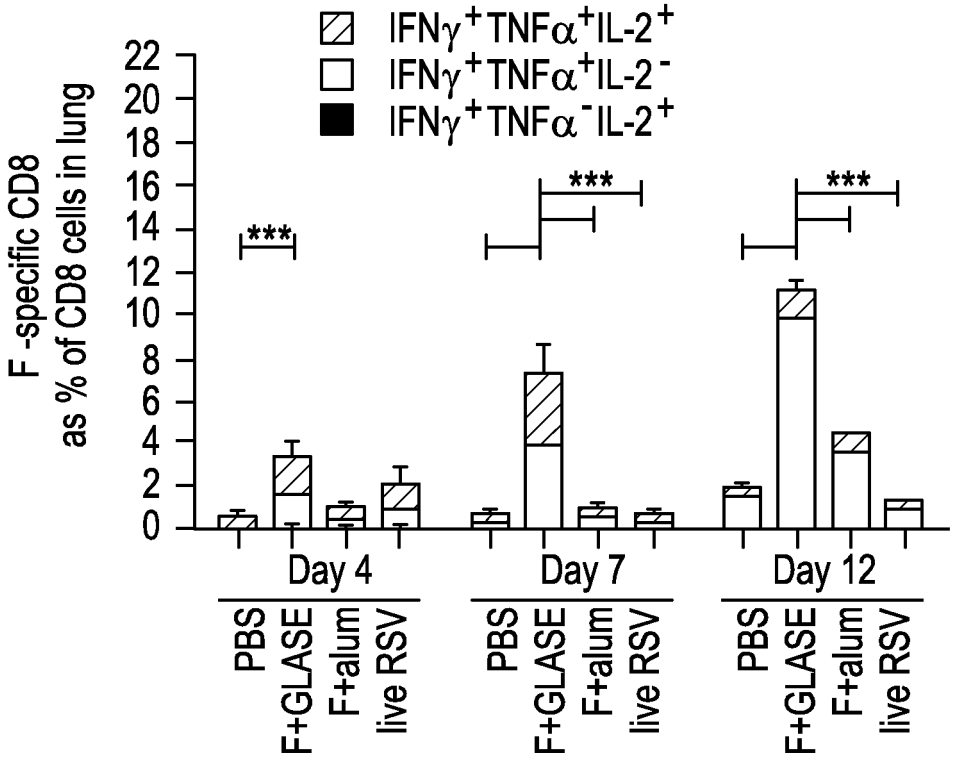

IFNγ+TNFα+IL-2+
IFNγ+TNFα+IL-2-
IFNγ+TNFα-IL-2+
F -specific CD8
as % of CD8 cells in lung
22
20
18
16
14
12
10
8
6
4
2
0
***
***
***
Day 4
Day 7
Day 12
PBS
F+GLASE
F+alum
live RSV

FIG. 4B

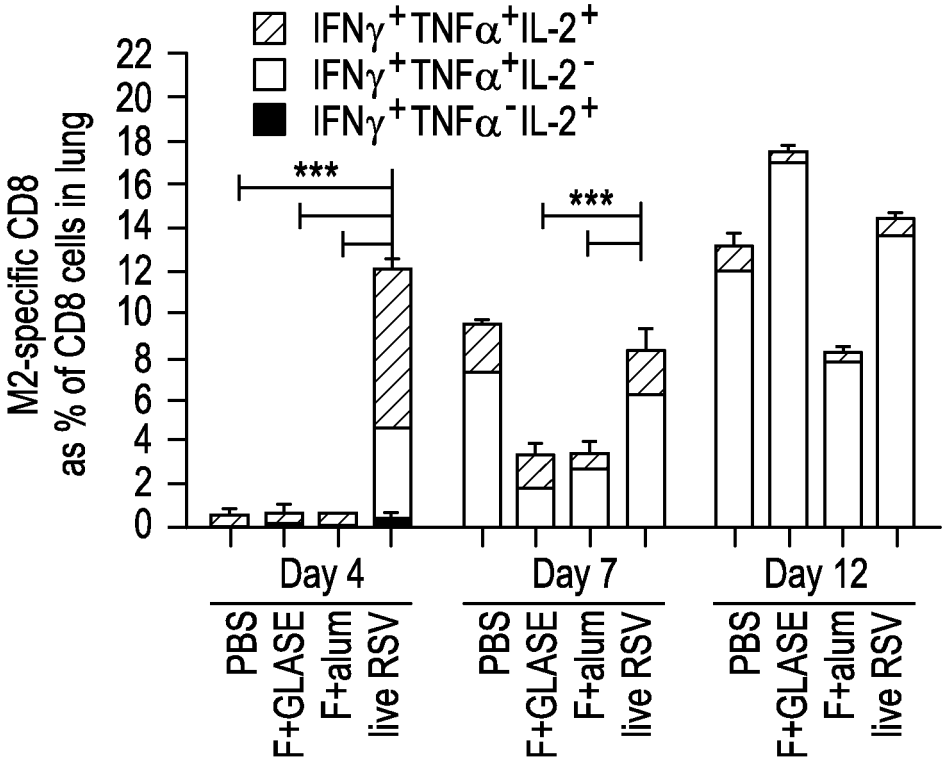

IFNγ+TNFα+IL-2+
IFNγ+TNFα+IL-2-
IFNγ+TNFα-IL-2+
M2-specific CD8
as % of CD8 cells in lung
22
20
18
16
14
12
10
8
6
4
2
0
***
***
Day 4
Day 7
Day 12
PBS
F+GLASE
F+alum
live RSV

FIG. 5A

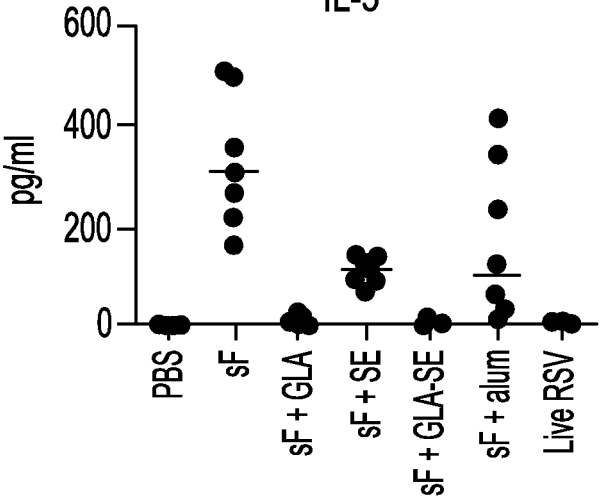


FIG. 5B

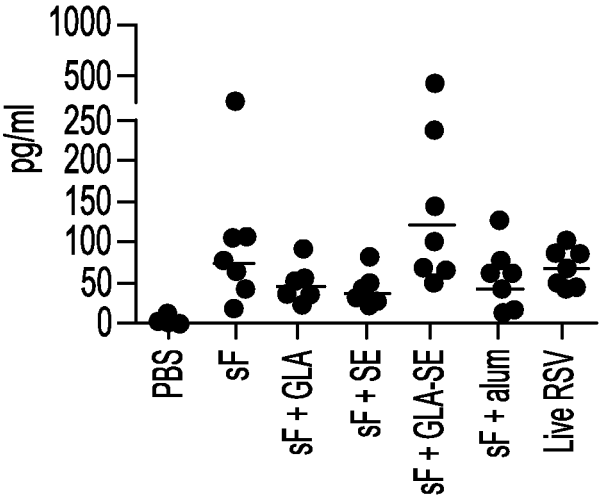


FIG. 5C

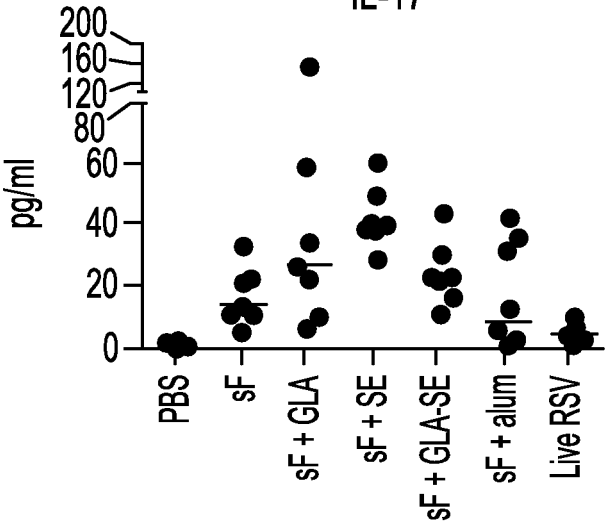


FIG. 5D

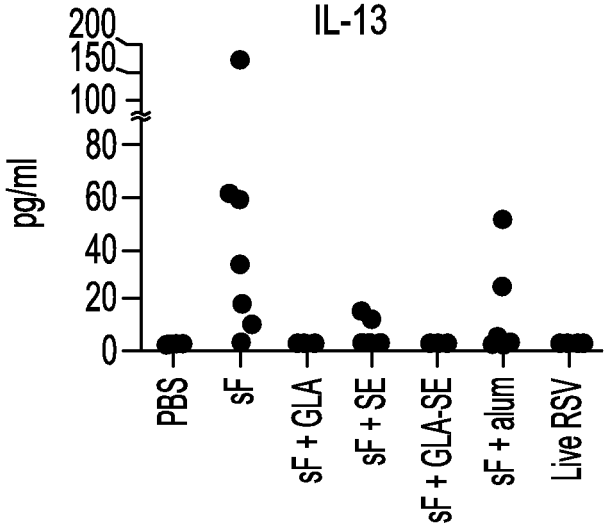


FIG. 5E

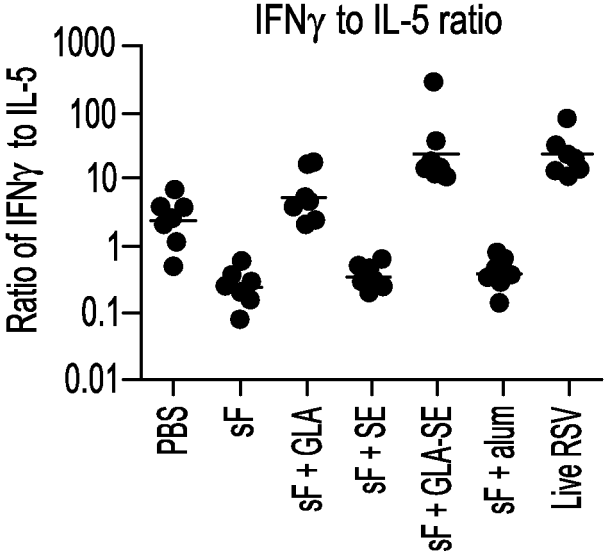


FIG. 5F

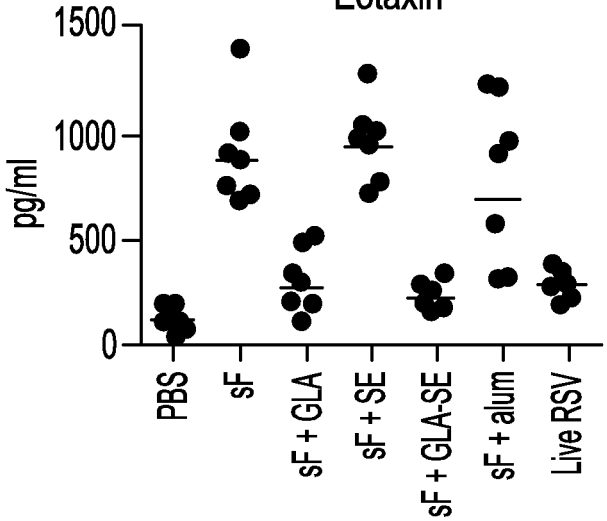


FIG. 6A

PBS

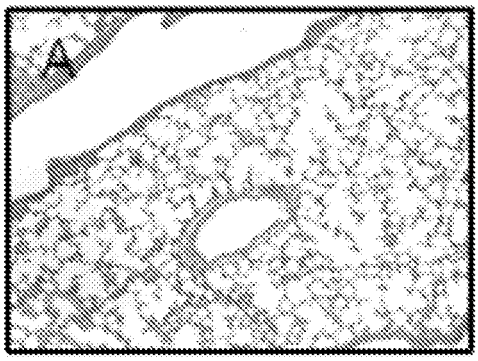


FIG. 6B

sF + GLA

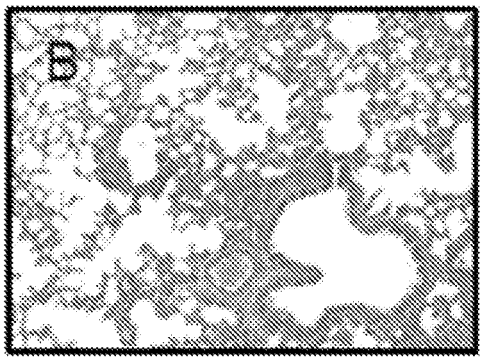


FIG. 6C

sF + SE

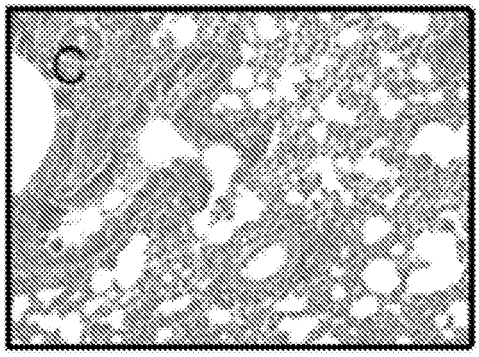


FIG. 6D

sF + GLA-SE

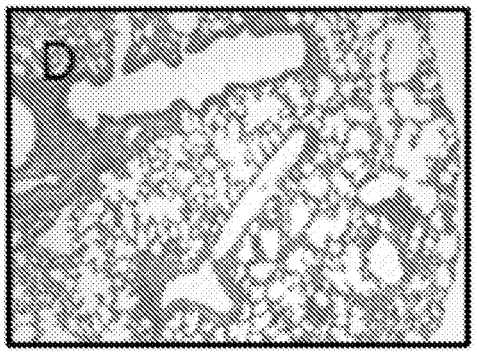


FIG. 6E

sF + alum

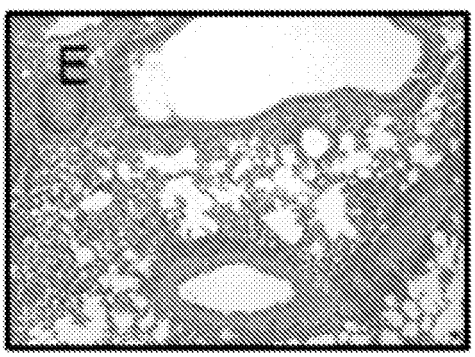


FIG. 6F

Live RSV

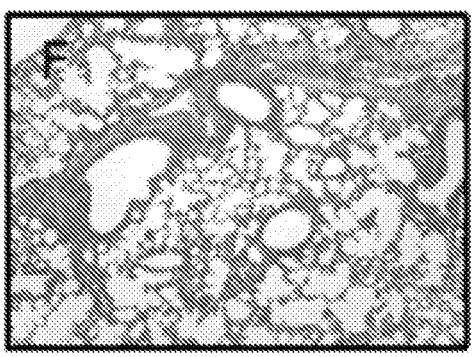


FIG. 7A

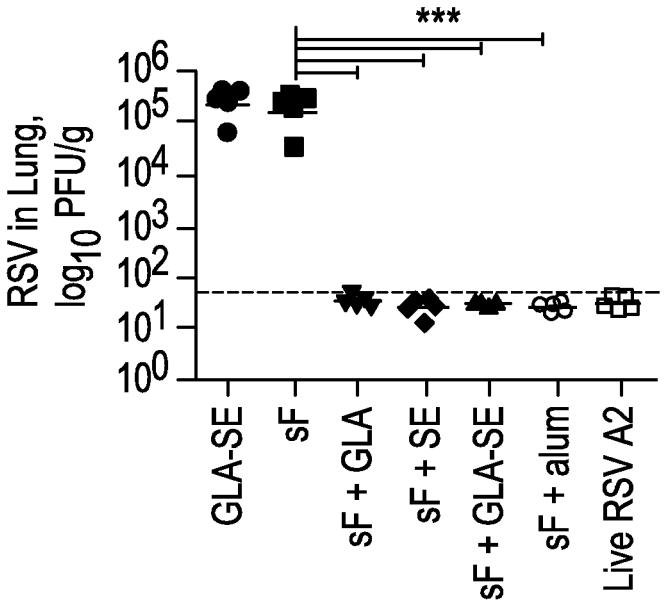


FIG. 7B

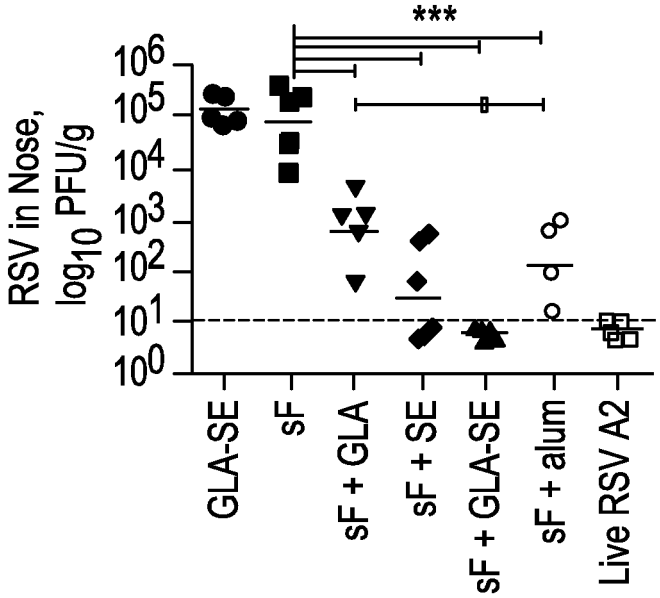


FIG. 7C

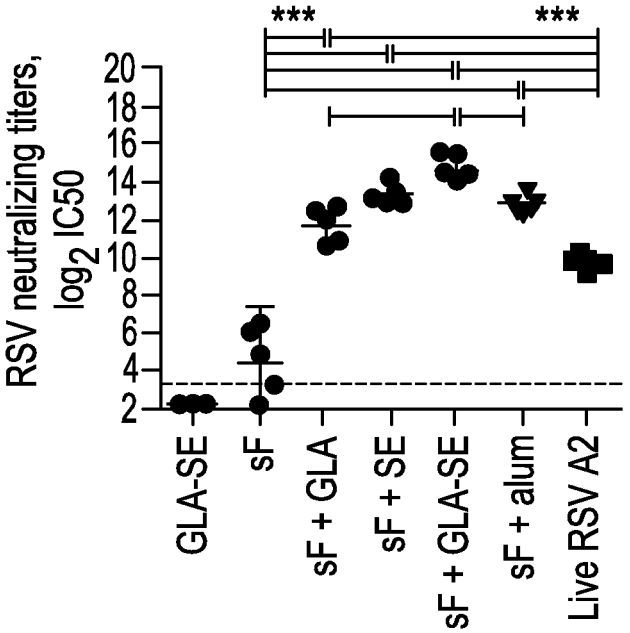


FIG. 7D

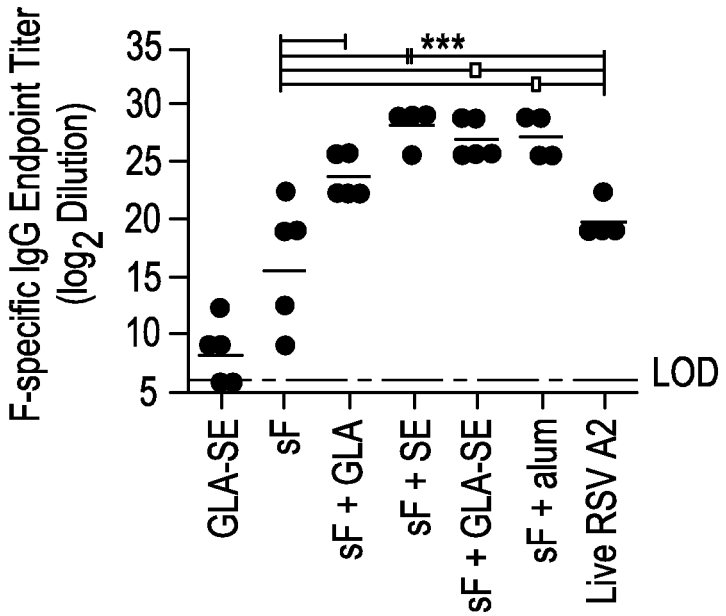


FIG. 7E

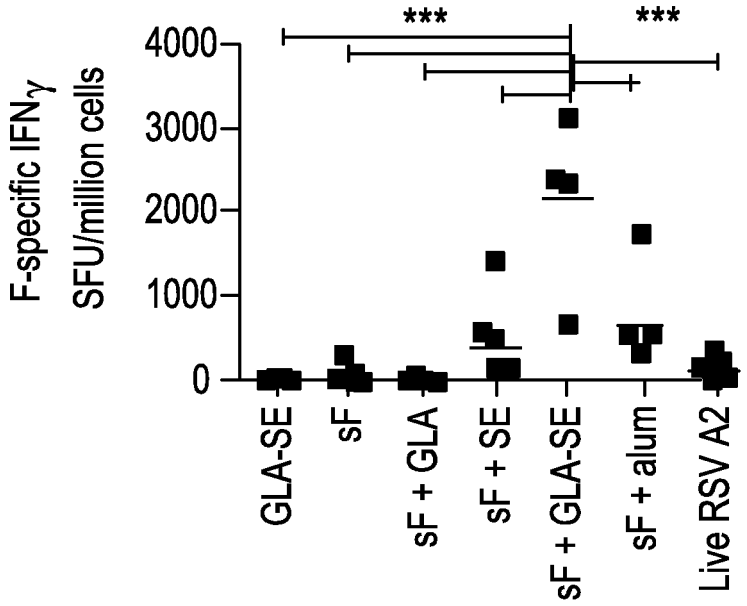


FIG. 7F

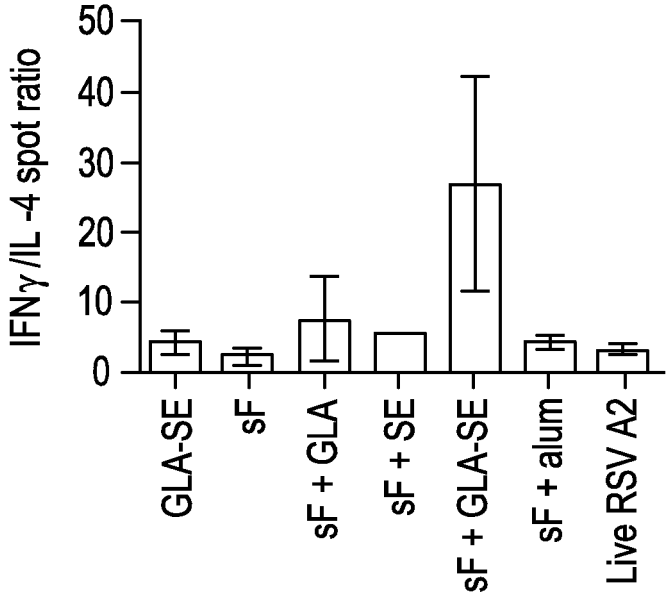


FIG. 8A

sF



FIG. 8B

sF + GLA

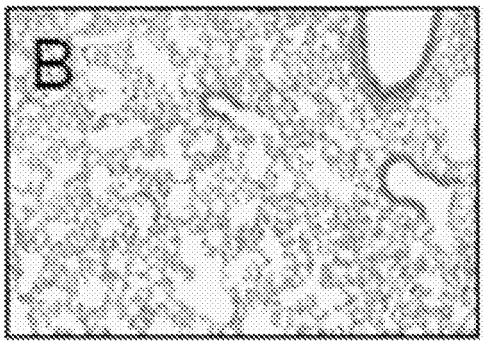


FIG. 8C

sF + SE

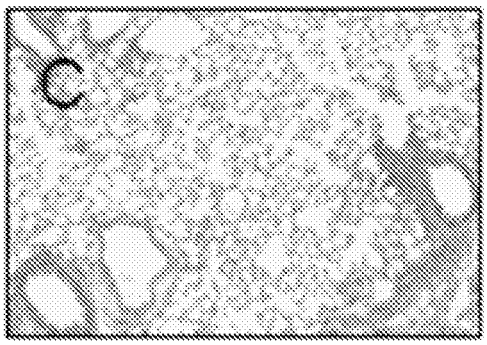


FIG. 8D

sF + GLA-SE

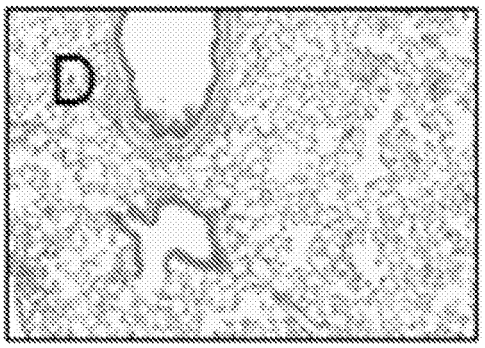


FIG. 8E

sF + alum

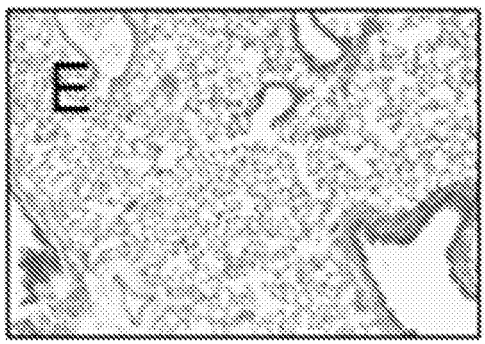


FIG. 8F

Live RSV

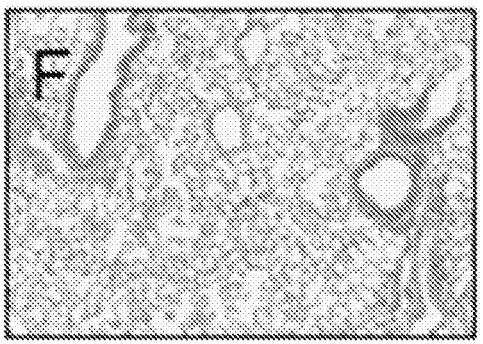


FIG. 9A

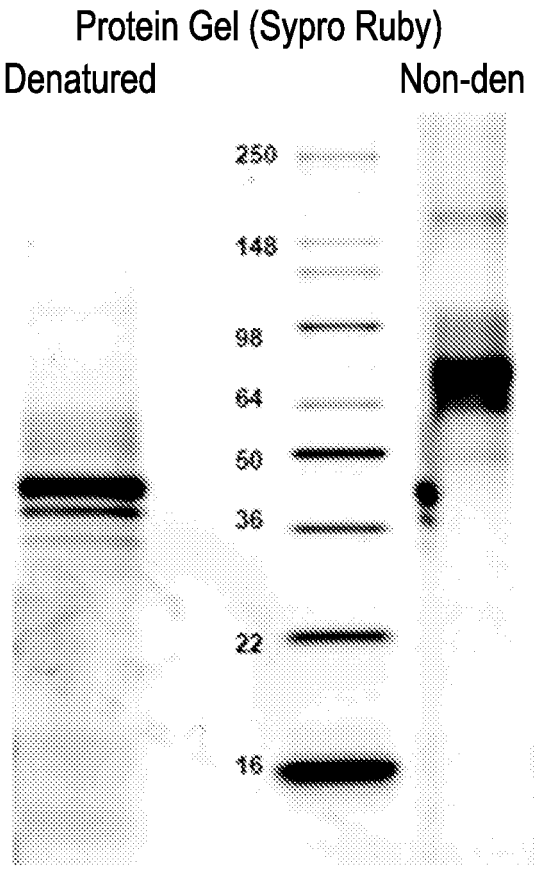

Protein Gel (Sypro Ruby)
Denatured
Non-den
250
148
98
64
50
36
22
16

FIG. 9B

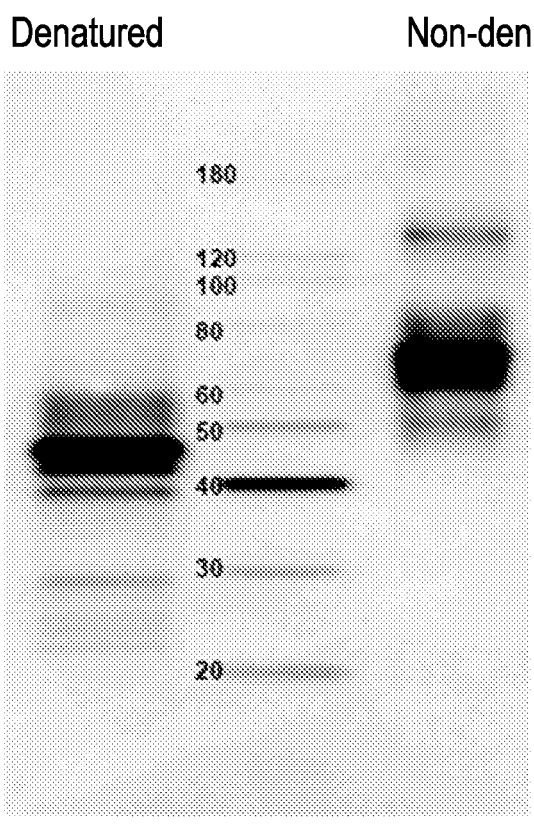

Western Blot (mota)
Denatured
Non-den
160
120
100
80
60
50
40
30
20

FIG. 10A

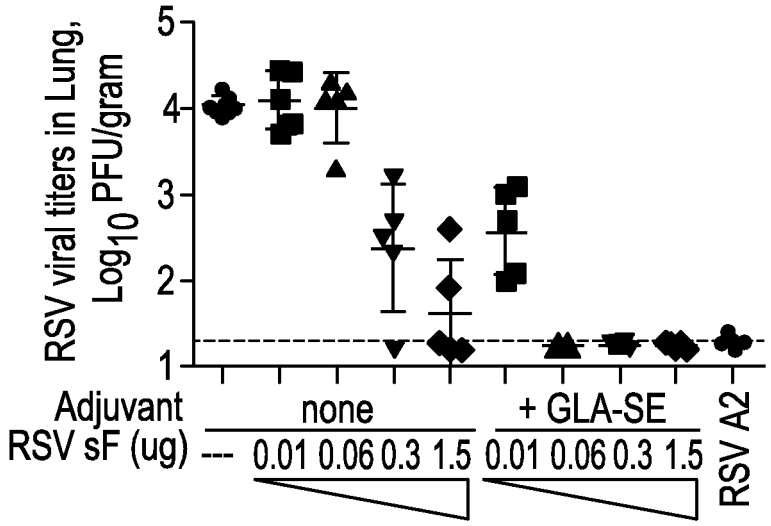


FIG. 10B

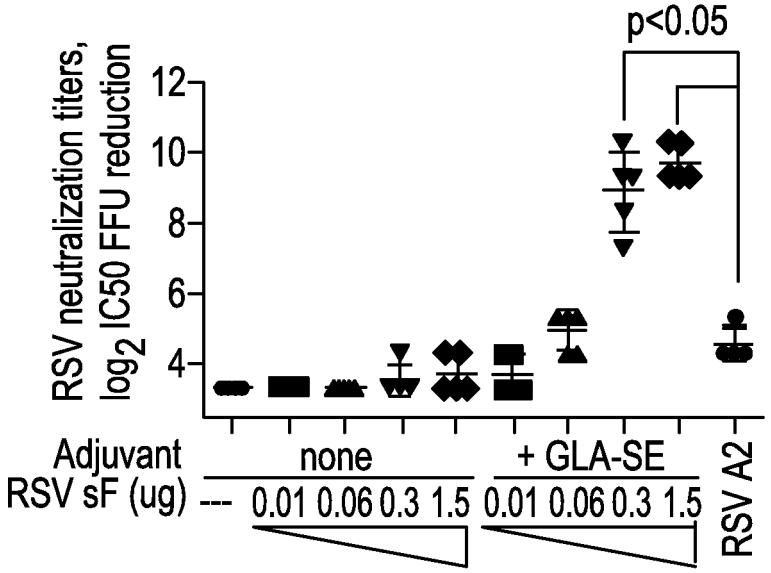


FIG. 11A

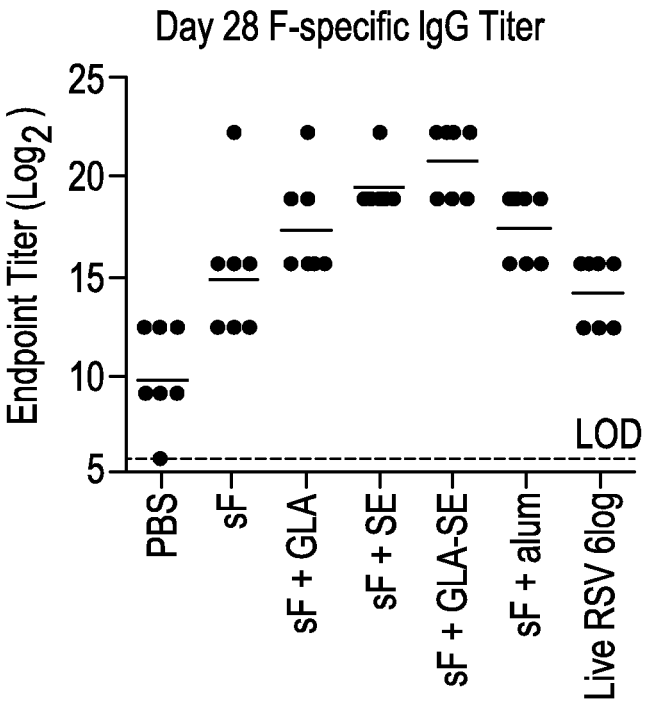


FIG. 11B

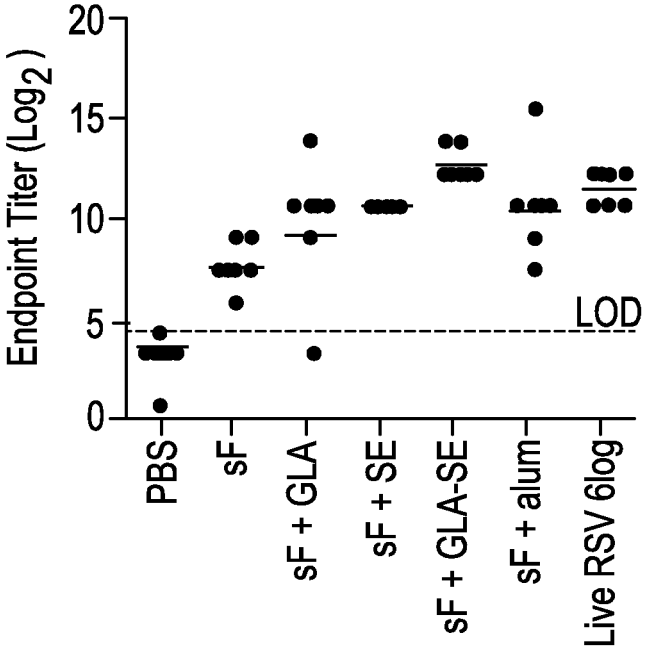


FIG. 12

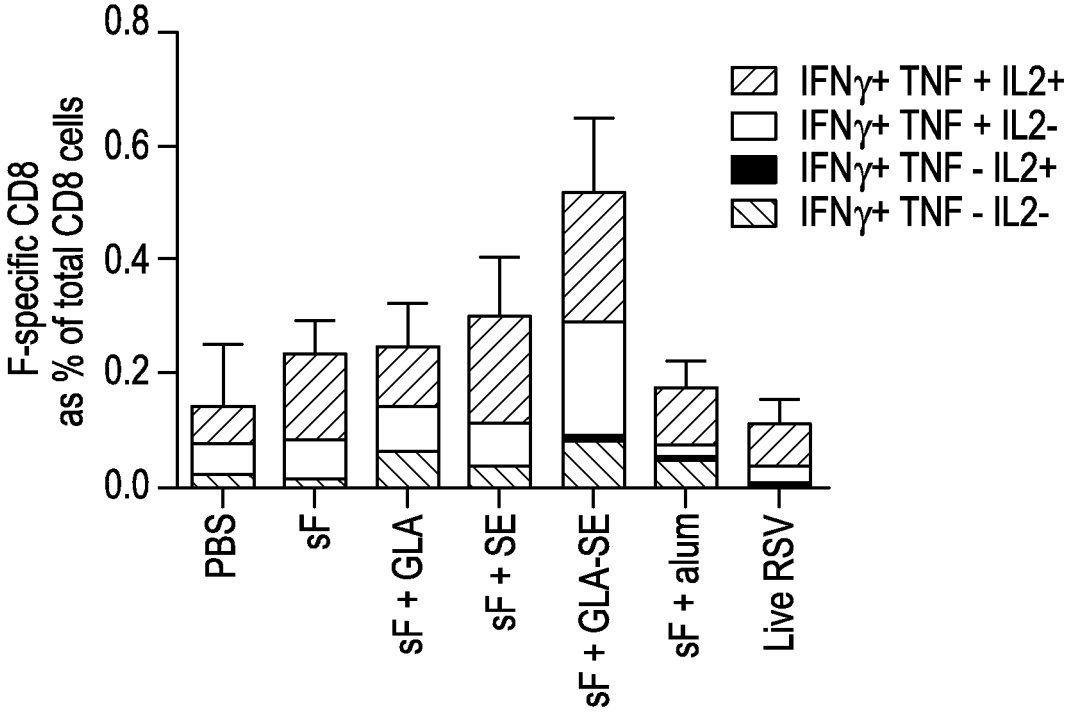


FIG. 13

		Neutralization Titer (log_2)	
Subgroup	Virus	sF+GLASE Immunized BALB/c Sera	Negative BALB/c Sera
A (A2 strain)	RSVA2-Delta G	11.3	<4.3 (LOD)
	RSV A2-GFP	9.3	<4.3
A subgroup	RSVA NW VB050407	9.3	<4.3
	RSVA M96-33	9.3	<4.3
	RSVA M96-76	13.3	<4.3
	RSVA CA-8	9.3	<4.3
B subgroup	RSVB NW VB051507	9.3	<4.3
	RSVB 15	11.3	<4.3

FIG. 14A

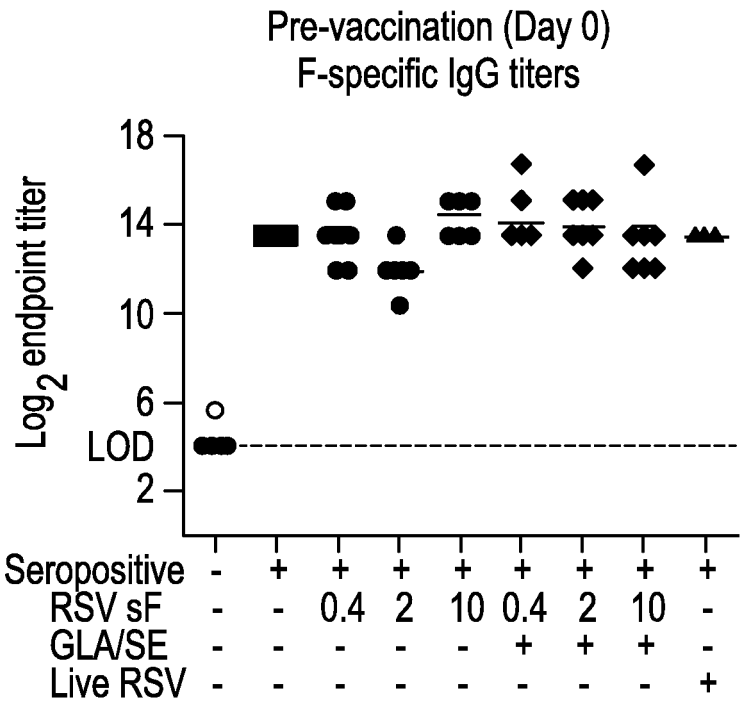


FIG. 14B

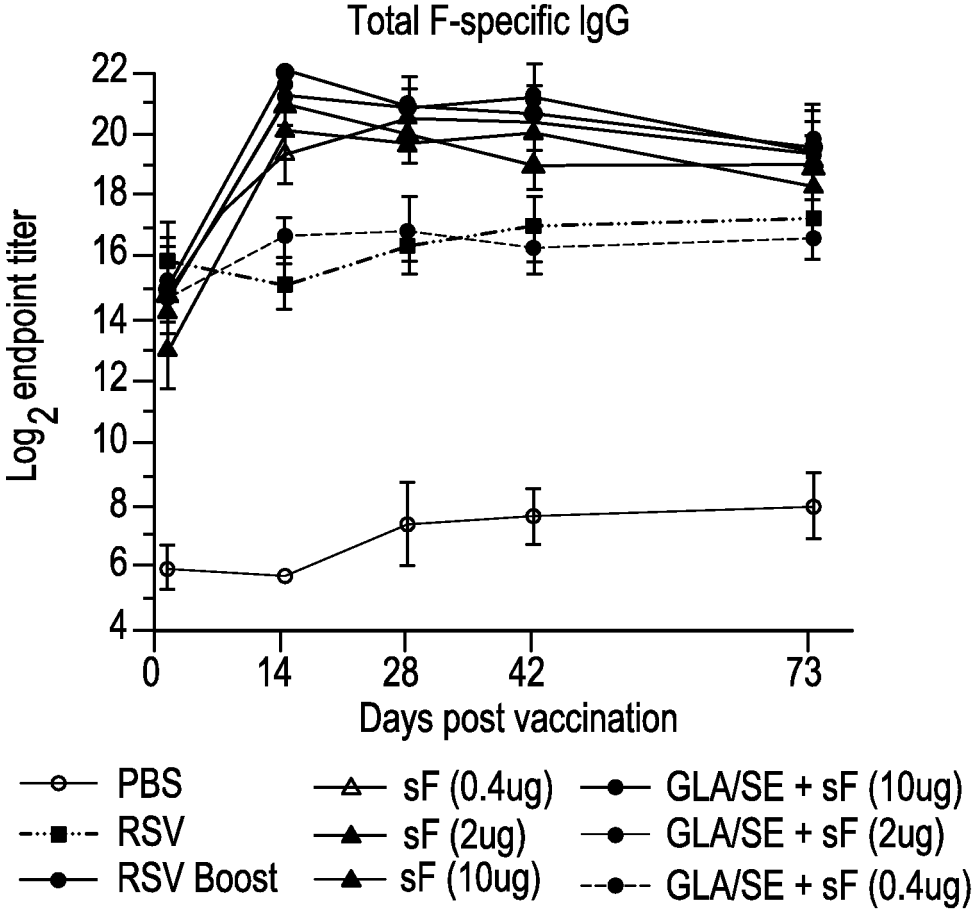


FIG. 15

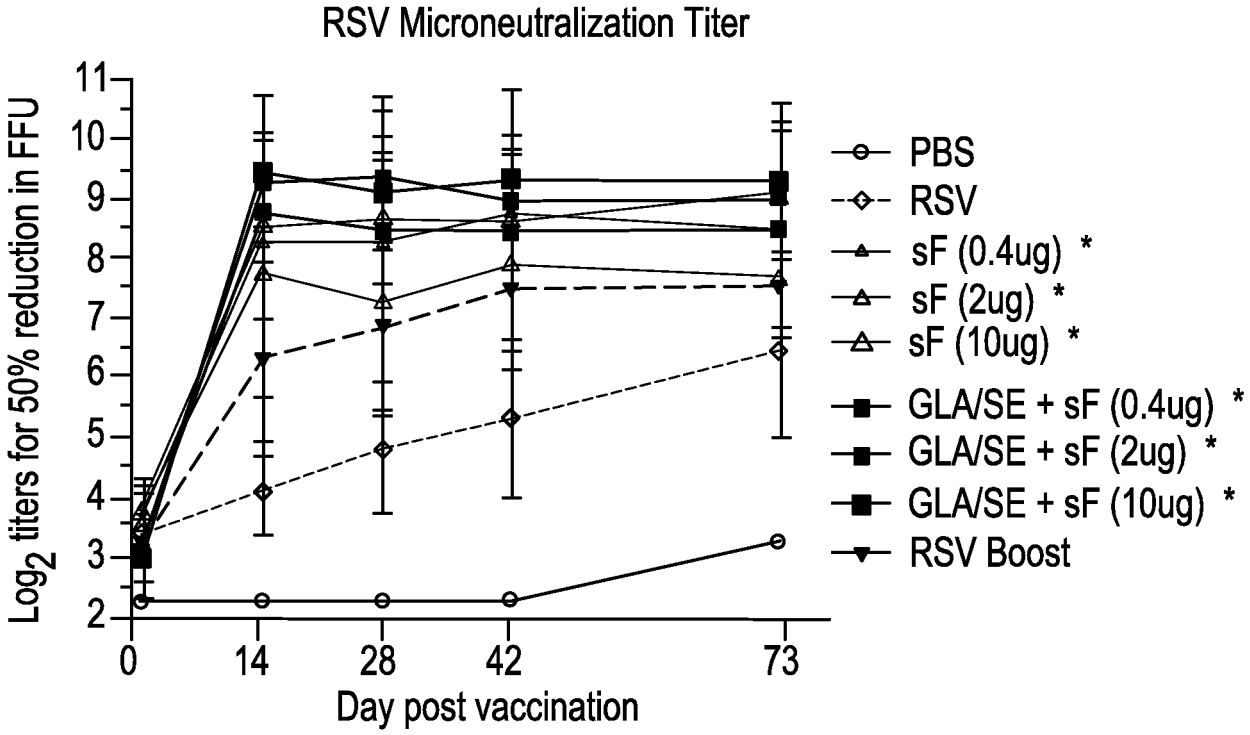

RSV Microneutralization Titer
Log2 titers for 50% reduction in FFU
11
10
9
8
7
6
5
4
3
2
0
14
28
42
73
Day post vaccination
PBS
RSV
sF (0.4ug) *
sF (2ug) *
sF (10ug) *
GLA/SE + sF (0.4ug) *
GLA/SE + sF (2ug) *
GLA/SE + sF (10ug) *
RSV Boost

FIG. 16

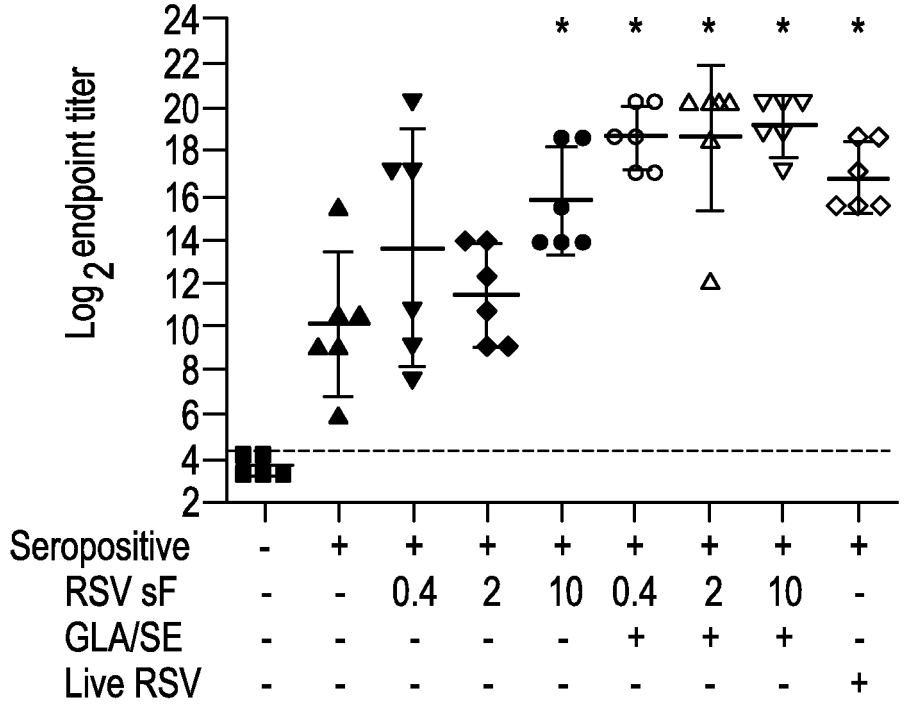

Serum F-specific IgA titers
Log2 endpoint titer
24
22
20
18
16
14
12
10
8
6
4
2
Seropositive - + + + + + + + +
RSV sF - - 0.4 2 10 0.4 2 10 -
GLA/SE - - - - - + + + -
Live RSV - - - - - - - - +

FIG. 17A

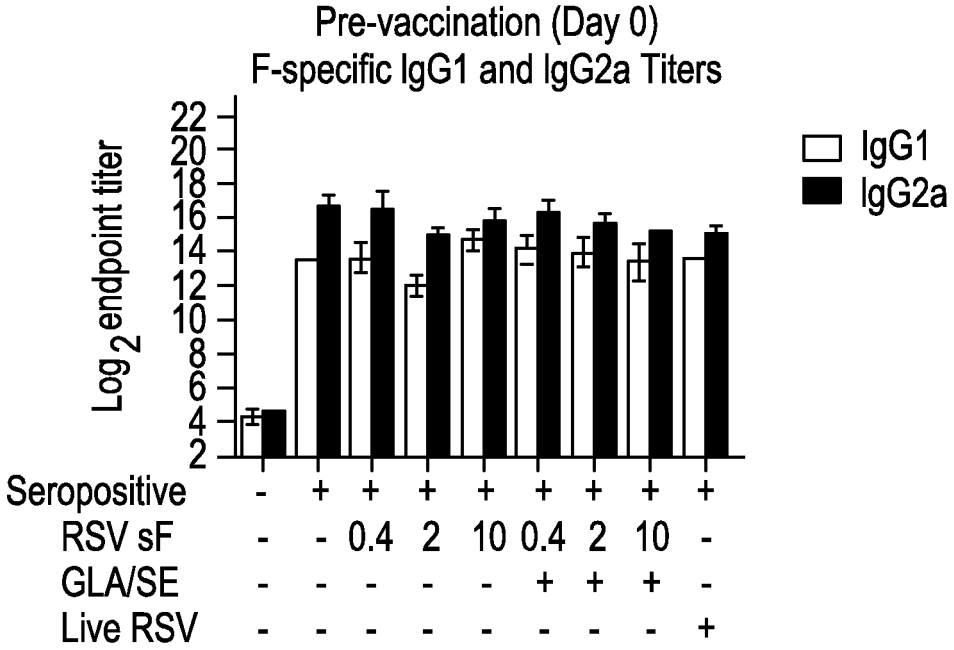


FIG. 17B

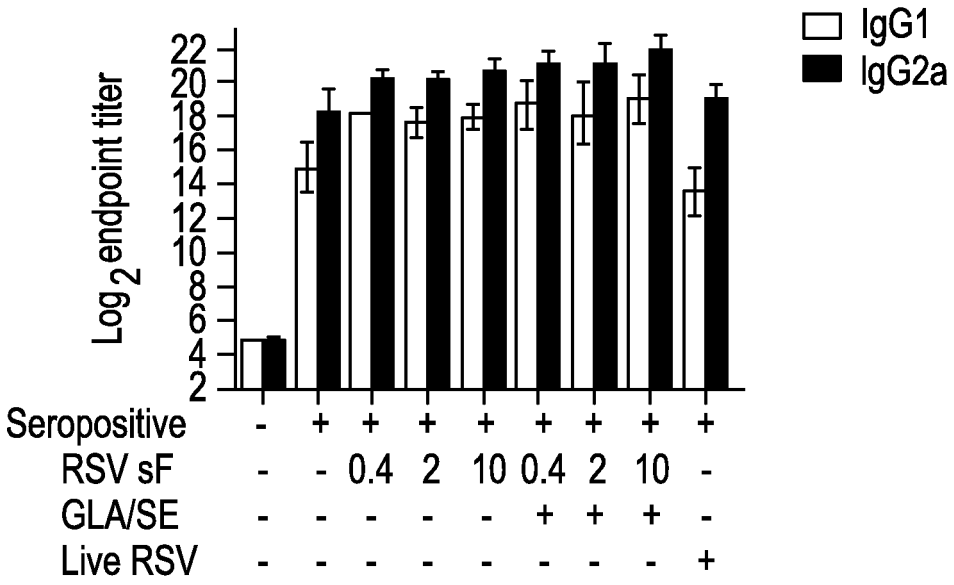


FIG. 18A

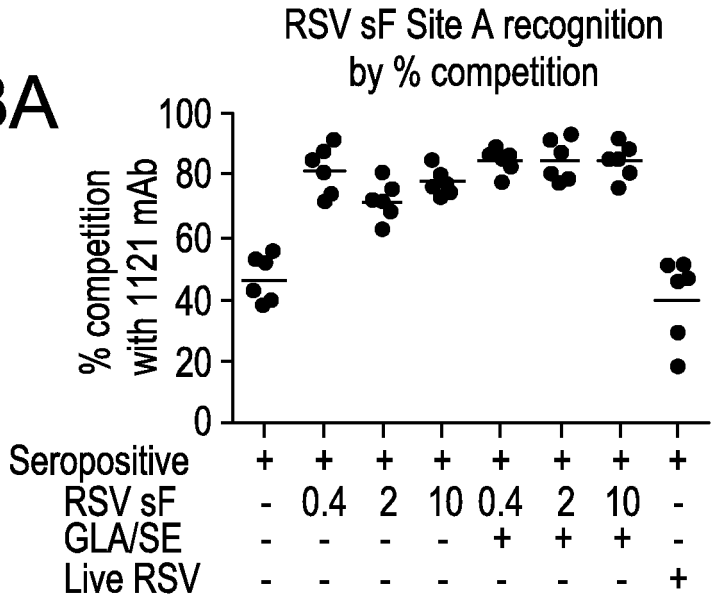


FIG. 18B

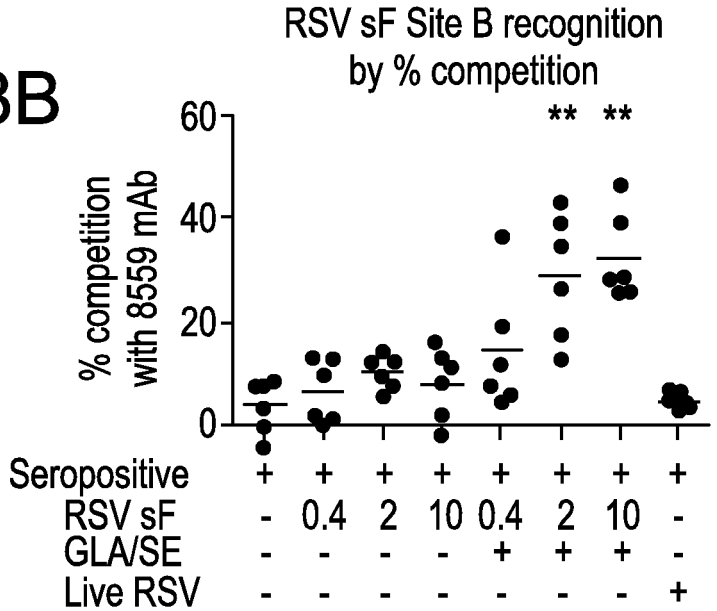


FIG. 18C

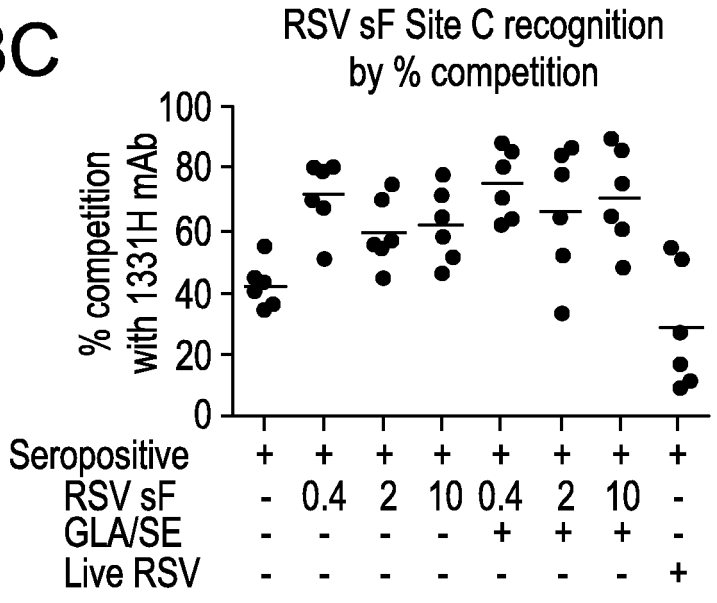


FIG. 19A

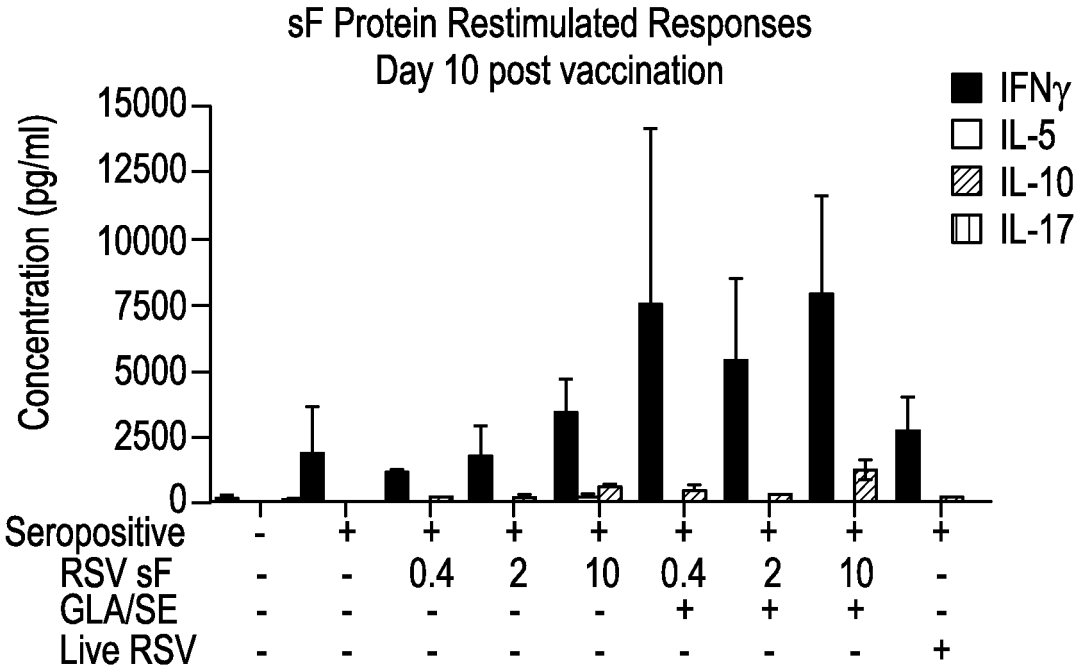


FIG. 19B

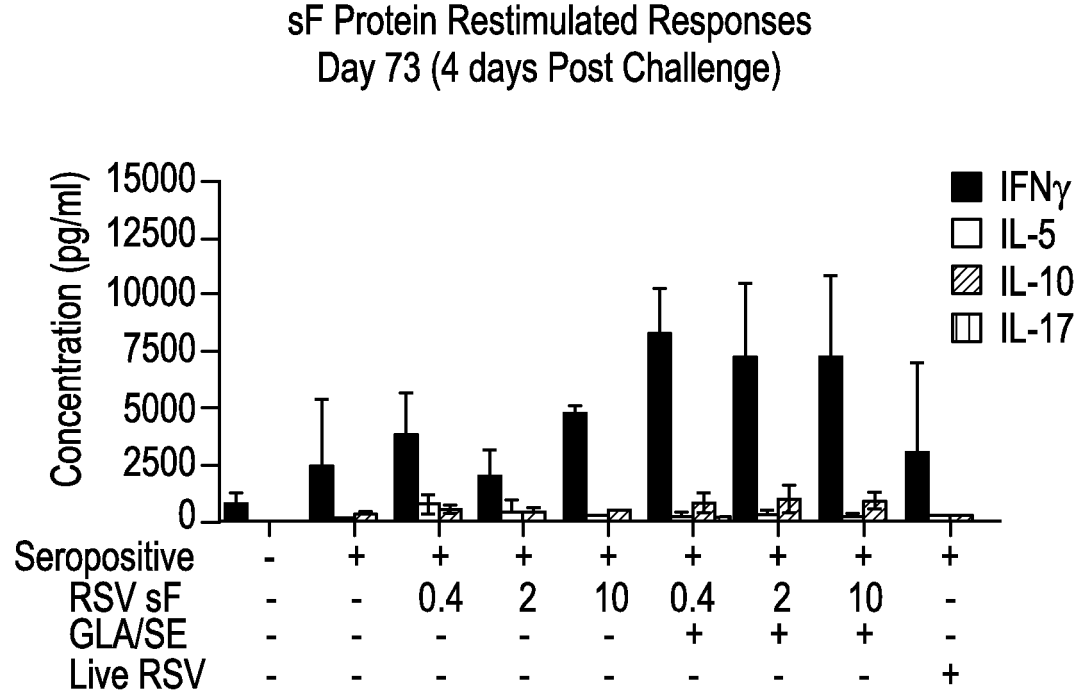


FIG. 20A

IFNγ ELISPOT for F-specific CD8 T cells
Day 10 Post Vaccination

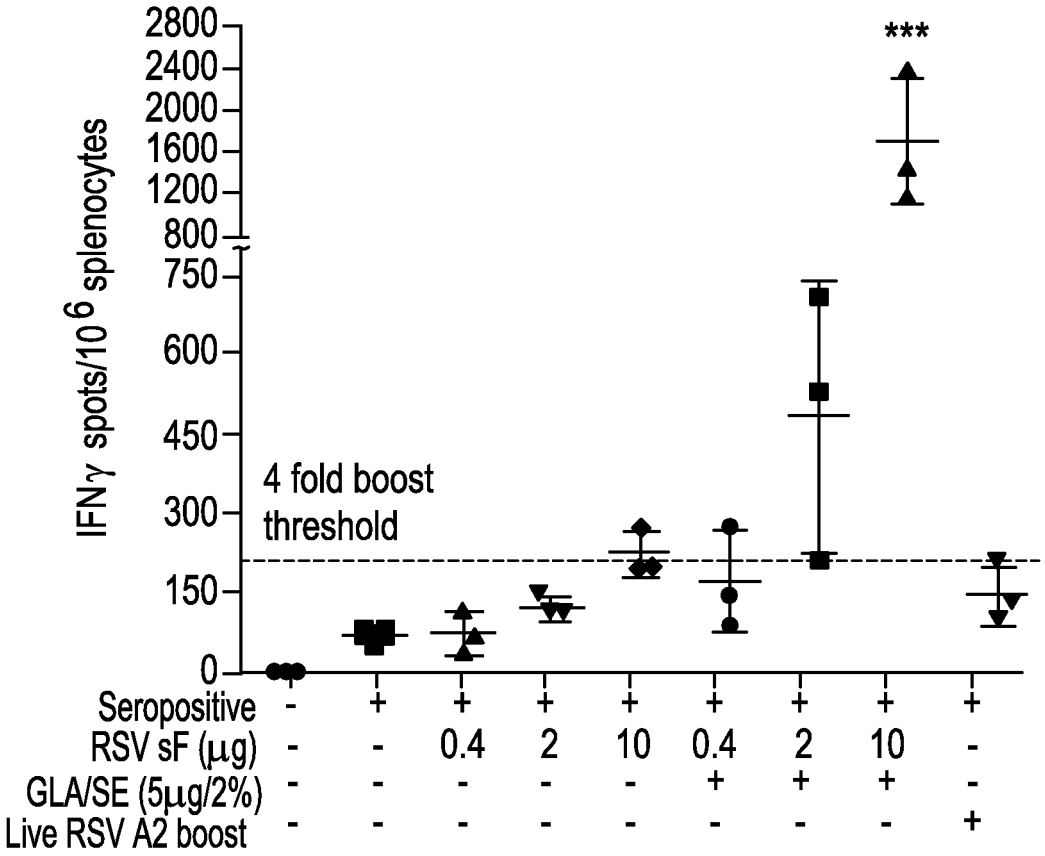


FIG. 20B

ICS for Polyfunctional F-specific CD8 T cells
Day 10 Post Vaccination

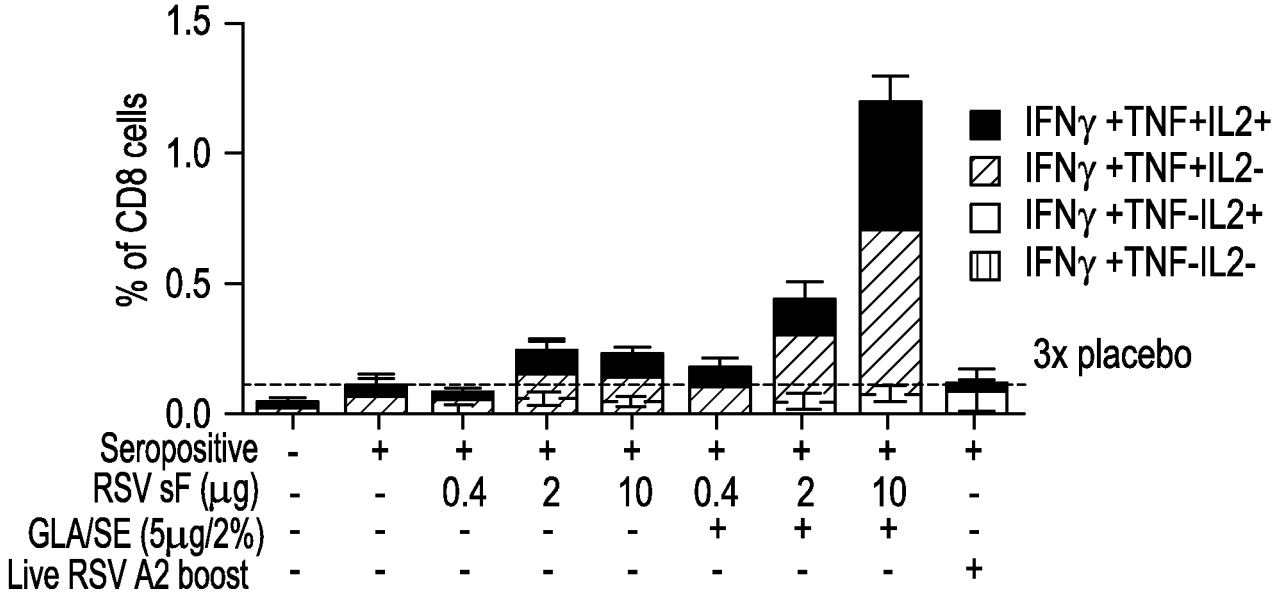


FIG. 21A

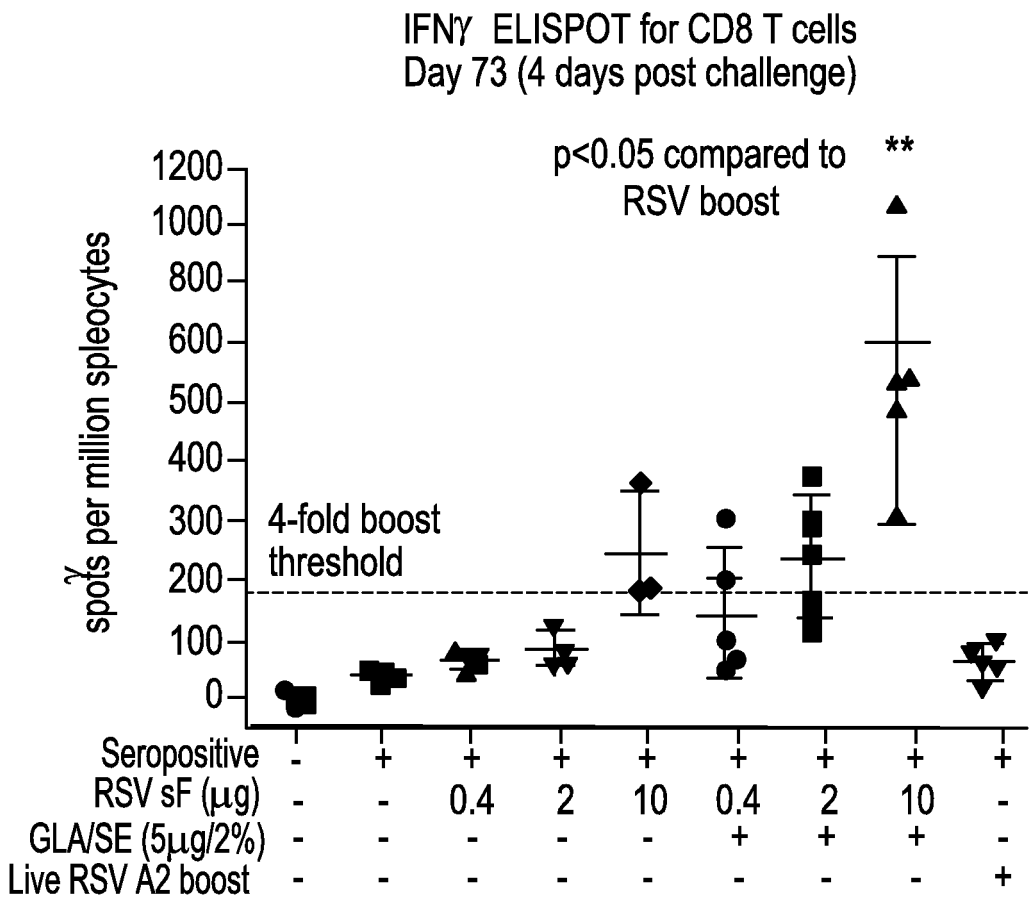


FIG. 21B

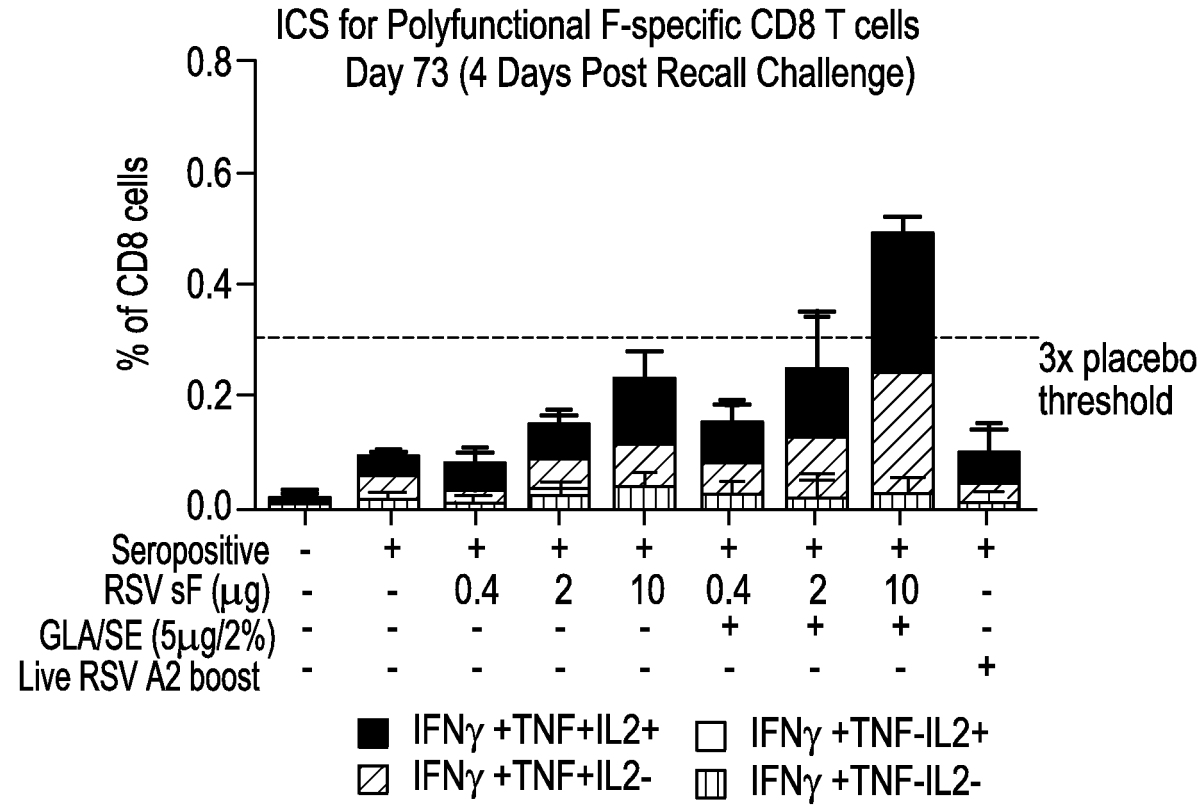


FIG. 22

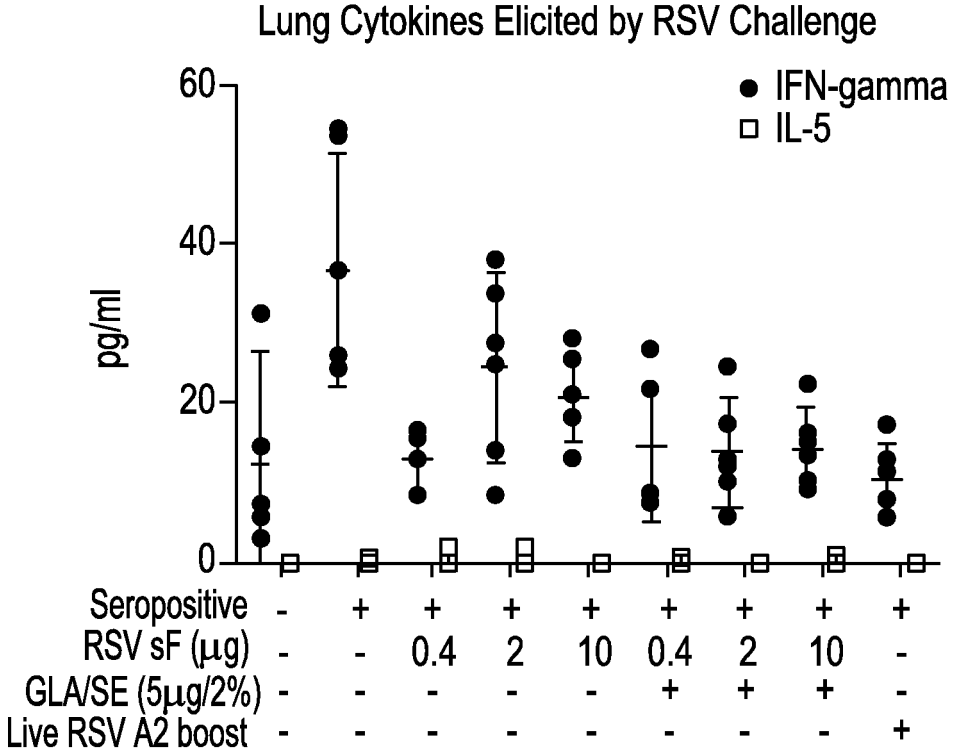

Lung Cytokines Elicited by RSV Challenge
IFN-gamma
IL-5
pg/ml
60
40
20
0
Seropositive - + + + + + + + +
RSV sF (µg) - - 0.4 2 10 0.4 2 10 -
GLA/SE (5µg/2%) - - - - - + + + -
Live RSV A2 boost - - - - - - - - +

FIG. 23

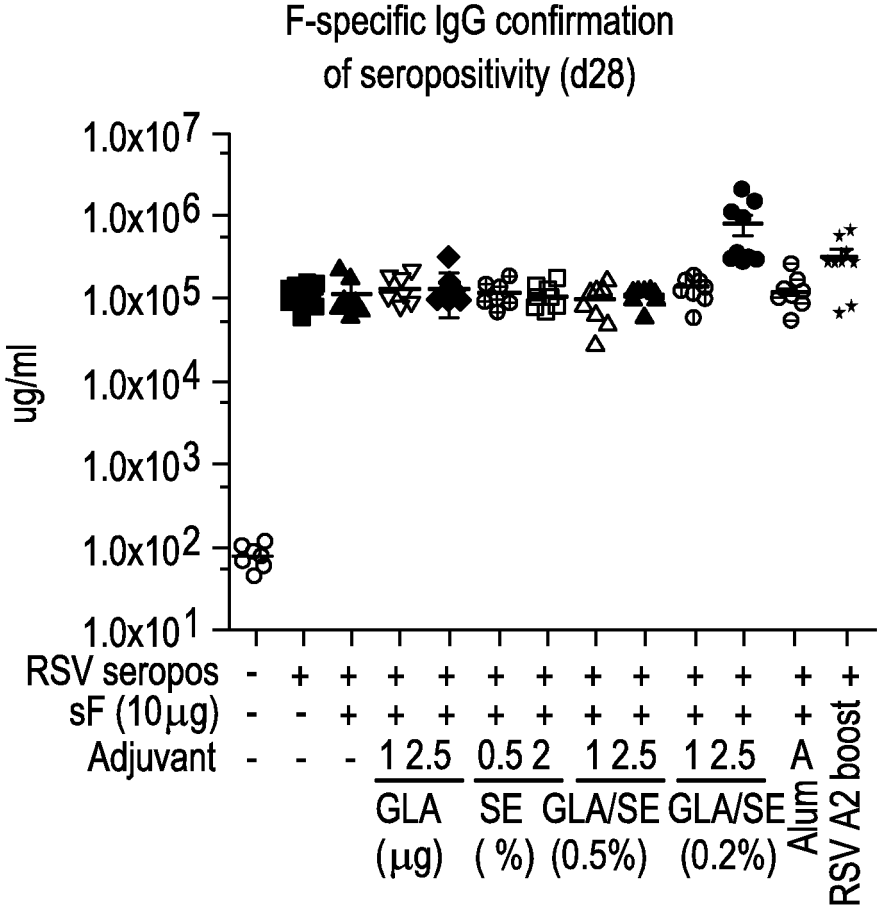

F-specific IgG confirmation
of seropositivity (d28)
ug/ml
1.0x10^7
1.0x10^6
1.0x10^5
1.0x10^4
1.0x10^3
1.0x10^2
1.0x10^1
RSV seropos - + + + + + + + + + + + +
sF (10µg) - - + + + + + + + + + + +
Adjuvant - - - 1 2.5 0.5 2 1 2.5 1 2.5 A
GLA (µg)
SE (%)
GLA/SE (0.5%)
GLA/SE (0.2%)
Alum
RSV A2 boost

FIG. 24

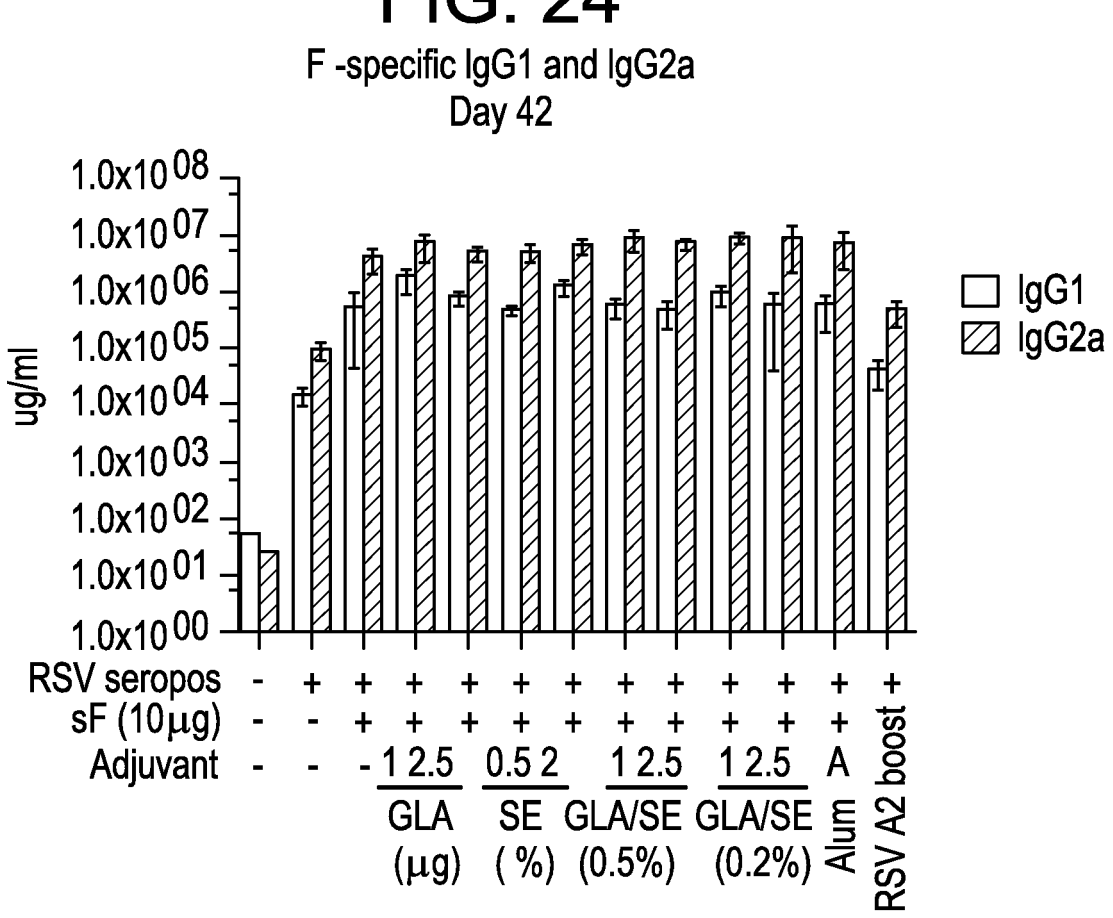

F -specific IgG1 and IgG2a
Day 42
ug/ml
1.0x10 08
1.0x10 07
1.0x10 06
1.0x10 05
1.0x10 04
1.0x10 03
1.0x10 02
1.0x10 01
1.0x10 00
IgG1
IgG2a
RSV seropos - + + + + + + + + + + + +
sF (10µg) - - + + + + + + + + + + +
Adjuvant - - - 1 2.5 0.5 2 1 2.5 1 2.5 A
GLA (µg)
SE (%)
GLA/SE (0.5%)
GLA/SE (0.2%)
Alum
RSV A2 boost

FIG. 25

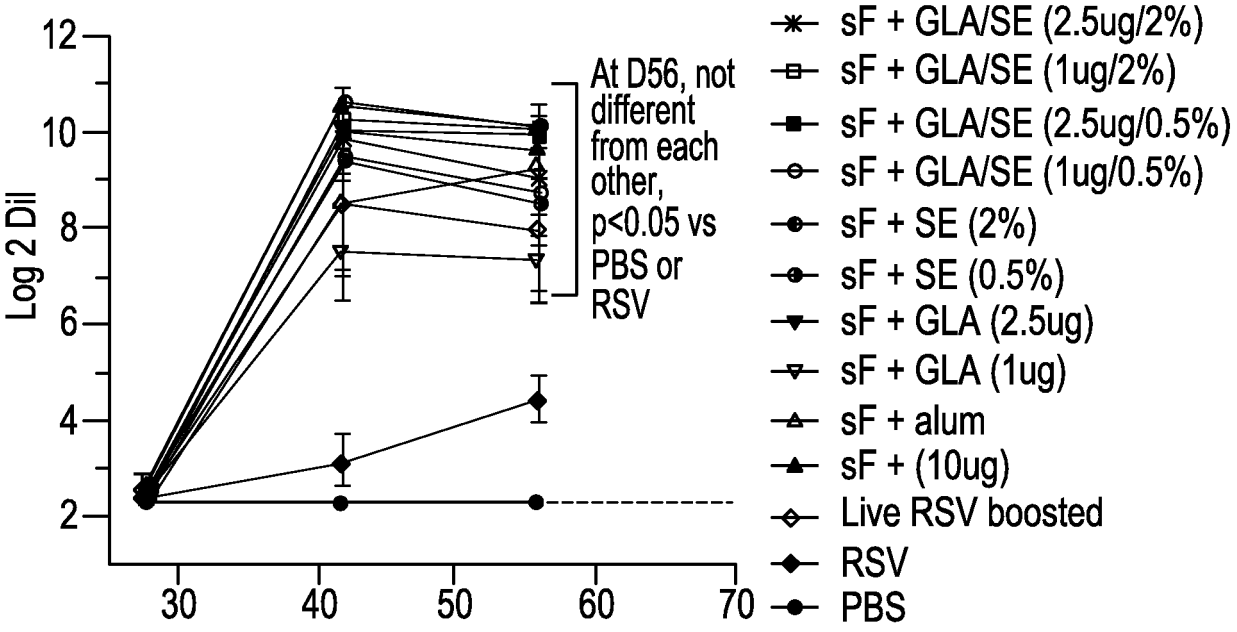
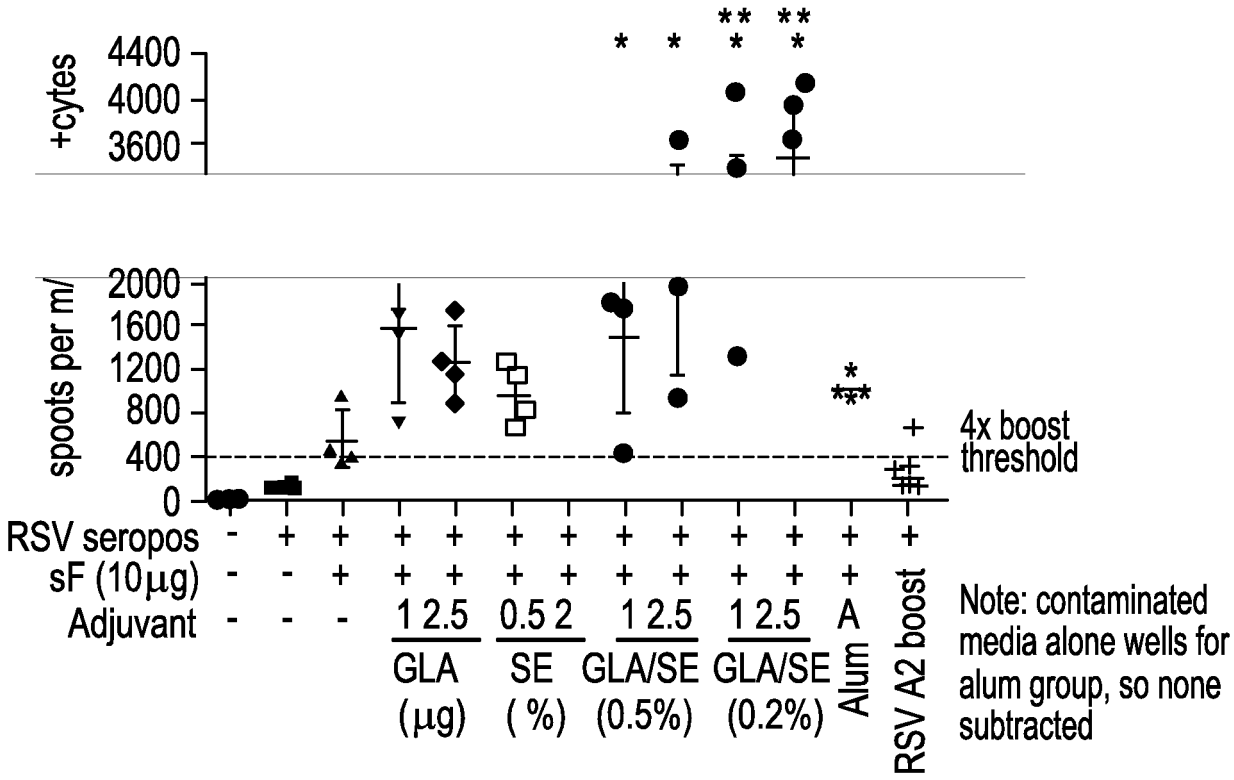

Serum RSV neutralizing titers
(timecourse)
Log 2 Dil
12
10
8
6
4
2
30
40
50
60
70
At D56, not different from each other, p<0.05 vs PBS or RSV
sF + GLA/SE (2.5ug/2%)
sF + GLA/SE (1ug/2%)
sF + GLA/SE (2.5ug/0.5%)
sF + GLA/SE (1ug/0.5%)
sF + SE (2%)
sF + SE (0.5%)
sF + GLA (2.5ug)
sF + GLA (1ug)
sF + alum
sF + (10ug)
Live RSV boosted
RSV
PBS

FIG. 26A

CD8 IFNγ ELISpot (d32)



* p<0.05 compared to seropositive given sF

** p<0.05 compared to seropositive given sF + alum

FIG. 26B

Polyfunctional CD8 T cells by ICS

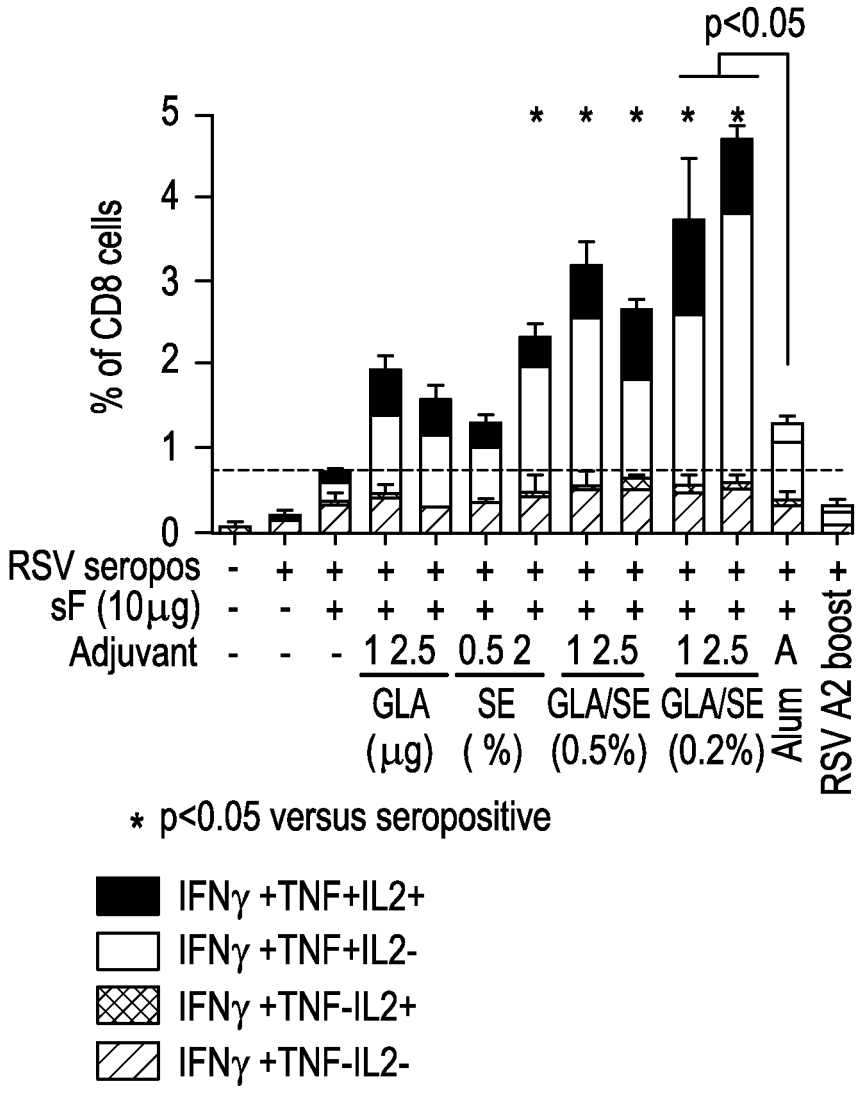


FIG. 27

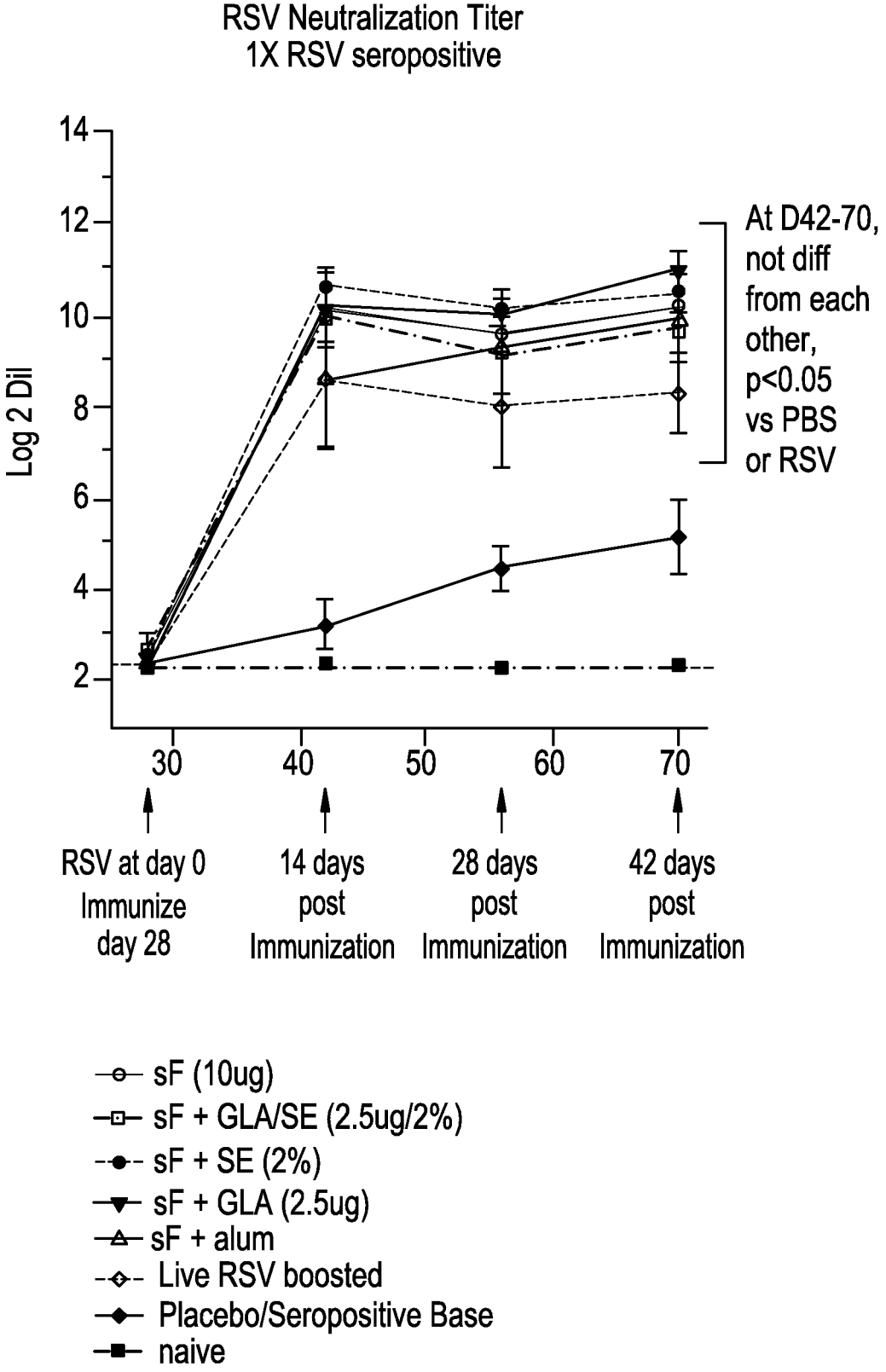

RSV Neutralization Titer
1X RSV seropositive
Log 2 Dil
14
12
10
8
6
4
2
30
40
50
60
70
At D42-70, not diff from each other, p<0.05 vs PBS or RSV
RSV at day 0 Immunize day 28
14 days post Immunization
28 days post Immunization
42 days post Immunization
sF (10ug)
sF + GLA/SE (2.5ug/2%)
sF + SE (2%)
sF + GLA (2.5ug)
sF + alum
Live RSV boosted
Placebo/Seropositive Base
naive

FIG. 28A

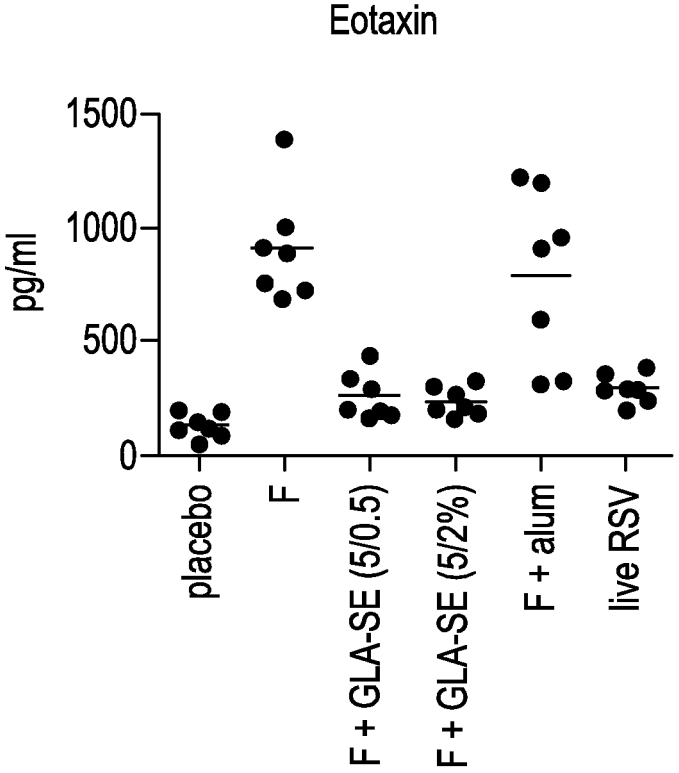


FIG. 28B

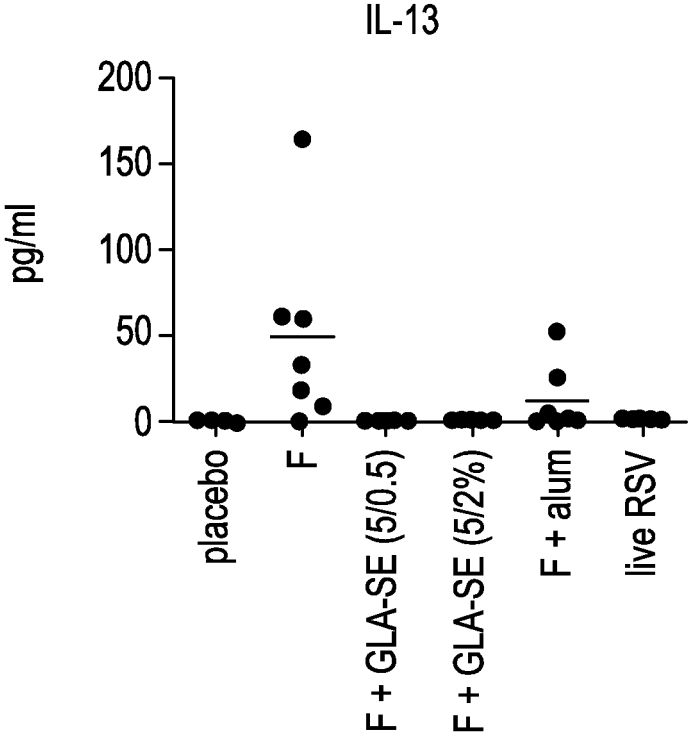


FIG. 29A

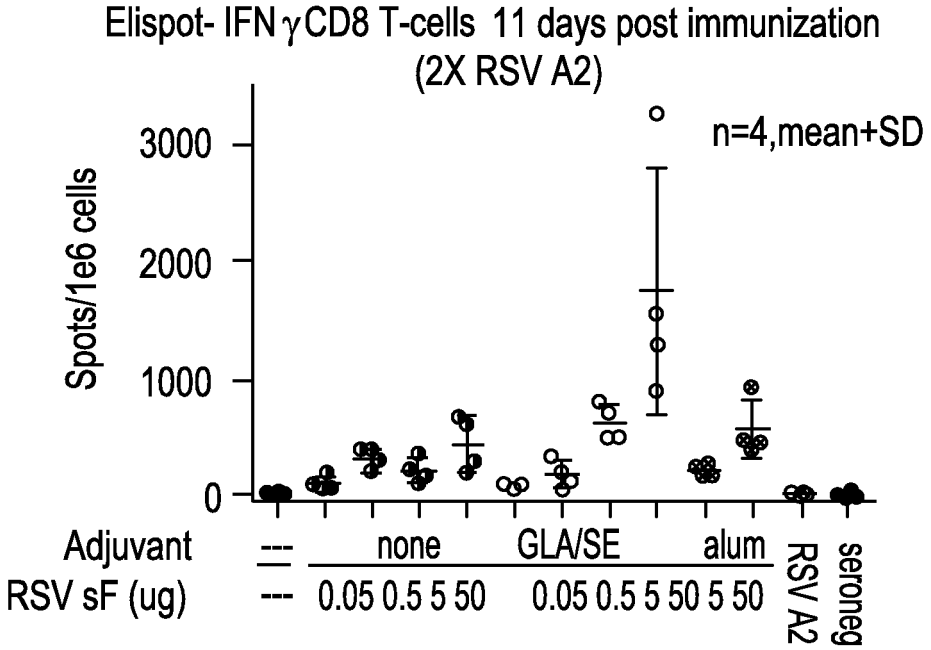
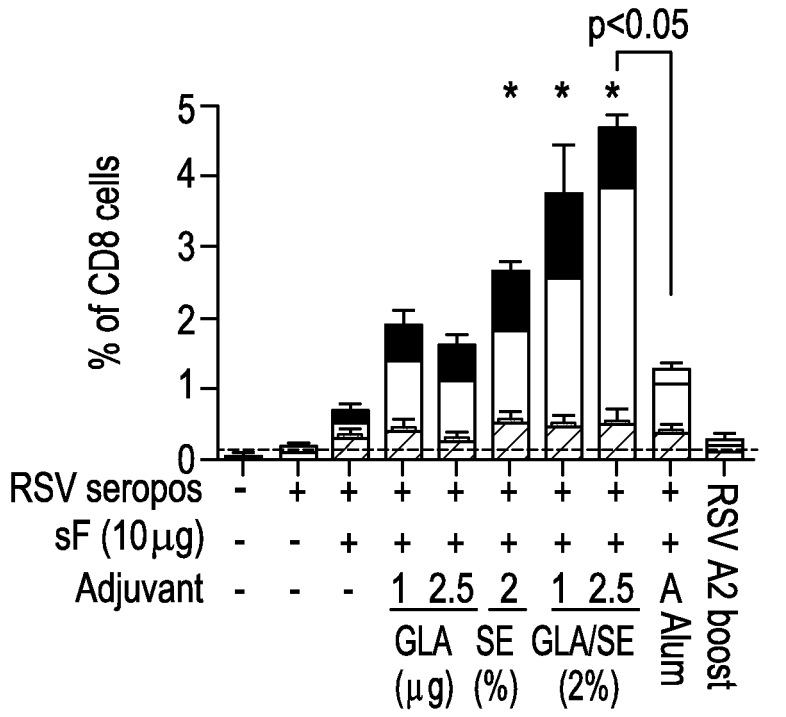


FIG. 29B



* p<0.05 versus seropositive

IFNγ +TNF+IL2+ IFNγ +TNF-IL2+

IFNγ +TNF+IL2- IFNγ +TNF-IL2-

FIG. 30A

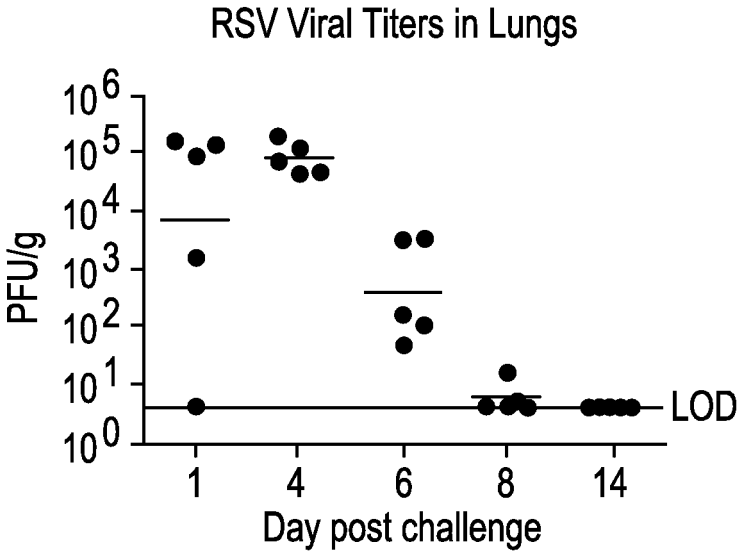


FIG. 30B

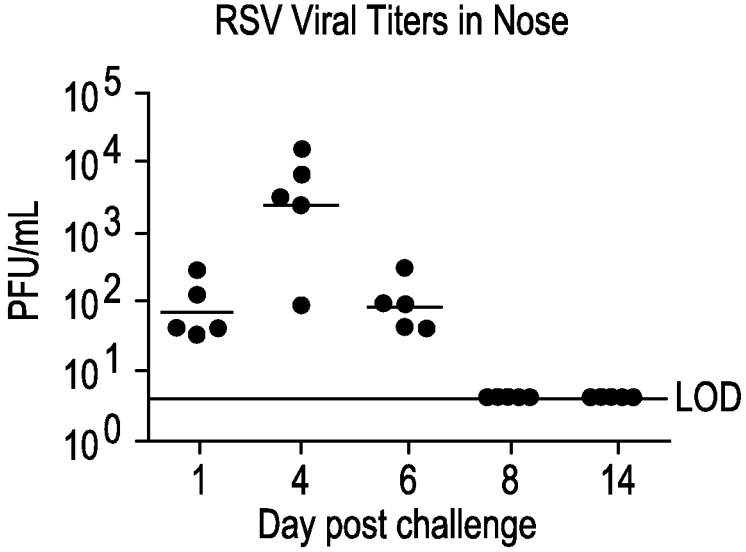


FIG. 31A

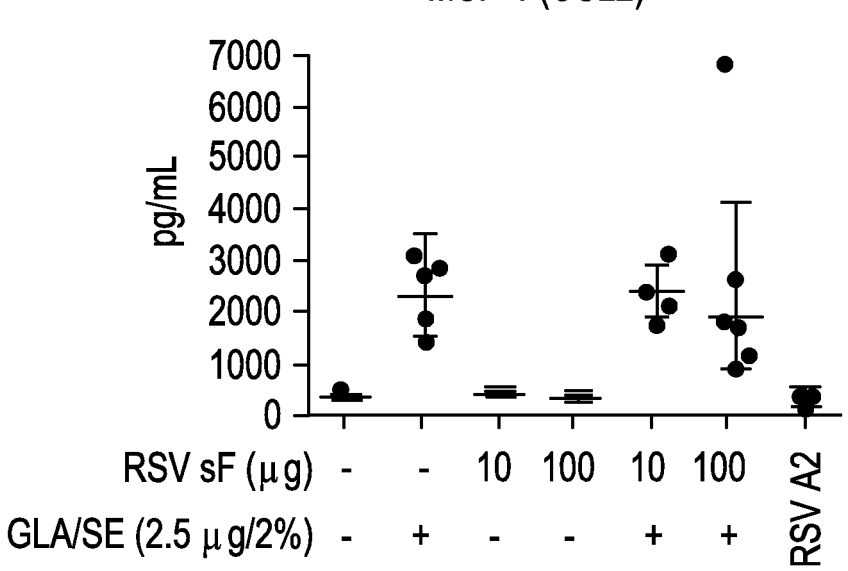


FIG. 31B

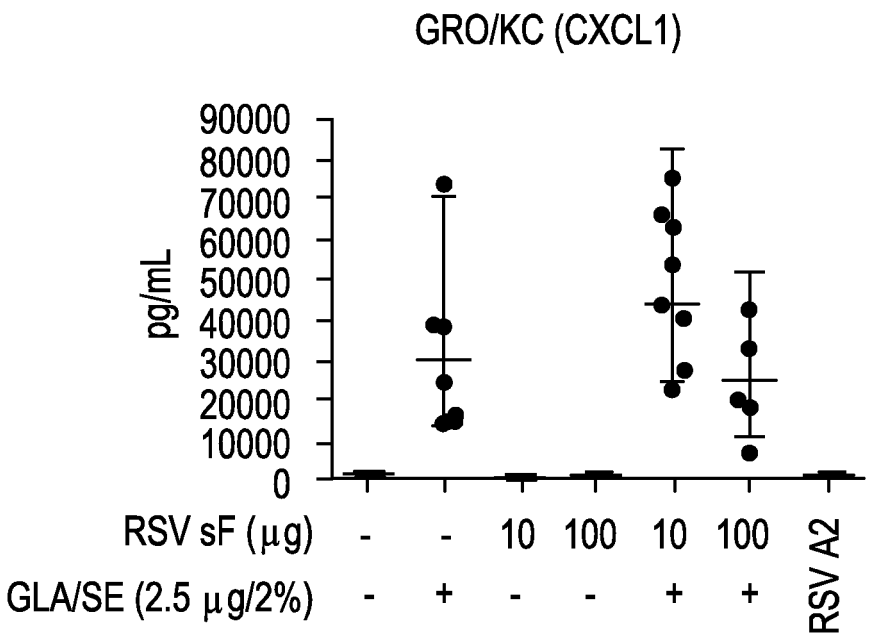


FIG. 31C

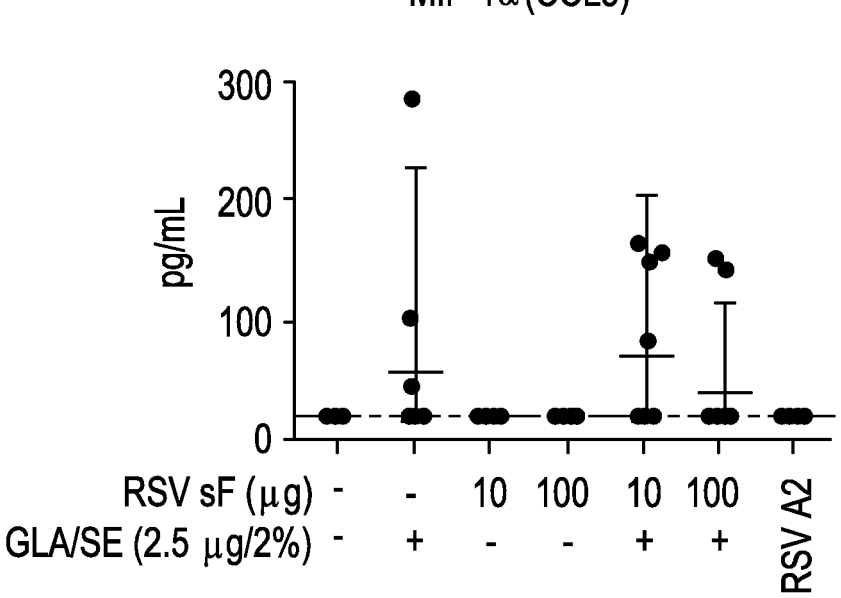


FIG. 31D

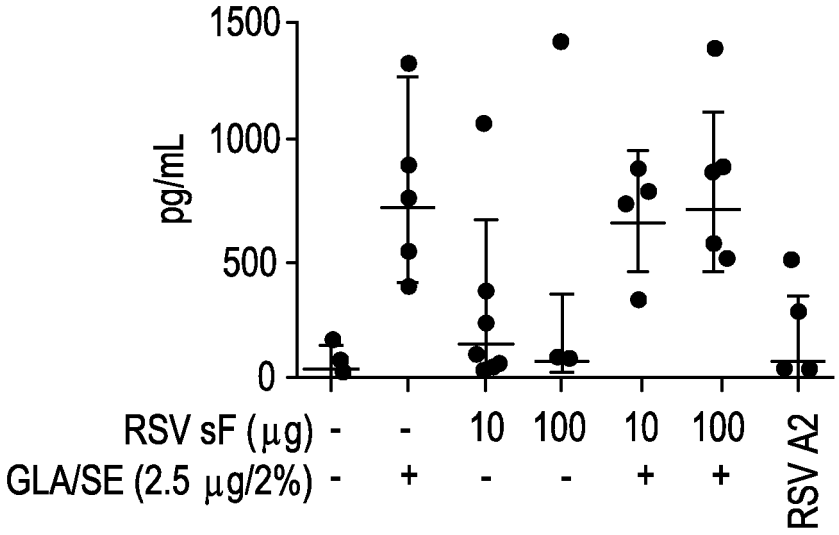


FIG. 32A

Day 14

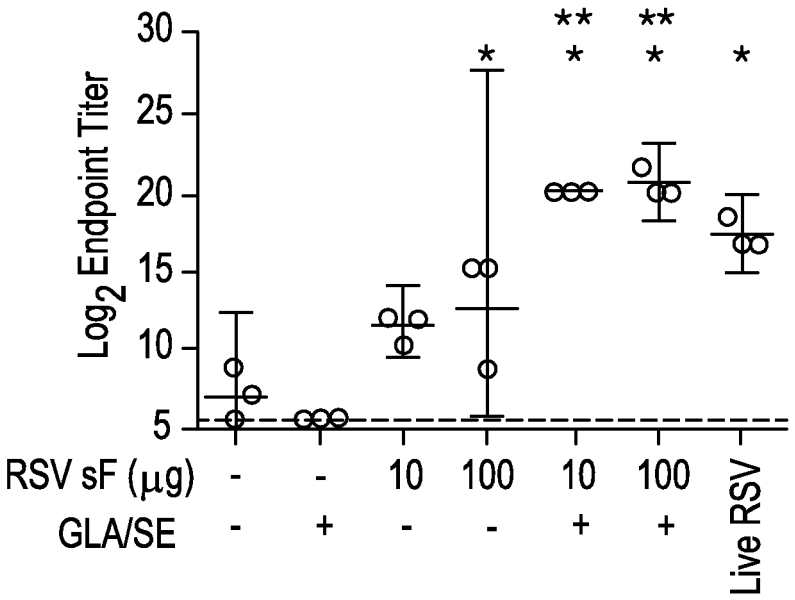


FIG. 32B

Day 22

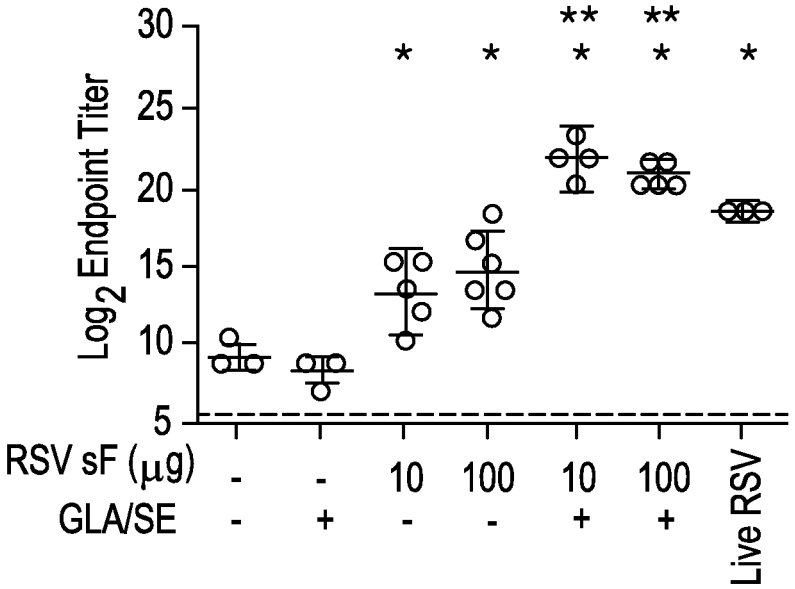


FIG. 32C

Day 42

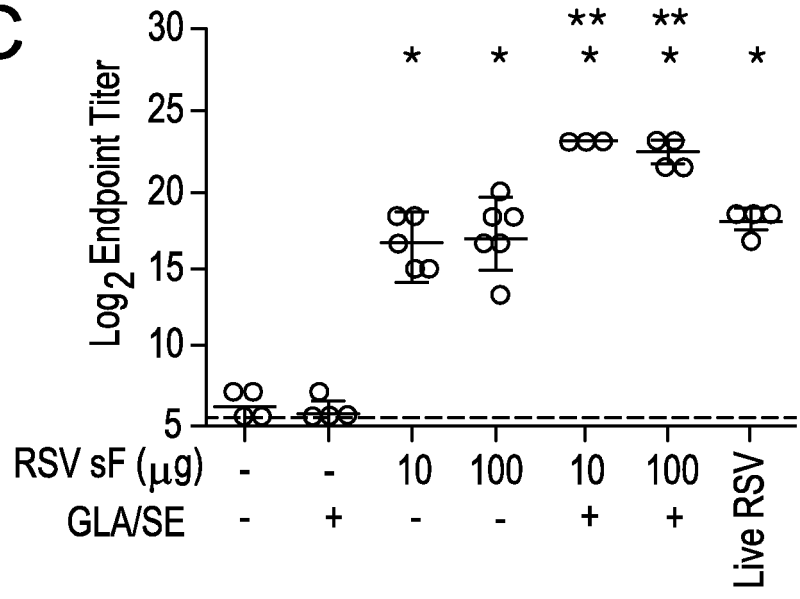


FIG. 33

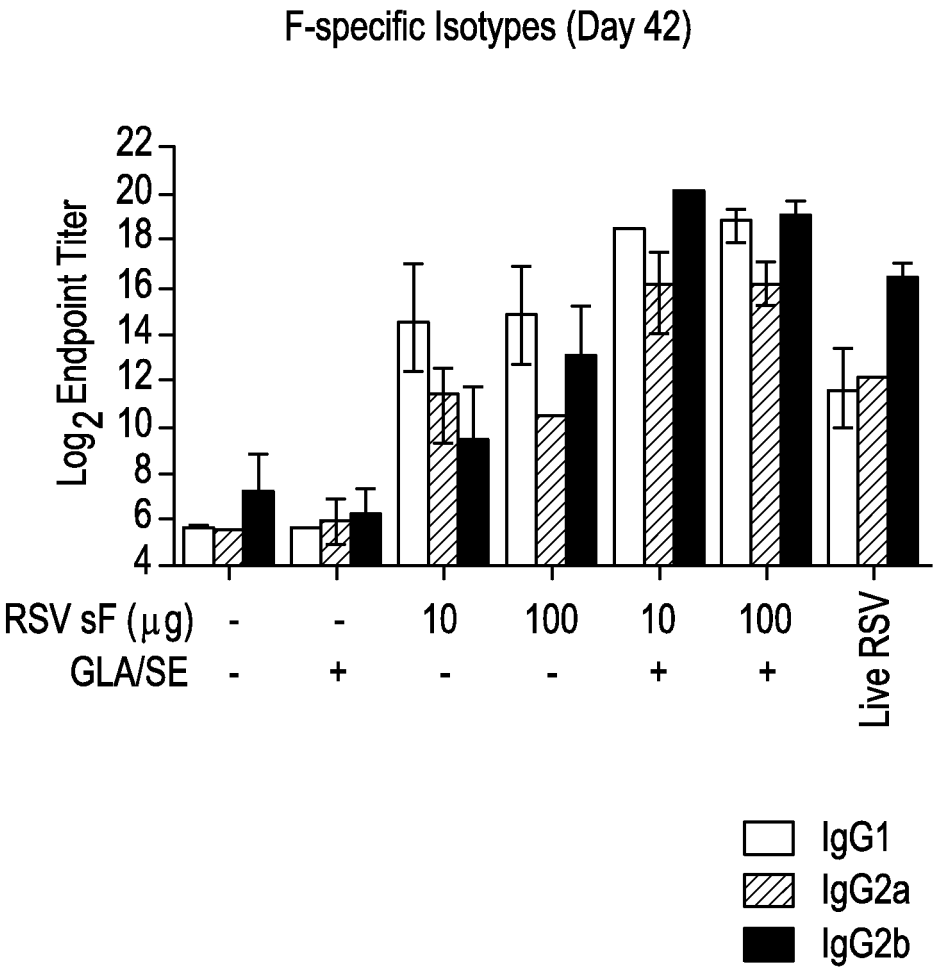

F-specific Isotypes (Day 42)
Log2 Endpoint Titer
22
20
18
16
14
12
10
8
6
4
RSV sF (μg) - - 10 100 10 100
GLA/SE - + - - + +
Live RSV
IgG1
IgG2a
IgG2b

FIG. 34A

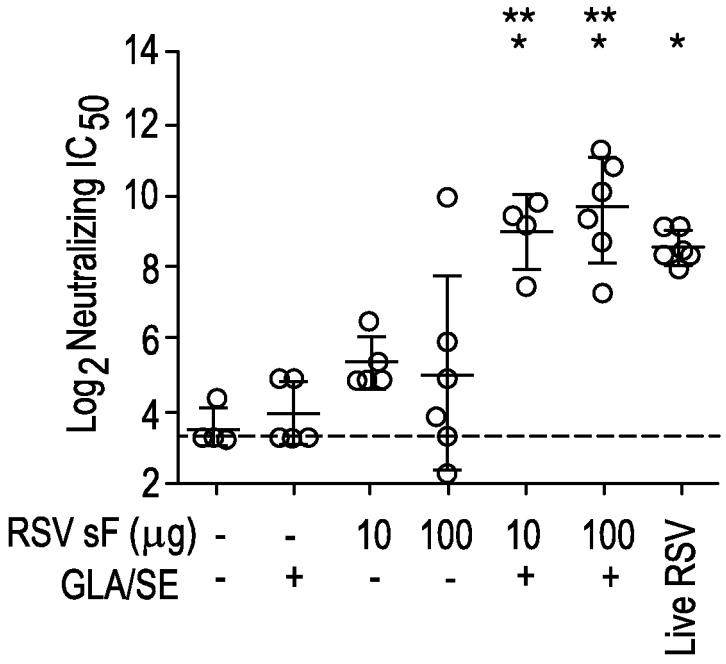


FIG. 34B

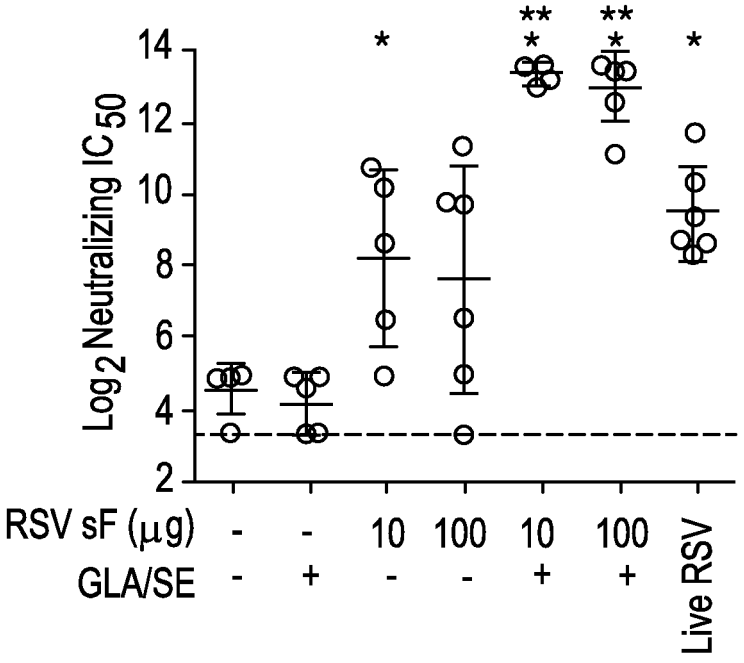


FIG. 35

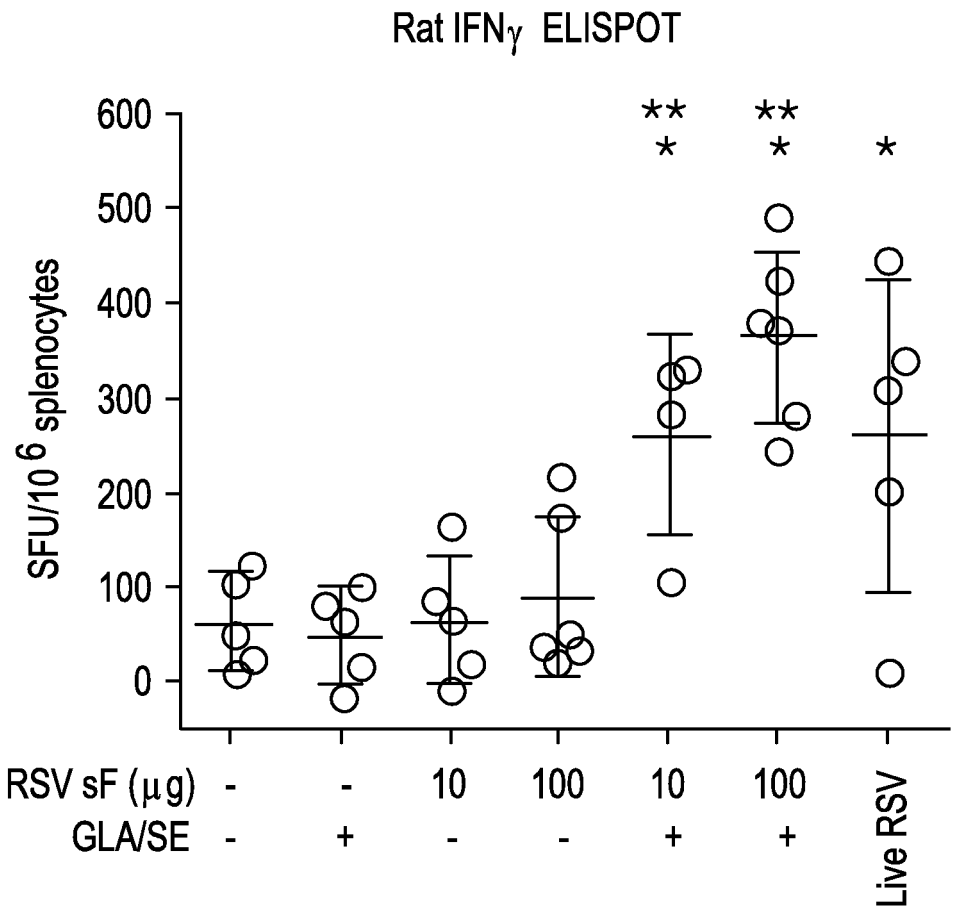

Rat IFNγ ELISPOT
SFU/10^6 splenocytes
600
500
400
300
200
100
0
** * ** * *
RSV sF (µg) - - 10 100 10 100
GLA/SE - + - - + +
Live RSV

FIG. 36A

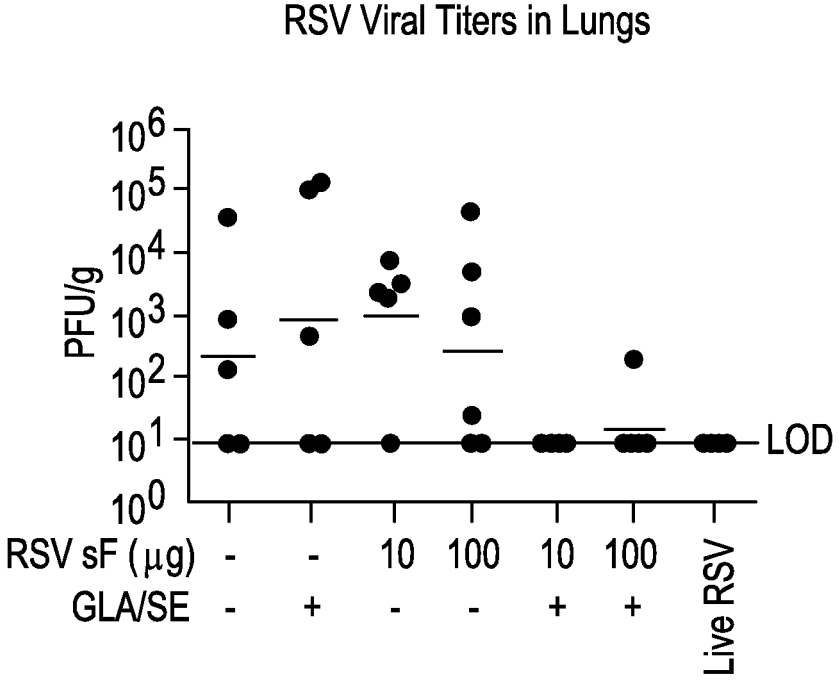


FIG. 36B

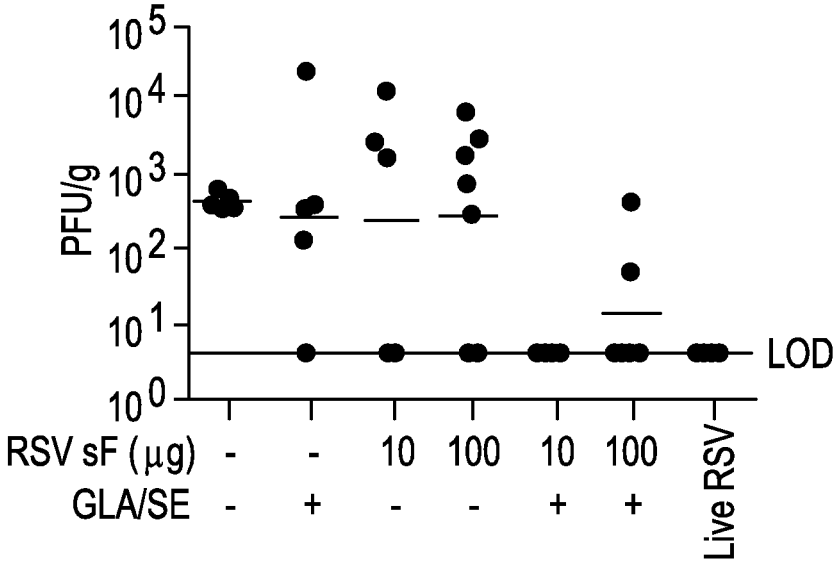


FIG. 37A

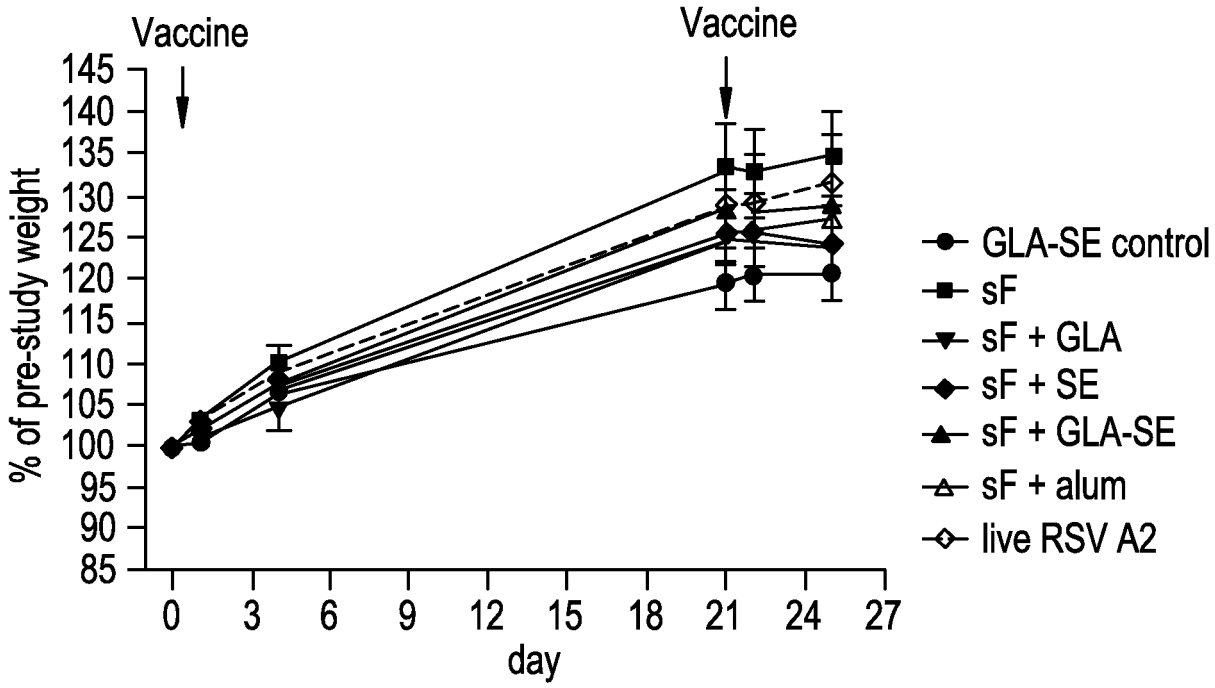


FIG. 37B

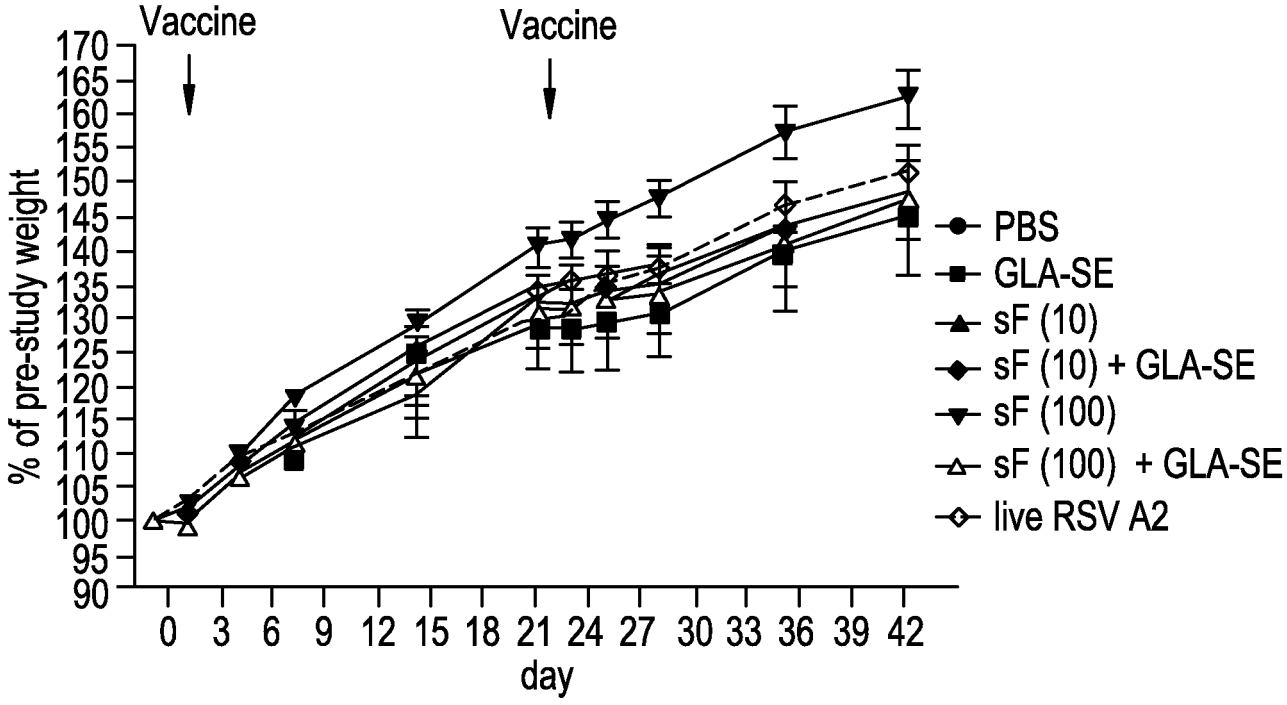


FIG. 38

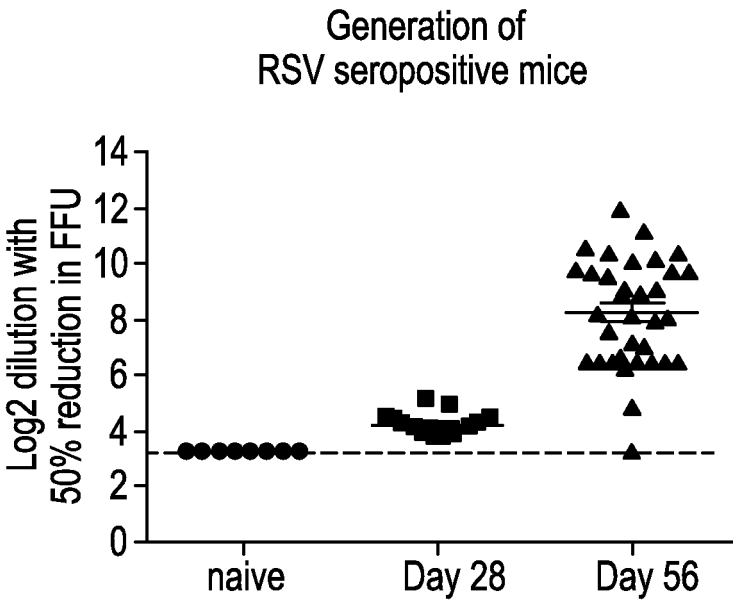

Generation of
RSV seropositive mice
Log2 dilution with
50% reduction in FFU
14
12
10
8
6
4
2
0
naive
Day 28
Day 56

FIG. 39

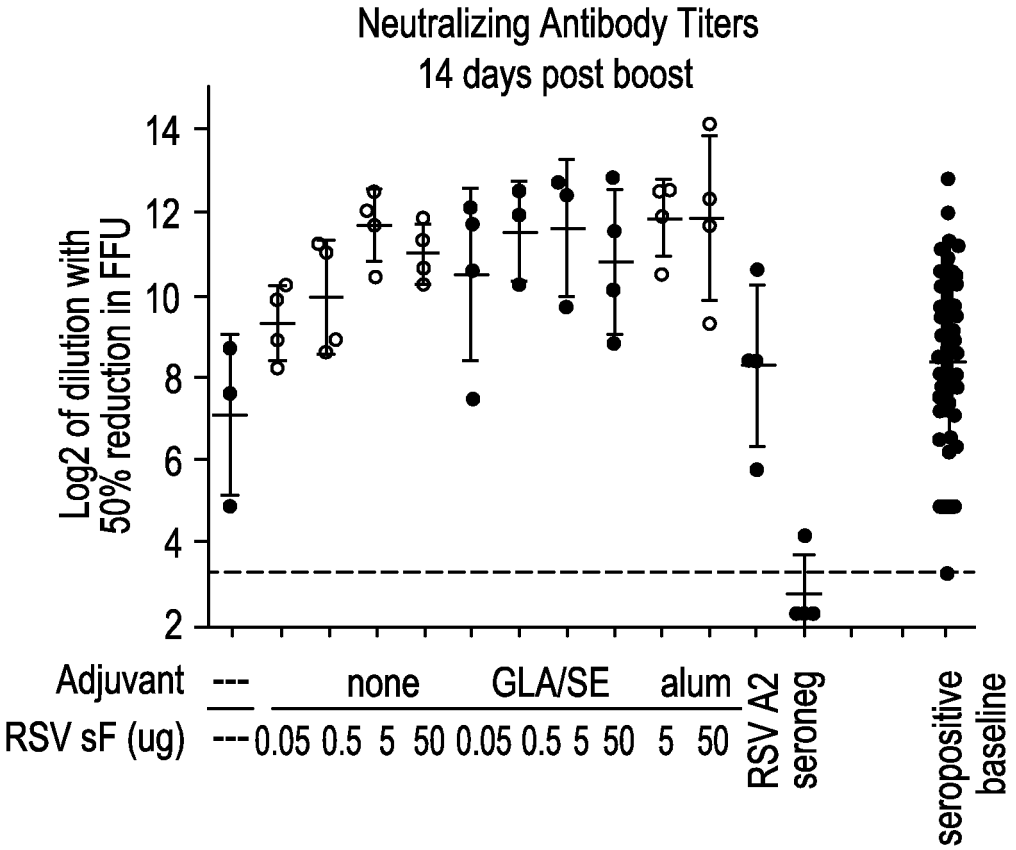

Neutralizing Antibody Titers
14 days post boost
Log2 of dilution with
50% reduction in FFU
14
12
10
8
6
4
2
Adjuvant --- none GLA/SE alum RSV A2 seroneg seropositive baseline
RSV sF (ug) --- 0.05 0.5 5 50 0.05 0.5 5 50 5 50

FIG. 40

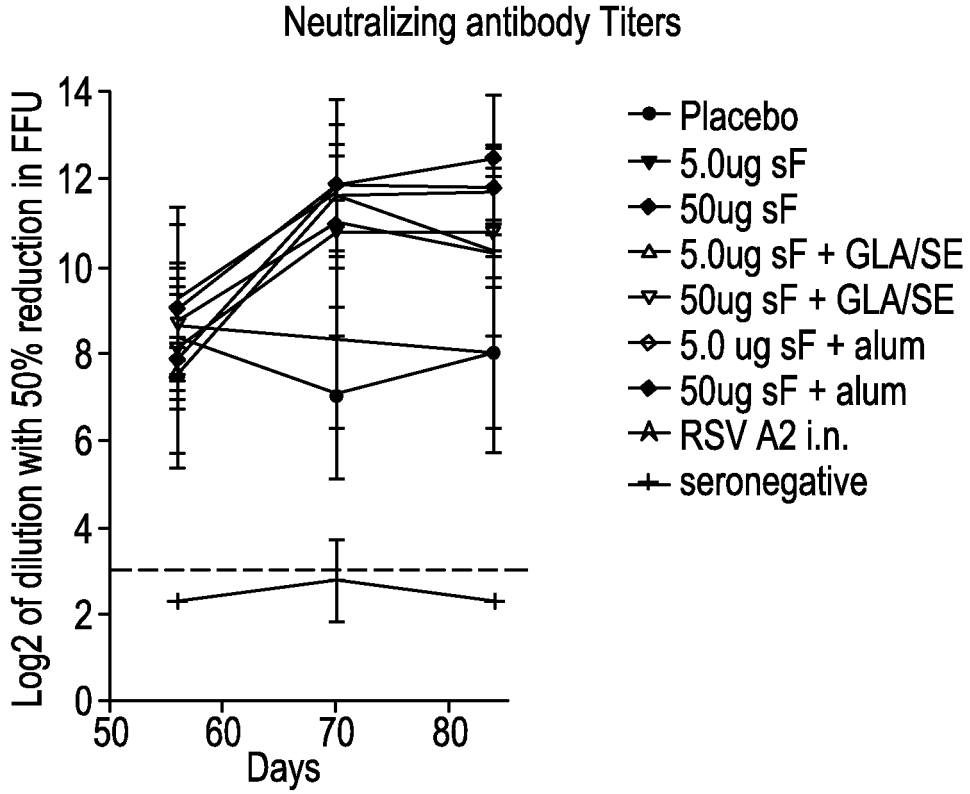

Neutralizing antibody Titers
Log2 of dilution with 50% reduction in FFU
14
12
10
8
6
4
2
0
50
60
70
80
Days
Placebo
5.0ug sF
50ug sF
5.0ug sF + GLA/SE
50ug sF + GLA/SE
5.0 ug sF + alum
50ug sF + alum
RSV A2 i.n.
seronegative

FIG. 41

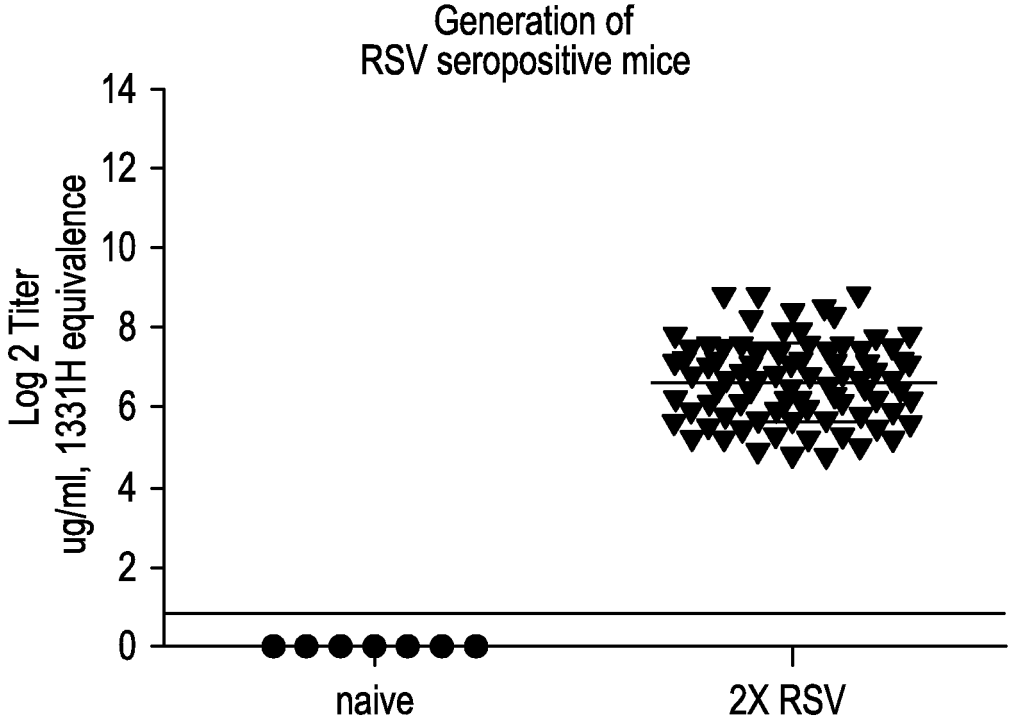

Generation of
RSV seropositive mice
Log 2 Titer
ug/ml, 1331H equivalence
14
12
10
8
6
4
2
0
naive
2X RSV

FIG. 42

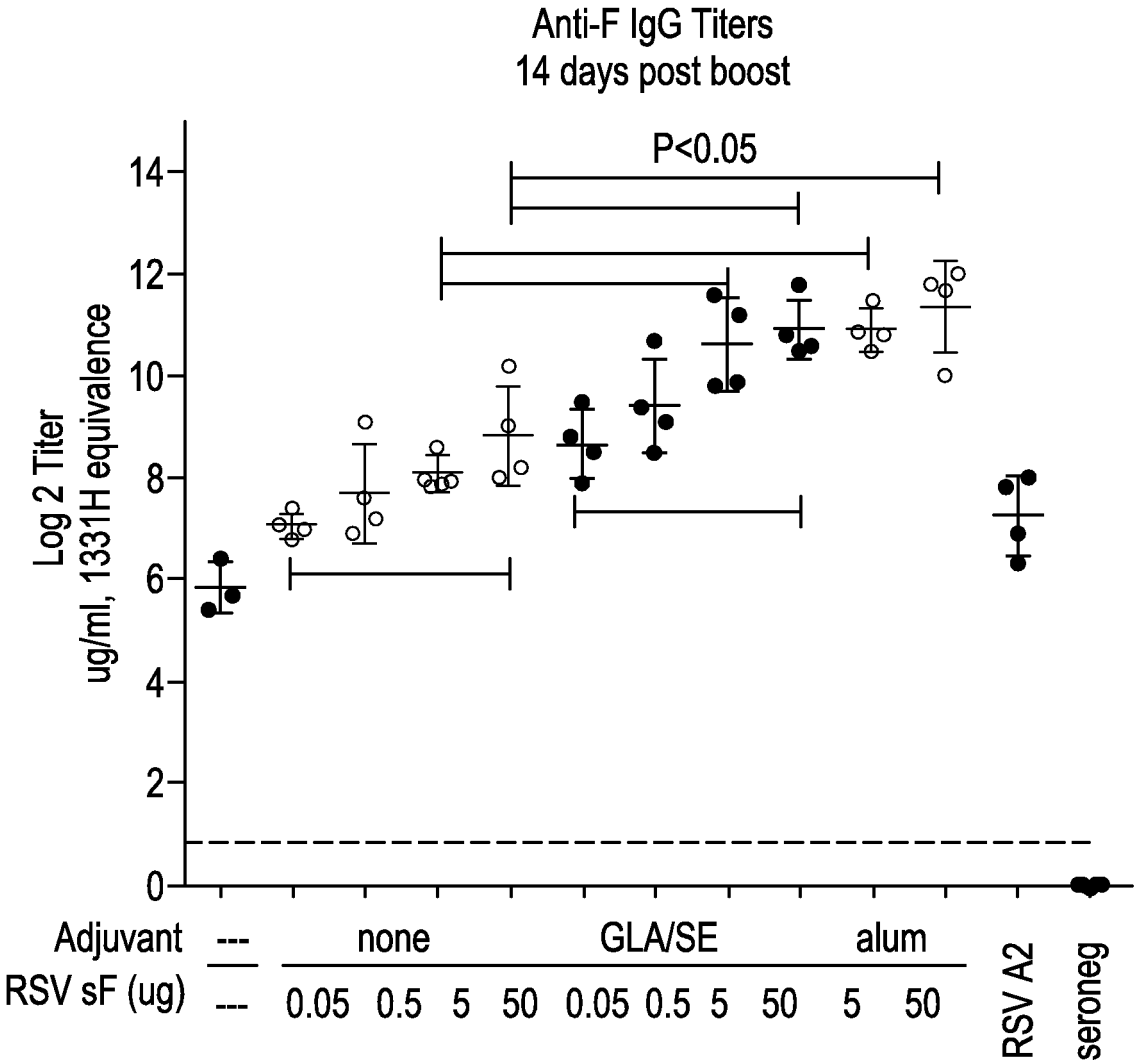

Anti-F IgG Titers
14 days post boost
P<0.05
Log 2 Titer
ug/ml, 1331H equivalence
14
12
10
8
6
4
2
0
Adjuvant --- none GLA/SE alum
RSV sF (ug) --- 0.05 0.5 5 50 0.05 0.5 5 50 5 50
RSV A2
seroneg

FIG. 43

Anti-F IgG Titer

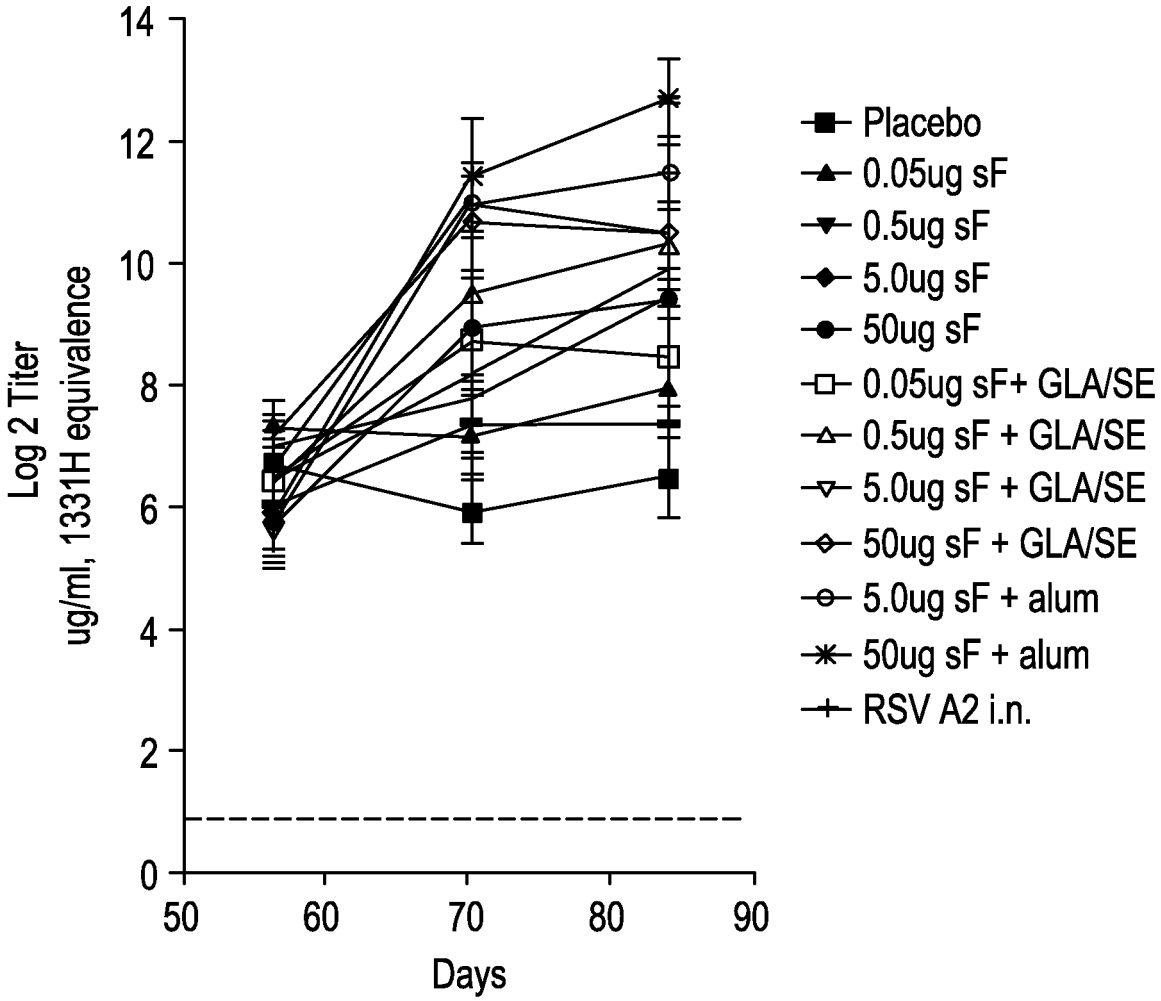


FIG. 44

Anti-F IgG1 and IgG2a titers

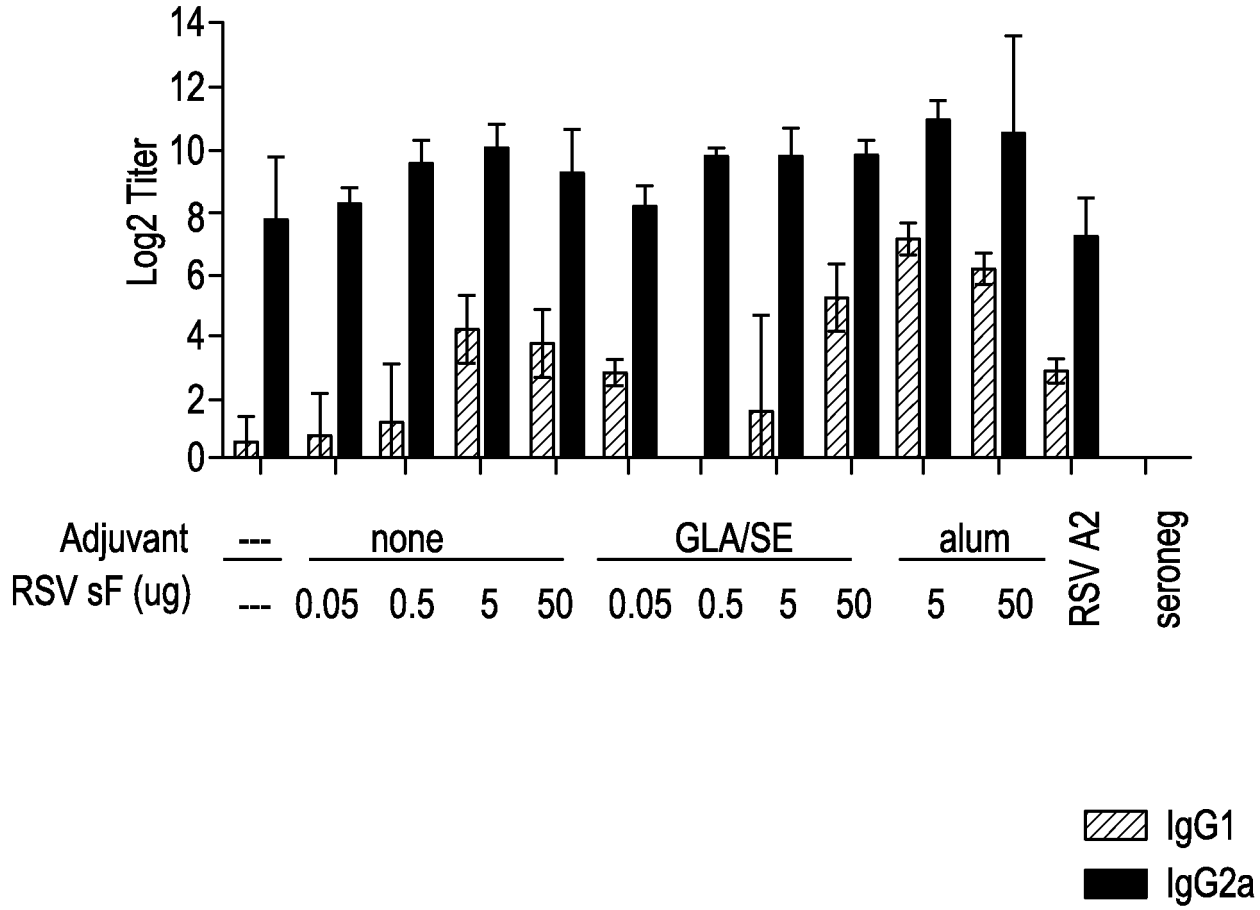
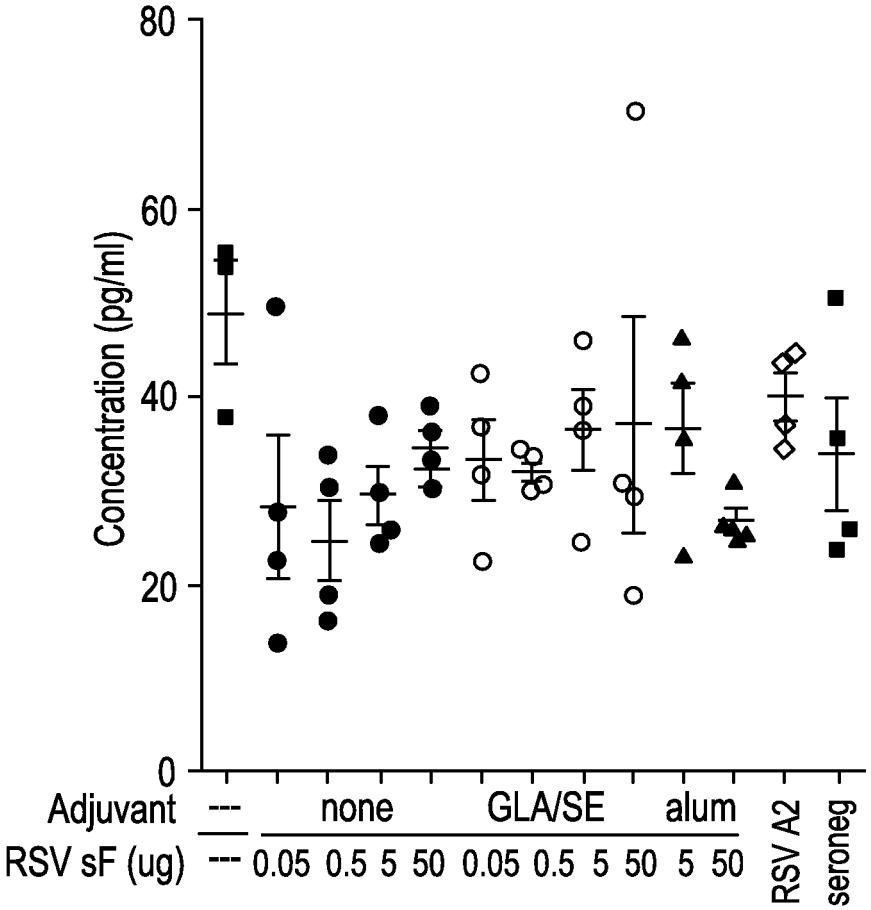


FIG. 45A


IFN-gamma (Th1)
Lungs, 4 days post-challenge
Concentration (pg/ml)
80
60
40
20
0
Adjuvant
---
none
GLA/SE
alum
RSV sF (ug)

0.05
0.5
5
50
0.05
0.5
5
50
5
50
RSV A2
seroneg

FIG. 45B

IL-5 (Th2)
Lungs, 4 days post-challenge

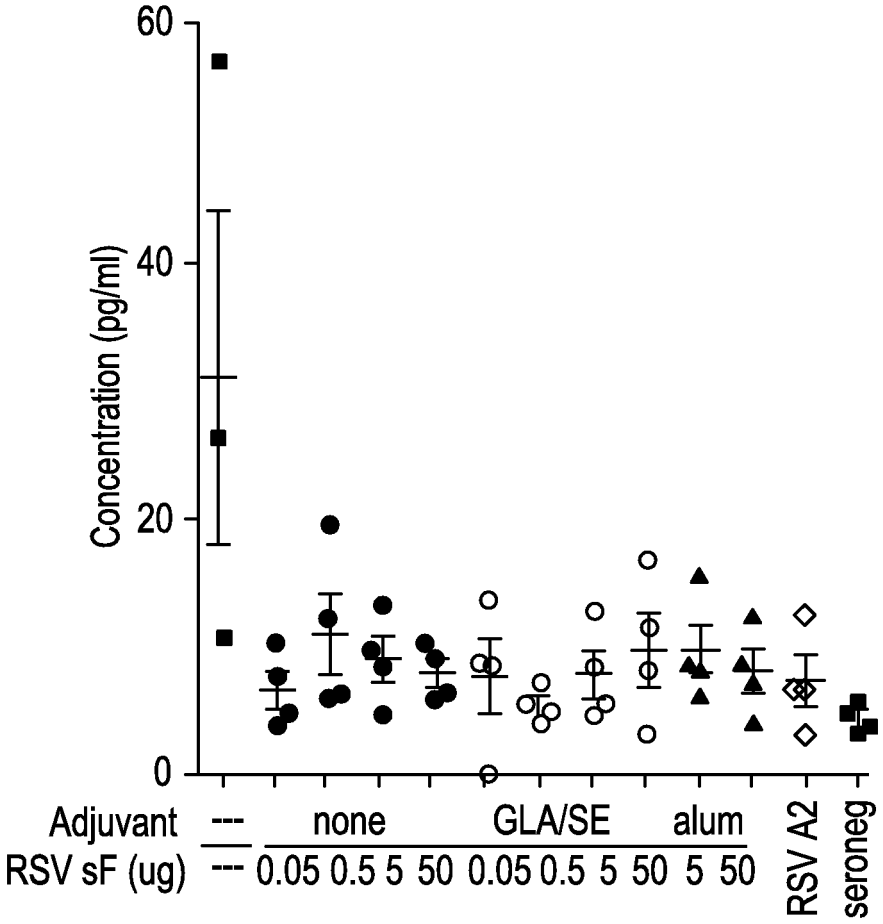


FIG. 46A

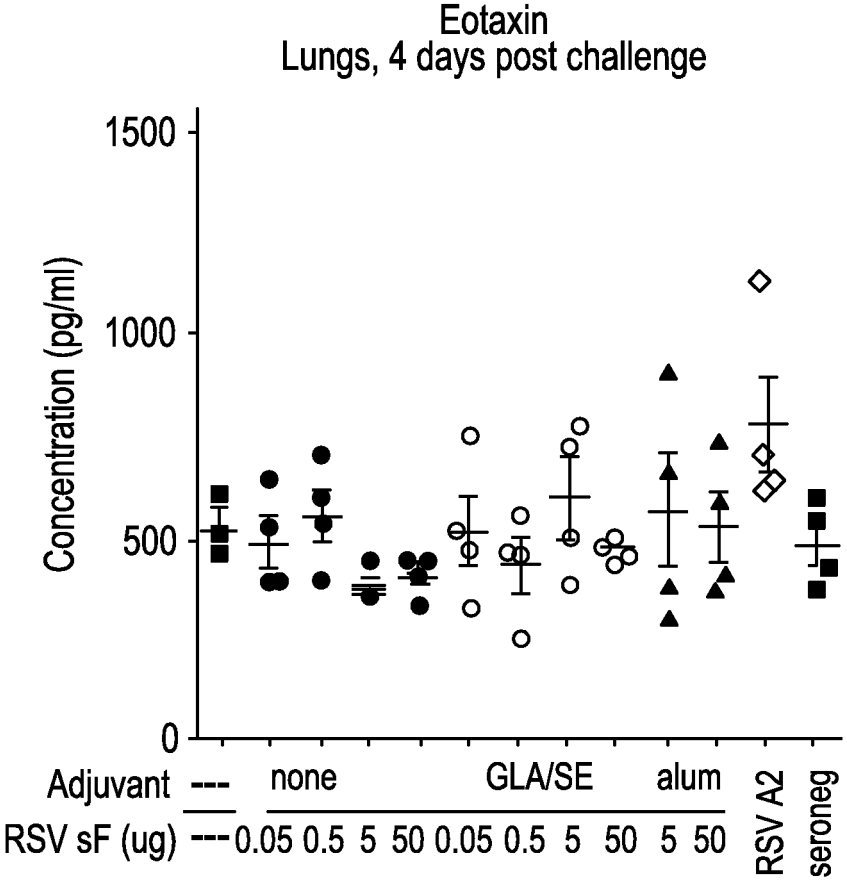


FIG. 46B

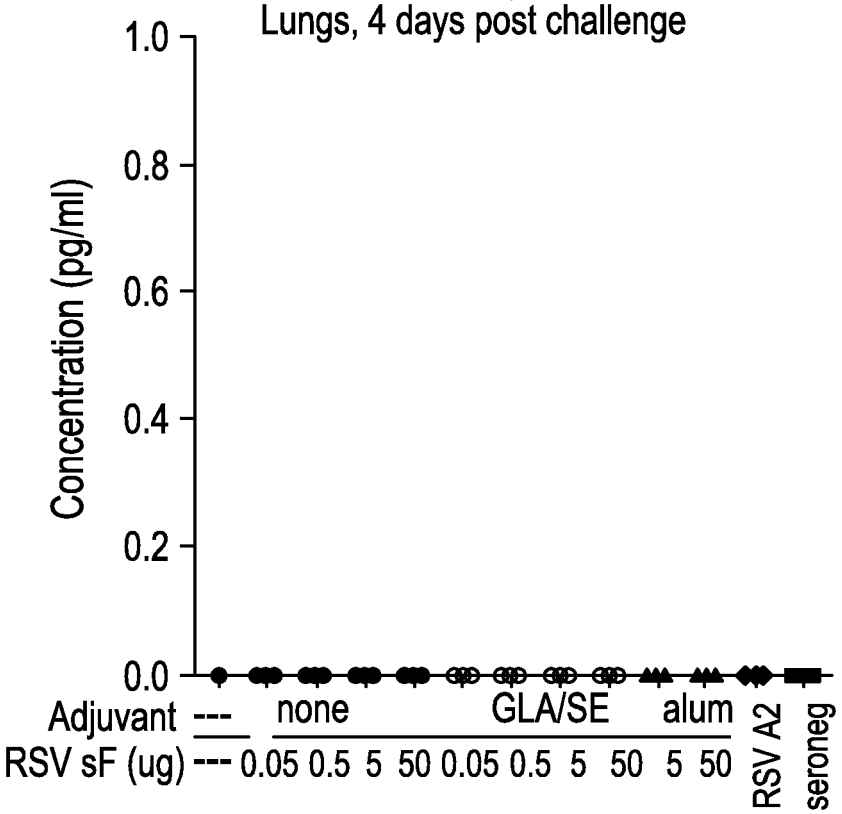


FIG. 46C

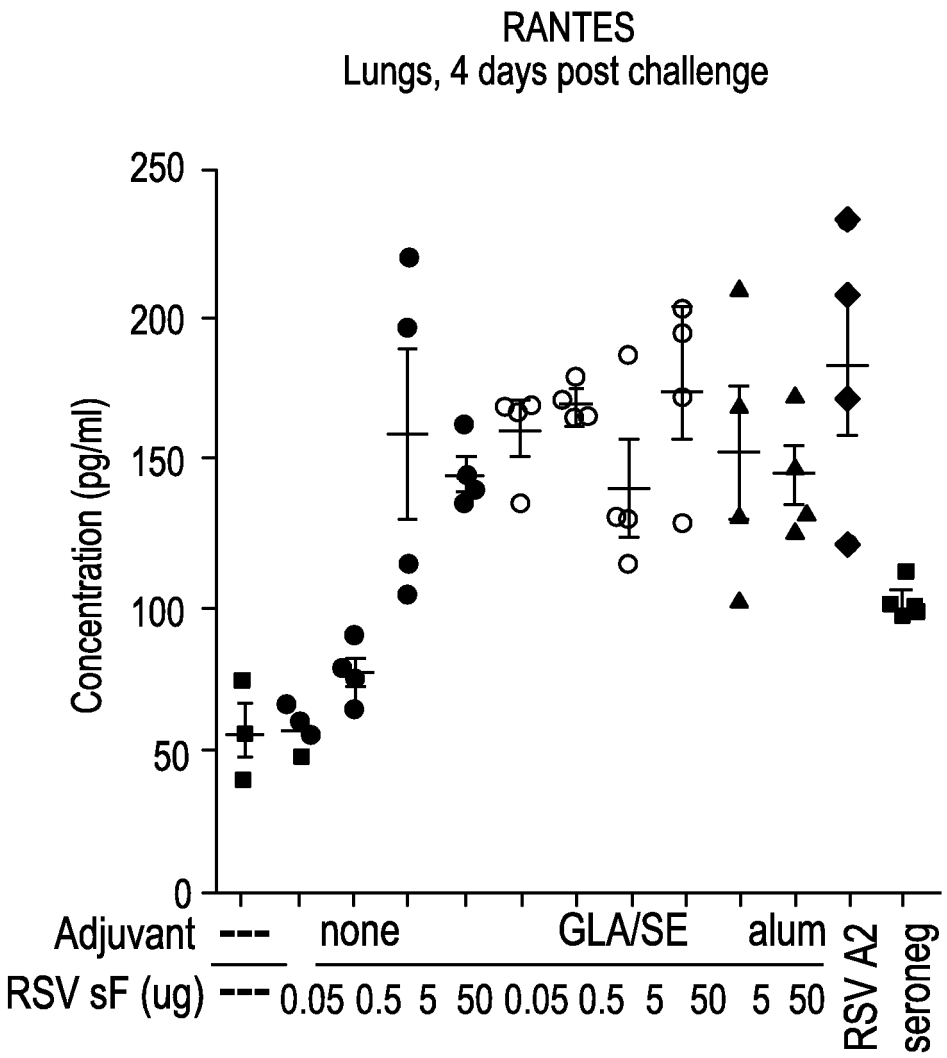

RANTES
Lungs, 4 days post challenge
Concentration (pg/ml)
250
200
150
100
50
0
Adjuvant --- none GLA/SE alum
RSV sF (ug) --- 0.05 0.5 5 50 0.05 0.5 5 50 5 50
RSV A2
seroneg

FIG. 47A

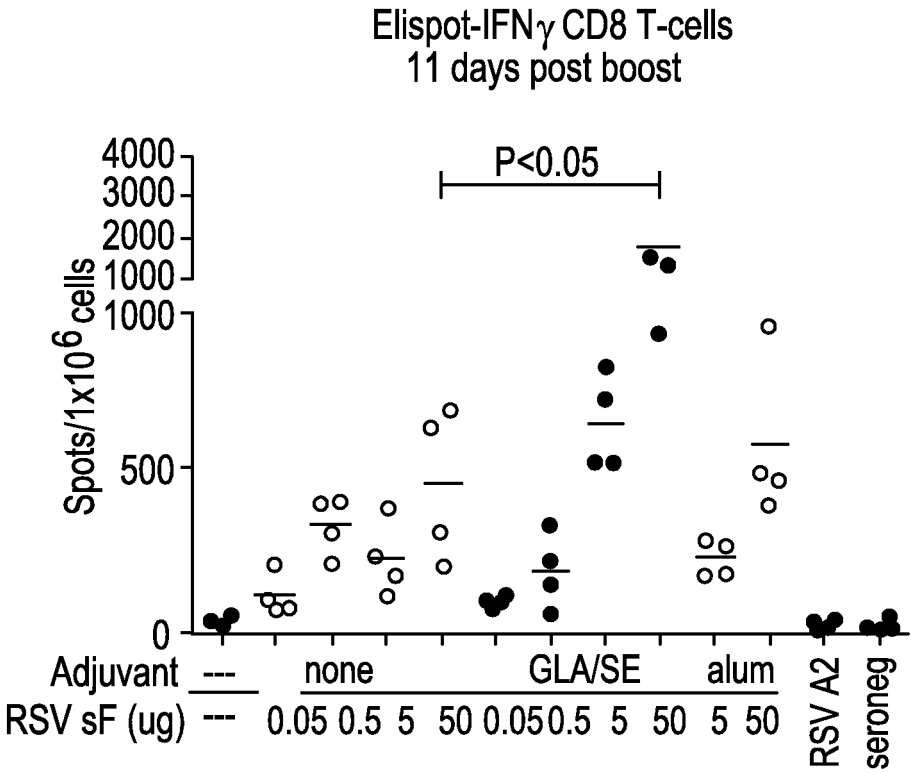


FIG. 47B

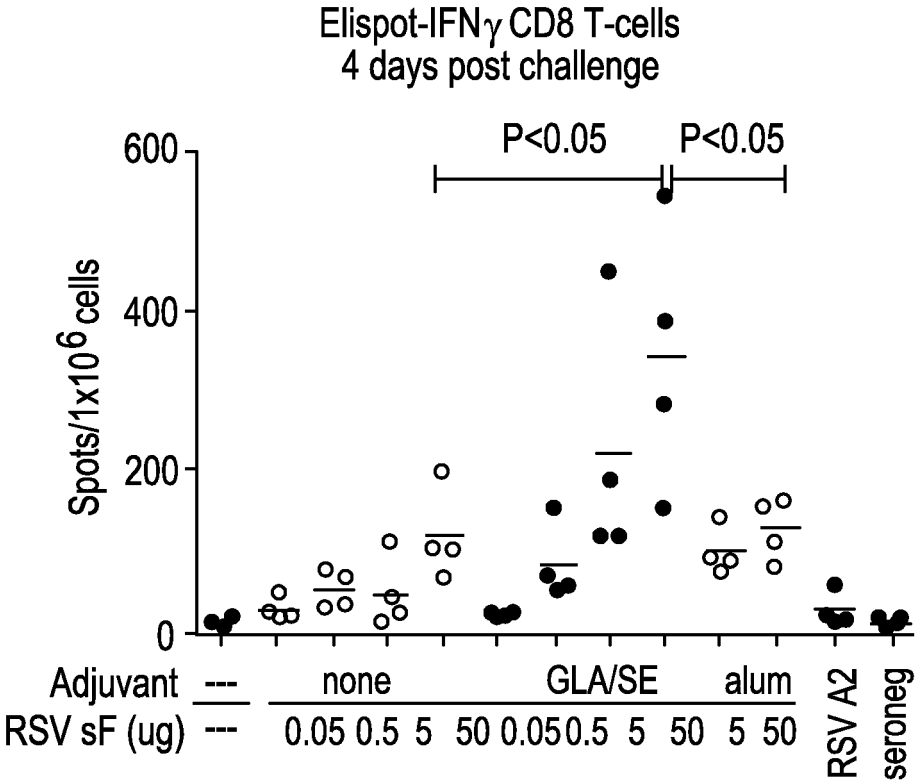


FIG. 48A

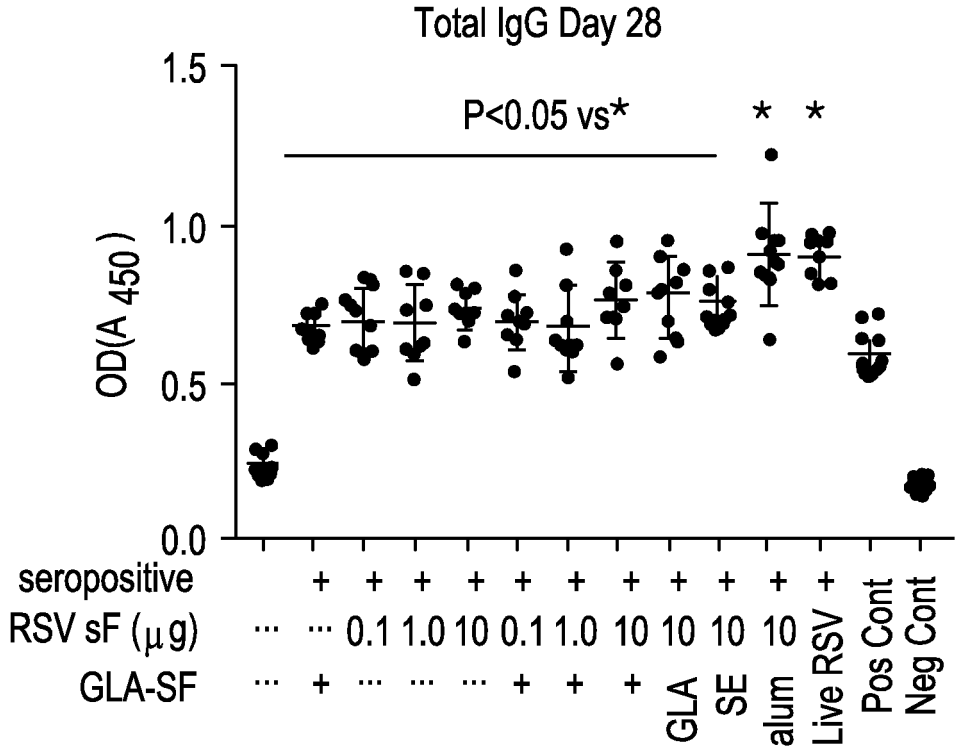


FIG. 48B

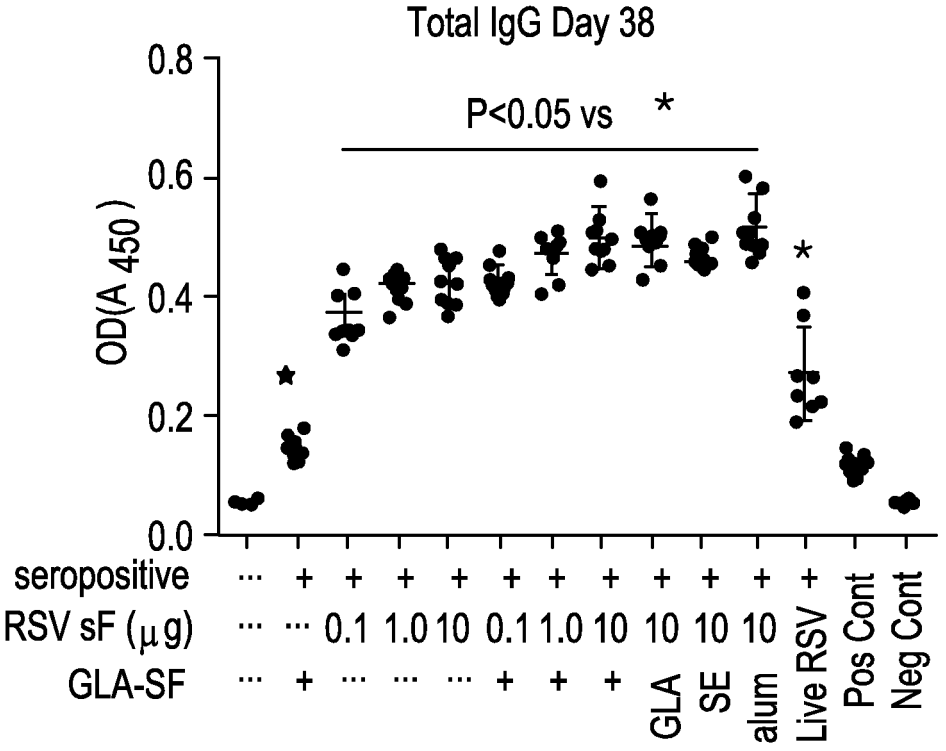


FIG. 48C

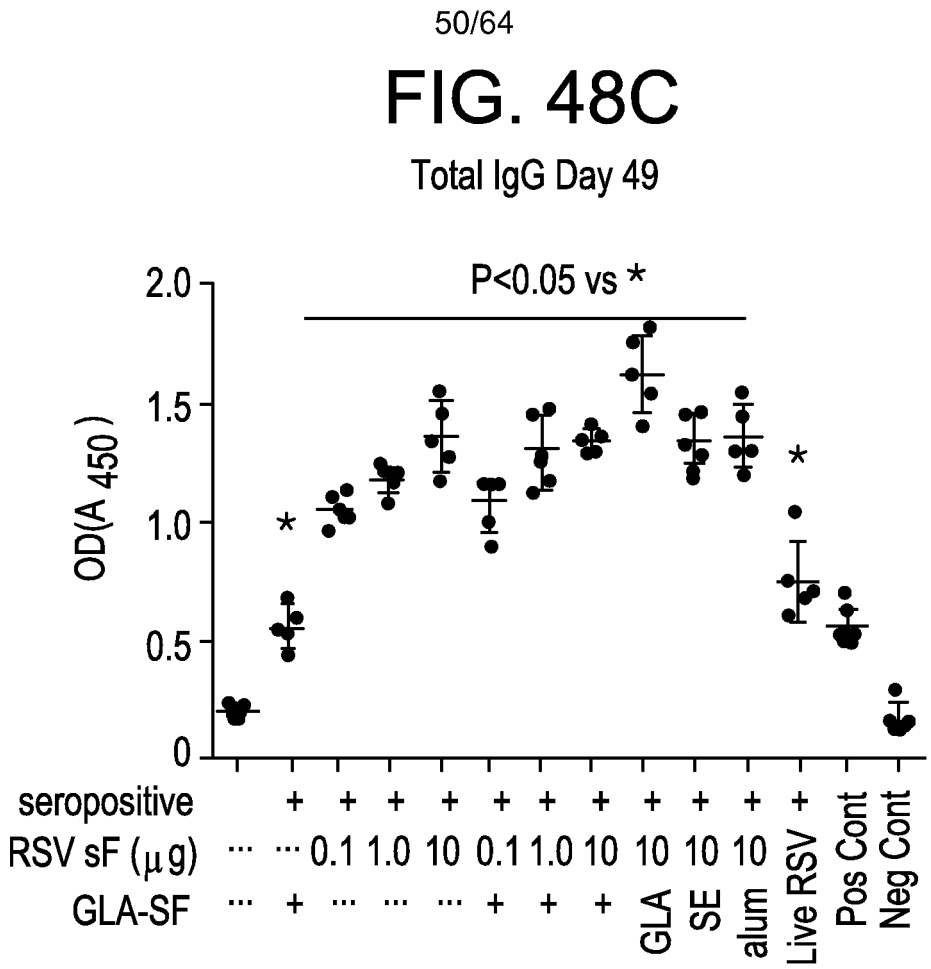


FIG. 48D

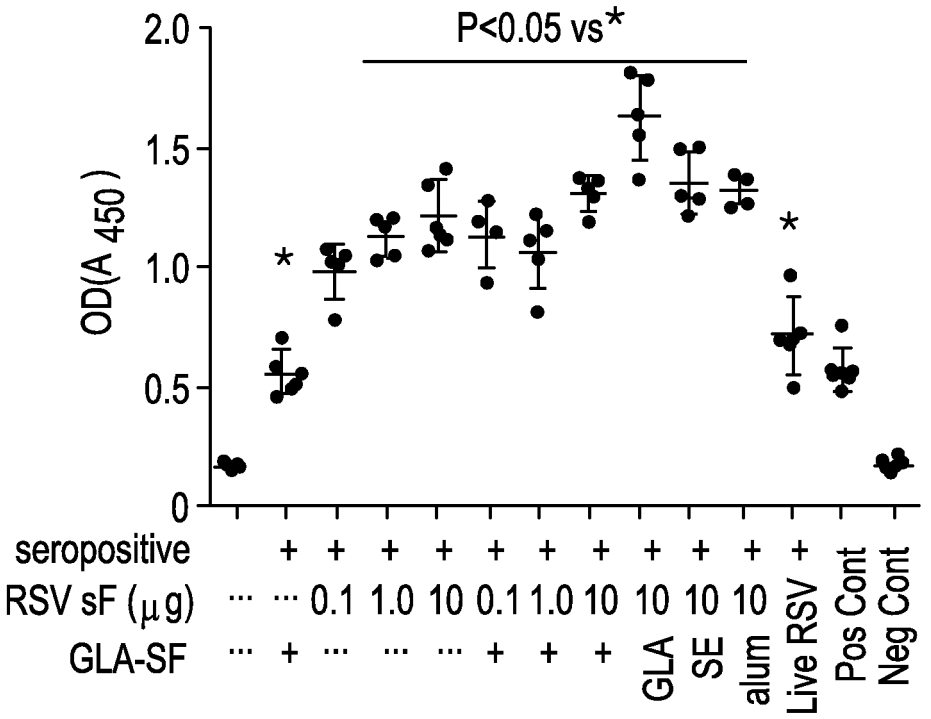


FIG. 49A

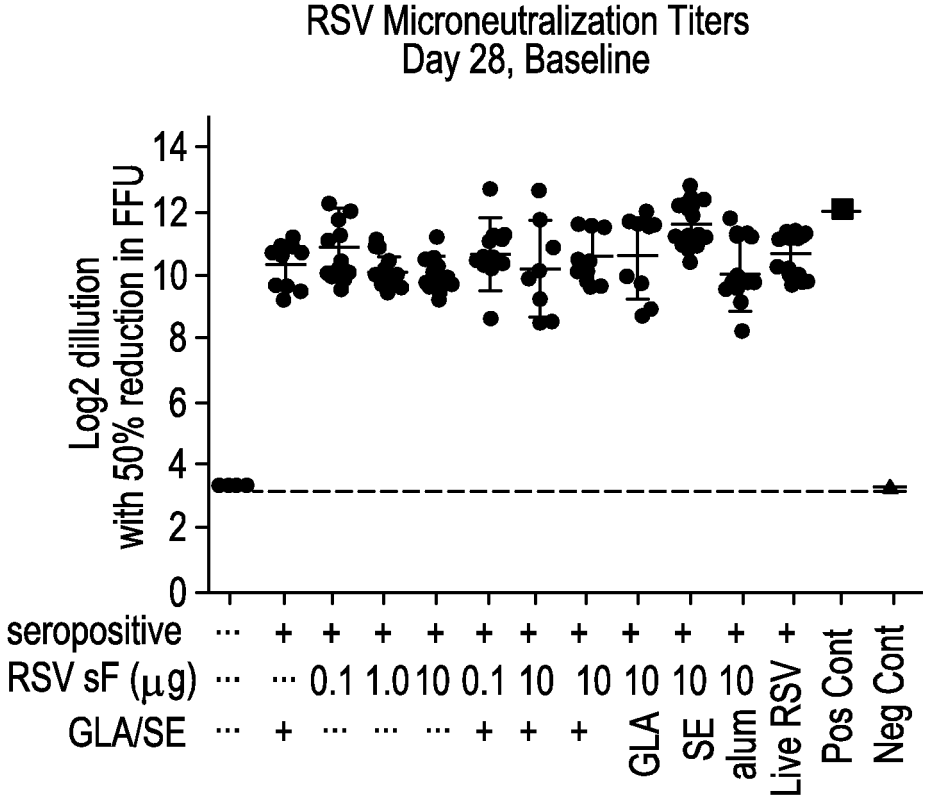


FIG. 49B

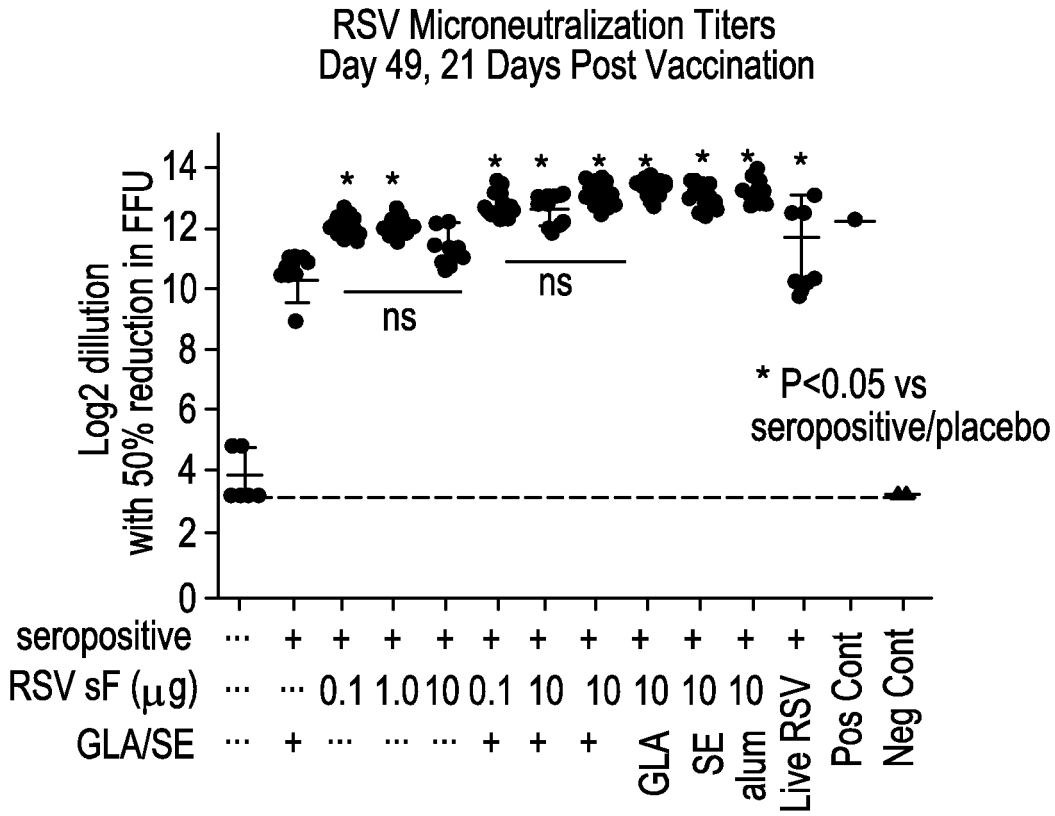


FIG. 50A

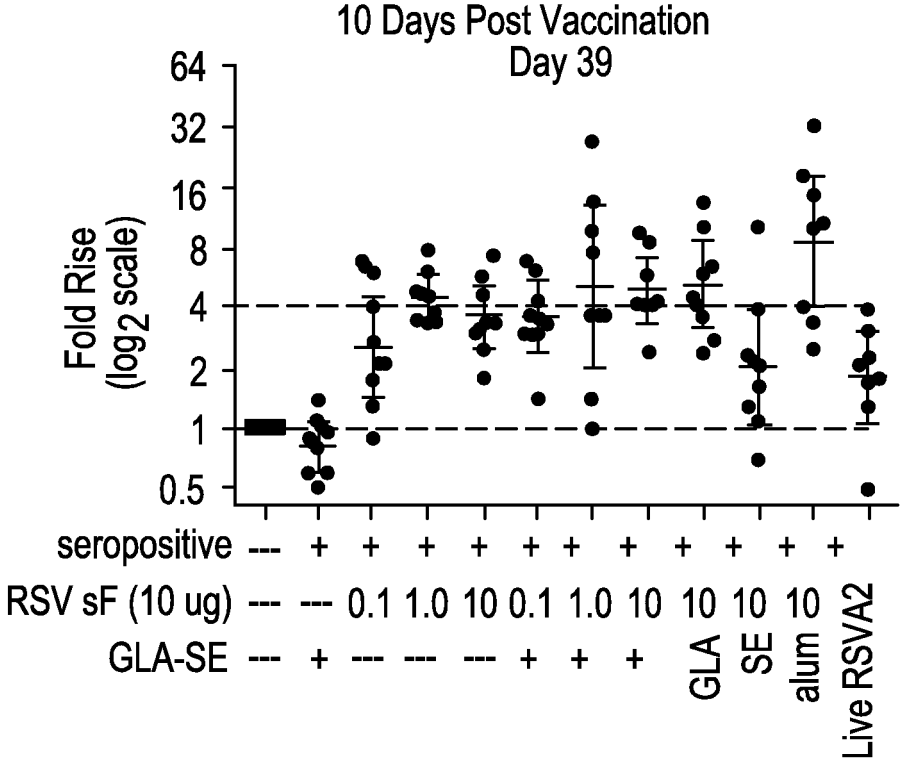


FIG. 50B

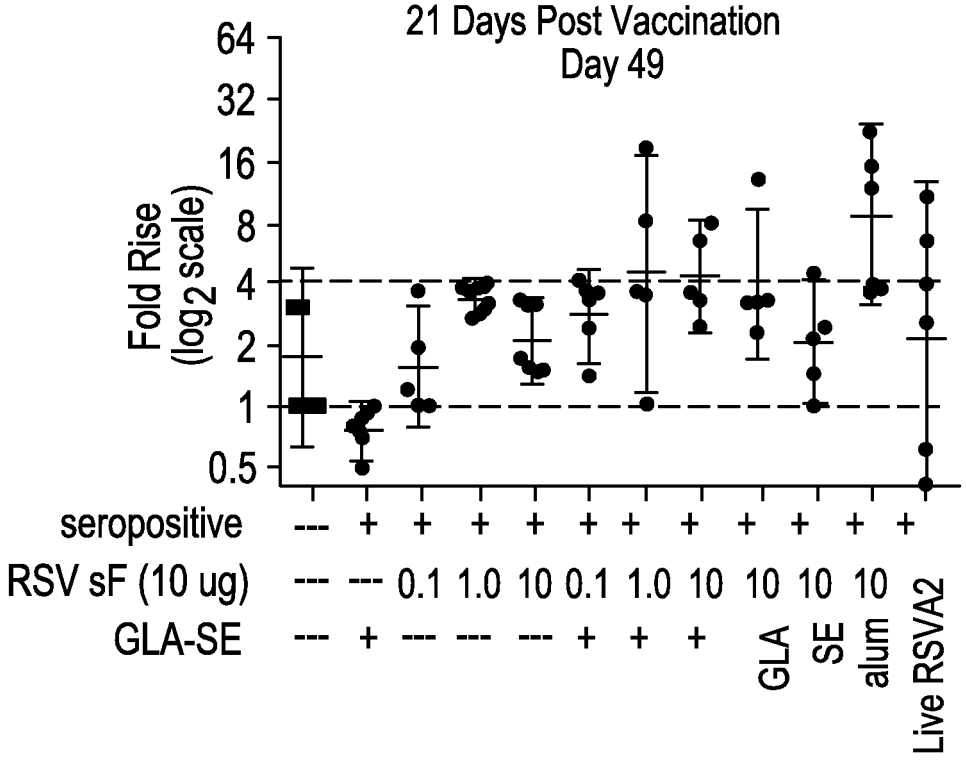


FIG. 50C

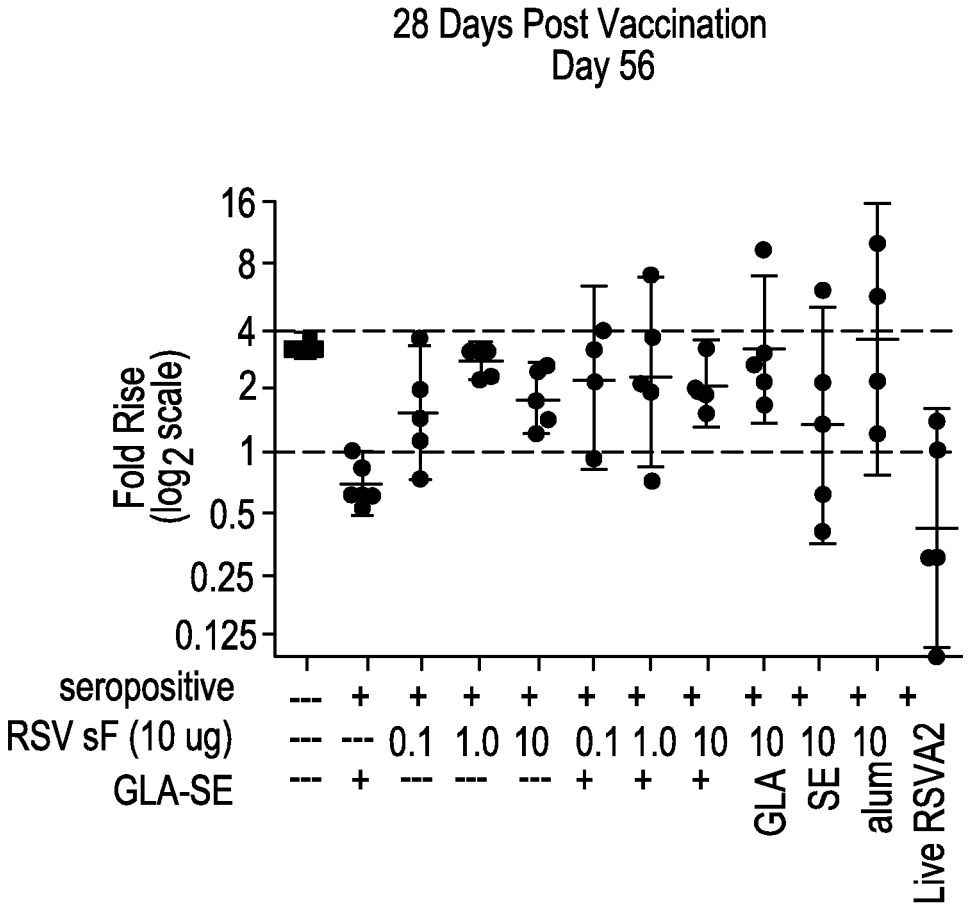

28 Days Post Vaccination
Day 56
Fold Rise
(log2 scale)
16
8
4
2
1
0.5
0.25
0.125
seropositive
RSV sF (10 ug)
GLA-SE
--- + + + + + + + + + + +
--- --- 0.1 1.0 10 0.1 1.0 10 10 10 10
--- + --- --- --- + + + GLA SE alum
Live RSVA2

FIG. 51A

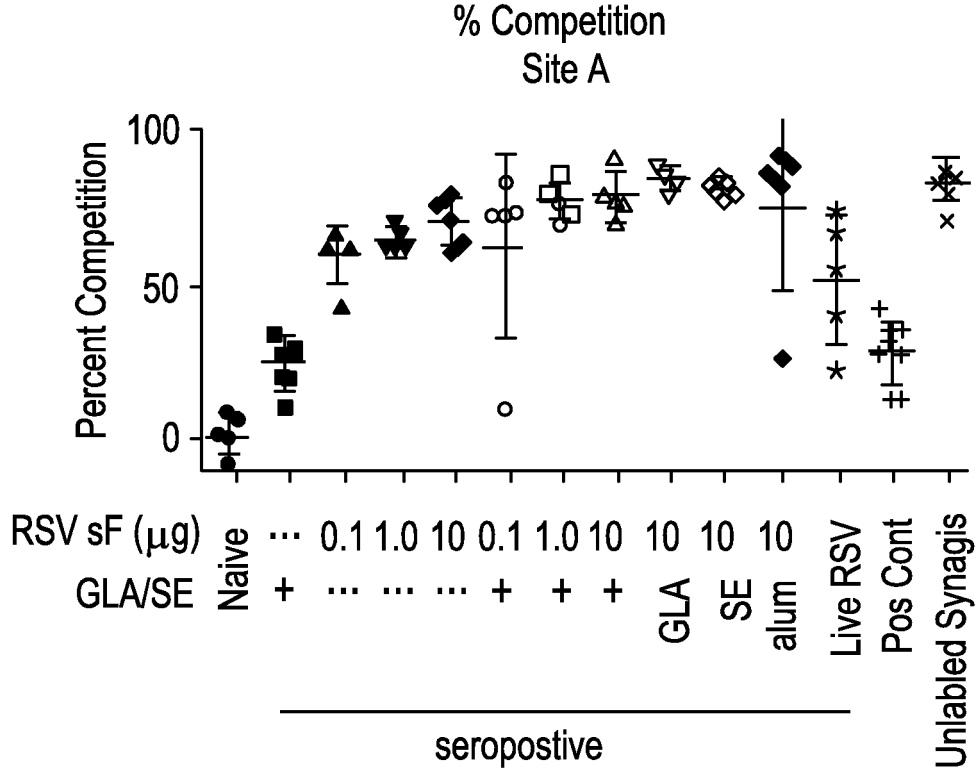


FIG. 51B

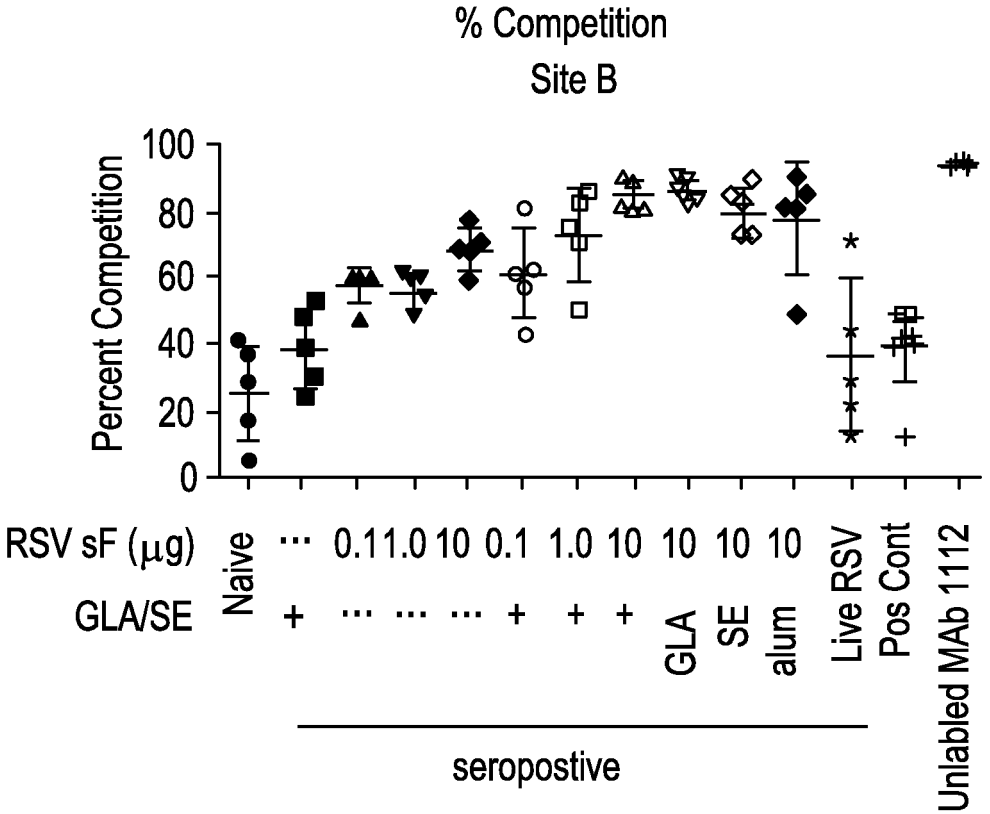


FIG. 51C

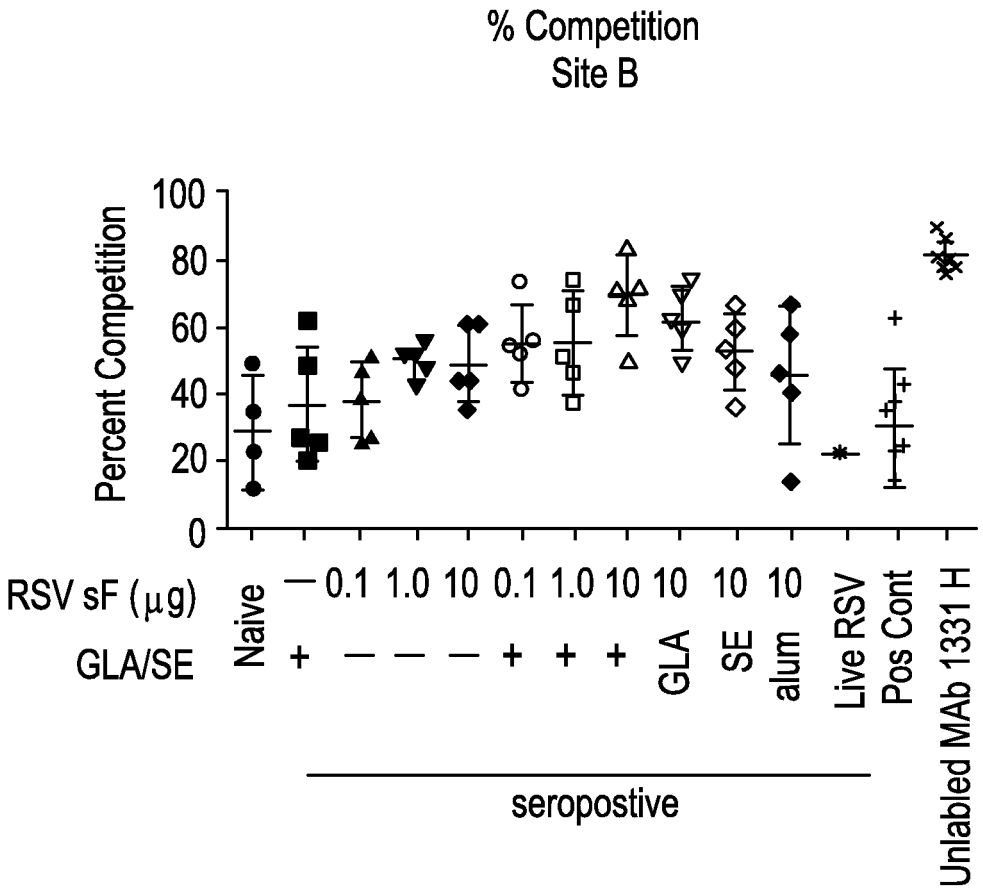

% Competition
Site B
Percent Competition
100
80
60
40
20
0
RSV sF (µg)
GLA/SE
Naive
—
0.1
1.0
10
0.1
1.0
10
10
10
10
+
—
—
—
+
+
+
GLA
SE
alum
Live RSV
Pos Cont
Unlabled MAb 1331 H
seropostive

FIG. 52A

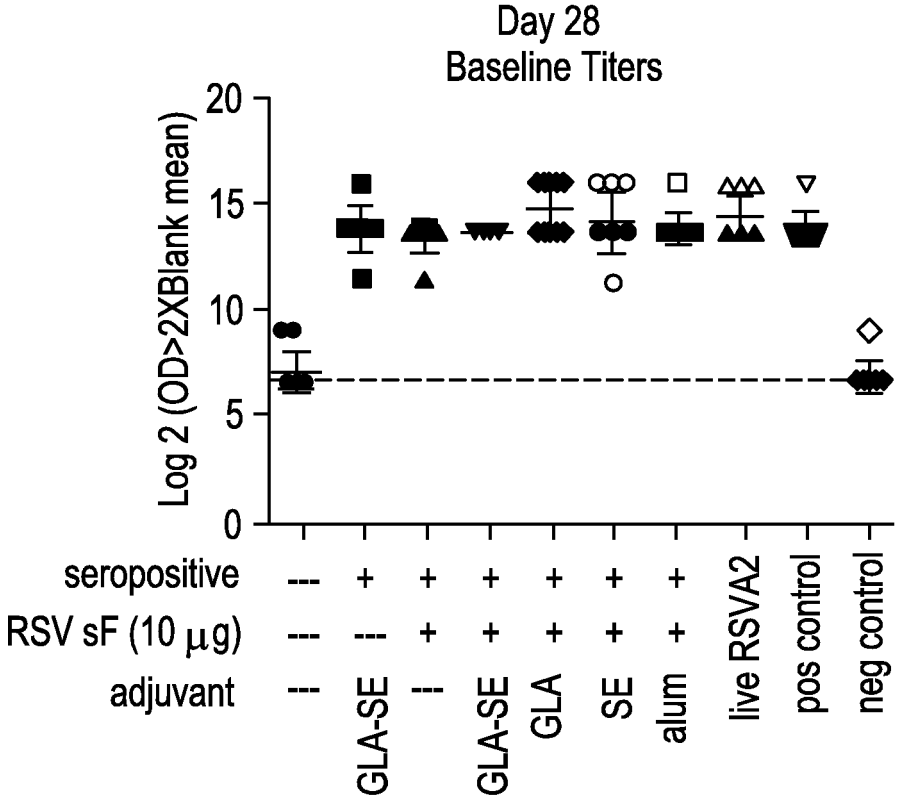


FIG. 52B

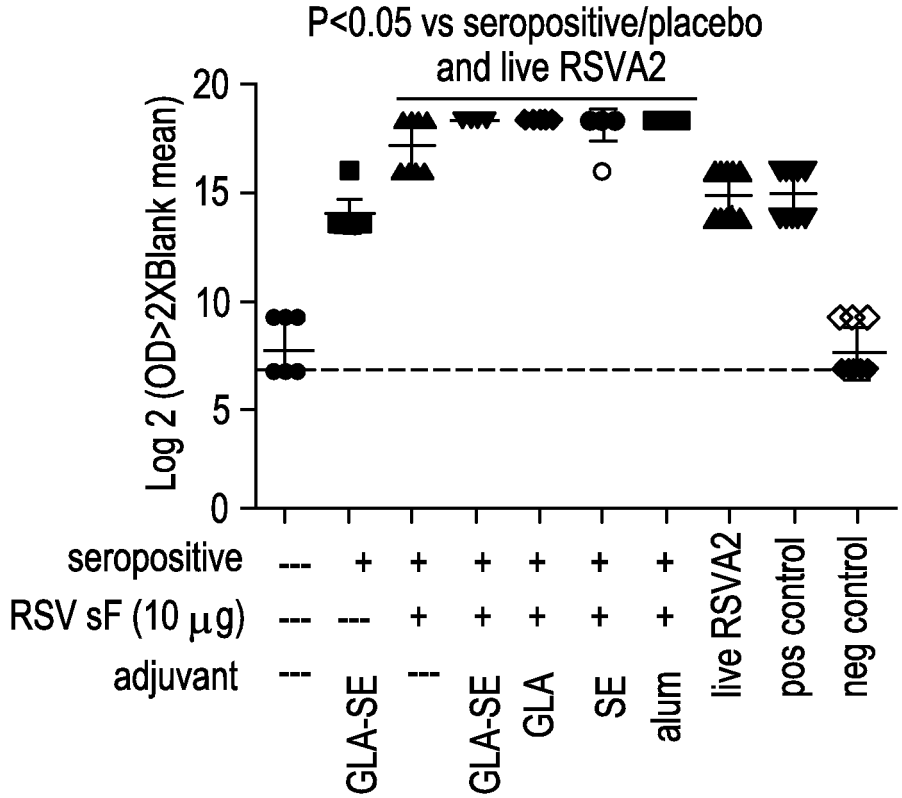


FIG. 53

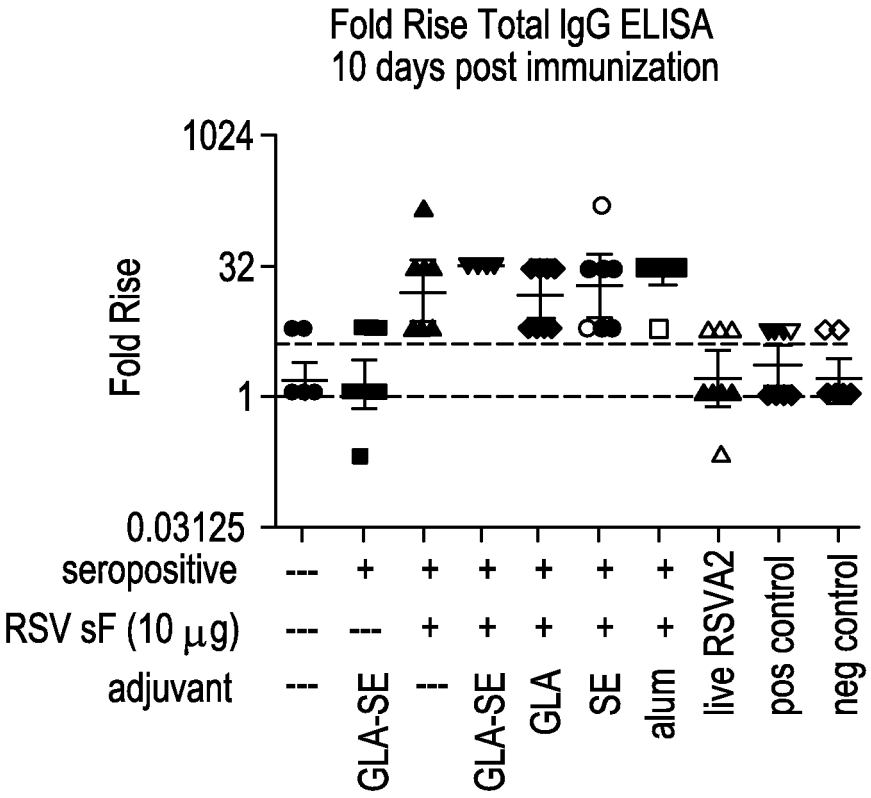

Fold Rise Total IgG ELISA
10 days post immunization
1024
32
1
0.03125
Fold Rise
seropositive --- + + + + + + + + +
RSV sF (10 μg) --- --- + + + + + + + +
adjuvant --- GLA-SE --- GLA-SE GLA SE alum live RSVA2 pos control neg control

FIG. 54A

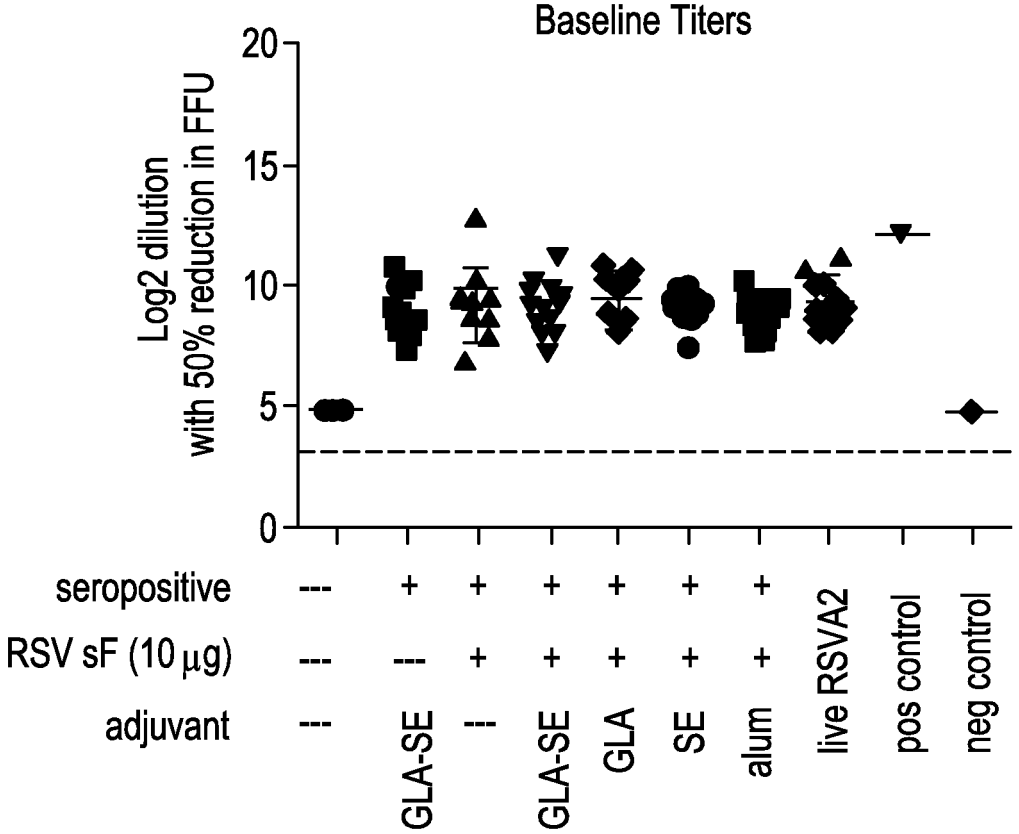


FIG. 54B

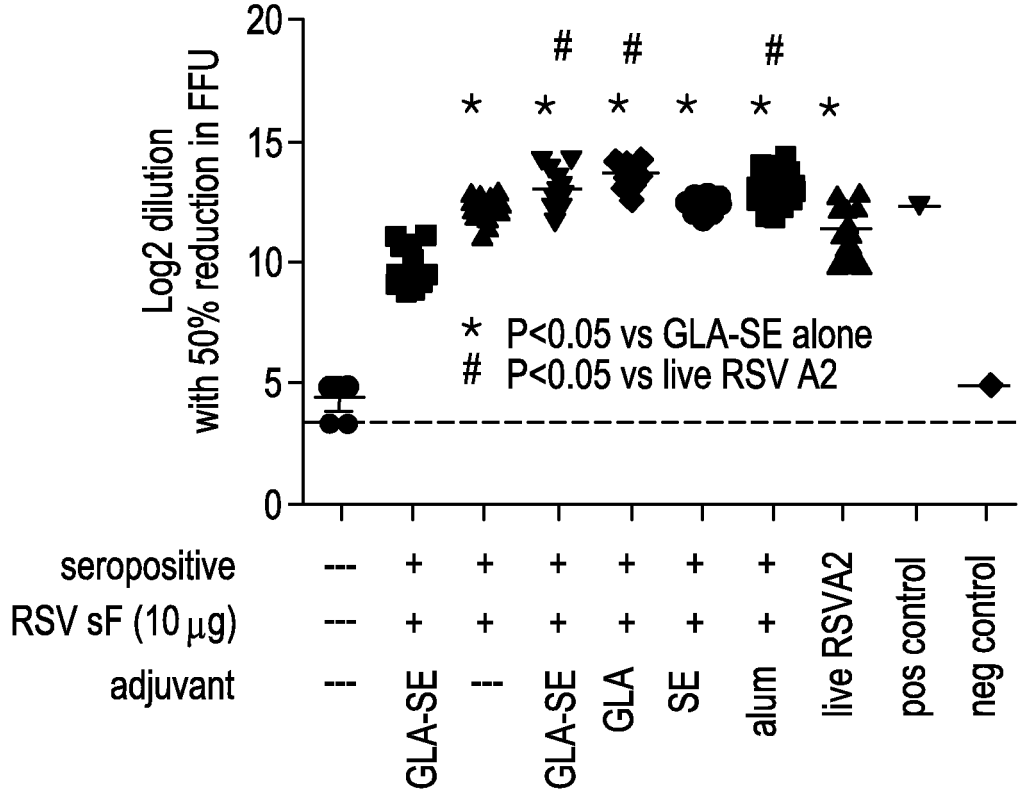


FIG. 55

Fold Rise RSV Neutralization Titers
10 days post immunization

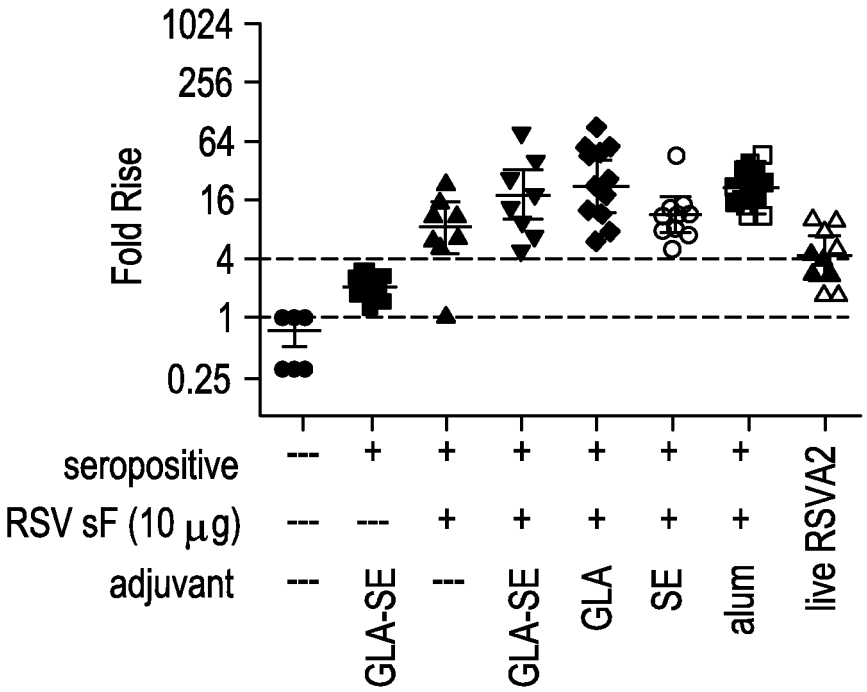


FIG. 56A

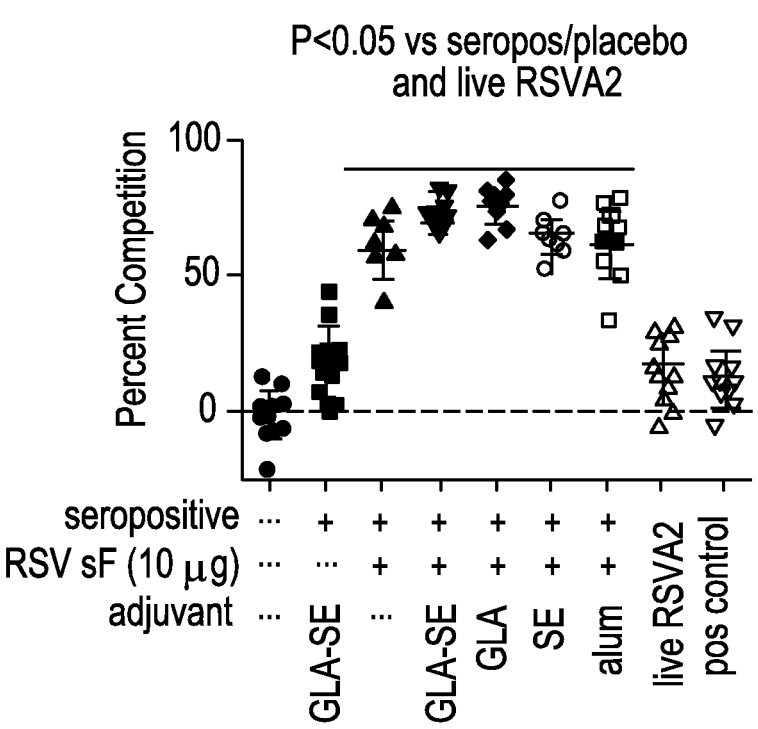


FIG. 56B

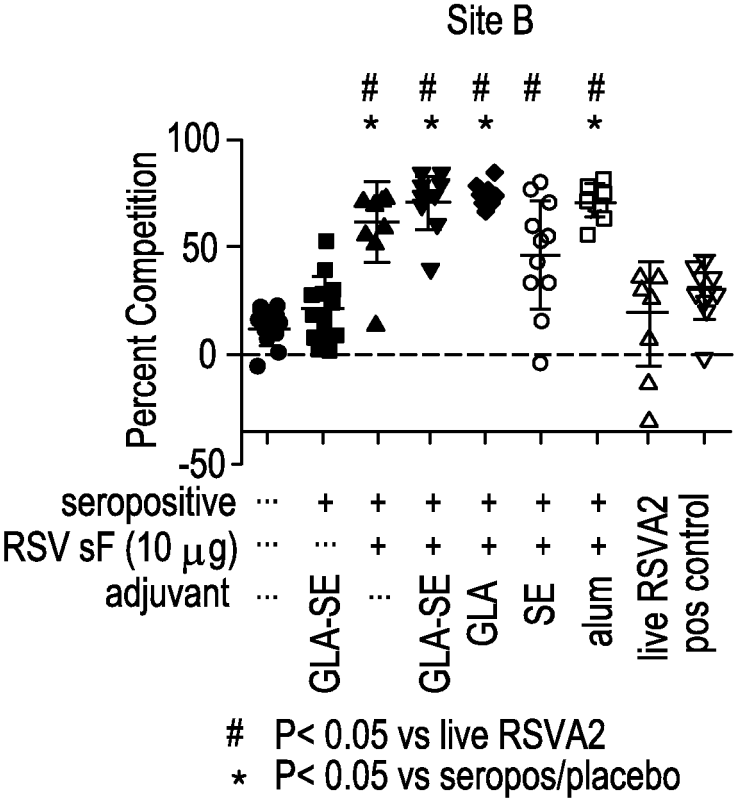


FIG. 56C

Site C

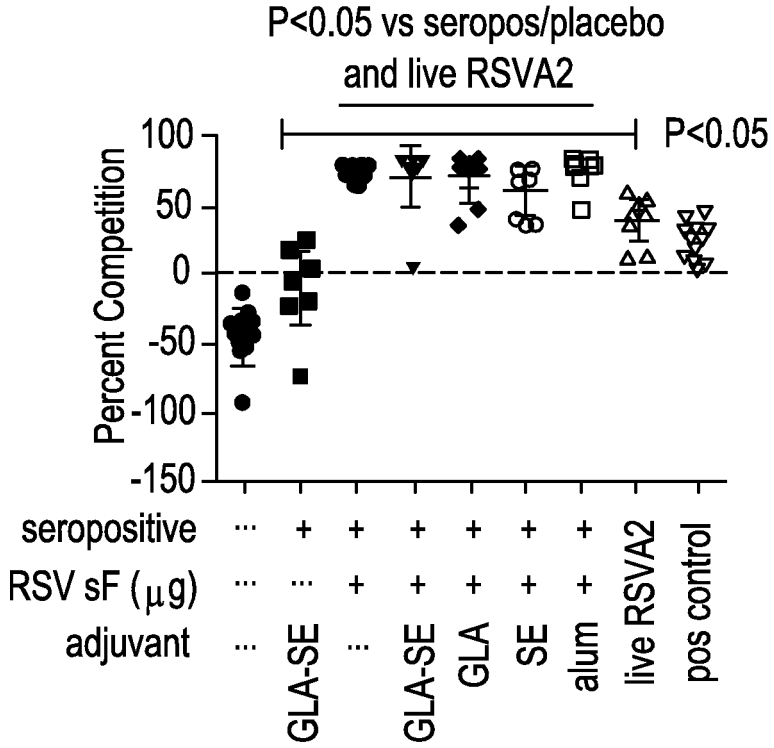


FIG. 57A

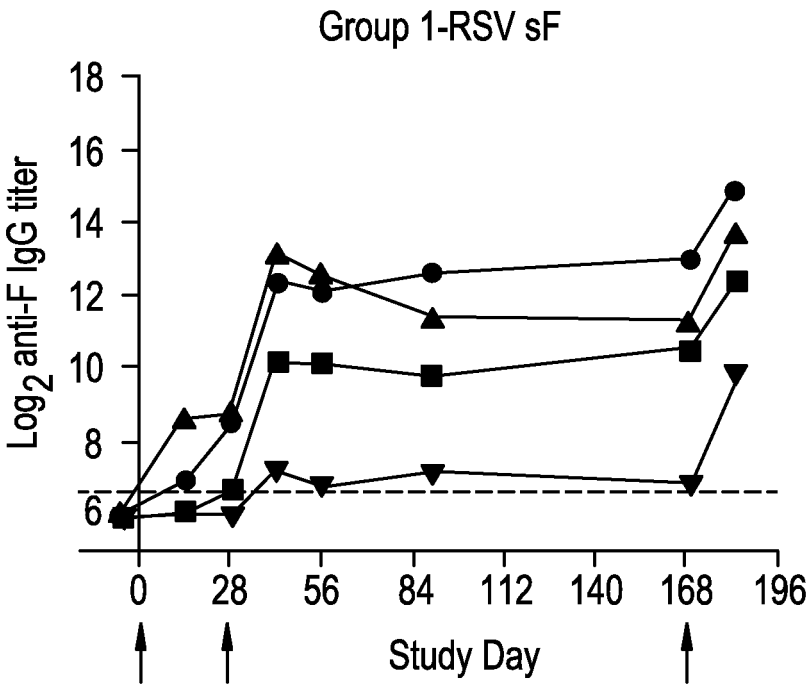


FIG. 57B

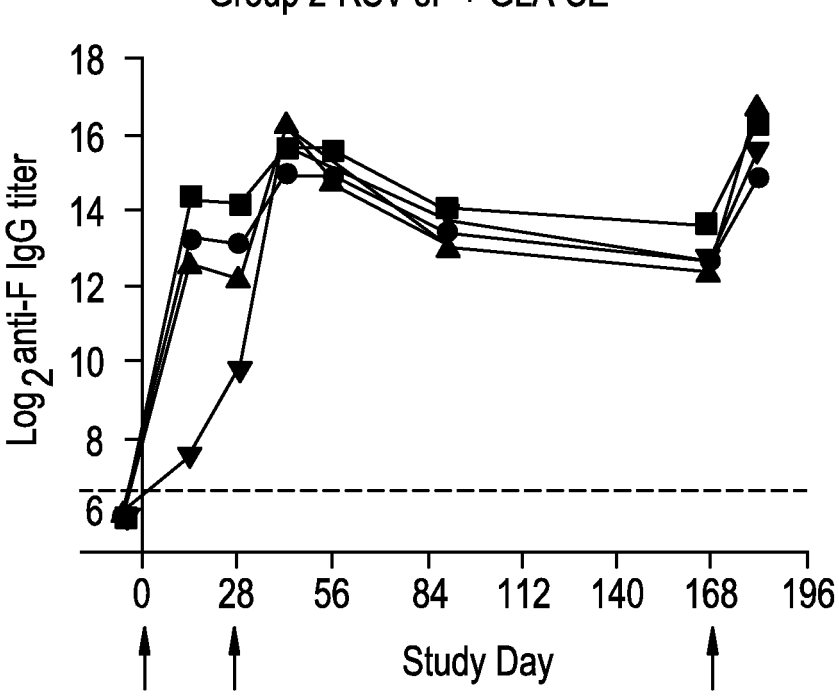


FIG. 58A

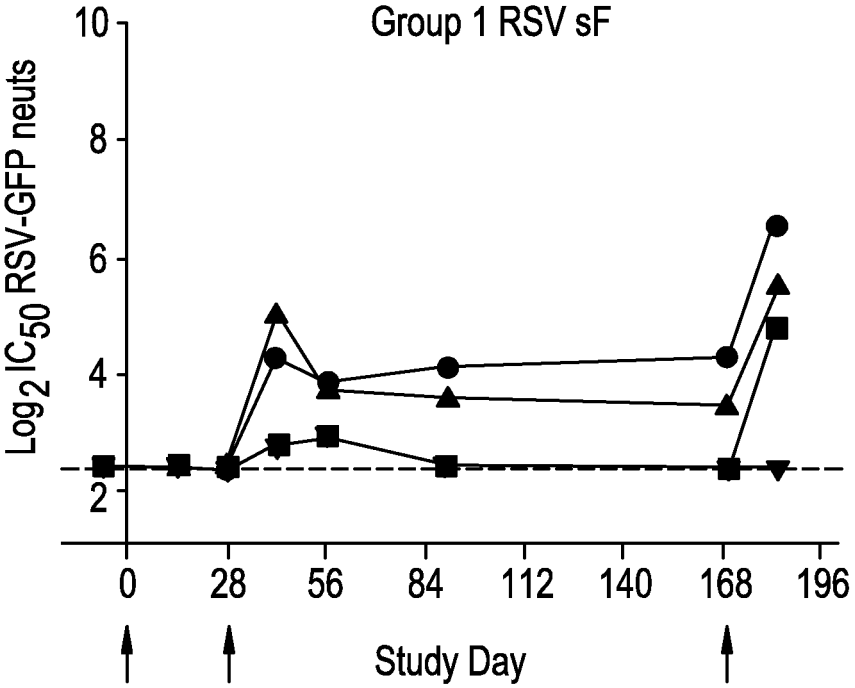


FIG. 58B

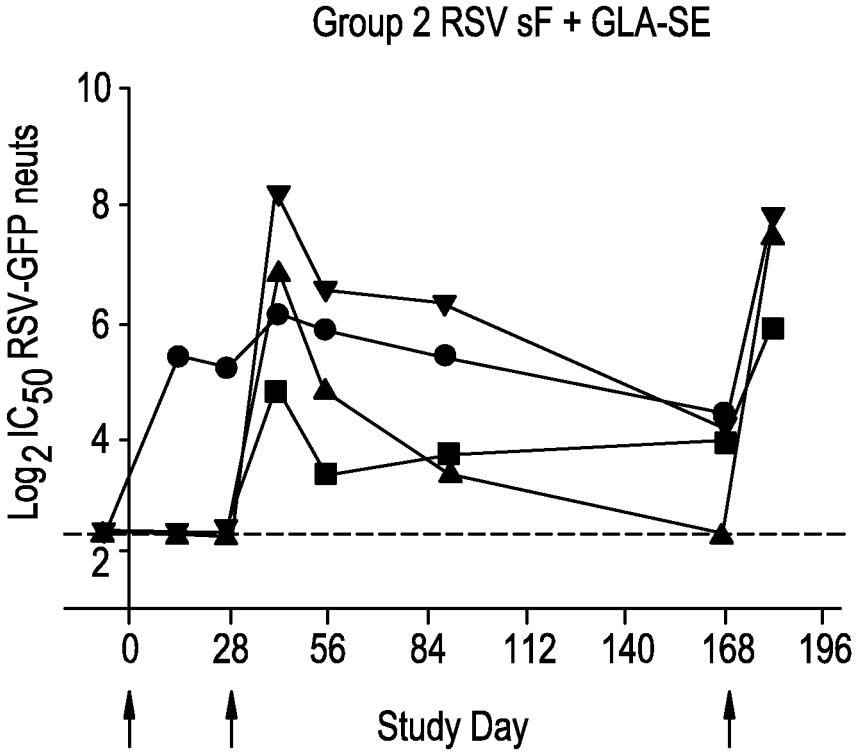


FIG. 59A

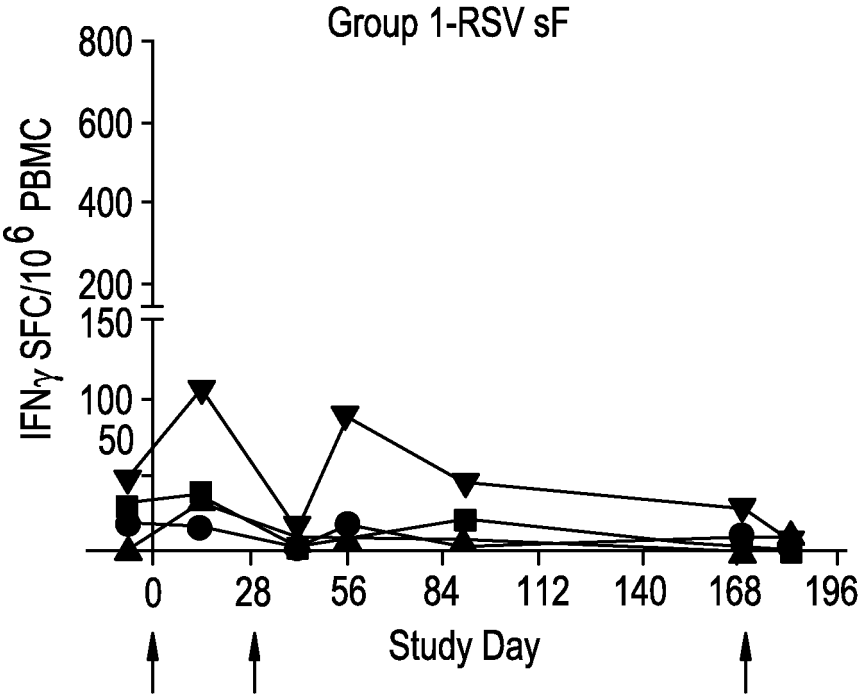
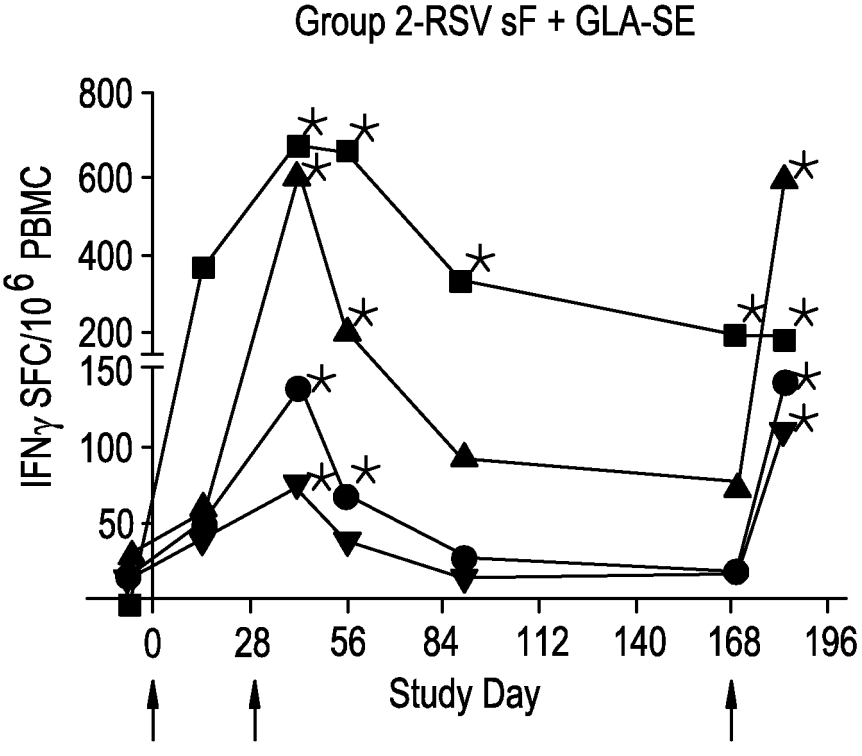


FIG. 59B



✶ = responder