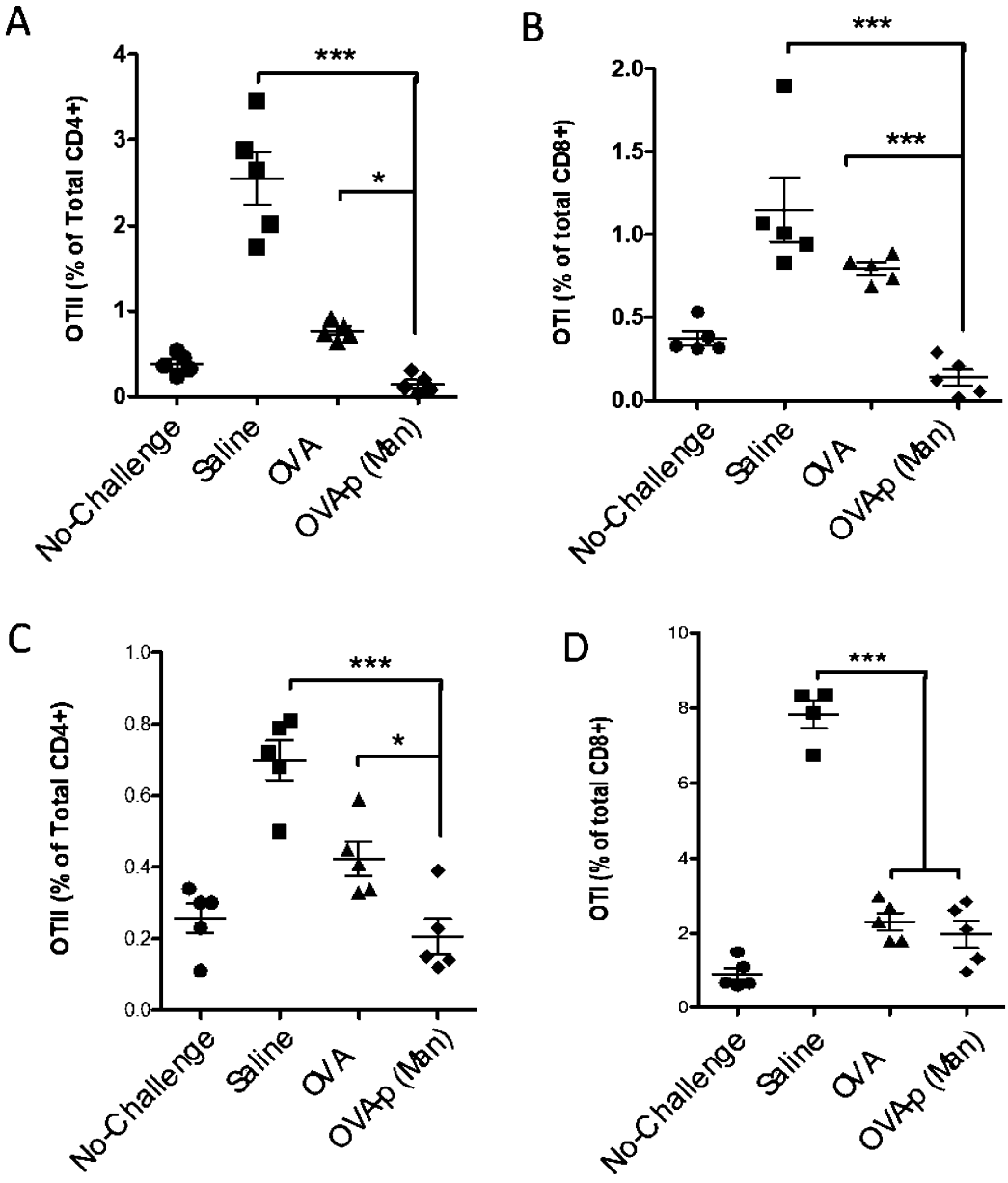
A
OTII (% of Total CD4+)
***
*
No-Challenge
Saline
OVA
OVAp (Man)
B
OTI (% of total CD8+)
***
***
No-Challenge
Saline
OVA
OVAp (Man)
C
OTII (% of Total CD4+)
***
*
No-Challenge
Saline
OVA
OVAp (Man)
D
OTI (% of total CD8+)
***
No-Challenge
Saline
OVA
OVAp (Man)

FIG. 1A-D

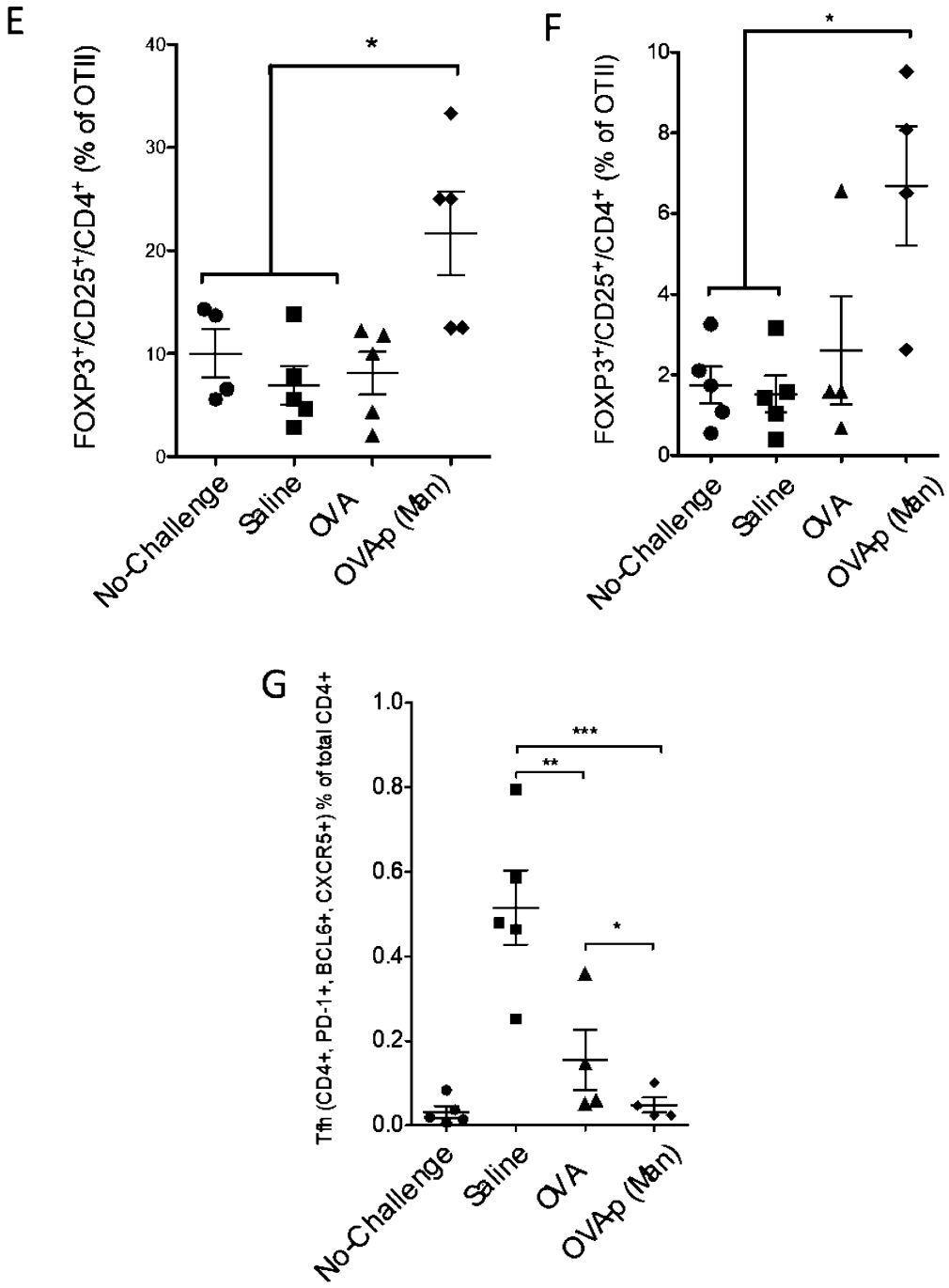
E
FOXP3+/CD25+/CD4+ (% of OTII)
40
30
20
10
0
*
No-Challenge
Saline
OVA
OVAp (Man)
F
FOXP3+/CD25+/CD4+ (% of OTII)
10
8
6
4
2
0
*
No-Challenge
Saline
OVA
OVAp (Man)
G
Tfh (CD4+, PD-1+, BCL6+, CXCR5+) % of total CD4+
1.0
0.8
0.6
0.4
0.2
0.0
***
**
*
No-Challenge
Saline
OVA
OVAp (Man)

FIG. 1E-G

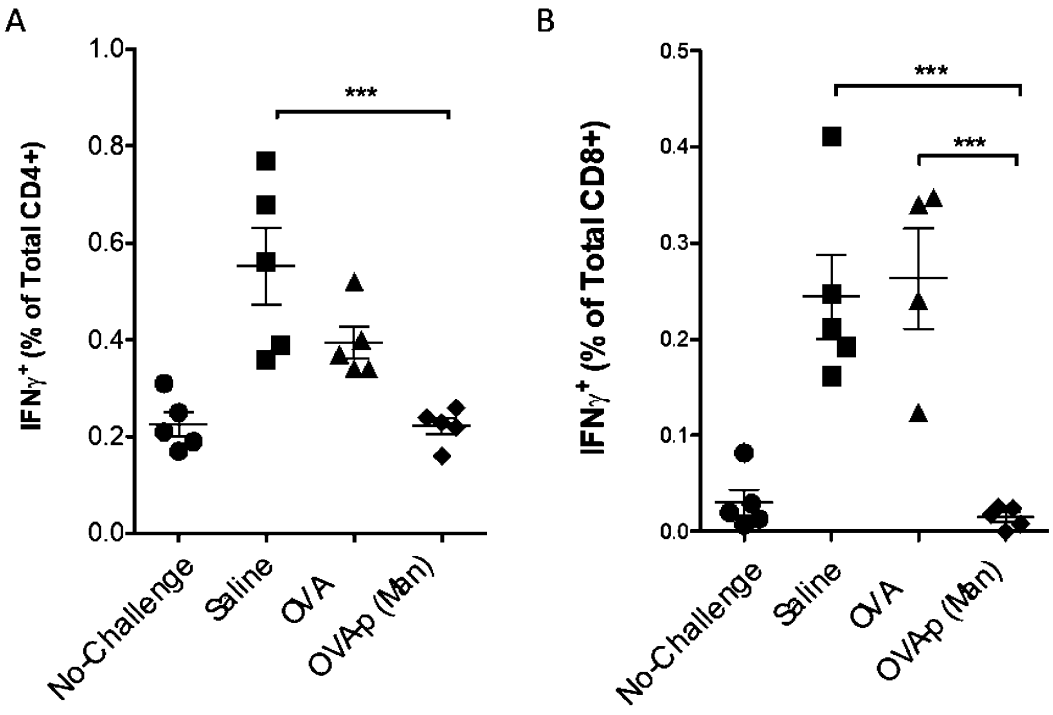
A
B
IFNγ+ (% of Total CD4+)
IFNγ+ (% of Total CD8+)
1.0
0.8
0.6
0.4
0.2
0.0
0.5
0.4
0.3
0.2
0.1
0.0
***
***
***
No-Challenge
Saline
OVA
OVA-p (Man)

FIG. 2A-B

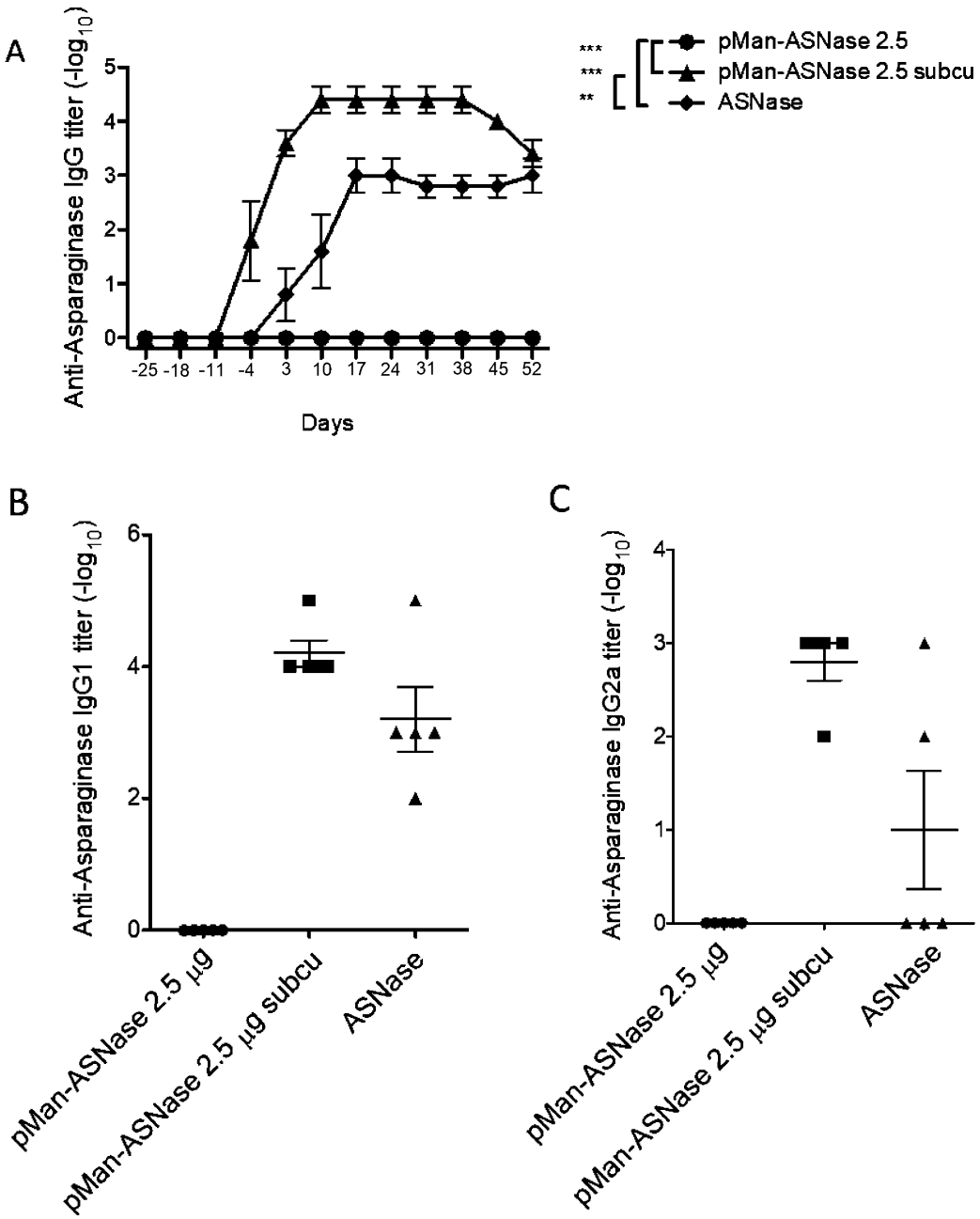
A
Anti-Asparaginase IgG titer (-log10)
5
4
3
2
1
0
-25 -18 -11 -4 3 10 17 24 31 38 45 52
Days
***
***
**
pMan-ASNase 2.5
pMan-ASNase 2.5 subcu
ASNase
B
Anti-Asparaginase IgG1 titer (-log10)
6
4
2
0
pMan-ASNase 2.5 µg
pMan-ASNase 2.5 µg subcu
ASNase
C
Anti-Asparaginase IgG2a titer (-log10)
4
3
2
1
0
pMan-ASNase 2.5 µg
pMan-ASNase 2.5 µg subcu
ASNase

FIG. 3A-C

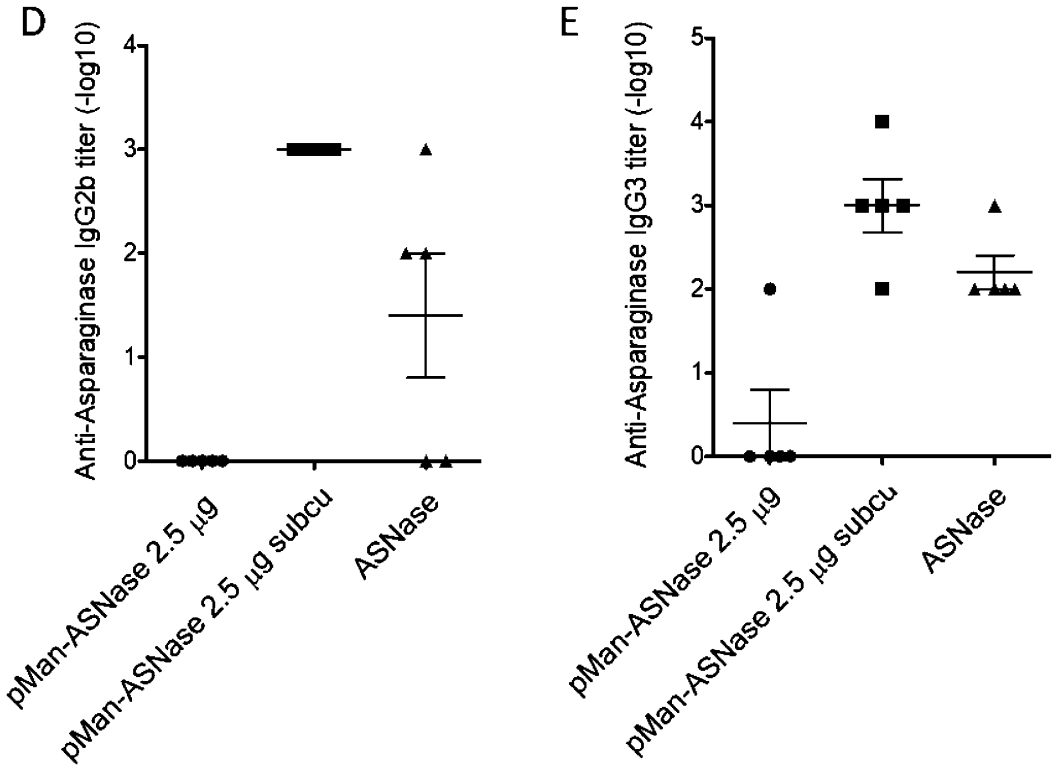
D
Anti-Asparaginase IgG2b titer (-log10)
0
1
2
3
4
pMan-ASNase 2.5 µg
pMan-ASNase 2.5 µg subcu
ASNase
E
Anti-Asparaginase IgG3 titer (-log10)
0
1
2
3
4
5
pMan-ASNase 2.5 µg
pMan-ASNase 2.5 µg subcu
ASNase

FIG. 3D-E

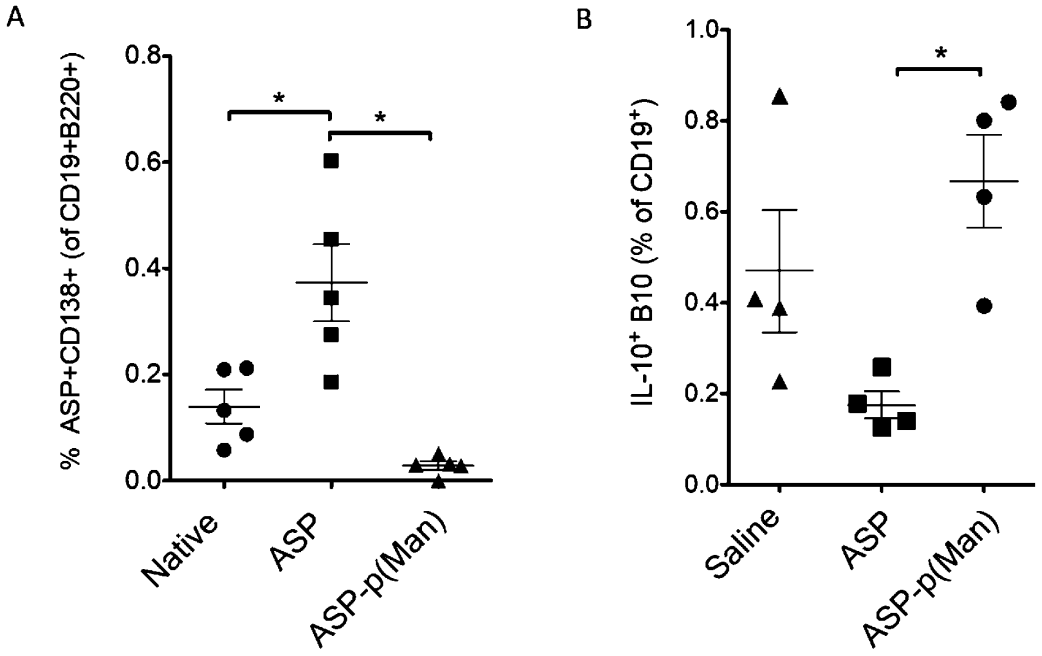
A
% ASP+CD138+ (of CD19+B220+)
0.8
0.6
0.4
0.2
0.0
*
*
Native
ASP
ASP-p(Man)
B
IL-10+ B10 (% of CD19+)
1.0
0.8
0.6
0.4
0.2
0.0
*
Saline
ASP
ASP-p(Man)

FIG. 4A-B

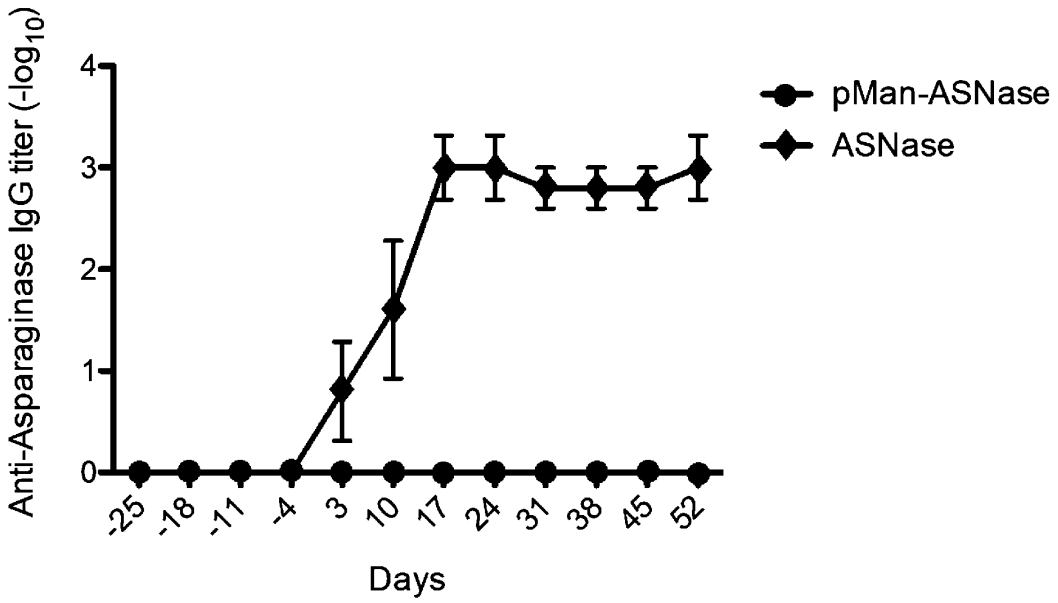
Anti-Asparaginase IgG titer (-log10)
4
3
2
1
0
-25
-18
-11
-4
3
10
17
24
31
38
45
52
Days
pMan-ASNase
ASNase

FIG. 5

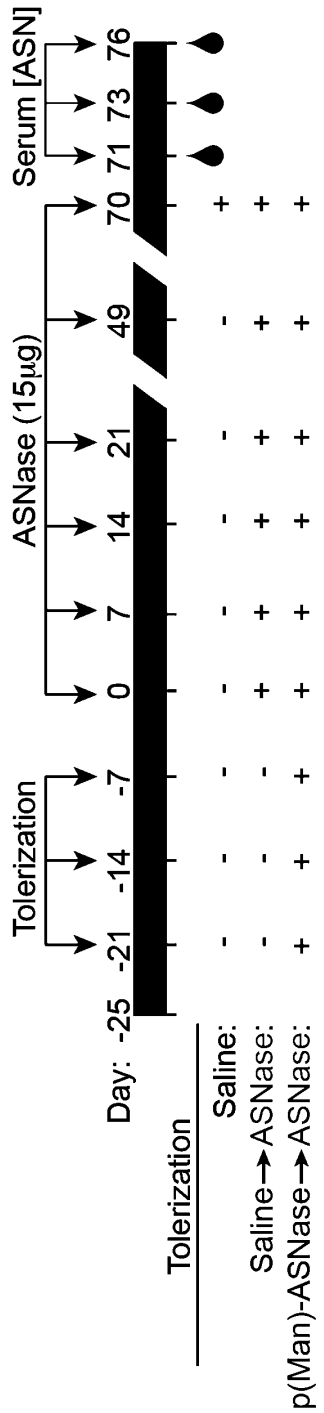
Tolerization
ASNase (15μg)
Serum [ASN]
Day: -25 -21 -14 -7 0 7 14 21 49 70 71 73 76
Tolerization
Saline: - - - - + + + + + + + + +
Saline→ASNase: - - - - + + + + + + + + +
p(Man)-ASNase→ASNase: + + + + + + + + + + + + +

FIG. 6

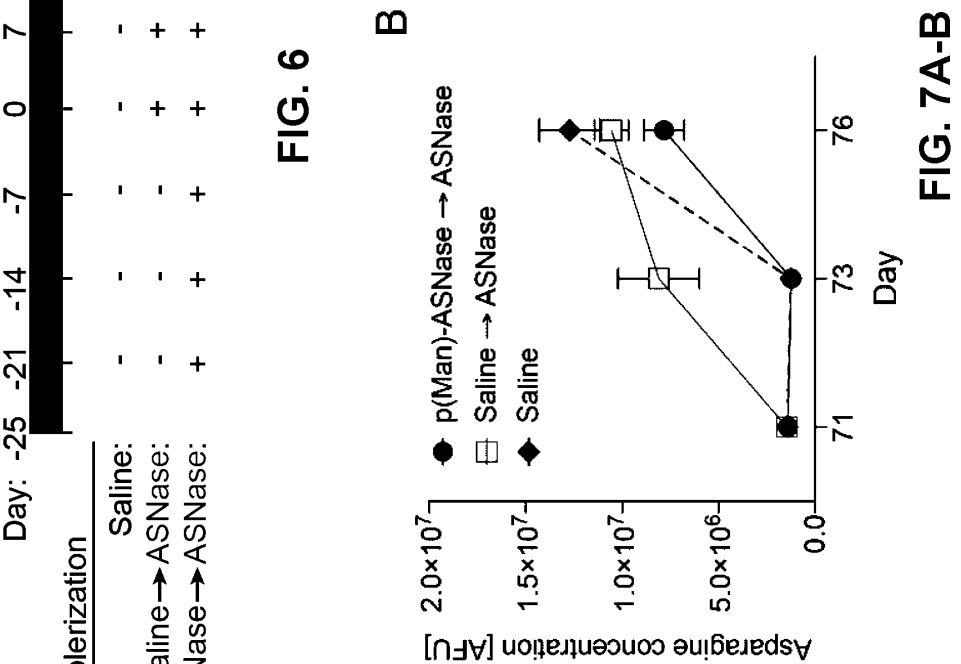
A
Asparagine concentration [AFU]
2.0×10^7
1.5×10^7
1.0×10^7
5.0×10^6
0.0
71
73
76
Day
p(Man)-ASNase → ASNase
Saline → ASNase
Saline
B
Asparagine Con. Day 73 [AFU]
10^8
10^7
10^6
r = 0.8
0
1
2
3
4
αASNase IgG Titer (-Log10)
p(Man)-ASNase→ASNase
Saline→ASNase

FIG. 7A-B