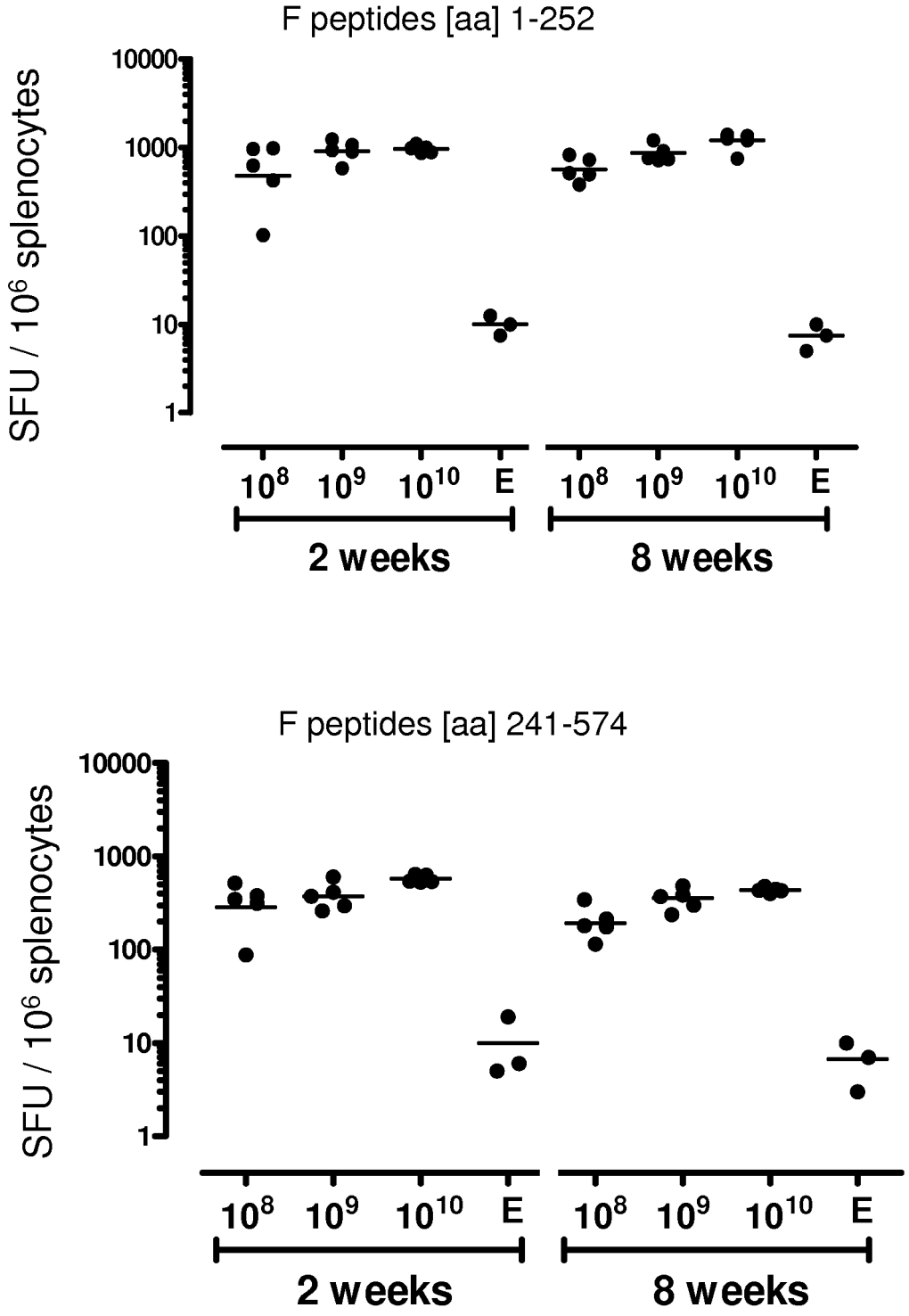

F peptides [aa] 1-252
SFU / 10^6 splenocytes
10000
1000
100
10
1
10^8 10^9 10^10 E
10^8 10^9 10^10 E
2 weeks
8 weeks
F peptides [aa] 241-574
SFU / 10^6 splenocytes
10000
1000
100
10
1
10^8 10^9 10^10 E
10^8 10^9 10^10 E
2 weeks
8 weeks

Fig. 1A

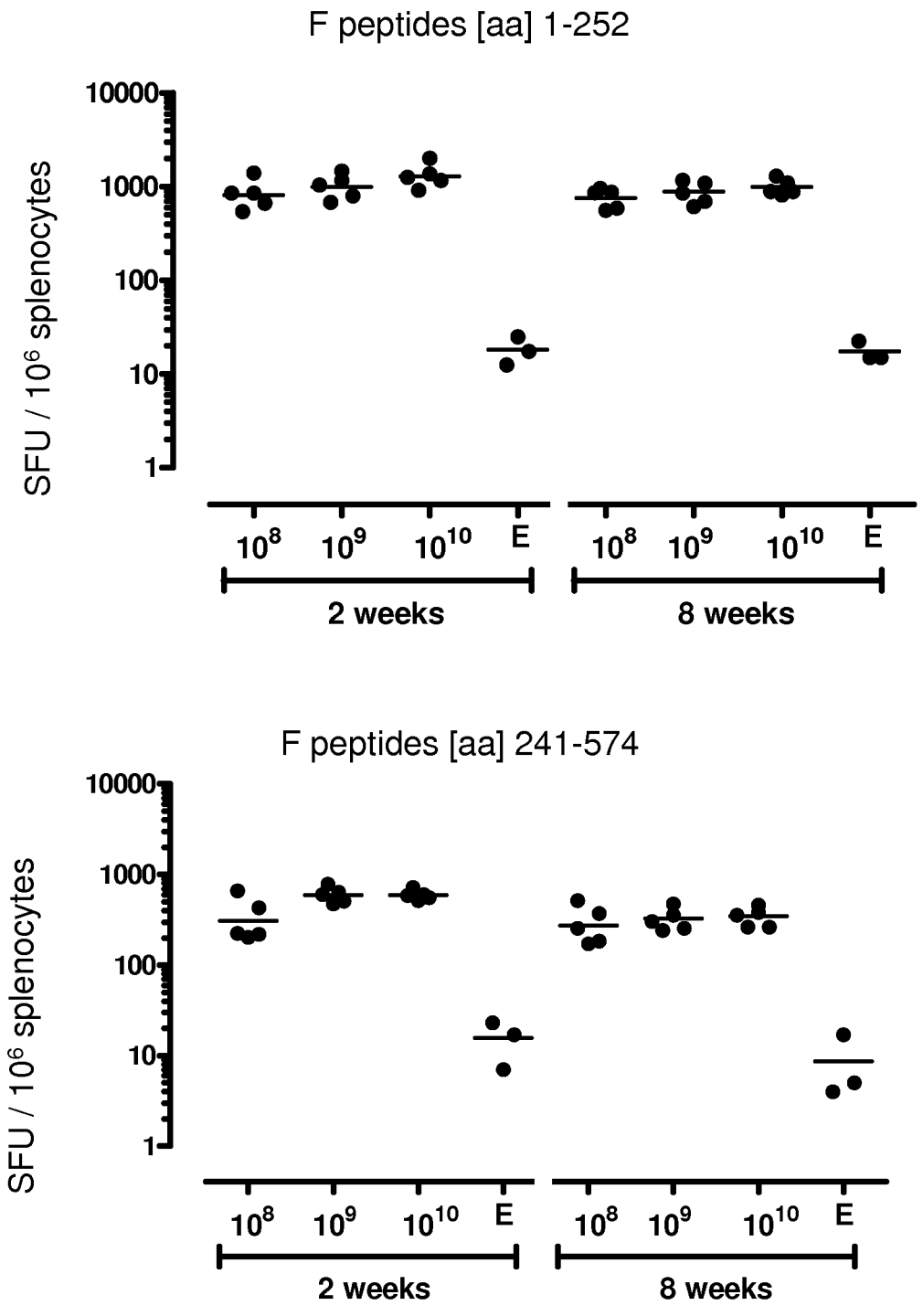

F peptides [aa] 1-252
SFU / 10^6 splenocytes
10000
1000
100
10
1
10^8
10^9
10^10
E
2 weeks
8 weeks
F peptides [aa] 241-574
SFU / 10^6 splenocytes
10000
1000
100
10
1
10^8
10^9
10^10
E
2 weeks
8 weeks

Fig. 1B

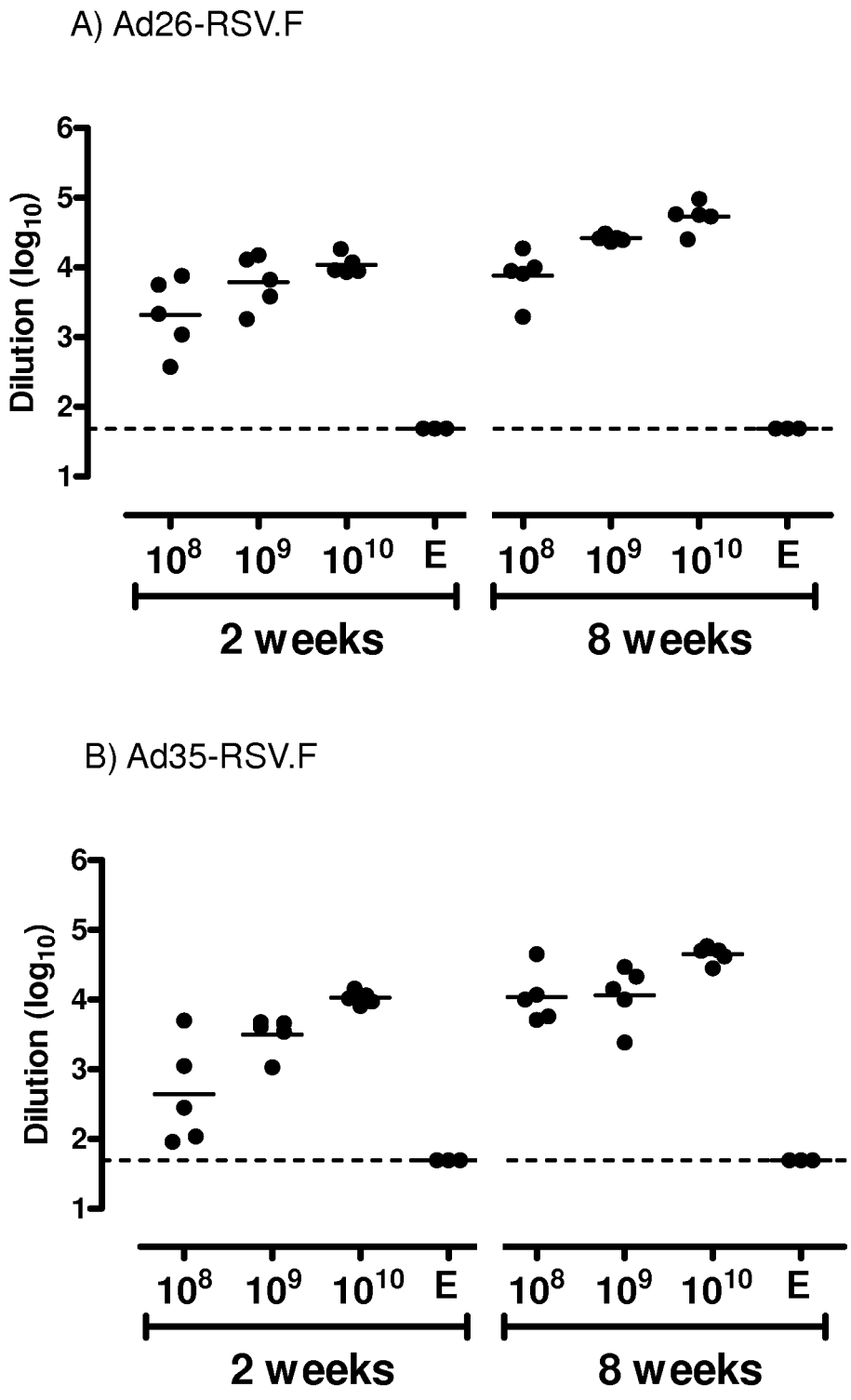

A) Ad26-RSV.F
Dilution (log_{10})
6
5
4
3
2
1
10^8 10^9 10^{10} E
10^8 10^9 10^{10} E
2 weeks
8 weeks
B) Ad35-RSV.F
Dilution (log_{10})
6
5
4
3
2
1
10^8 10^9 10^{10} E
10^8 10^9 10^{10} E
2 weeks
8 weeks

Fig. 2

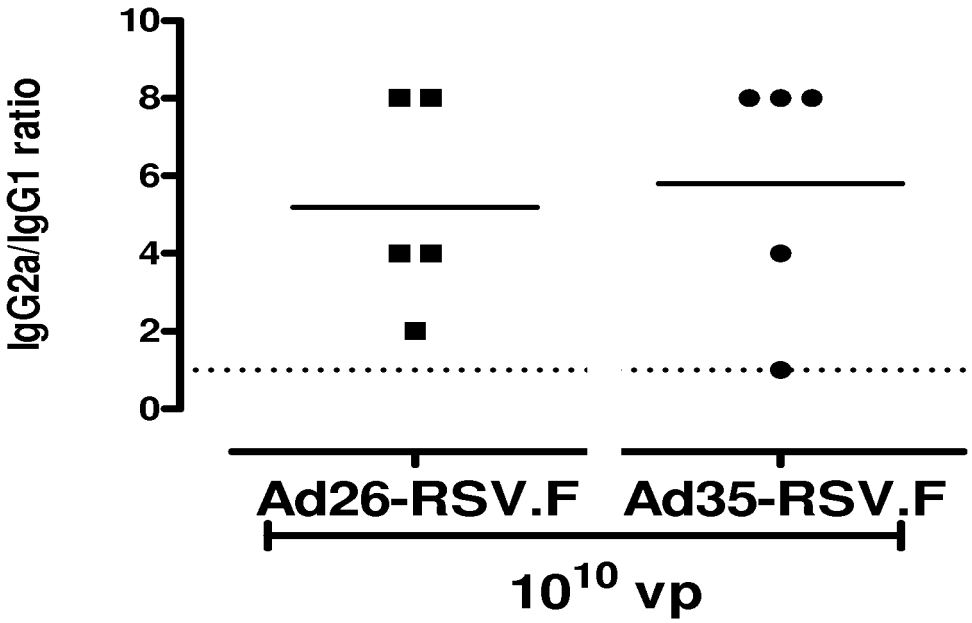
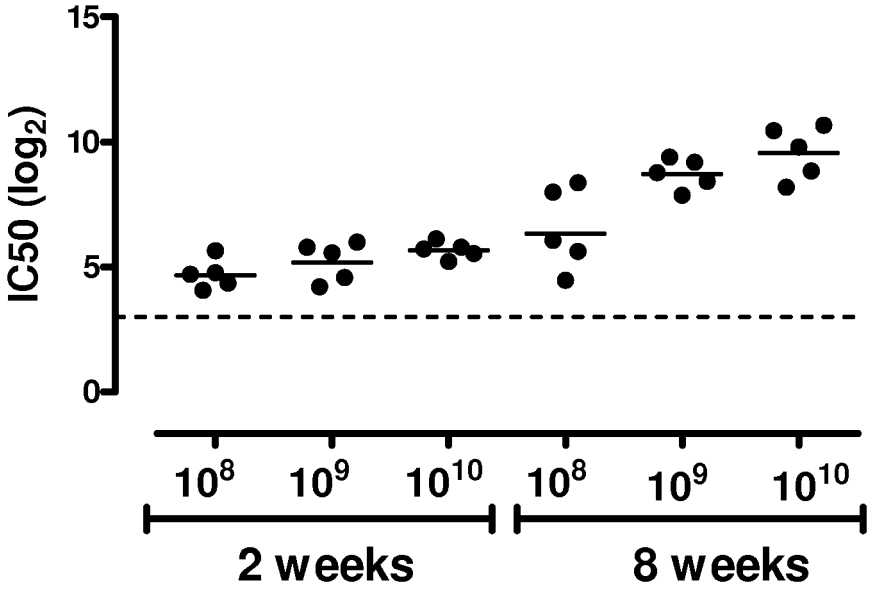


Fig. 3

A) Ad26-RSV.F



B) Ad35-RSV.F

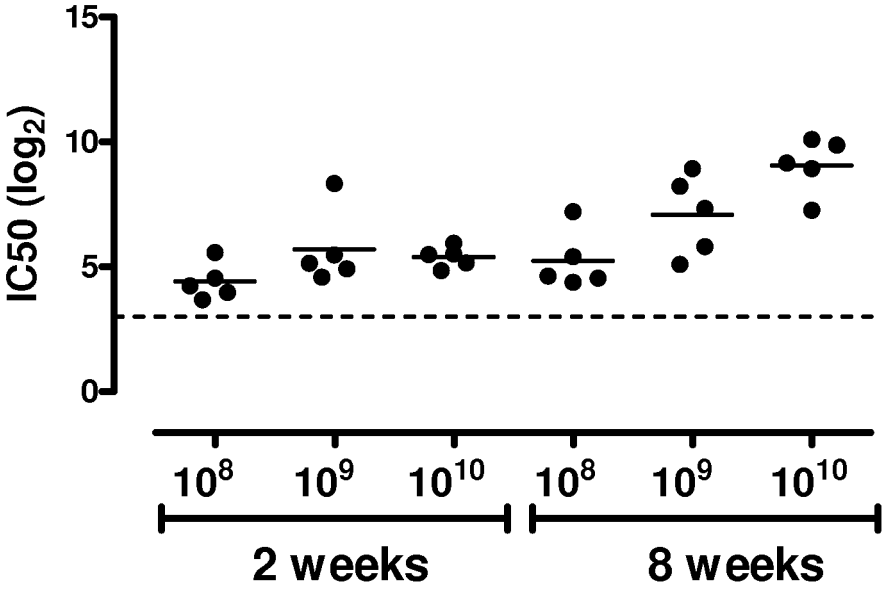
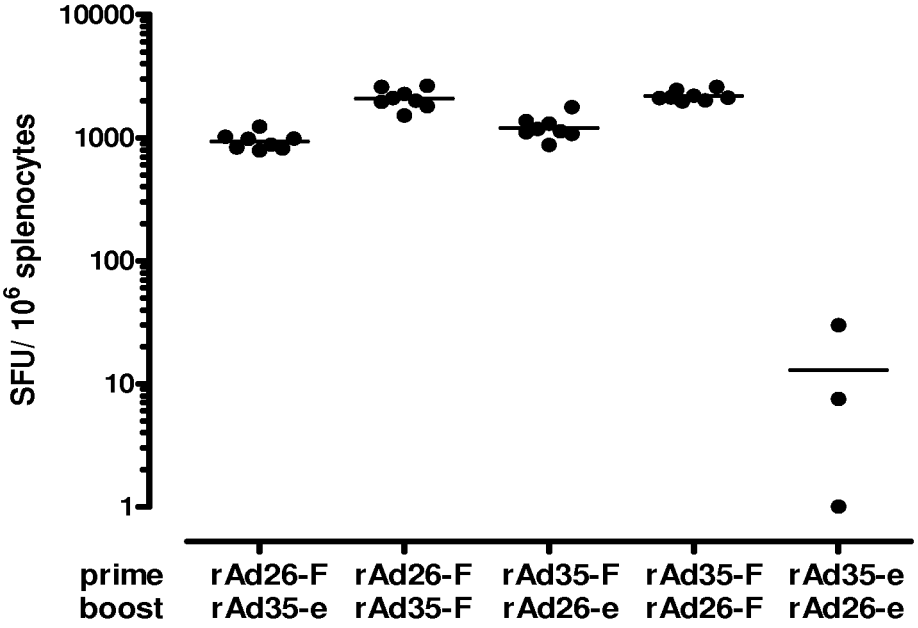


Fig. 4

F peptides [aa] 1-252

at 6 weeks



at 12 weeks

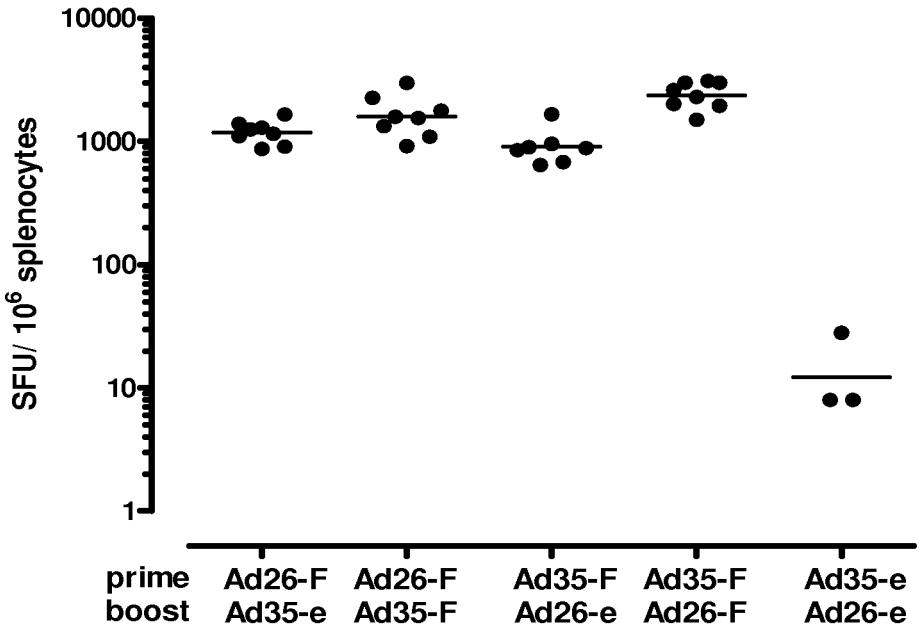
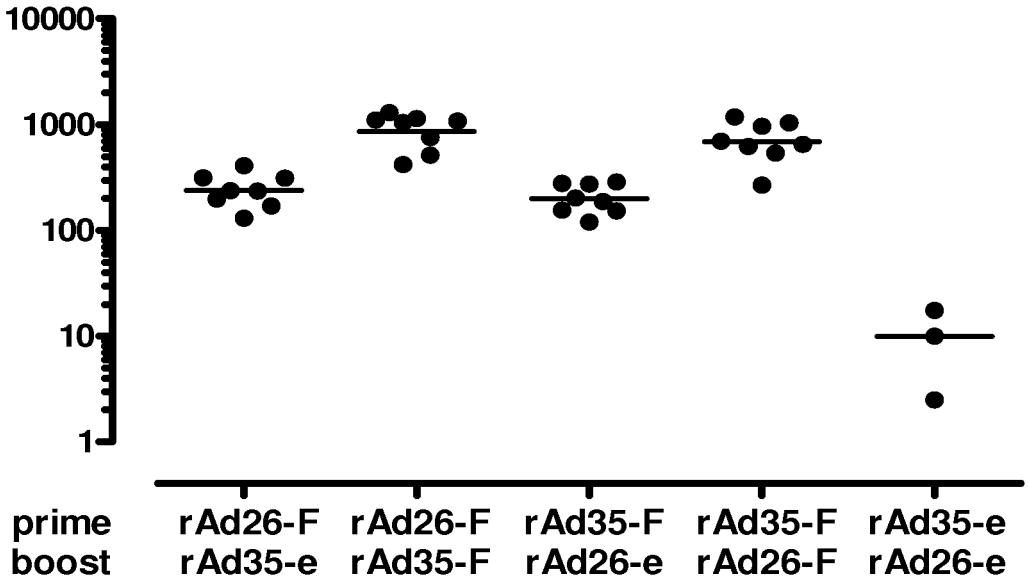


Fig. 5A

F peptides [aa] 241-574

at 6 weeks



at 12 weeks

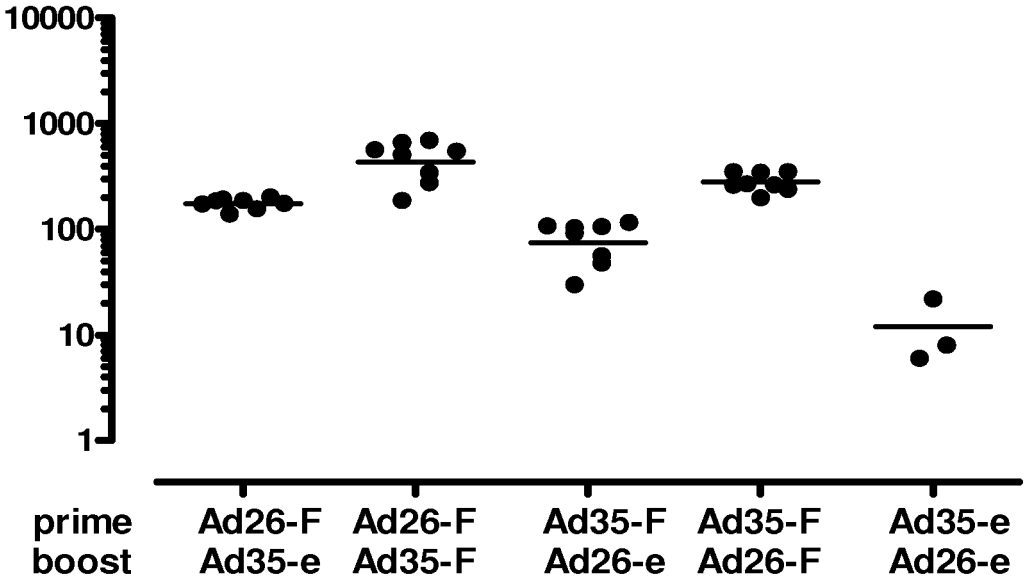


Fig. 5B

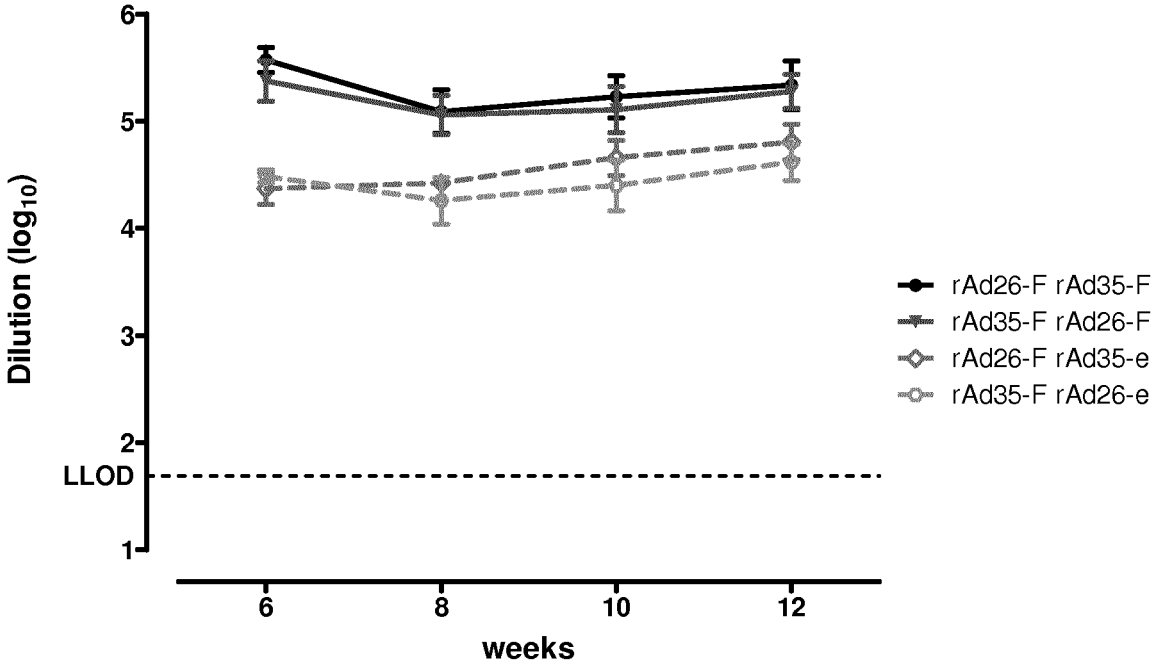

6
5
4
3
2
LLOD
1
Dilution (log_{10})
6
8
10
12
weeks
rAd26-F rAd35-F
rAd35-F rAd26-F
rAd26-F rAd35-e
rAd35-F rAd26-e

Fig. 6

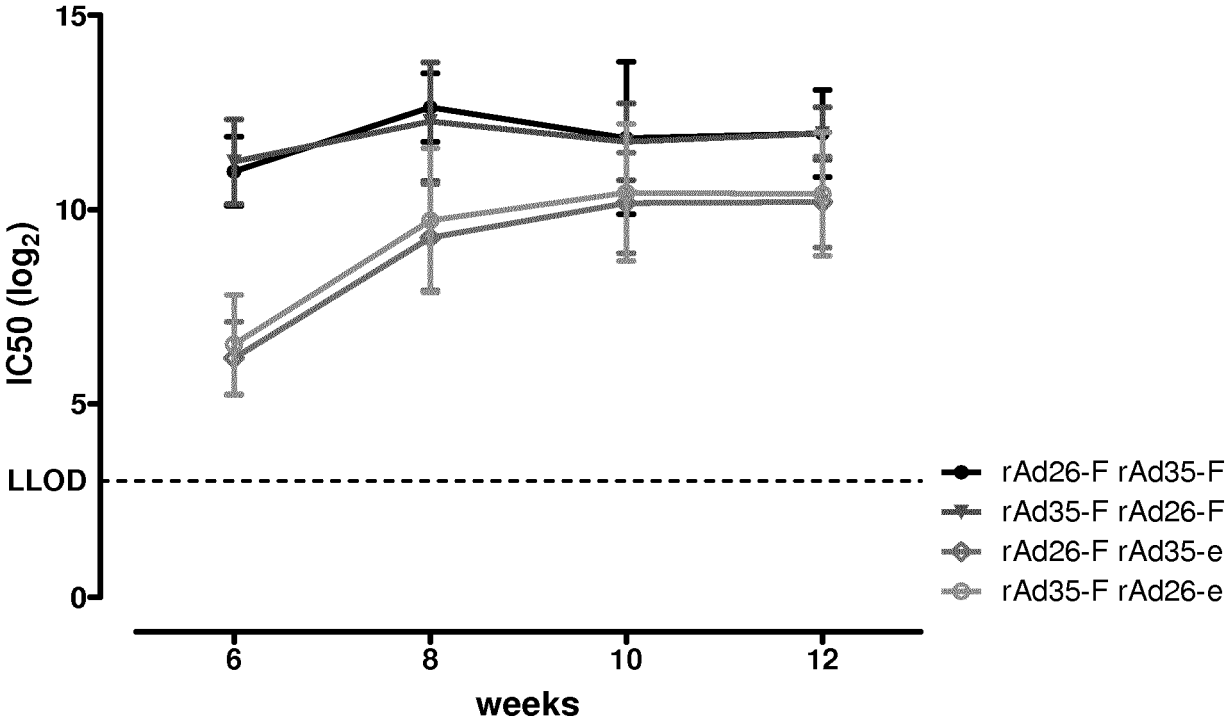
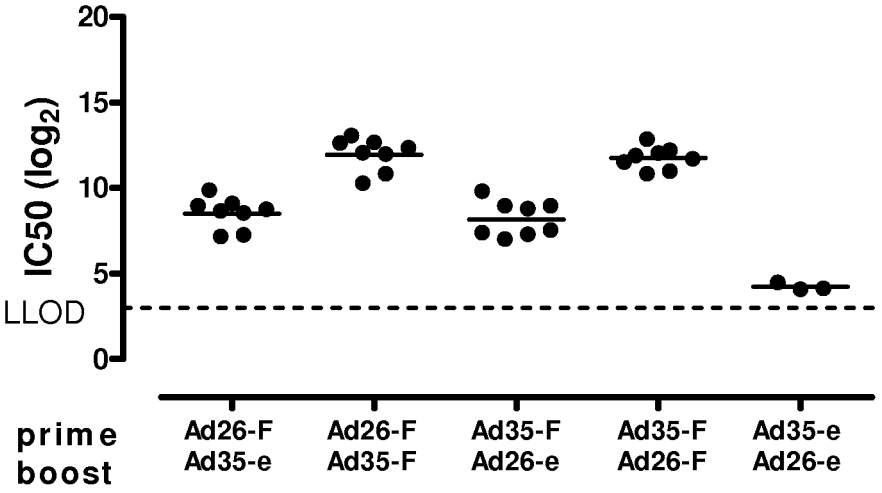

15
10
5
LLOD
0
IC50 (log2)
6
8
10
12
weeks
rAd26-F rAd35-F
rAd35-F rAd26-F
rAd26-F rAd35-e
rAd35-F rAd26-e

Fig. 7

at 6 weeks



at 12 weeks

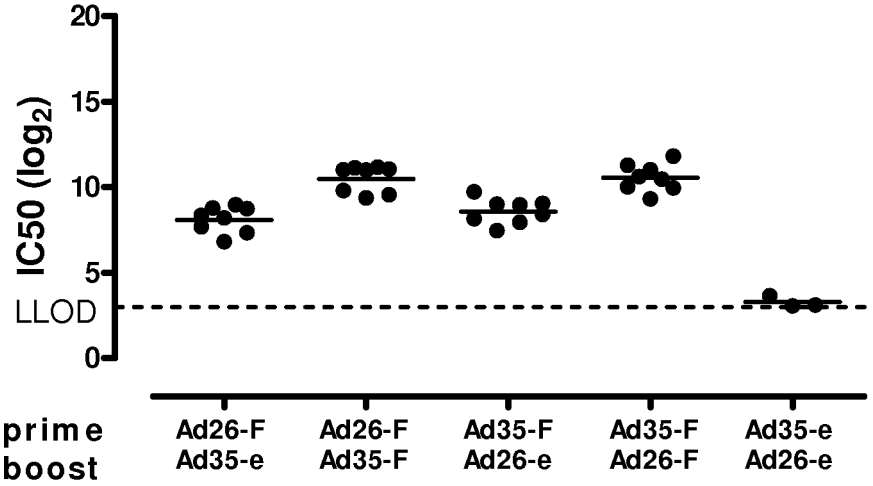


Fig. 8

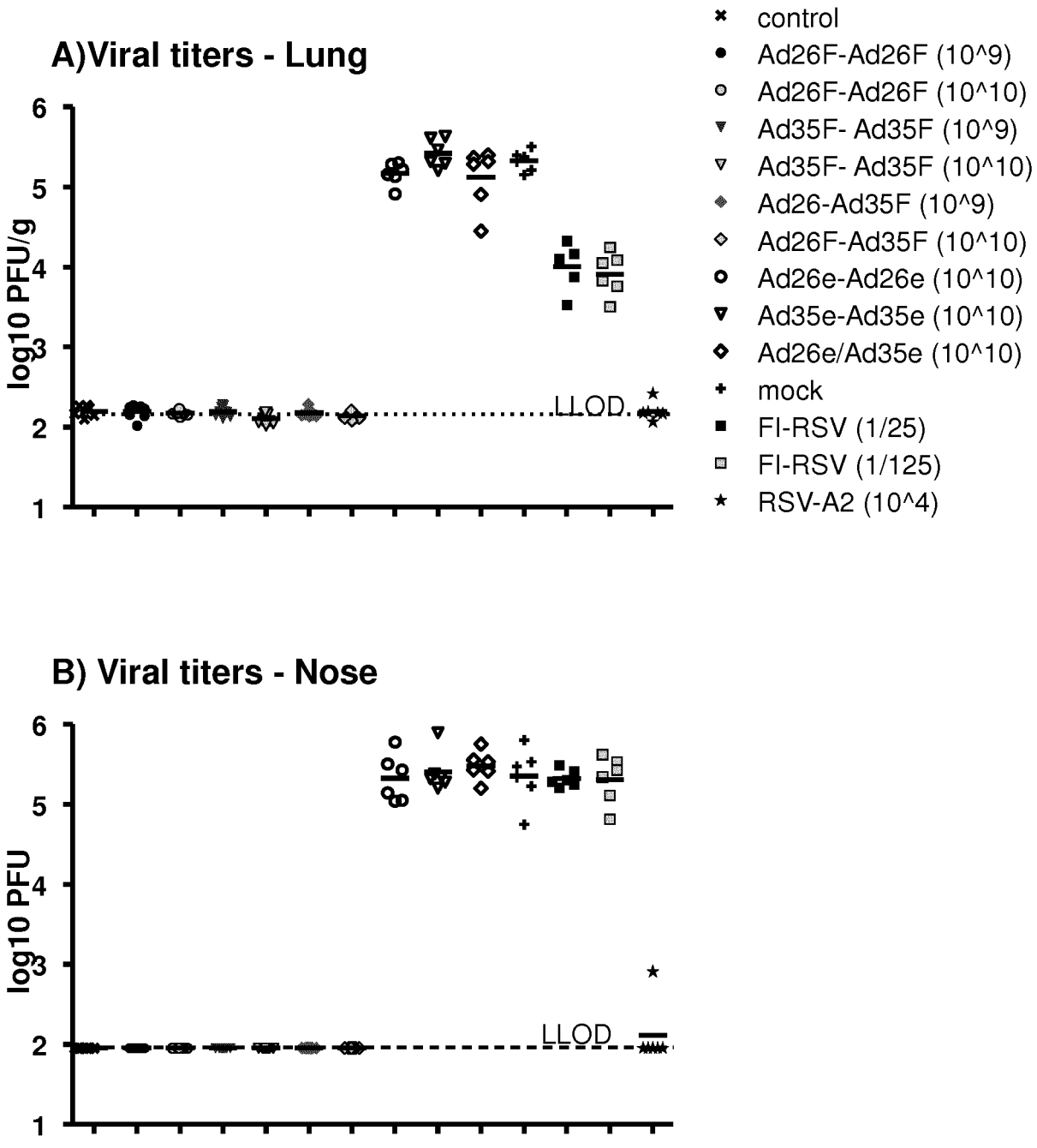

A)Viral titers - Lung
log10 PFU/g
6
5
4
3
2
1
LLOD
control
Ad26F-Ad26F (10^9)
Ad26F-Ad26F (10^10)
Ad35F- Ad35F (10^9)
Ad35F- Ad35F (10^10)
Ad26-Ad35F (10^9)
Ad26F-Ad35F (10^10)
Ad26e-Ad26e (10^10)
Ad35e-Ad35e (10^10)
Ad26e/Ad35e (10^10)
mock
FI-RSV (1/25)
FI-RSV (1/125)
RSV-A2 (10^4)
B) Viral titers - Nose
log10 PFU
6
5
4
3
2
1
LLOD

Fig. 9

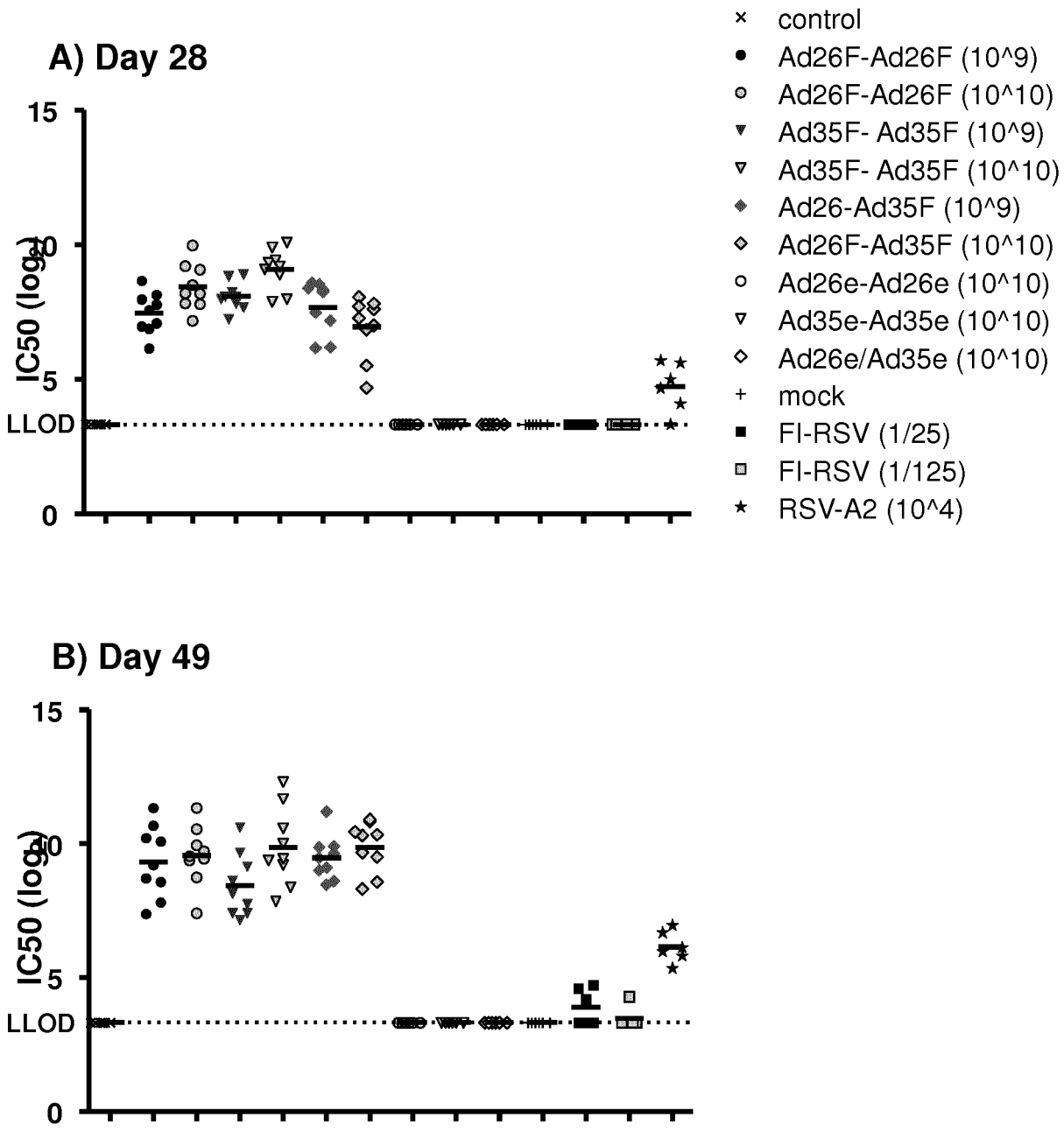

A) Day 28
B) Day 49
IC50 (log4)
15
10
5
0
LLOD
control
Ad26F-Ad26F (10^9)
Ad26F-Ad26F (10^10)
Ad35F- Ad35F (10^9)
Ad35F- Ad35F (10^10)
Ad26-Ad35F (10^9)
Ad26F-Ad35F (10^10)
Ad26e-Ad26e (10^10)
Ad35e-Ad35e (10^10)
Ad26e/Ad35e (10^10)
mock
FI-RSV (1/25)
FI-RSV (1/125)
RSV-A2 (10^4)

Fig. 10

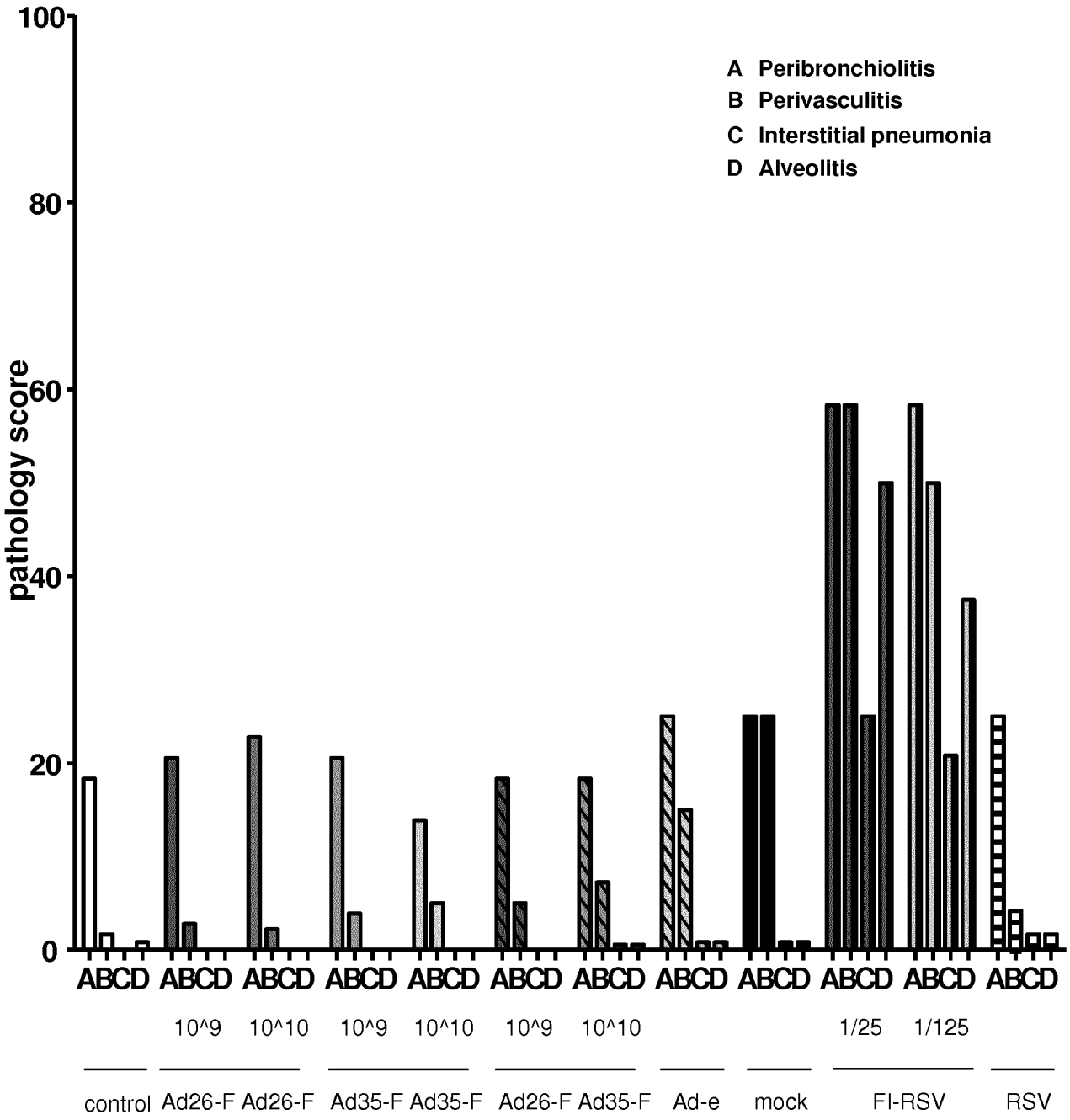

100
80
60
40
20
0
pathology score
A Peribronchiolitis
B Perivasculitis
C Interstitial pneumonia
D Alveolitis
ABCD
10^9
10^10
1/25
1/125
control
Ad26-F
Ad35-F
Ad-e
mock
FI-RSV
RSV

Fig. 11

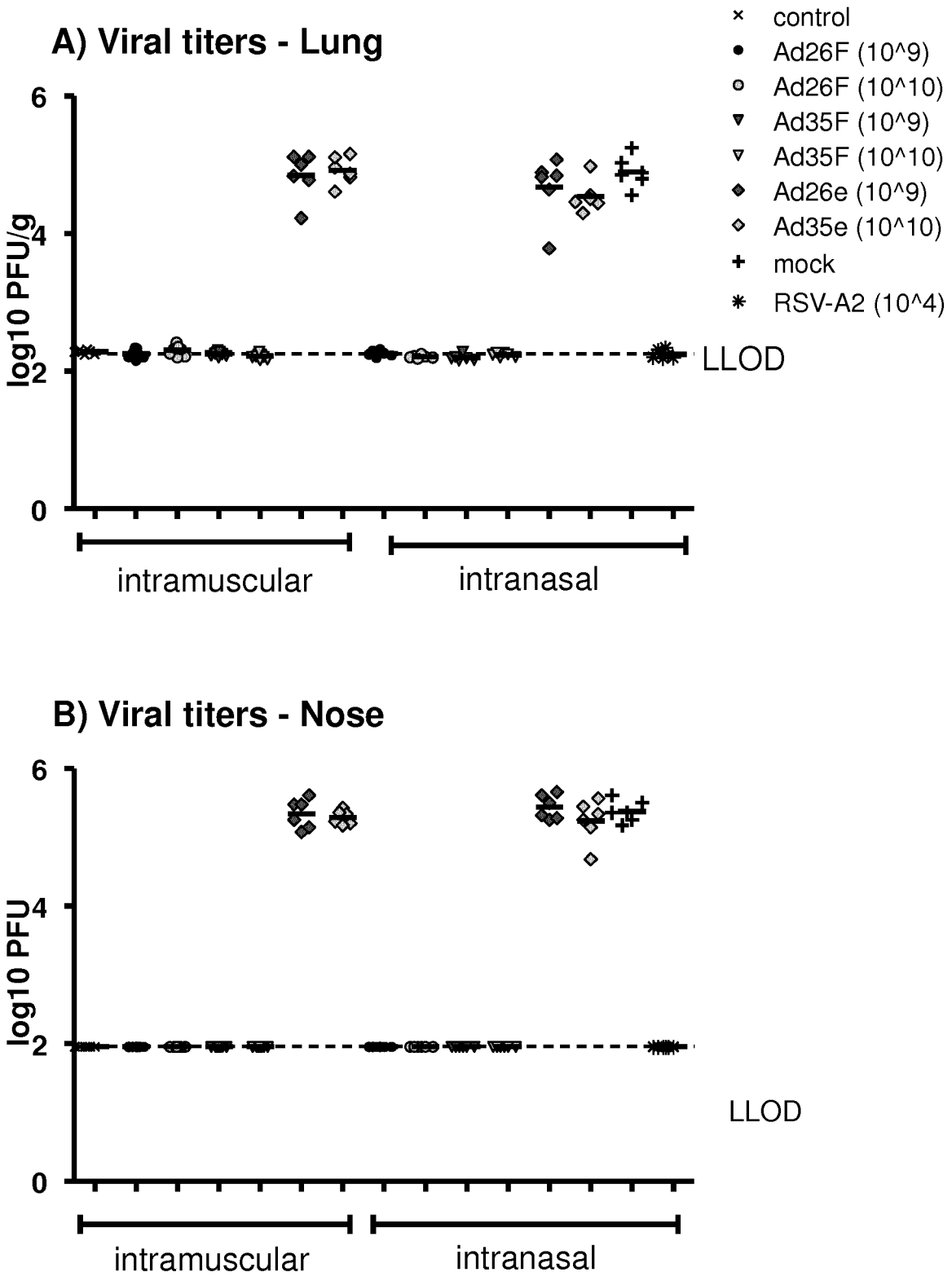

A) Viral titers - Lung
log10 PFU/g
6
4
2
0
LLOD
intramuscular
intranasal
control
Ad26F (10^9)
Ad26F (10^10)
Ad35F (10^9)
Ad35F (10^10)
Ad26e (10^9)
Ad35e (10^10)
mock
RSV-A2 (10^4)
B) Viral titers - Nose
log10 PFU
6
4
2
0
LLOD
intramuscular
intranasal

Fig. 12

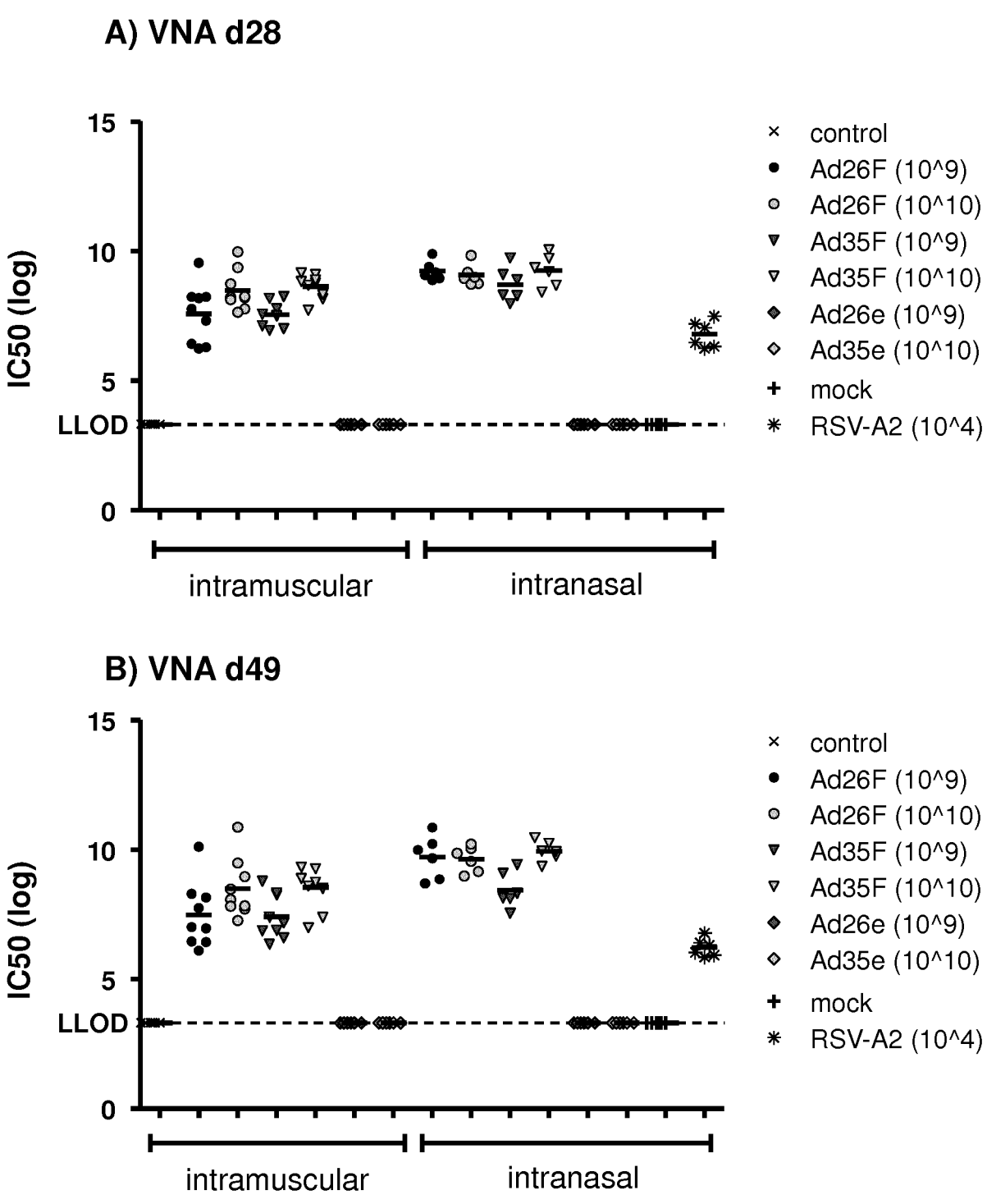

A) VNA d28
IC50 (log)
15
10
5
LLOD
0
intramuscular
intranasal
control
Ad26F (10^9)
Ad26F (10^10)
Ad35F (10^9)
Ad35F (10^10)
Ad26e (10^9)
Ad35e (10^10)
mock
RSV-A2 (10^4)
B) VNA d49
IC50 (log)
15
10
5
LLOD
0
intramuscular
intranasal
control
Ad26F (10^9)
Ad26F (10^10)
Ad35F (10^9)
Ad35F (10^10)
Ad26e (10^9)
Ad35e (10^10)
mock
RSV-A2 (10^4)

Fig. 13

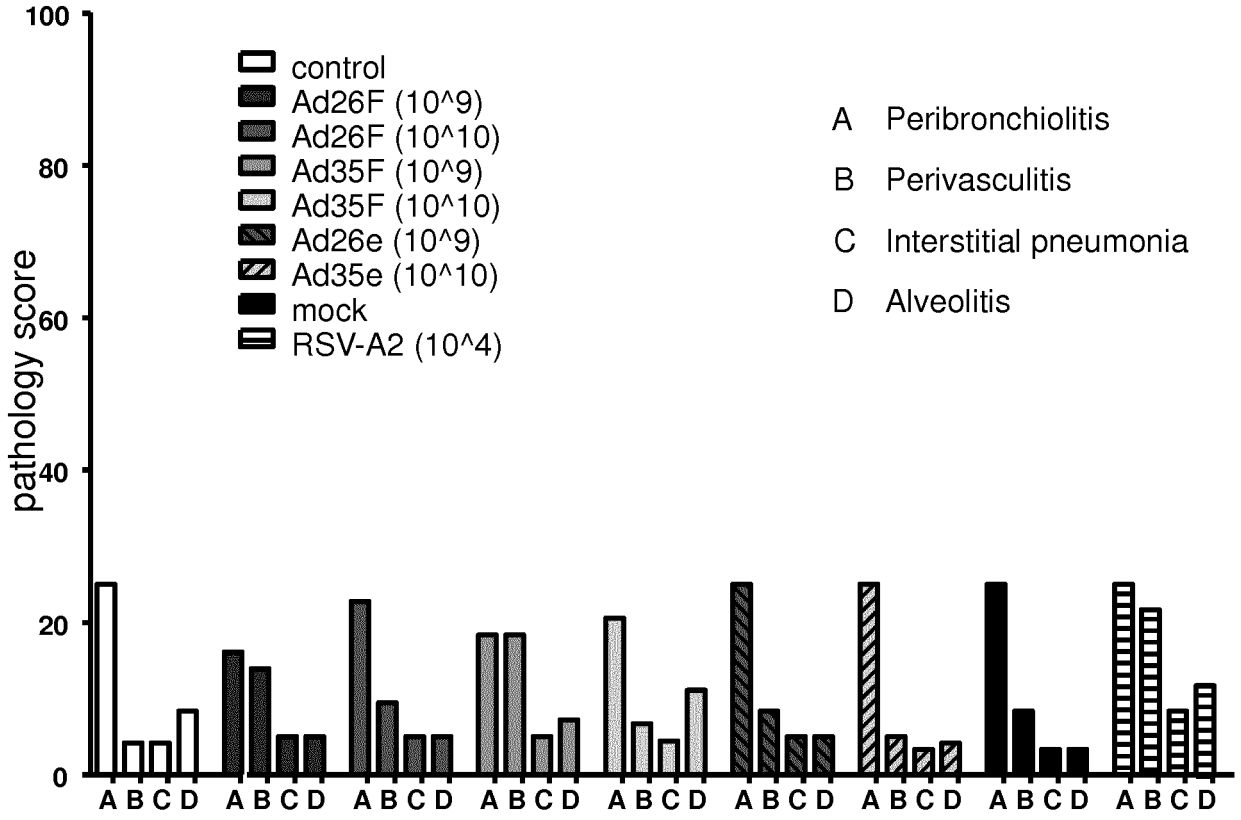

100
80
60
40
20
0
pathology score
control
Ad26F (10^9)
Ad26F (10^10)
Ad35F (10^9)
Ad35F (10^10)
Ad26e (10^9)
Ad35e (10^10)
mock
RSV-A2 (10^4)
A Peribronchiolitis
B Perivasculitis
C Interstitial pneumonia
D Alveolitis
A B C D A B C D A B C D A B C D A B C D A B C D A B C D A B C D

Fig. 14

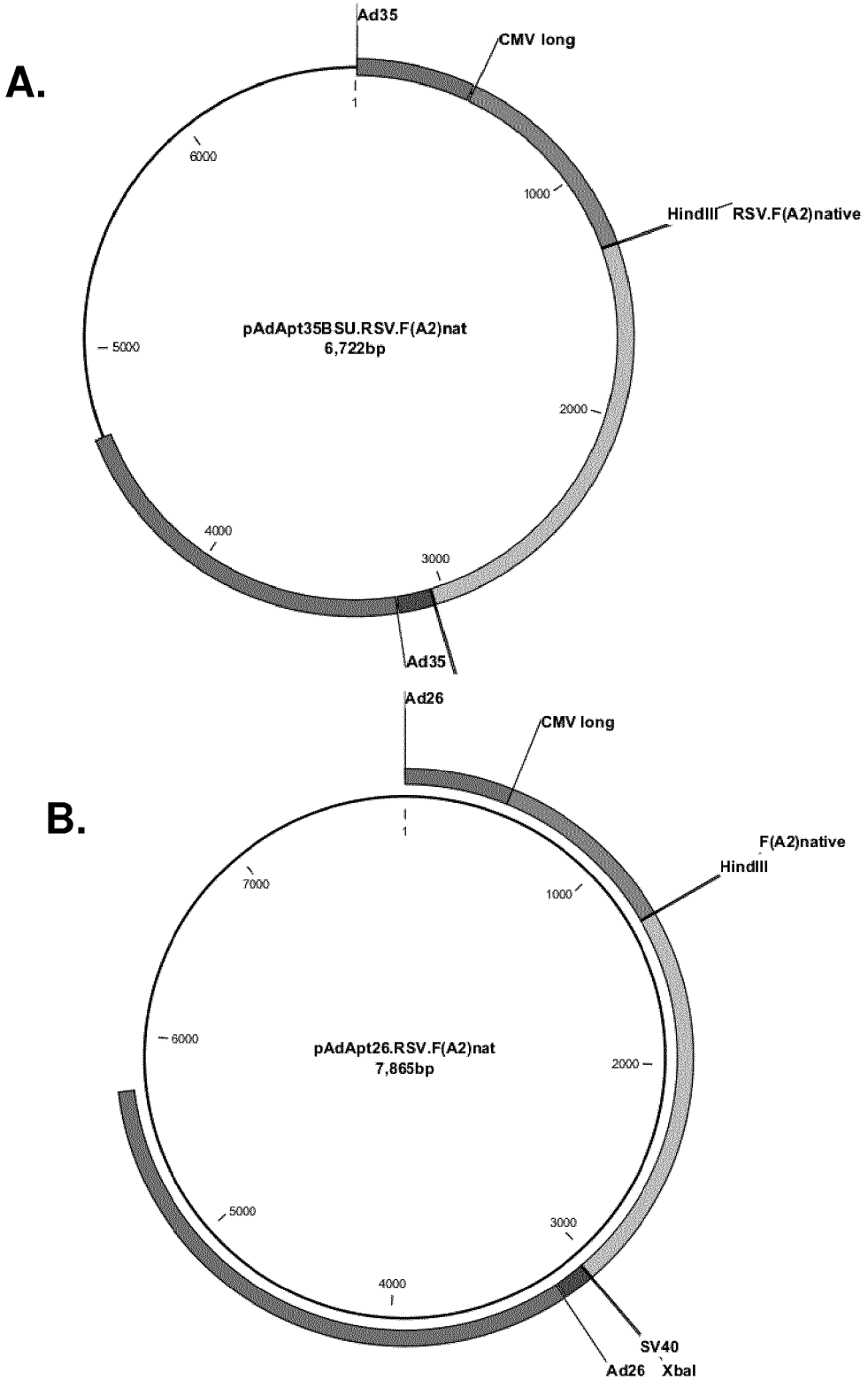

A.
Ad35
CMV long
1
1000
HindIII
RSV.F(A2)native
2000
3000
Ad35
4000
5000
6000
pAdApt35BSU.RSV.F(A2)nat
6,722bp
B.
Ad26
CMV long
1
1000
F(A2)native
HindIII
2000
3000
SV40
Ad26
XbaI
4000
5000
6000
7000
pAdApt26.RSV.F(A2)nat
7,865bp

Fig. 15

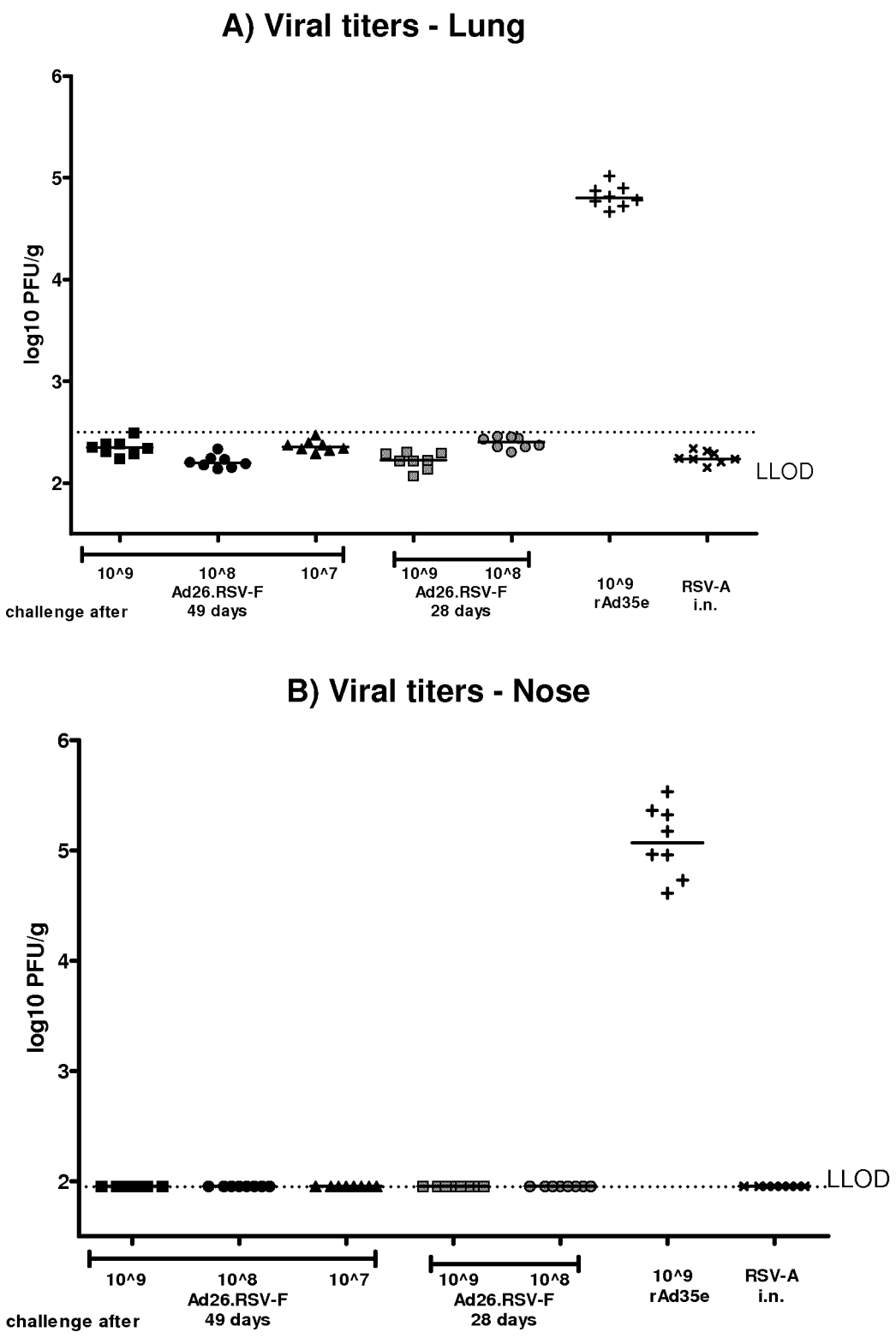

A) Viral titers - Lung
log10 PFU/g
6
5
4
3
2
LLOD
10^9
10^8
Ad26.RSV-F
49 days
10^7
10^9
10^8
Ad26.RSV-F
28 days
10^9
rAd35e
RSV-A
i.n.
challenge after
B) Viral titers - Nose
log10 PFU/g
6
5
4
3
2
LLOD
10^9
10^8
Ad26.RSV-F
49 days
10^7
10^9
10^8
Ad26.RSV-F
28 days
10^9
rAd35e
RSV-A
i.n.
challenge after

Fig. 16

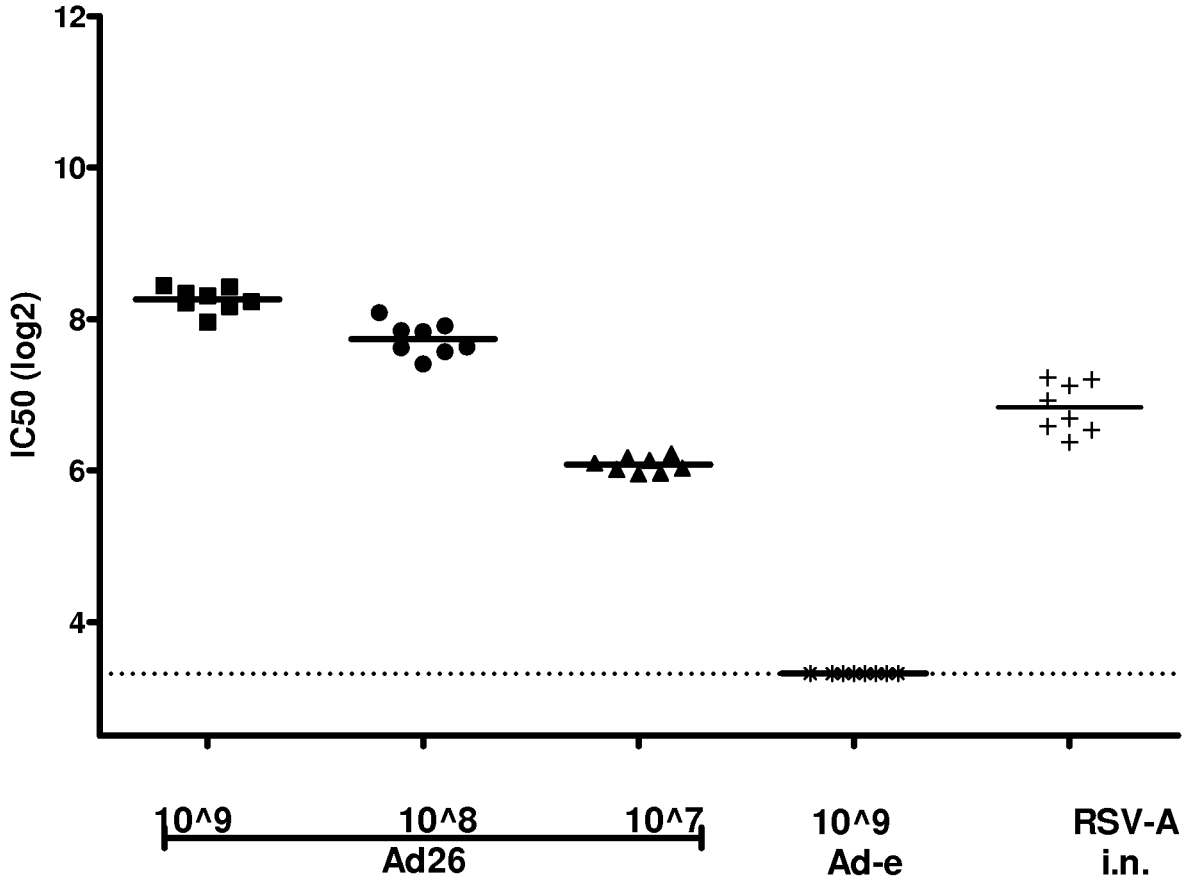


Fig. 17

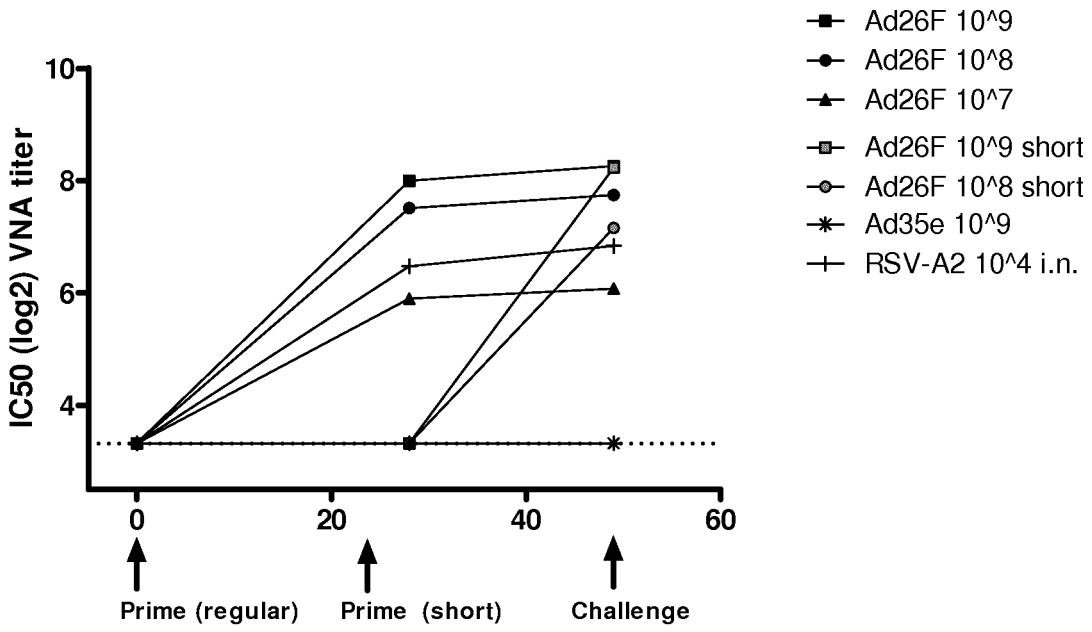

IC50 (log2) VNA titer
10
8
6
4
0
20
40
60
Prime (regular)
Prime (short)
Challenge
Ad26F 10^9
Ad26F 10^8
Ad26F 10^7
Ad26F 10^9 short
Ad26F 10^8 short
Ad35e 10^9
RSV-A2 10^4 i.n.

Fig. 18

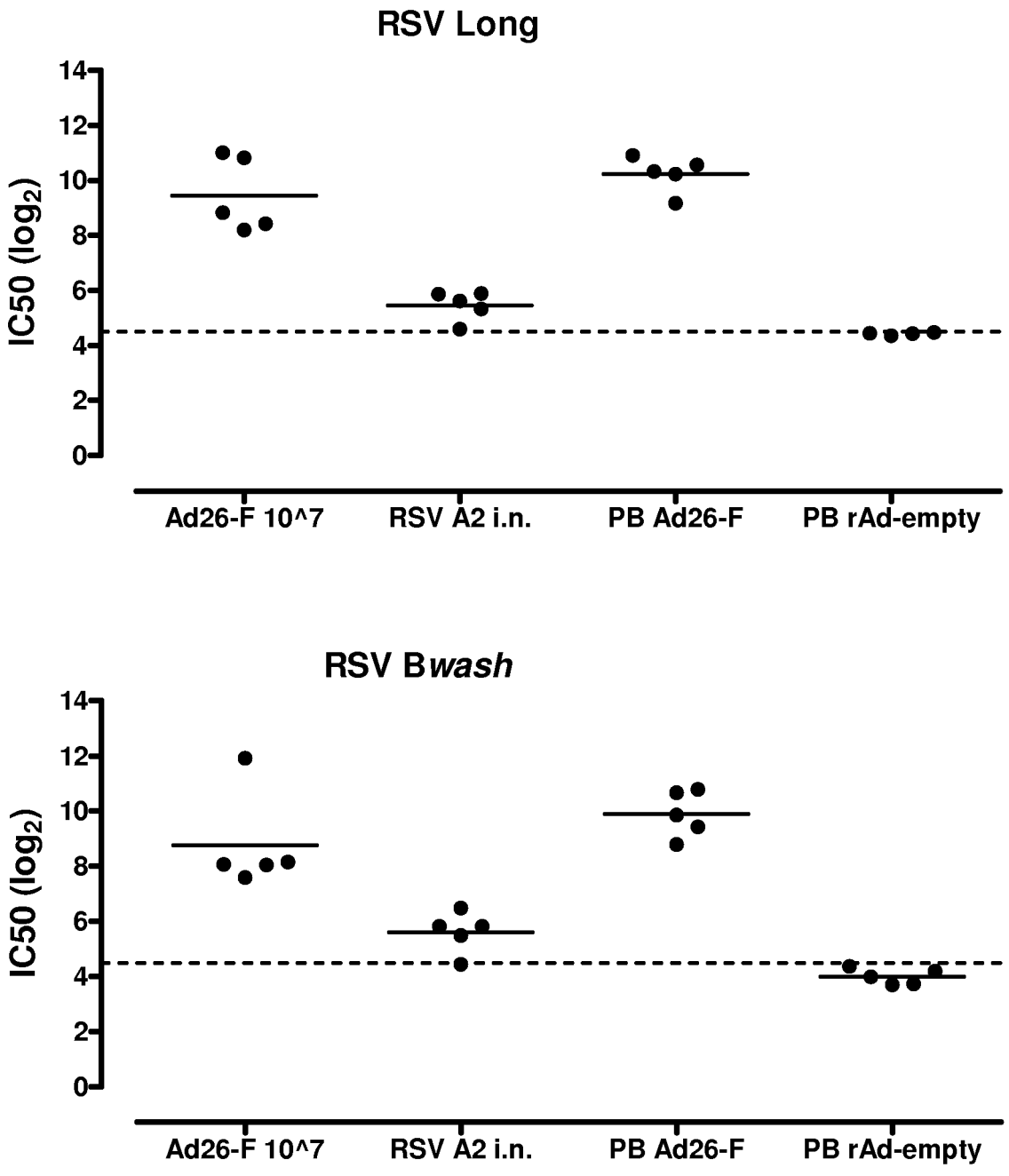
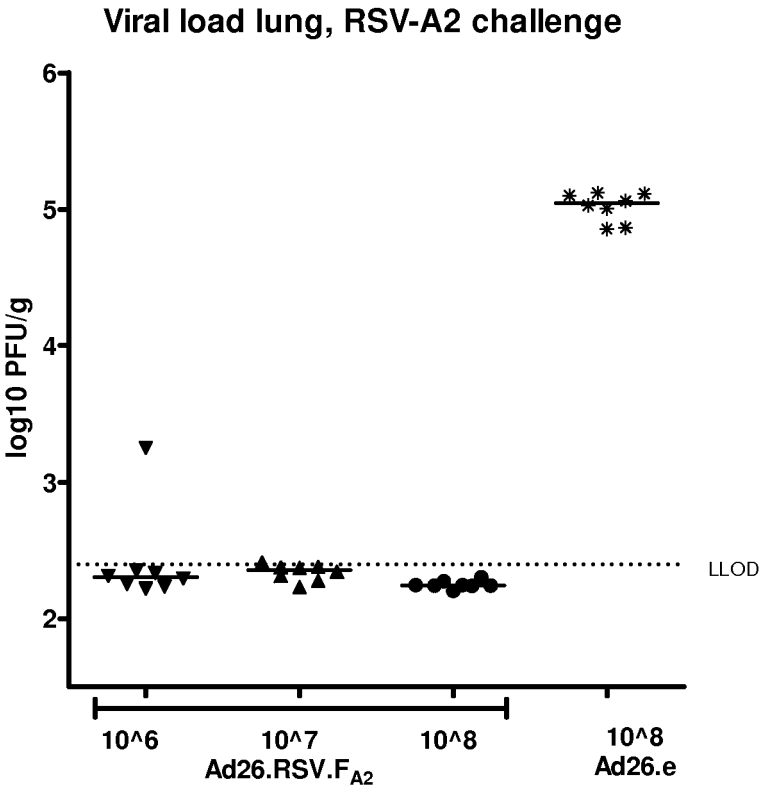

RSV Long
IC50 (log2)
14
12
10
8
6
4
2
0
Ad26-F 10^7
RSV A2 i.n.
PB Ad26-F
PB rAd-empty
RSV Bwash
IC50 (log2)
14
12
10
8
6
4
2
0
Ad26-F 10^7
RSV A2 i.n.
PB Ad26-F
PB rAd-empty

Fig. 19


Viral load lung, RSV-A2 challenge
log10 PFU/g
6
5
4
3
2
LLOD
10^6
10^7
Ad26.RSV.F$_{A2}$
10^8
10^8
Ad26.e

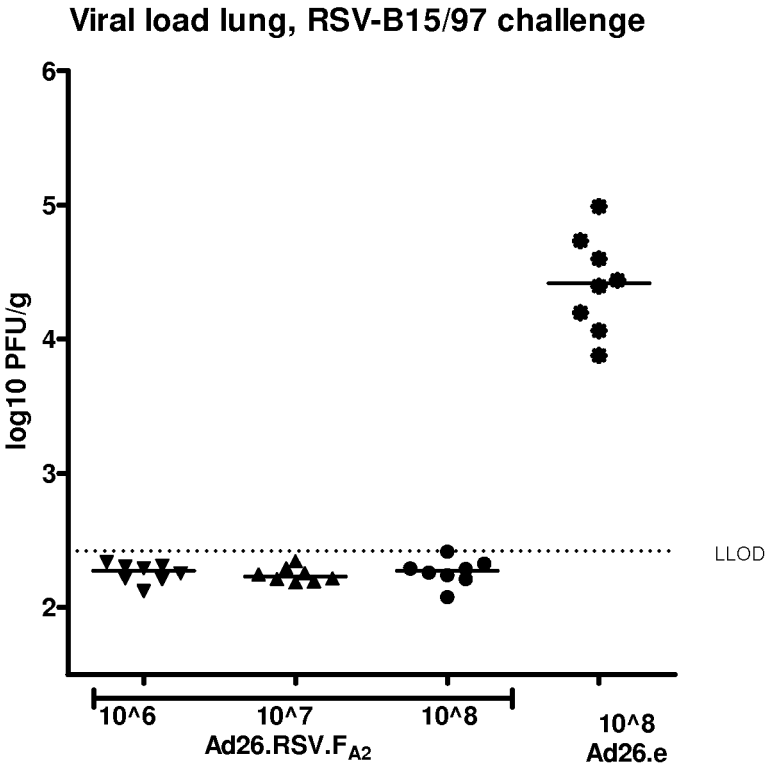

Viral load lung, RSV-B15/97 challenge
log10 PFU/g
6
5
4
3
2
LLOD
10^6
10^7
Ad26.RSV.F$_{A2}$
10^8
10^8
Ad26.e

Fig. 20

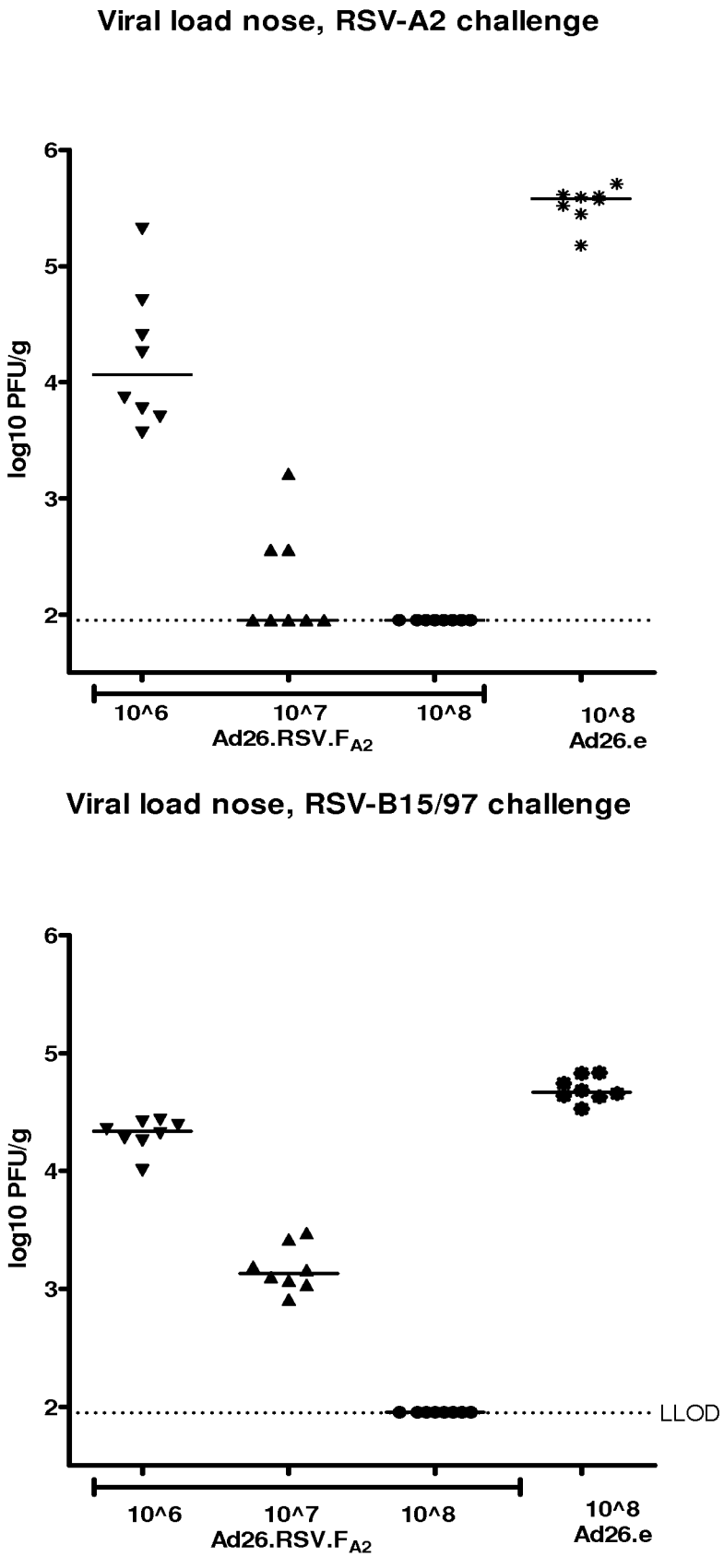

Viral load nose, RSV-A2 challenge
log10 PFU/g
6
5
4
3
2
10^6
10^7
Ad26.RSV.F$_{A2}$
10^8
10^8
Ad26.e
Viral load nose, RSV-B15/97 challenge
log10 PFU/g
6
5
4
3
2
LLOD
10^6
10^7
Ad26.RSV.F$_{A2}$
10^8
10^8
Ad26.e

Fig. 21

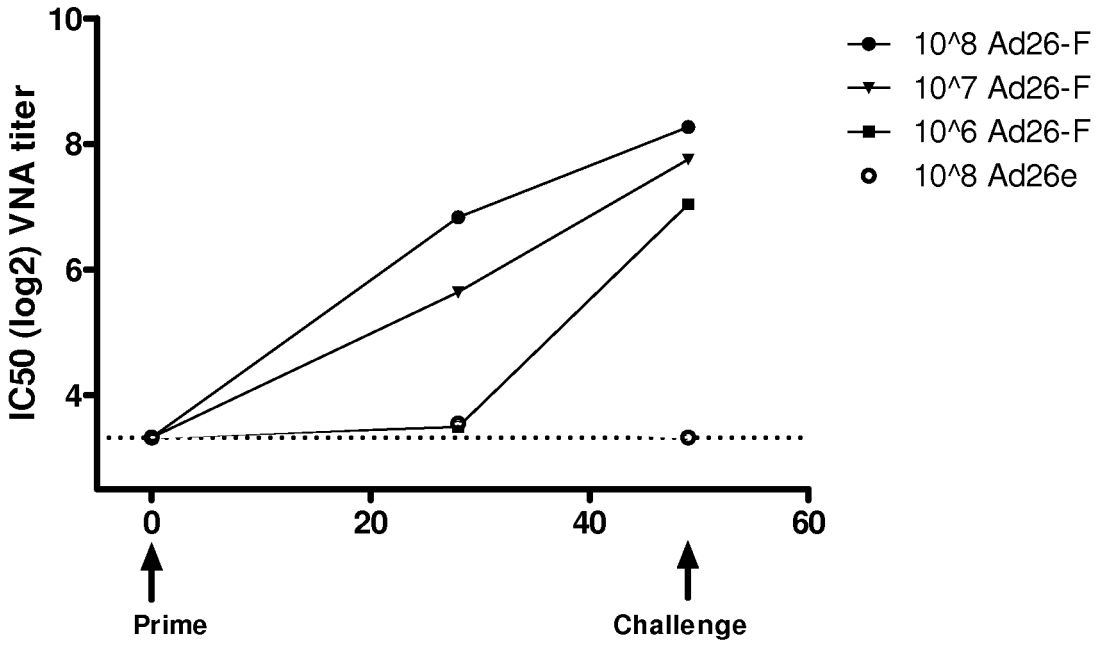

IC50 (log2) VNA titer
10
8
6
4
0
20
40
60
Prime
Challenge
10^8 Ad26-F
10^7 Ad26-F
10^6 Ad26-F
10^8 Ad26e

Fig. 22

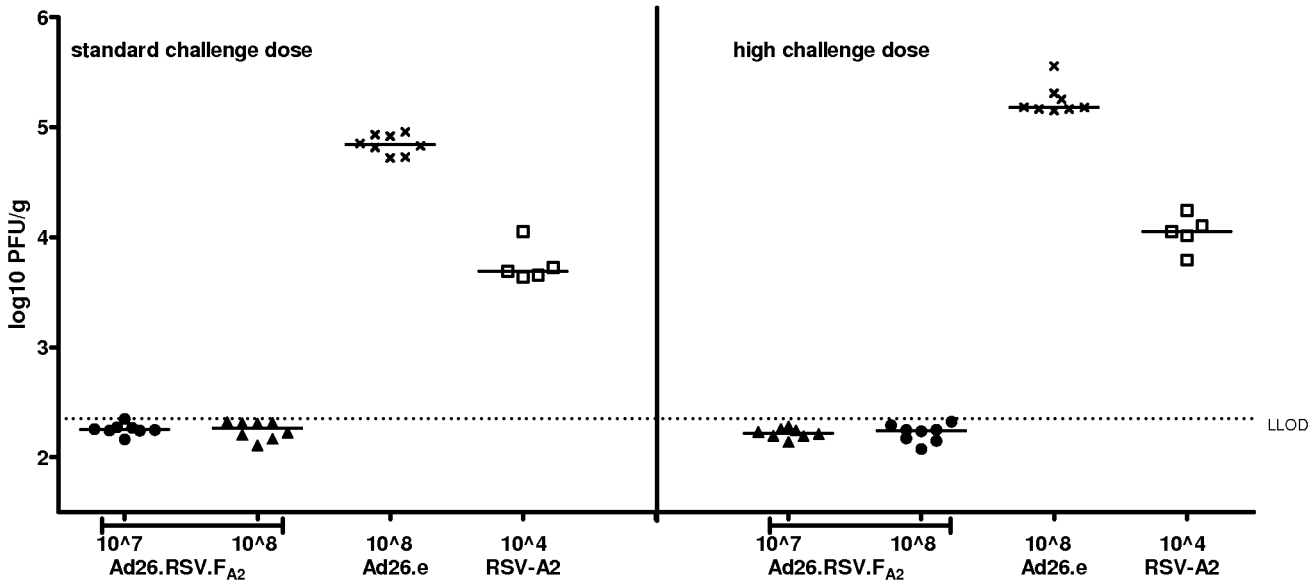

Lung viral load
standard challenge dose
high challenge dose
log10 PFU/g
6
5
4
3
2
LLOD
10^7
10^8
Ad26.RSV.F$_{A2}$
10^8
Ad26.e
10^4
RSV-A2
10^7
10^8
Ad26.RSV.F$_{A2}$
10^8
Ad26.e
10^4
RSV-A2

Fig. 23

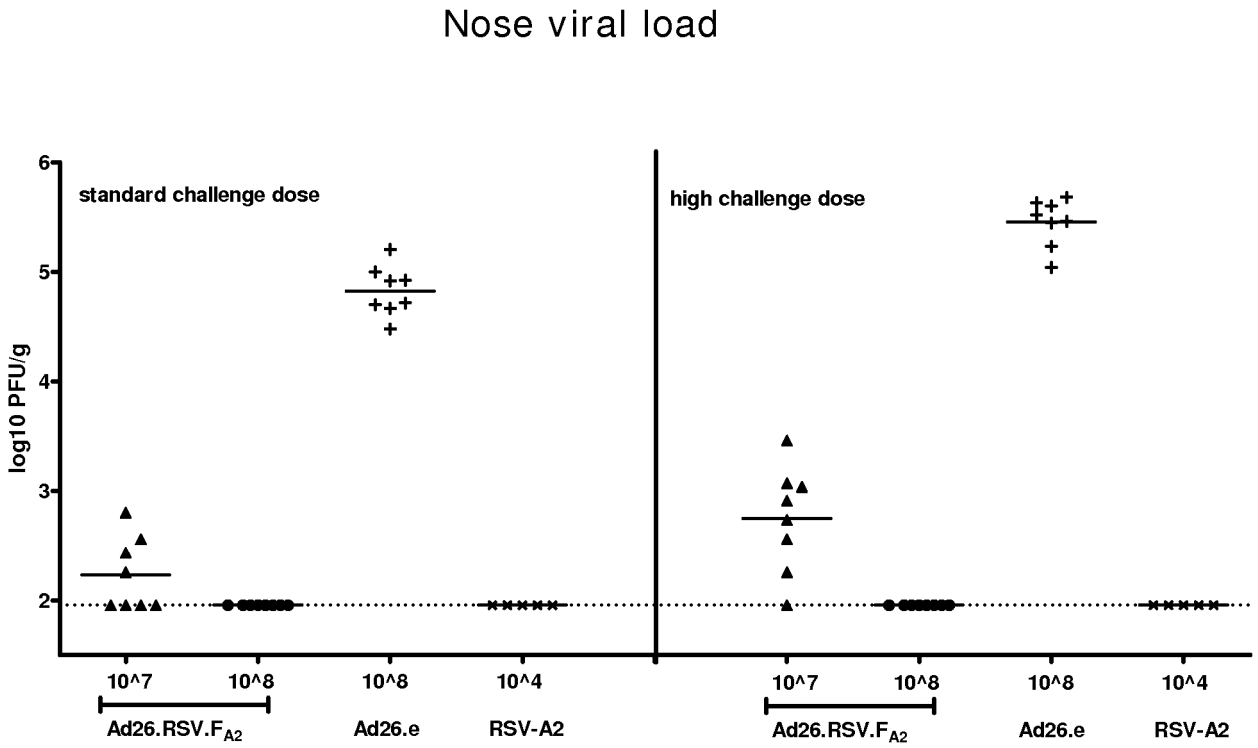
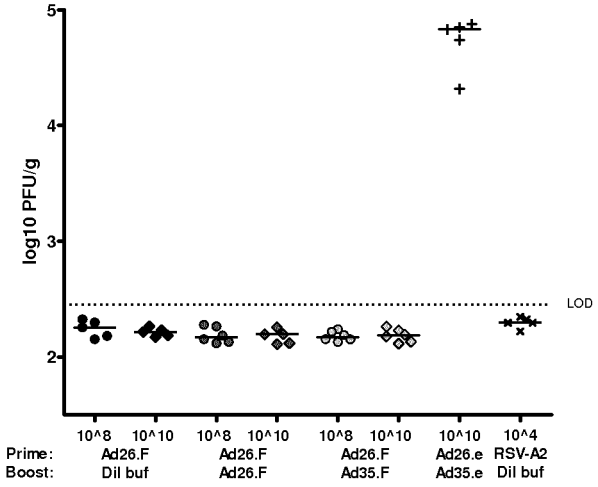

Nose viral load
standard challenge dose
high challenge dose
log10 PFU/g
6
5
4
3
2
10^7
10^8
10^8
10^4
Ad26.RSV.F$_{A2}$
Ad26.e
RSV-A2
10^7
10^8
10^8
10^4
Ad26.RSV.F$_{A2}$
Ad26.e
RSV-A2

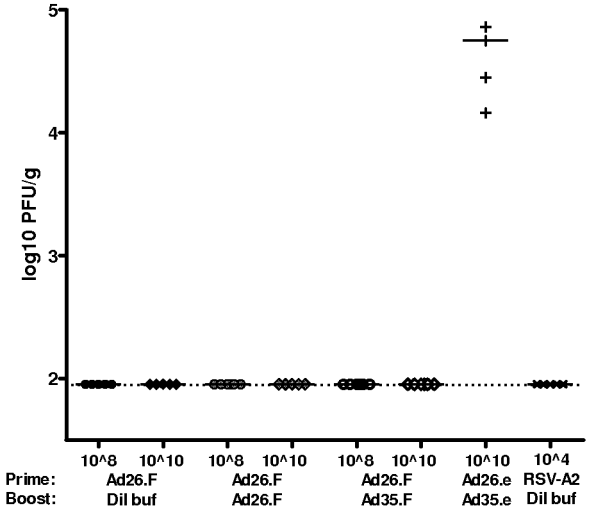
Fig. 24

Long term protection – lung & nose titers

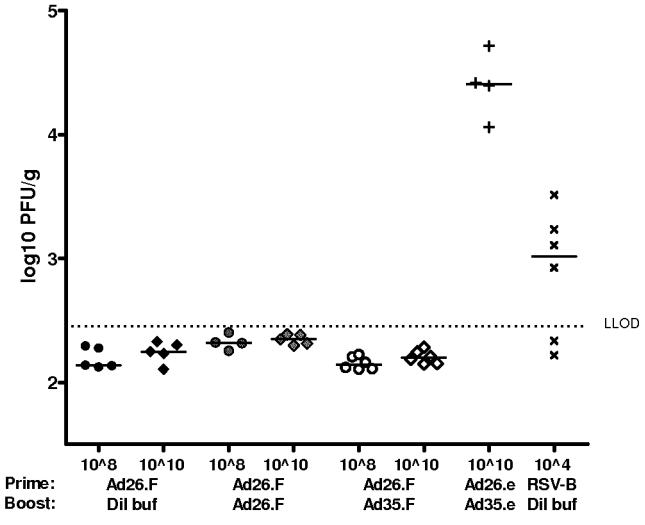
Viral titers – Lung
RSV-A2 challenge
t=31 wks



Viral titers – Nose
RSV-A2 challenge
t=31 wks



Viral titers – Lung
RSV-B15/97 challenge
t=31 wks



Viral titers – Nose
RSV-B15/97 challenge
t=31 wks

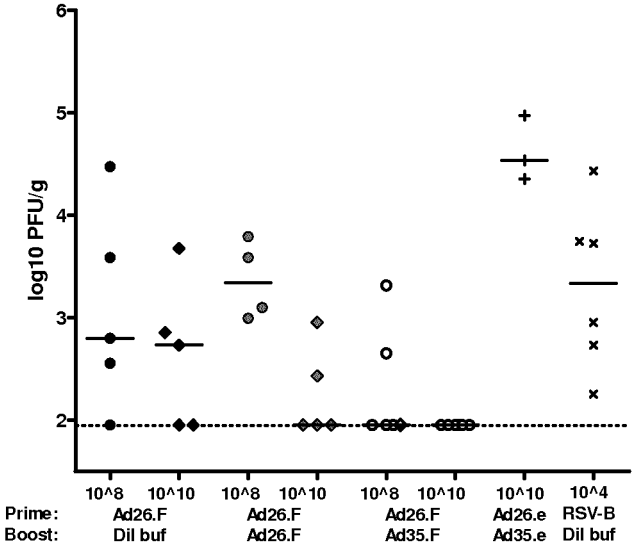


Fig. 25

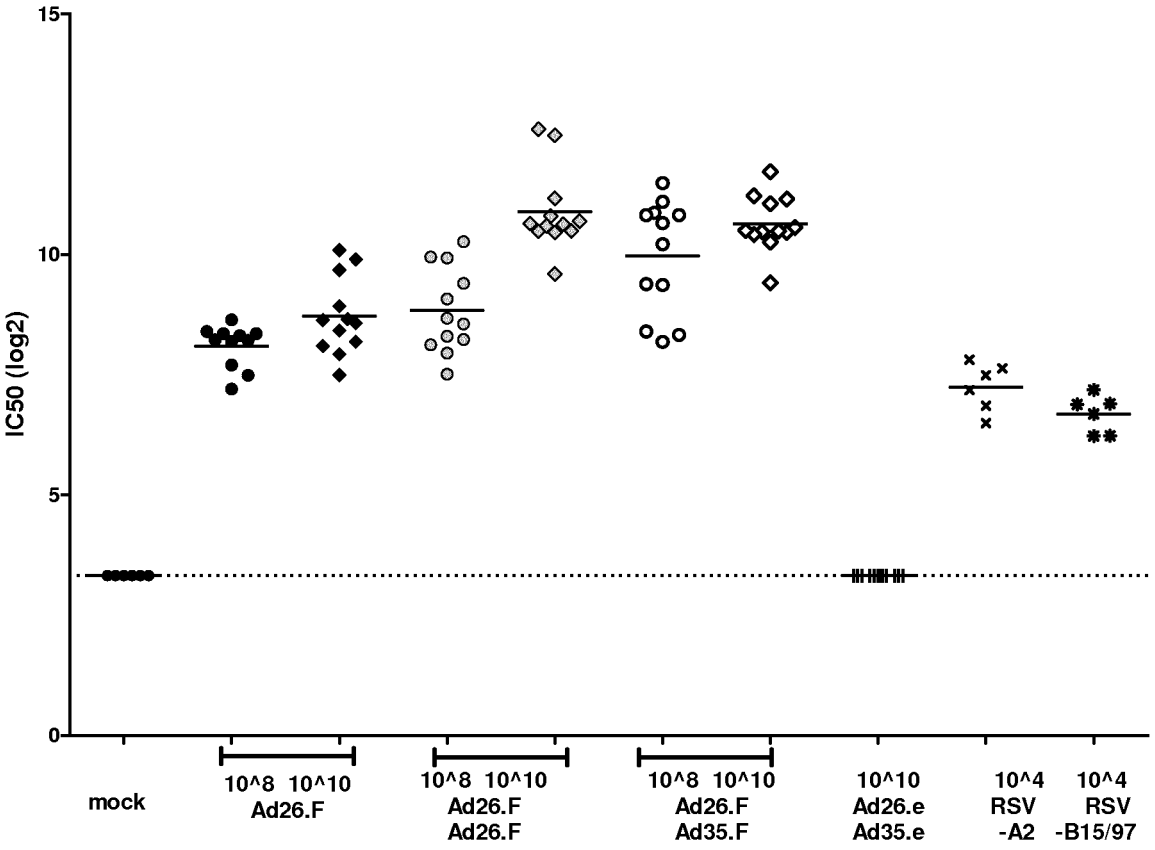

15
10
5
0
IC50 (log2)
mock
10^8 10^10
Ad26.F
10^8 10^10
Ad26.F
Ad26.F
10^8 10^10
Ad26.F
Ad35.F
10^10
Ad26.e
Ad35.e
10^4
RSV
-A2
10^4
RSV
-B15/97

Fig. 26

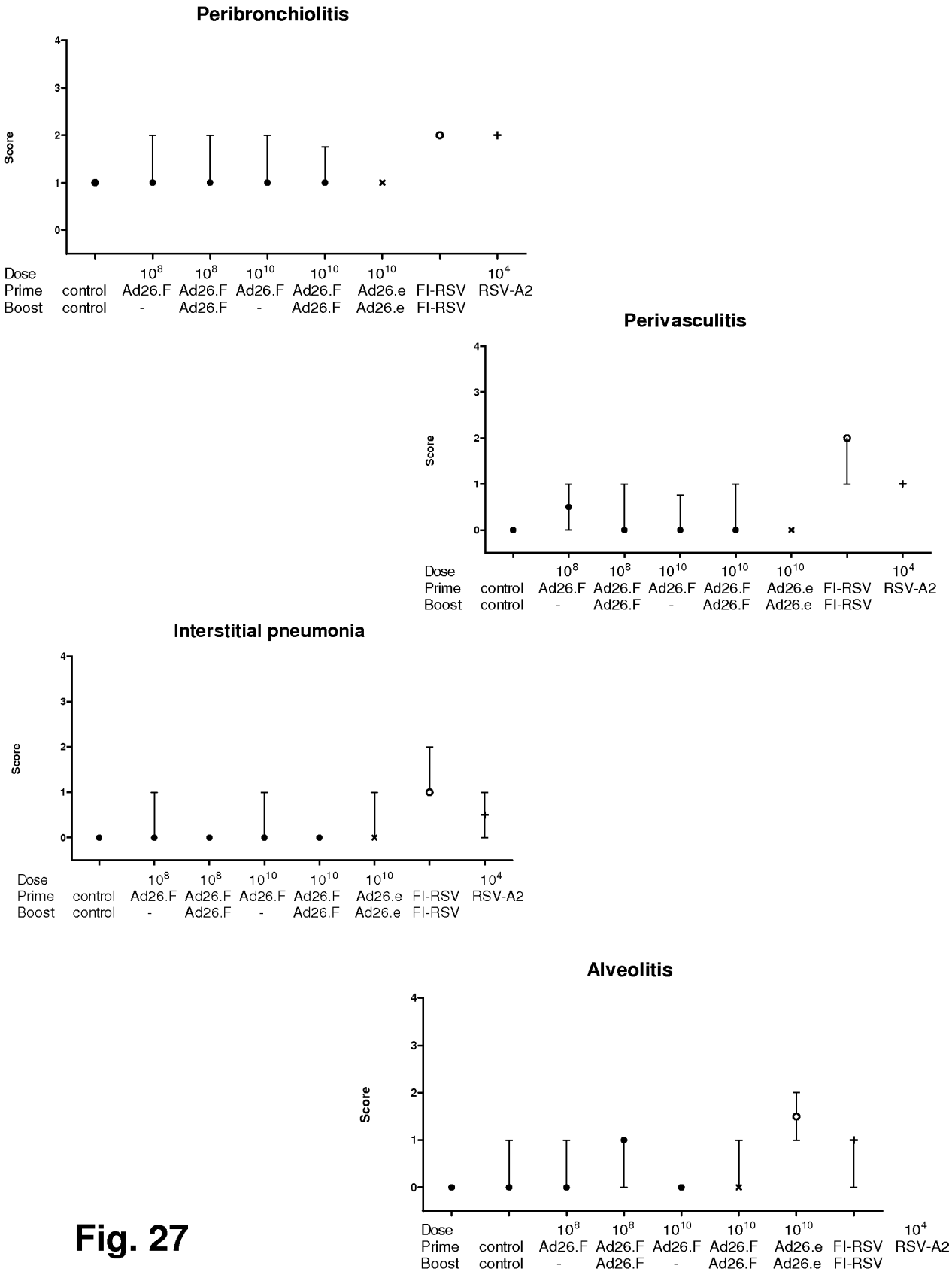
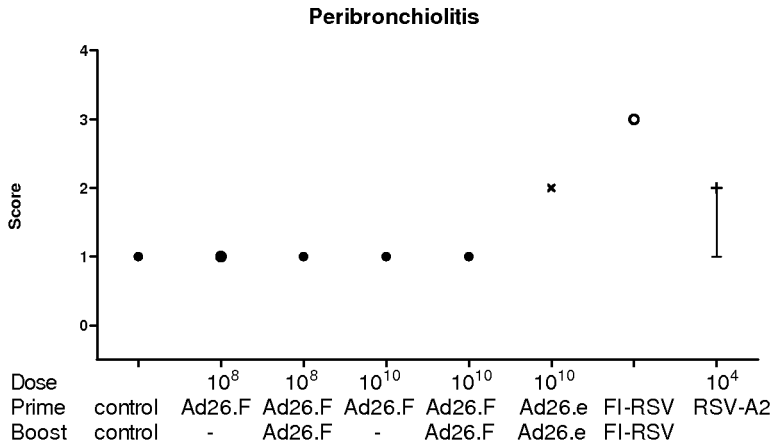
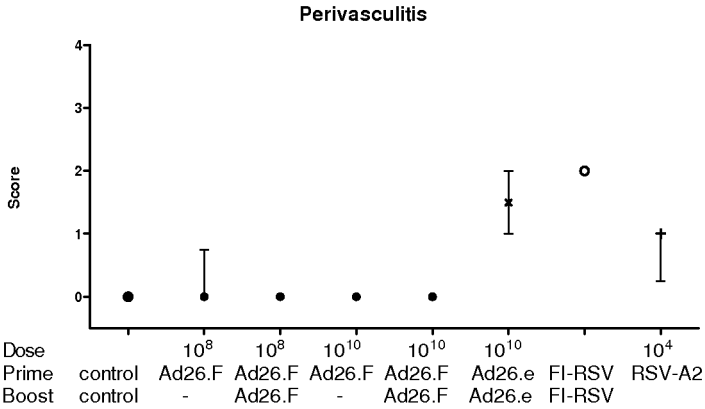
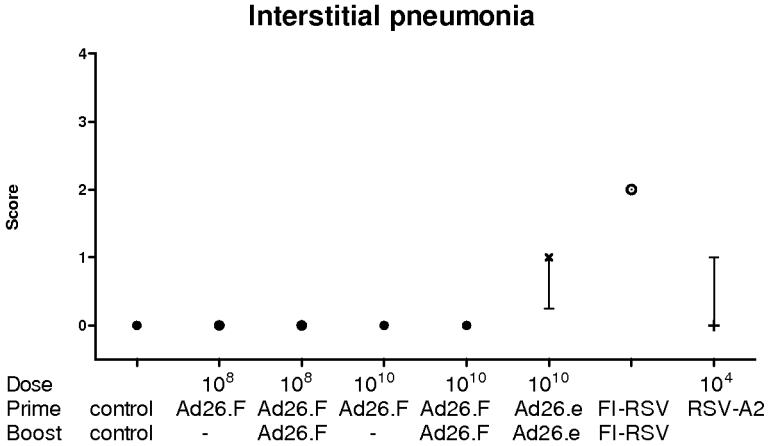

Peribronchiolitis
Score
0
1
2
3
4
Dose
Prime control
Boost control
10^8 Ad26.F -
10^8 Ad26.F Ad26.F
10^10 Ad26.F -
10^10 Ad26.F Ad26.F
10^10 Ad26.e Ad26.e
FI-RSV FI-RSV
10^4 RSV-A2
Perivasculitis
Score
0
1
2
3
4
Dose
Prime control
Boost control
10^8 Ad26.F -
10^8 Ad26.F Ad26.F
10^10 Ad26.F -
10^10 Ad26.F Ad26.F
10^10 Ad26.e Ad26.e
FI-RSV FI-RSV
10^4 RSV-A2
Interstitial pneumonia
Score
0
1
2
3
4
Dose
Prime control
Boost control
10^8 Ad26.F -
10^8 Ad26.F Ad26.F
10^10 Ad26.F -
10^10 Ad26.F Ad26.F
10^10 Ad26.e Ad26.e
FI-RSV FI-RSV
10^4 RSV-A2
Alveolitis
Score
0
1
2
3
4
Dose
Prime control
Boost control
10^8 Ad26.F -
10^8 Ad26.F Ad26.F
10^10 Ad26.F -
10^10 Ad26.F Ad26.F
10^10 Ad26.e Ad26.e
FI-RSV FI-RSV
10^4 RSV-A2

Fig. 27


Peribronchiolitis
Score
0
1
2
3
4
Dose 10^8 10^8 10^{10} 10^{10} 10^{10} 10^4
Prime control Ad26.F Ad26.F Ad26.F Ad26.F Ad26.e FI-RSV RSV-A2
Boost control - Ad26.F - Ad26.F Ad26.e FI-RSV


Perivasculitis
Score
0
1
2
3
4
Dose 10^8 10^8 10^{10} 10^{10} 10^{10} 10^4
Prime control Ad26.F Ad26.F Ad26.F Ad26.F Ad26.e FI-RSV RSV-A2
Boost control - Ad26.F - Ad26.F Ad26.e FI-RSV


Interstitial pneumonia
Score
0
1
2
3
4
Dose 10^8 10^8 10^{10} 10^{10} 10^{10} 10^4
Prime control Ad26.F Ad26.F Ad26.F Ad26.F Ad26.e FI-RSV RSV-A2
Boost control - Ad26.F - Ad26.F Ad26.e FI-RSV

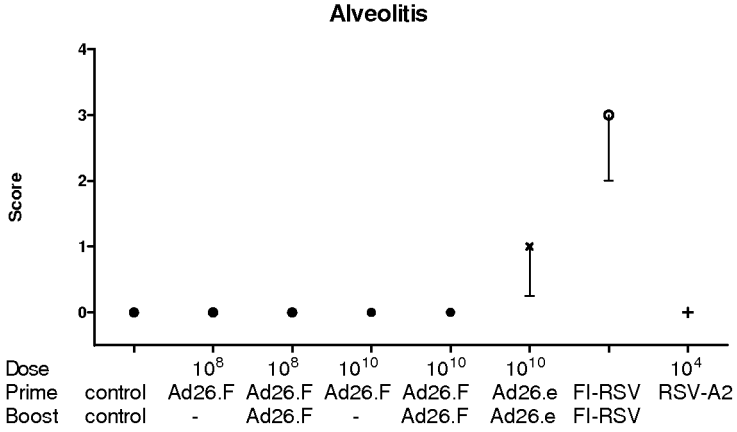

Alveolitis
Score
0
1
2
3
4
Dose 10^8 10^8 10^{10} 10^{10} 10^{10} 10^4
Prime control Ad26.F Ad26.F Ad26.F Ad26.F Ad26.e FI-RSV RSV-A2
Boost control - Ad26.F - Ad26.F Ad26.e FI-RSV

Fig. 28

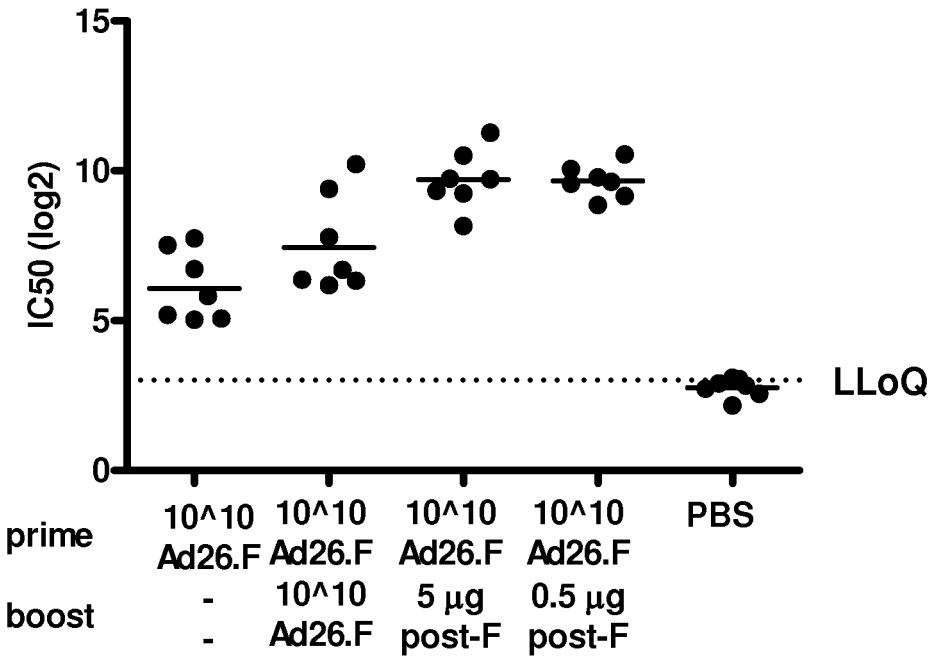
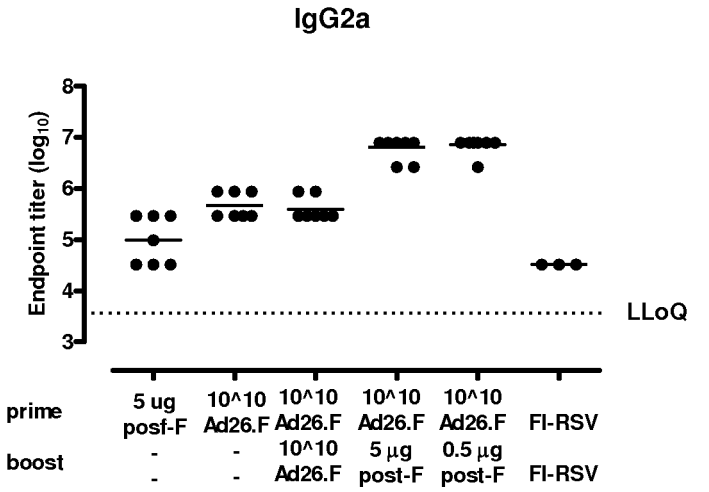
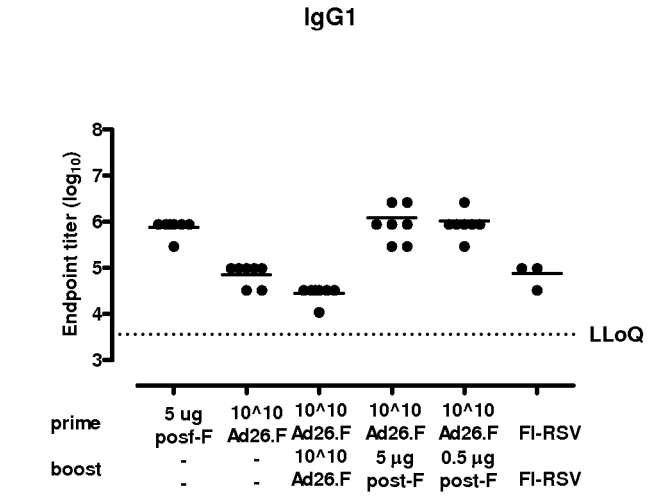

15
10
5
0
IC50 (log2)
LLoQ
prime
boost
10^10 Ad26.F
-
10^10 Ad26.F
10^10 Ad26.F
10^10 Ad26.F
5 µg post-F
10^10 Ad26.F
0.5 µg post-F
PBS

Fig. 29


IgG2a
Endpoint titer (log10)
8
7
6
5
4
3
LLoQ
prime
boost
5 ug posf-F
10^10 Ad26.F
10^10 Ad26.F
10^10 Ad26.F
10^10 Ad26.F
Fl-RSV
-
-
10^10 Ad26.F
5 µg post-F
0.5 µg post-F
Fl-RSV


IgG1
Endpoint titer (log10)
8
7
6
5
4
3
LLoQ
prime
boost
5 ug posf-F
10^10 Ad26.F
10^10 Ad26.F
10^10 Ad26.F
10^10 Ad26.F
Fl-RSV
-
-
10^10 Ad26.F
5 µg post-F
0.5 µg post-F
Fl-RSV

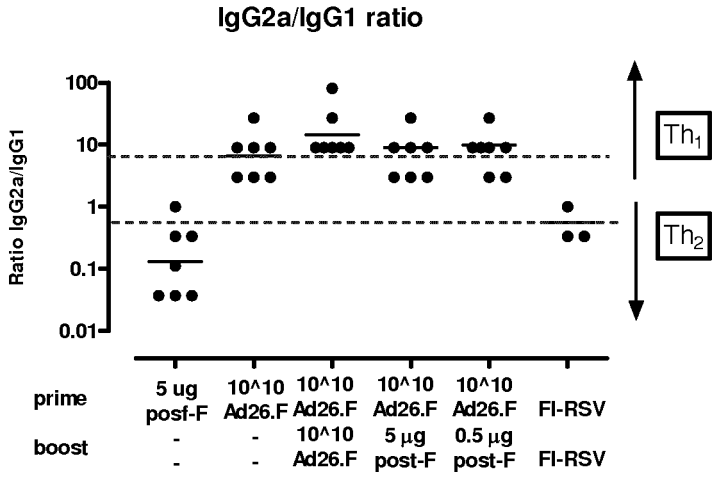

IgG2a/IgG1 ratio
Ratio IgG2a/IgG1
100
10
1
0.1
0.01
Th1
Th2
prime
boost
5 ug posf-F
10^10 Ad26.F
10^10 Ad26.F
10^10 Ad26.F
10^10 Ad26.F
Fl-RSV
-
-
10^10 Ad26.F
5 µg post-F
0.5 µg post-F
Fl-RSV

Fig. 30

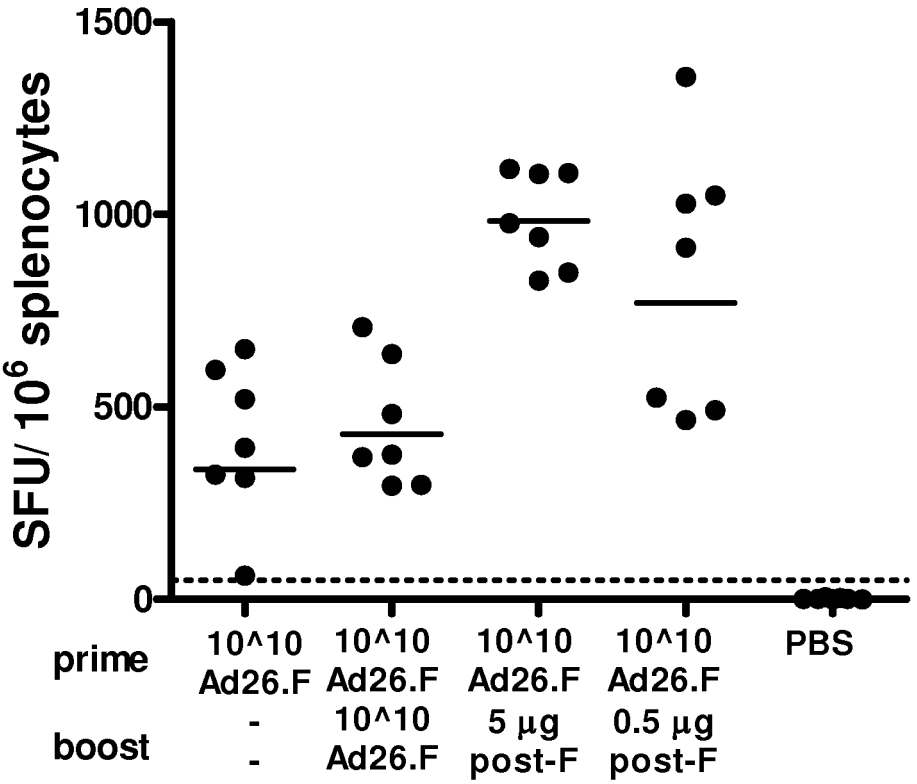

1500
1000
500
0
SFU/ 10^6 splenocytes
prime
boost
10^10 Ad26.F
-
10^10 Ad26.F
10^10 Ad26.F
5 µg post-F
10^10 Ad26.F
0.5 µg post-F
PBS

Fig. 31