FIG. 1

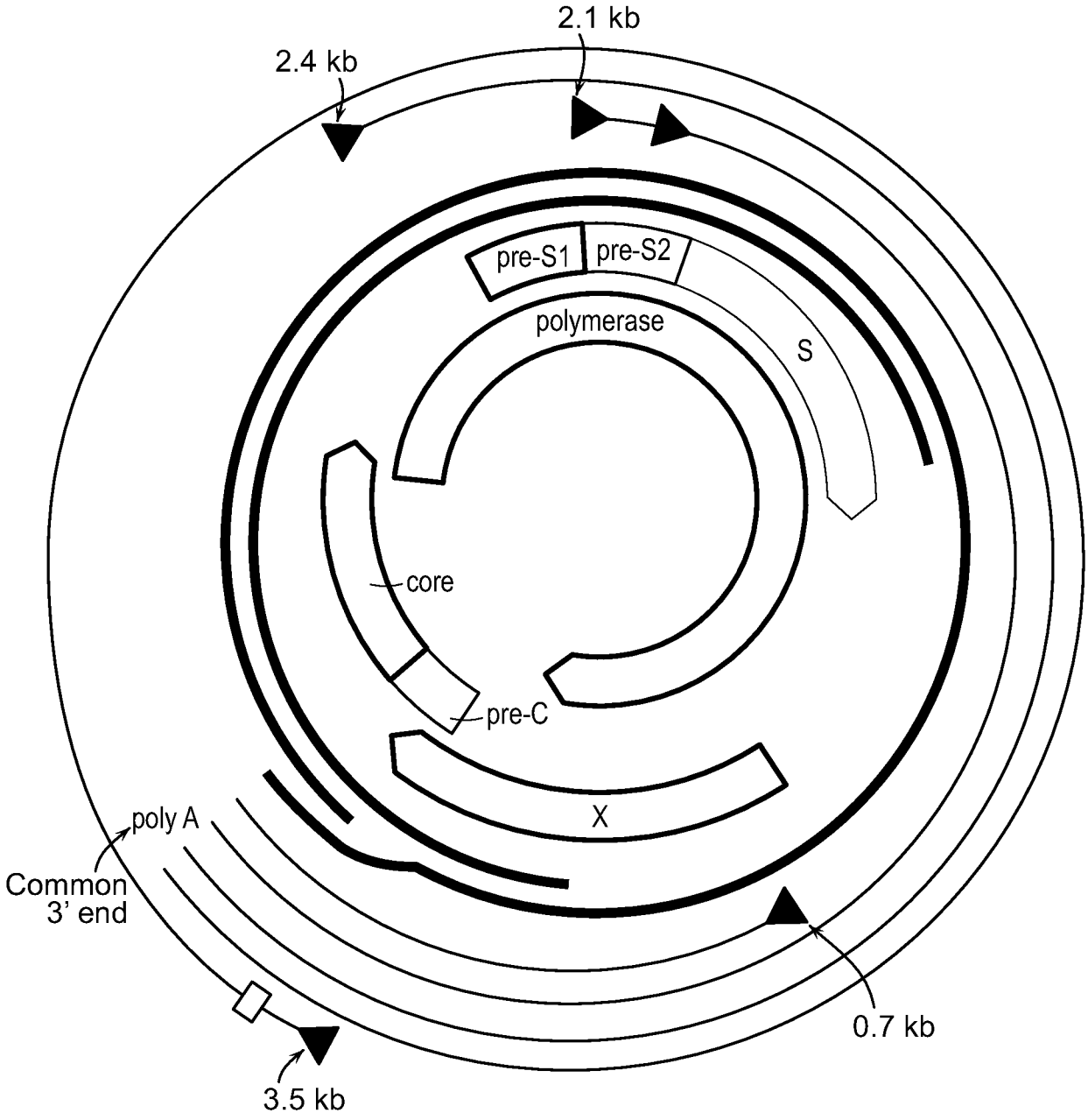

2.1 kb
2.4 kb
pre-S1
pre-S2
polymerase
S
core
pre-C
X
poly A
Common
3' end
0.7 kb
3.5 kb

FIG. 2A

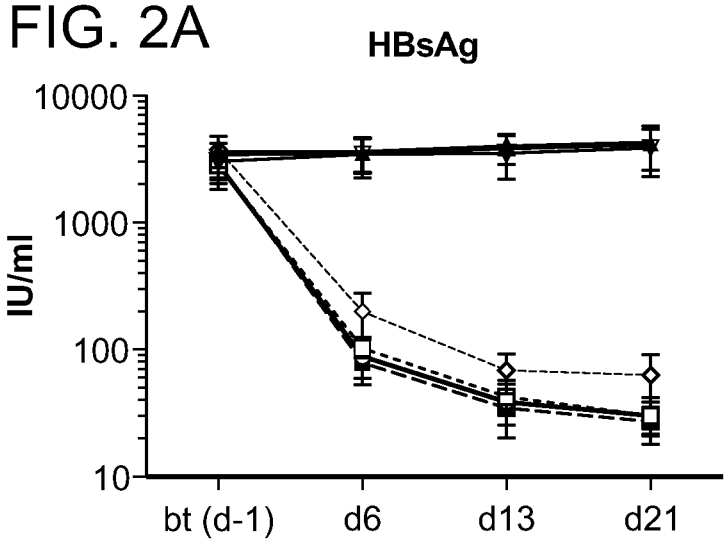


FIG. 2B

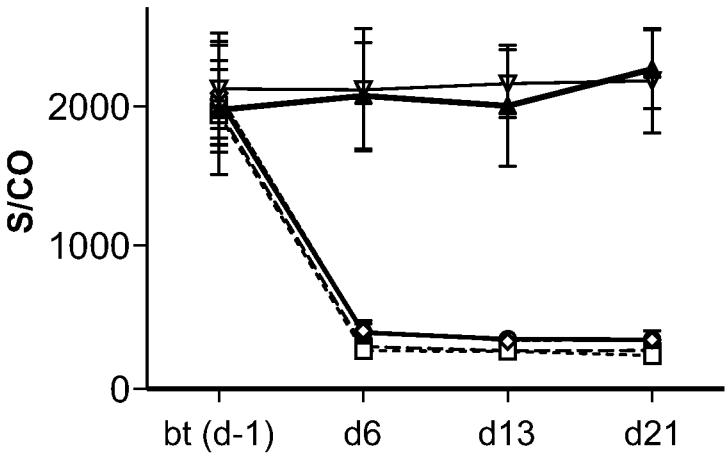


FIG. 2C

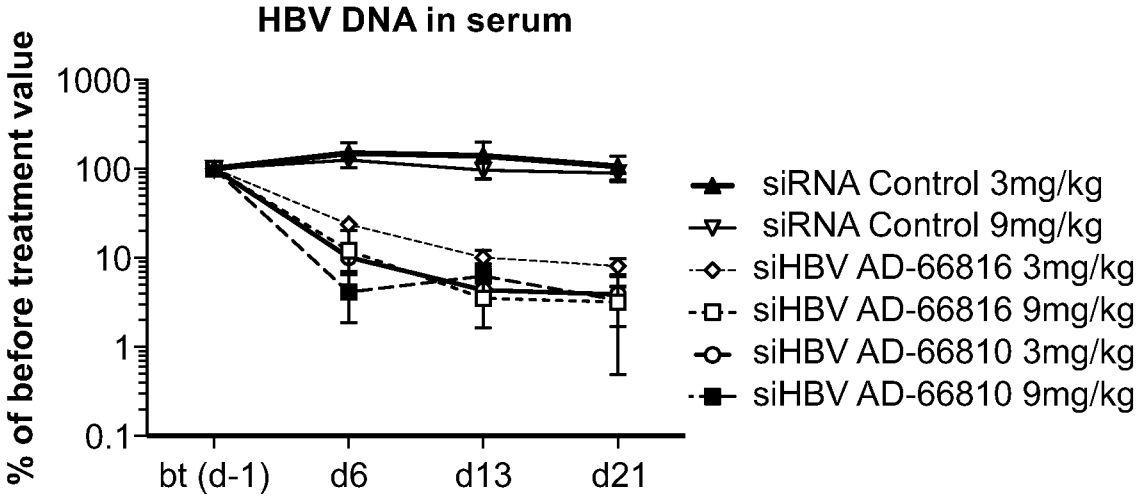


FIG. 2D

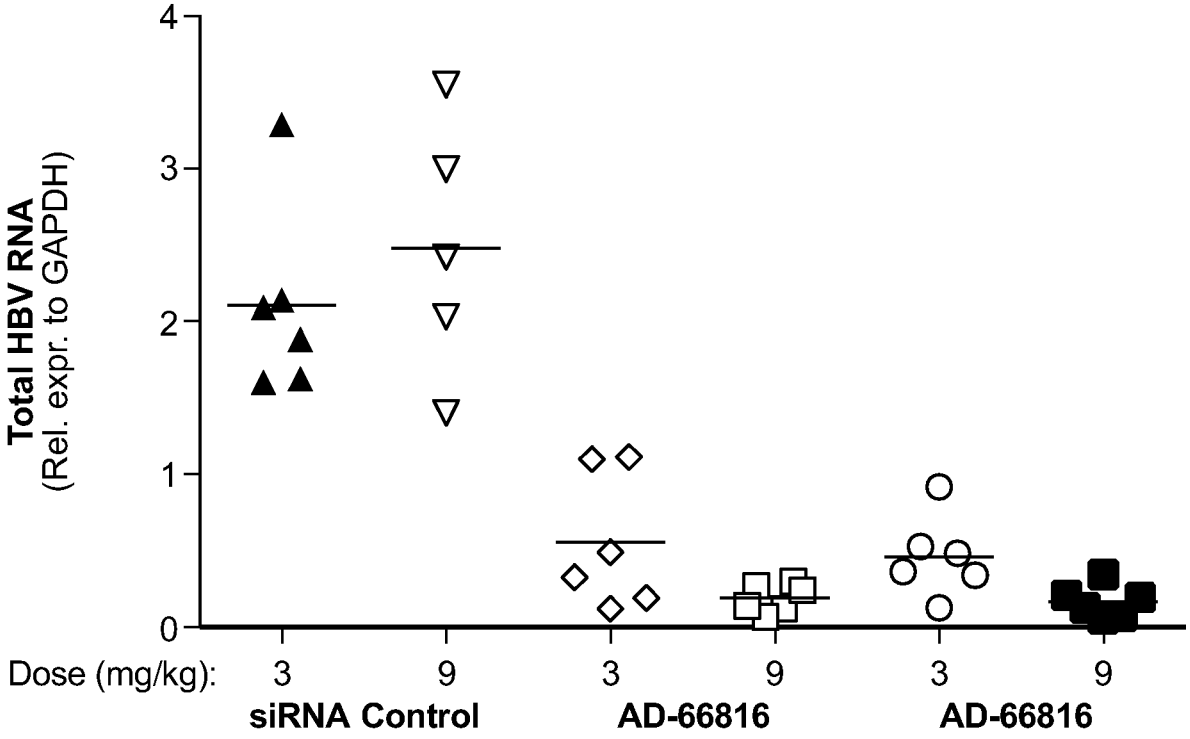

Total HBV RNA
(Rel. expr. to GAPDH)
4
3
2
1
0
Dose (mg/kg):
3
9
3
9
3
9
siRNA Control
AD-66816
AD-66816

FIG. 2E

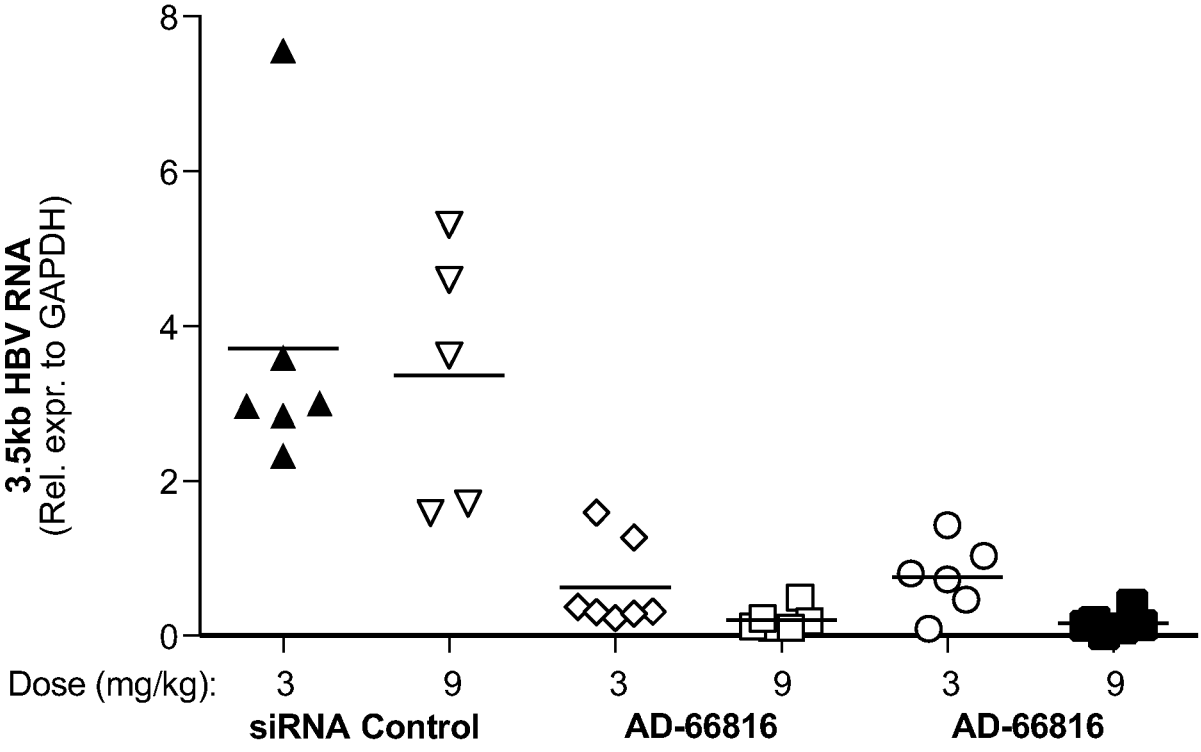
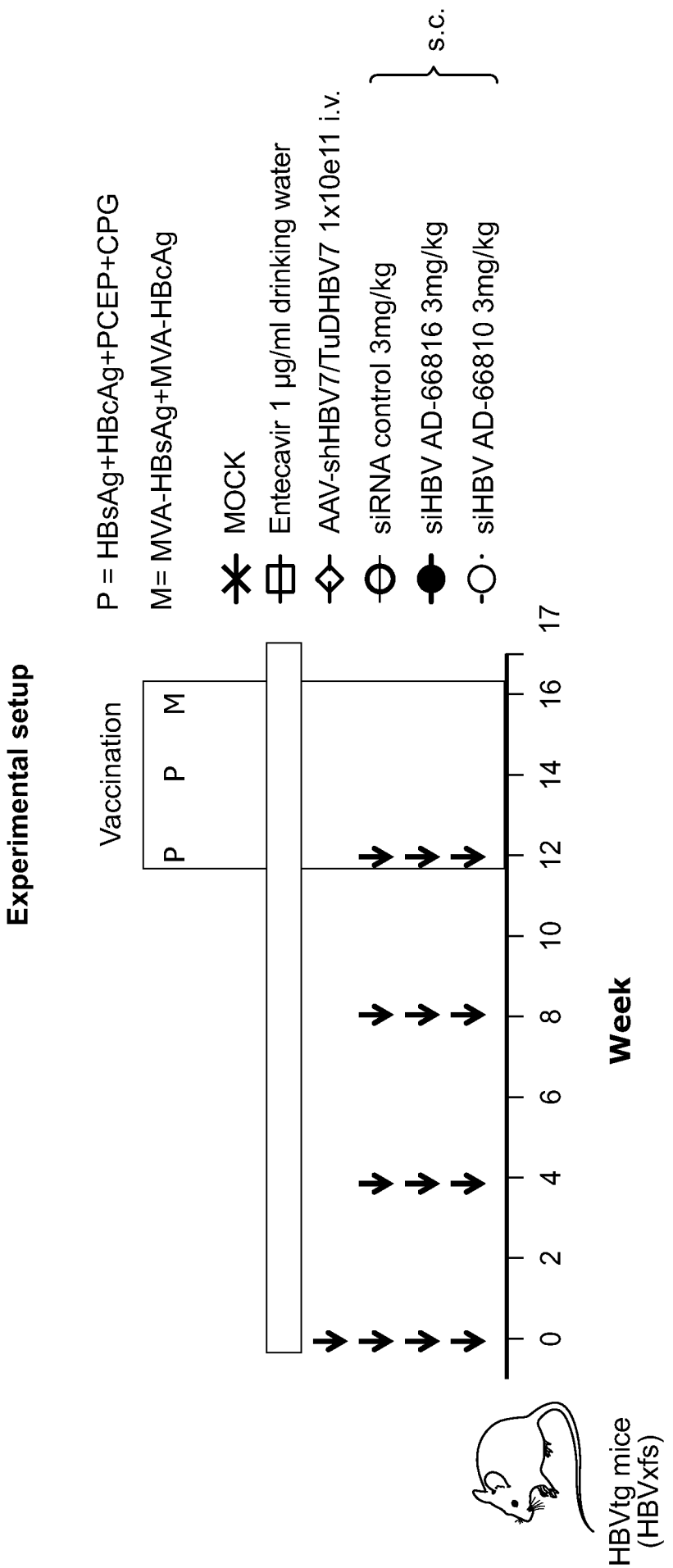

3.5kb HBV RNA
(Rel. expr. to GAPDH)
8
6
4
2
0
Dose (mg/kg):
3
9
3
9
3
9
siRNA Control
AD-66816
AD-66816

FIG. 3


Experimental setup
Vaccination
P P M
P = HBsAg+HBcAg+PCEP+CPG
M= MVA-HBsAg+MVA-HBcAg
MOCK
Entecavir 1 µg/ml drinking water
AAV-shHBV7/TuDHBV7 1x10e11 i.v.
siRNA control 3mg/kg
siHBV AD-66816 3mg/kg
siHBV AD-66810 3mg/kg
s.c.
0 2 4 6 8 10 12 14 16 17
Week
HBVtg mice
(HBVxfs)

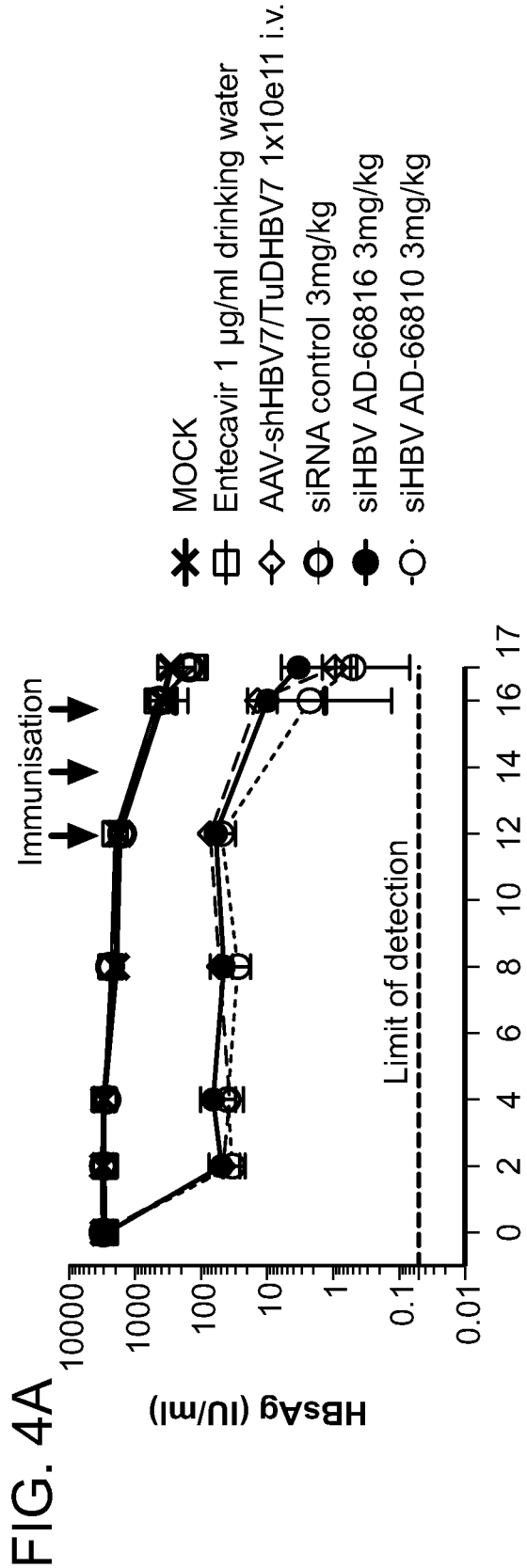


FIG. 4A

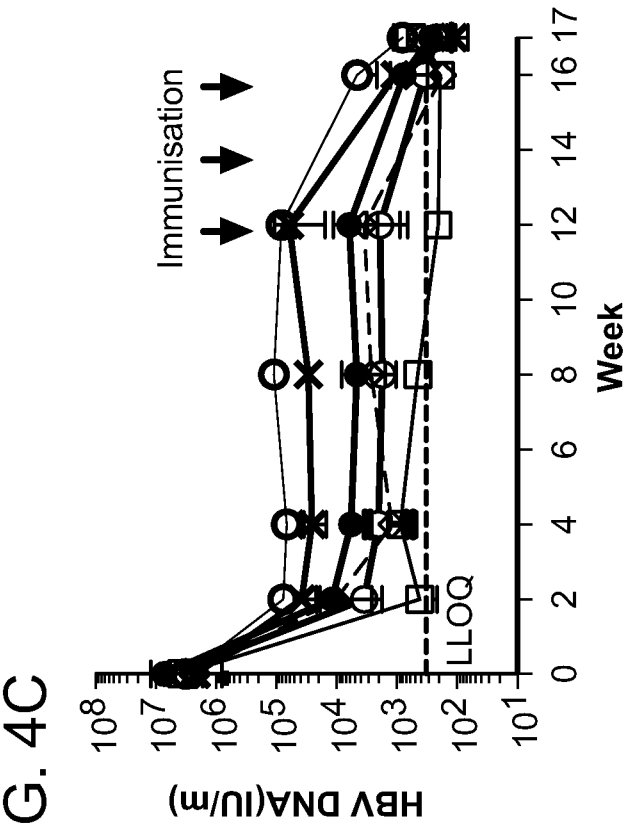


FIG. 4C

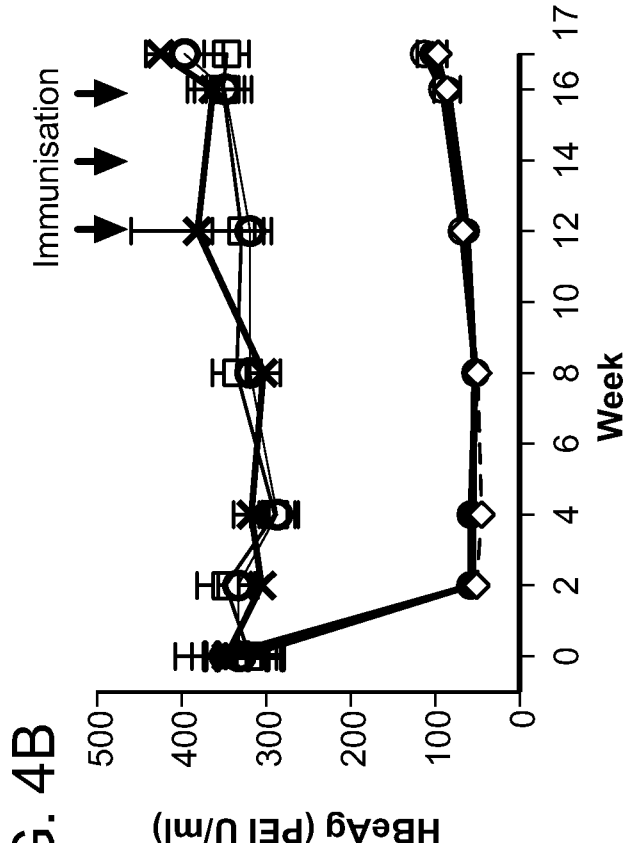


FIG. 4B

FIG. 5A

FIG. 5B

FIG. 5C

FIG. 5D

FIG. 5E

FIG. 5F

FIG. 6A

FIG. 6B

FIG. 6C

FIG. 7

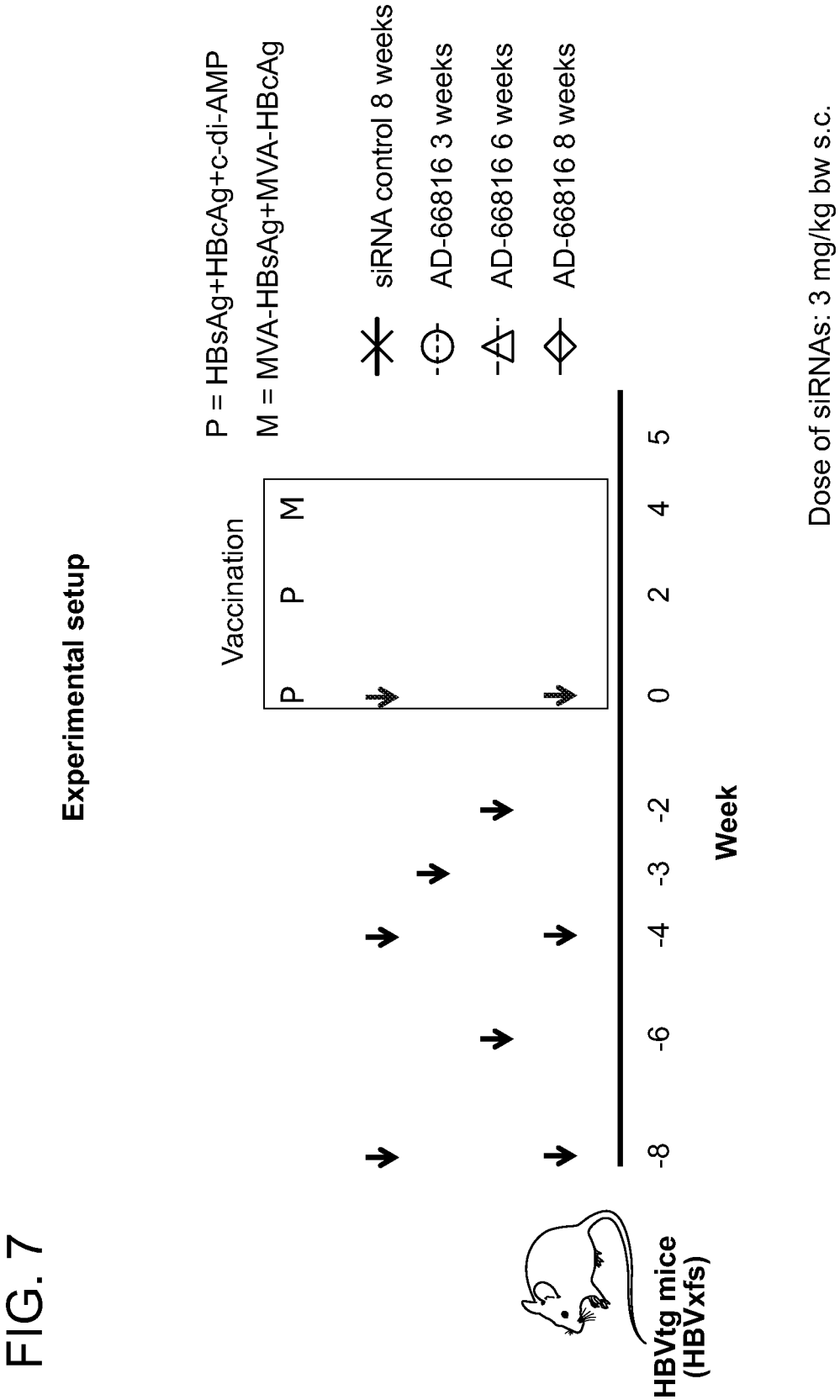

Experimental setup
P = HBsAg+HBcAg+c-di-AMP
M = MVA-HBsAg+MVA-HBcAg
Vaccination
P
P
M
siRNA control 8 weeks
AD-66816 3 weeks
AD-66816 6 weeks
AD-66816 8 weeks
-8
-6
-4
-3
-2
0
2
4
5
Week
HBVtg mice
(HBVxfs)
Dose of siRNAs: 3 mg/kg bw s.c.

FIG. 8A

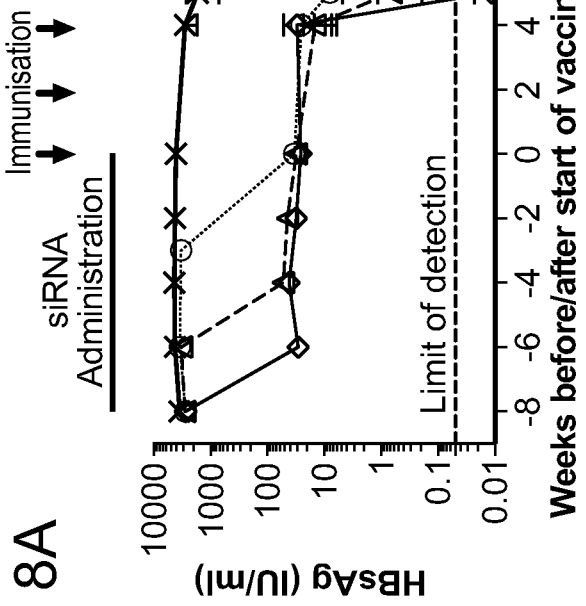


FIG. 8B

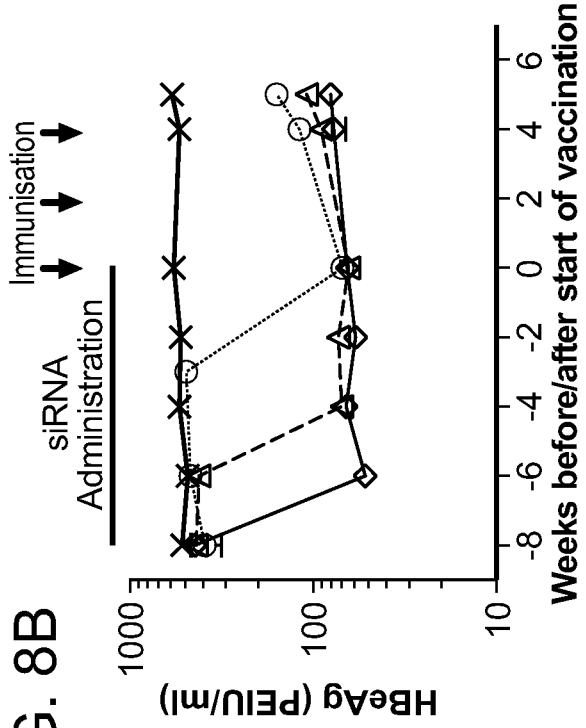
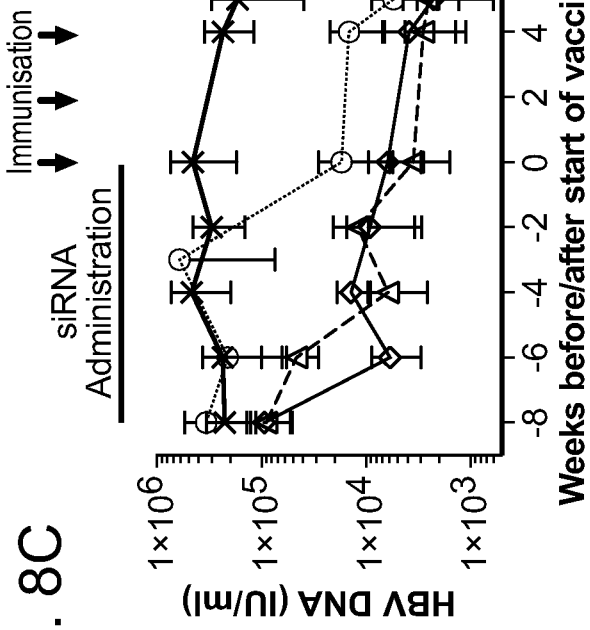


FIG. 8C



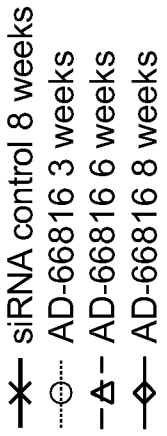


FIG. 9A

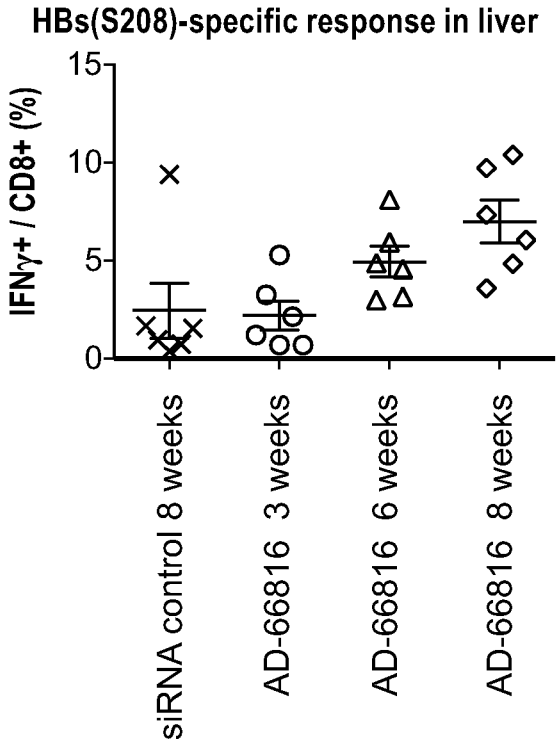


FIG. 9B

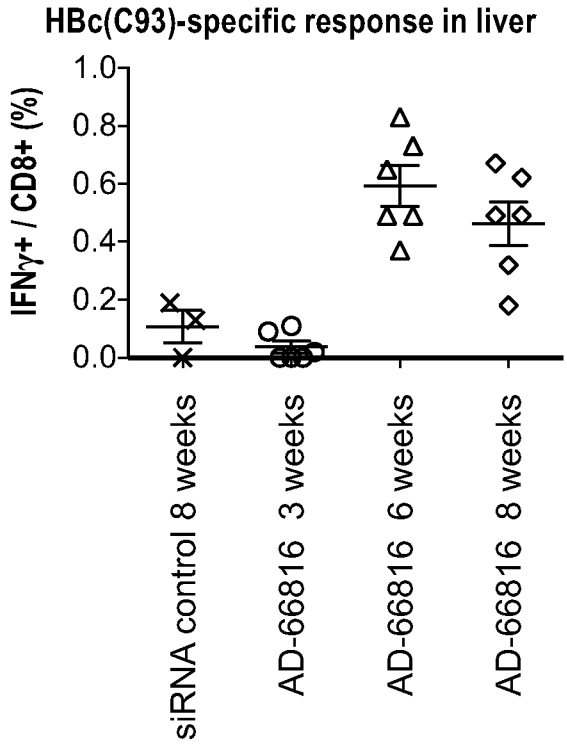


FIG. 9C

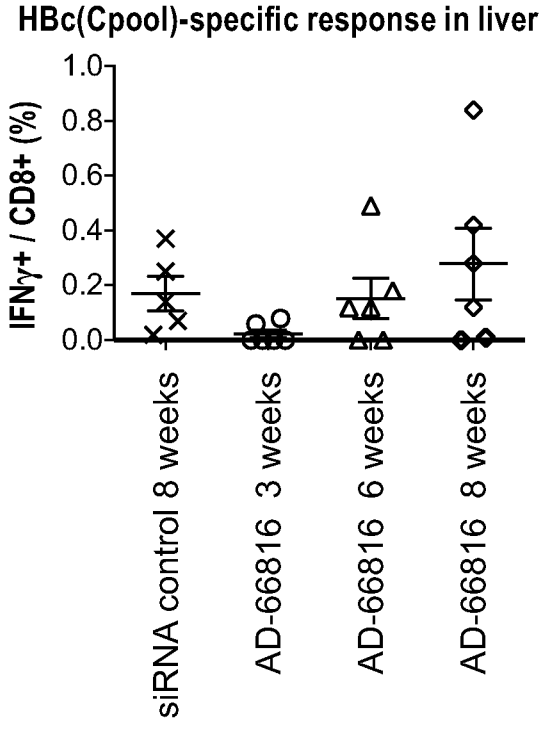


FIG. 9D

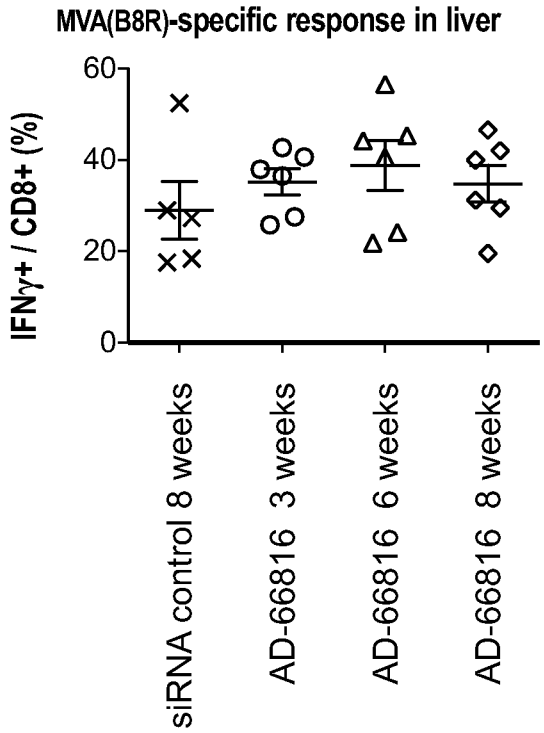


FIG. 10A

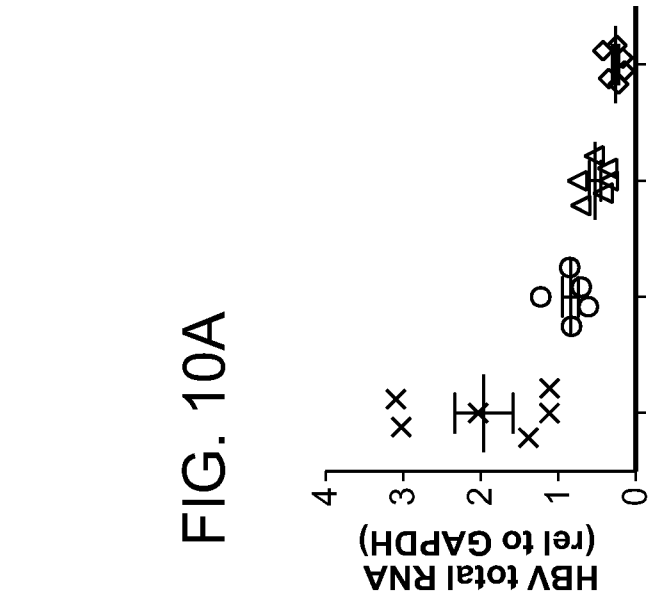


FIG. 10B

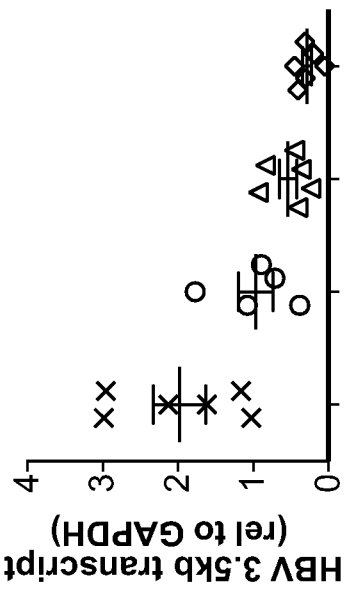
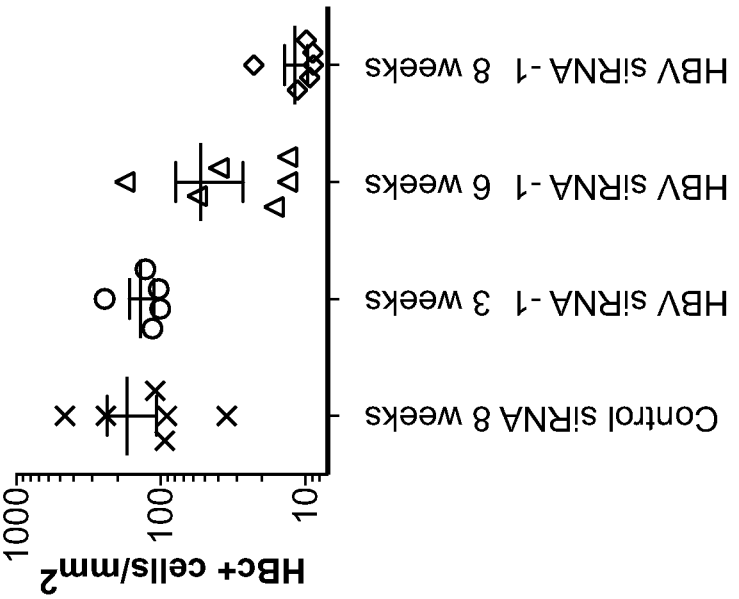


FIG. 10C



• All animals treated s.c. with 3 mg/kg bw AD-66816
• Termination 3 weeks after last vaccination

FIG. 11A

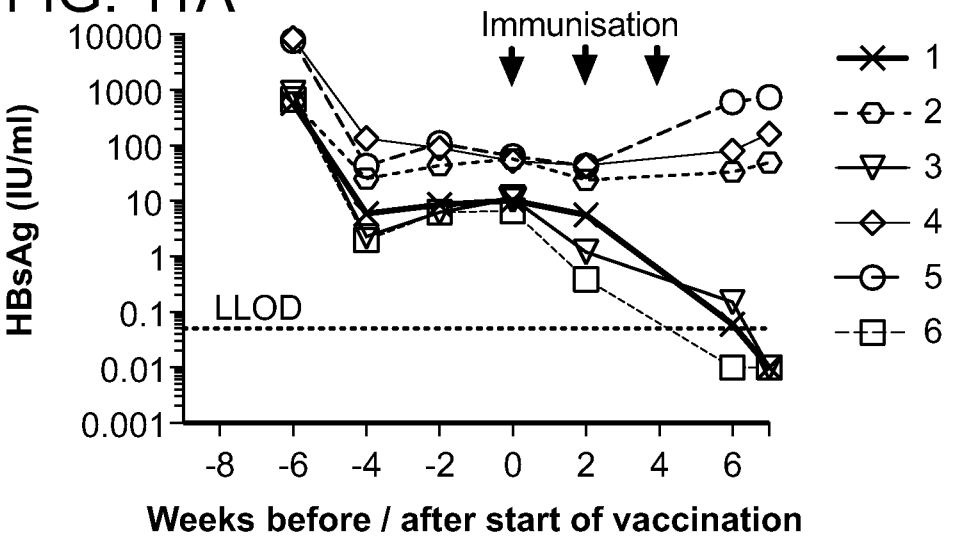


FIG. 11B

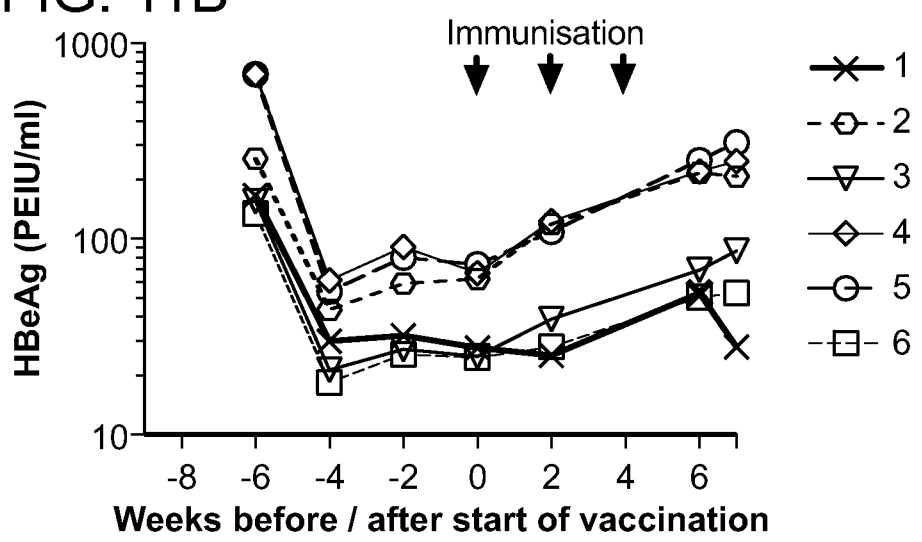


FIG. 11C

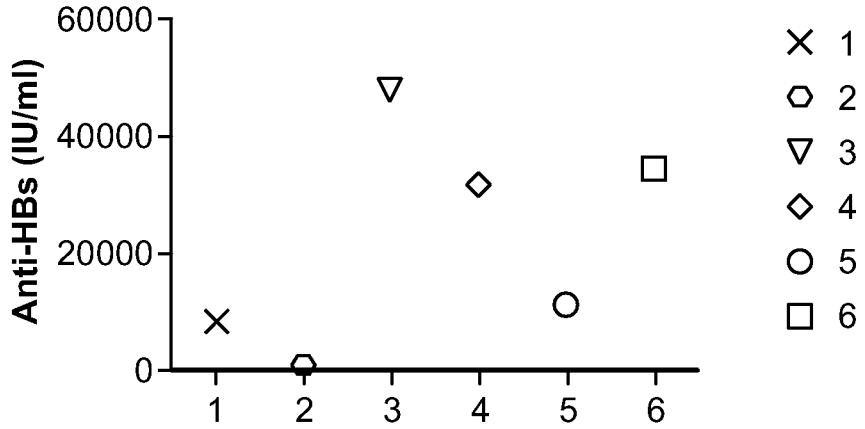


FIG. 11D

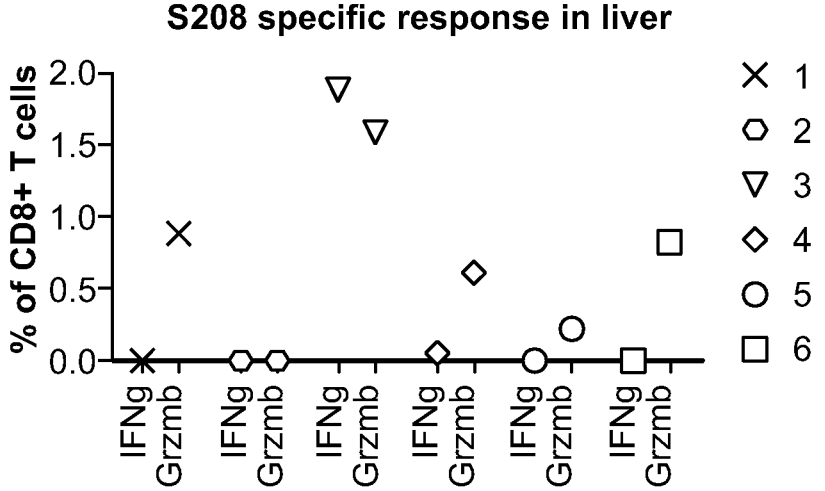


FIG. 12

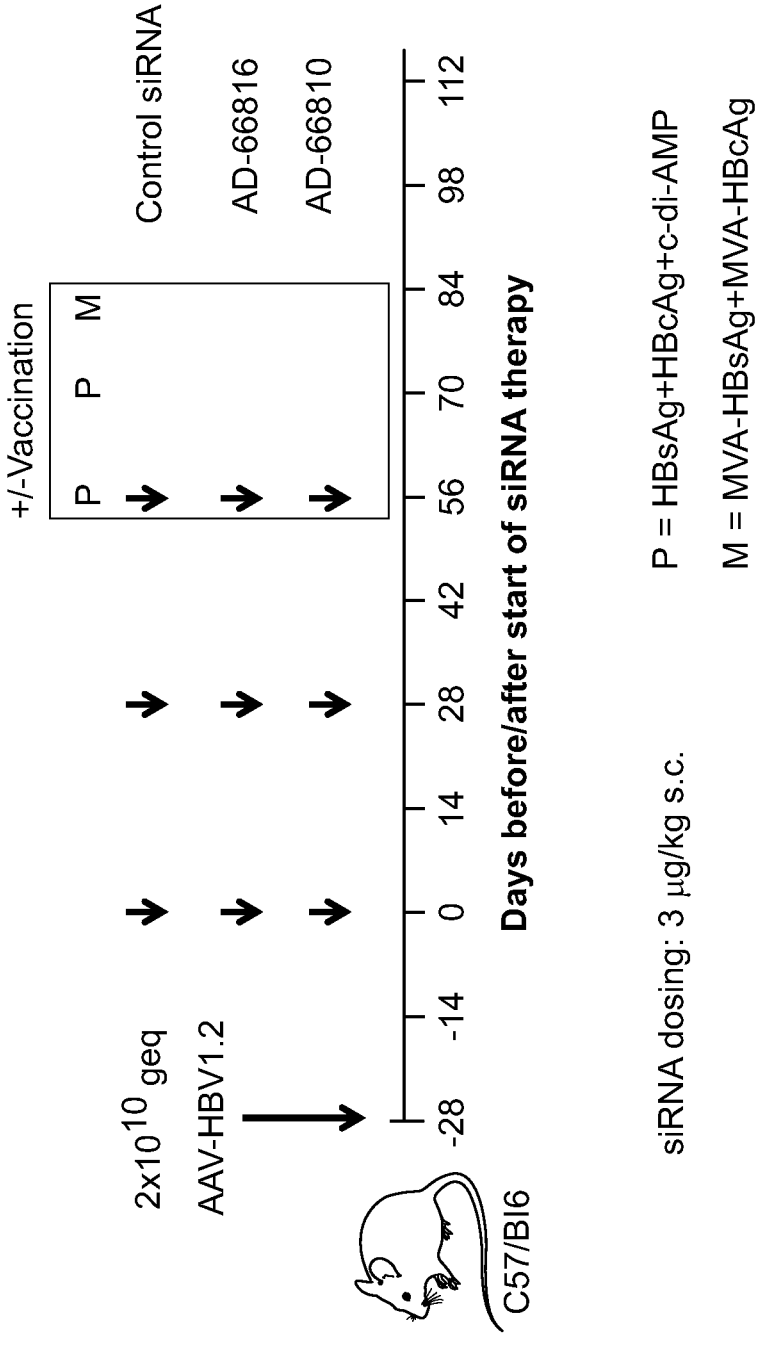

+/-Vaccination
P
P
M
Control siRNA
AD-66816
AD-66810
2x10^10 geq
AAV-HBV1.2
C57/Bl6
-28
-14
0
14
28
42
56
70
84
98
112
Days before/after start of siRNA therapy
siRNA dosing: 3 µg/kg s.c.
P = HBsAg+HBcAg+c-di-AMP
M = MVA-HBsAg+MVA-HBcAg

FIG. 13A

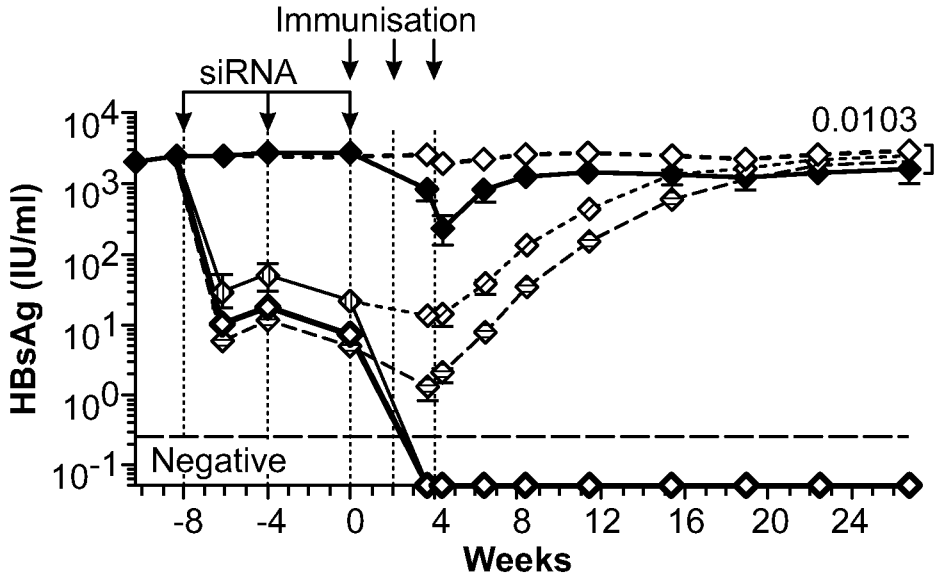
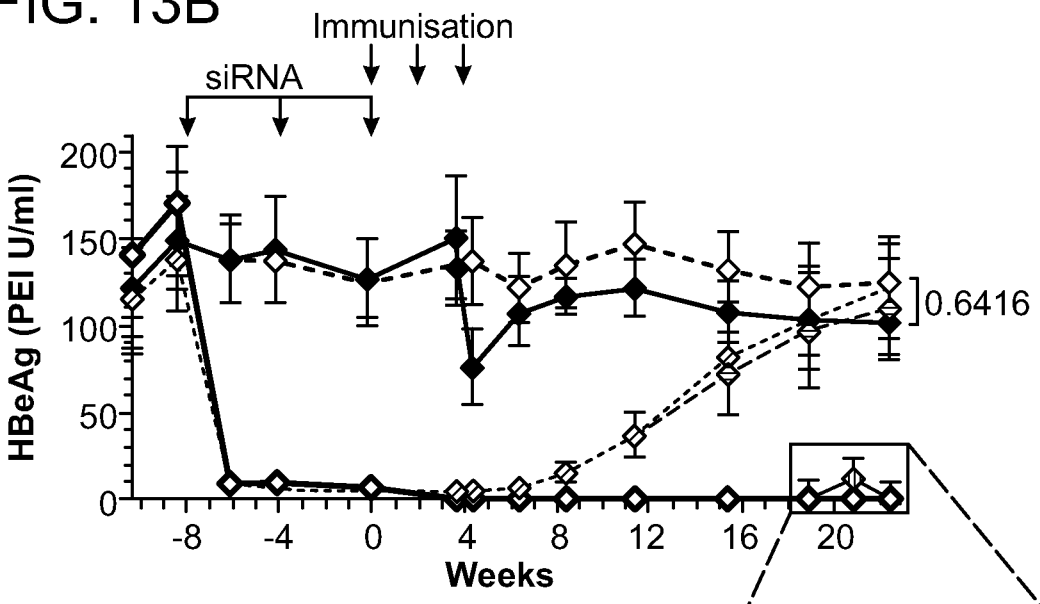


FIG. 13B



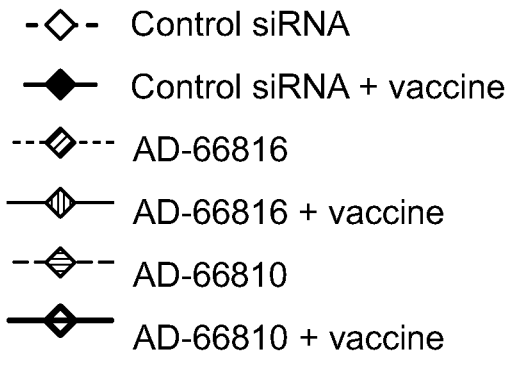
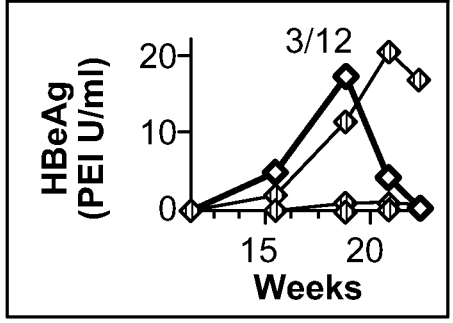


FIG. 13C



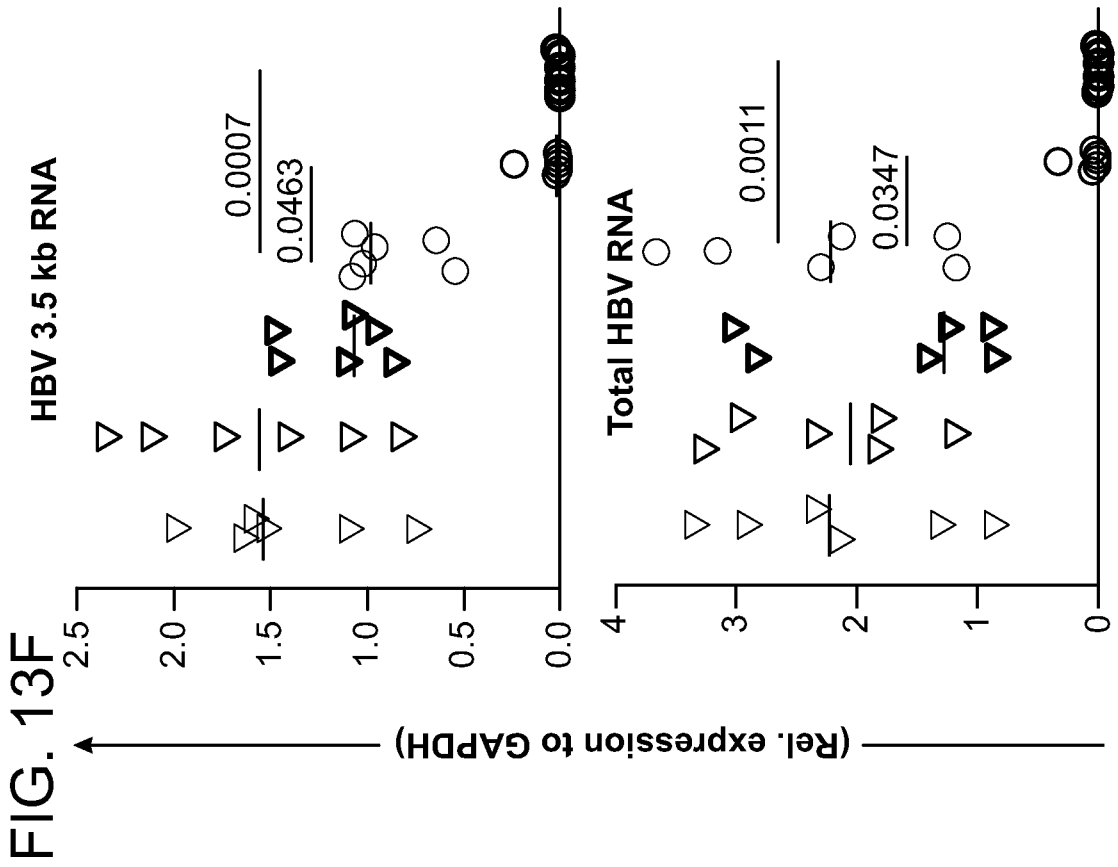


FIG. 13F

FIG. 13G

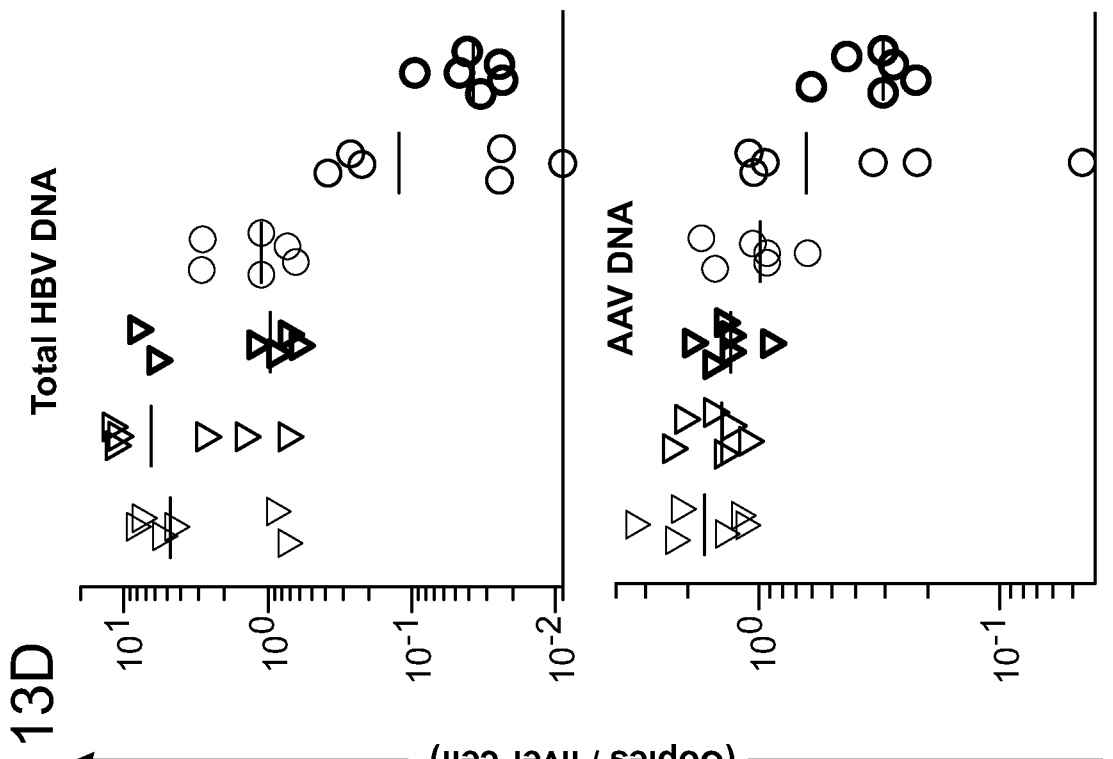


FIG. 13D

FIG. 13E

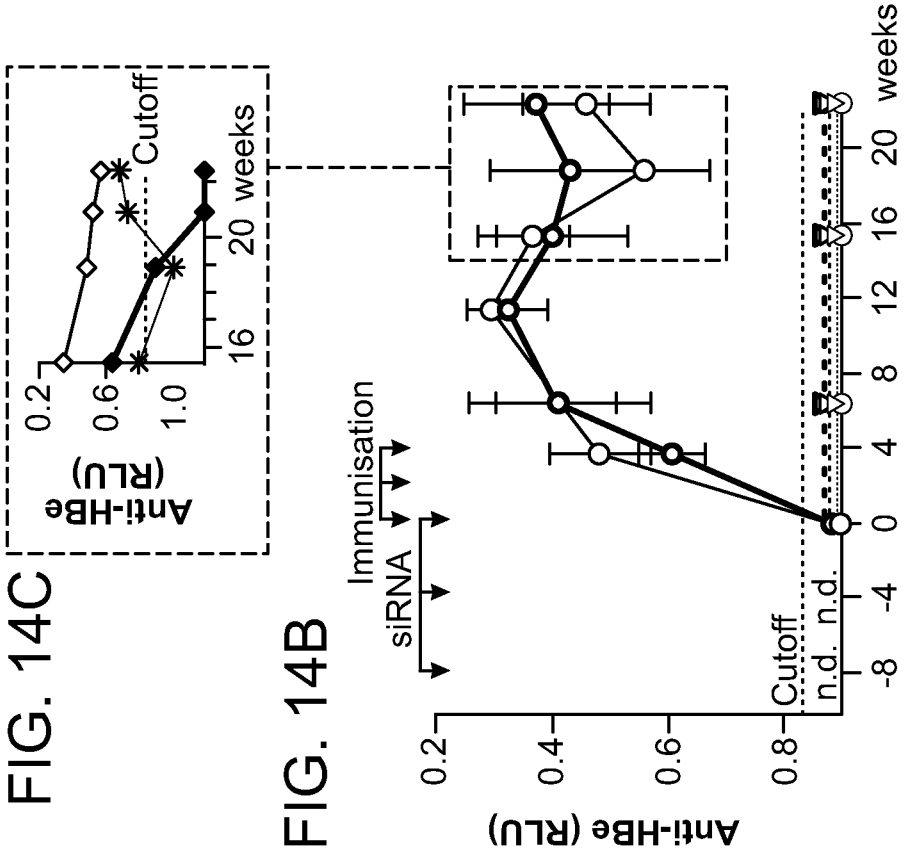


FIG. 14C

FIG. 14B

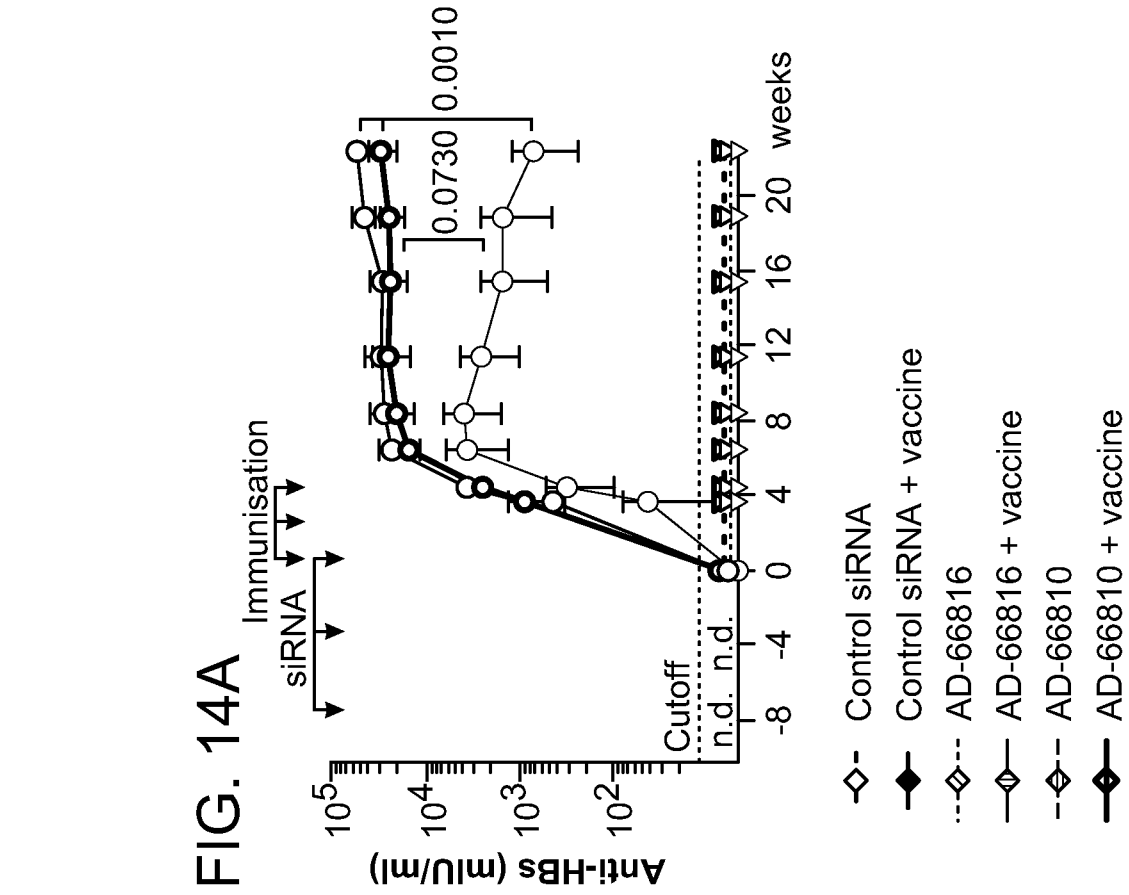


FIG. 14A

FIG. 15A

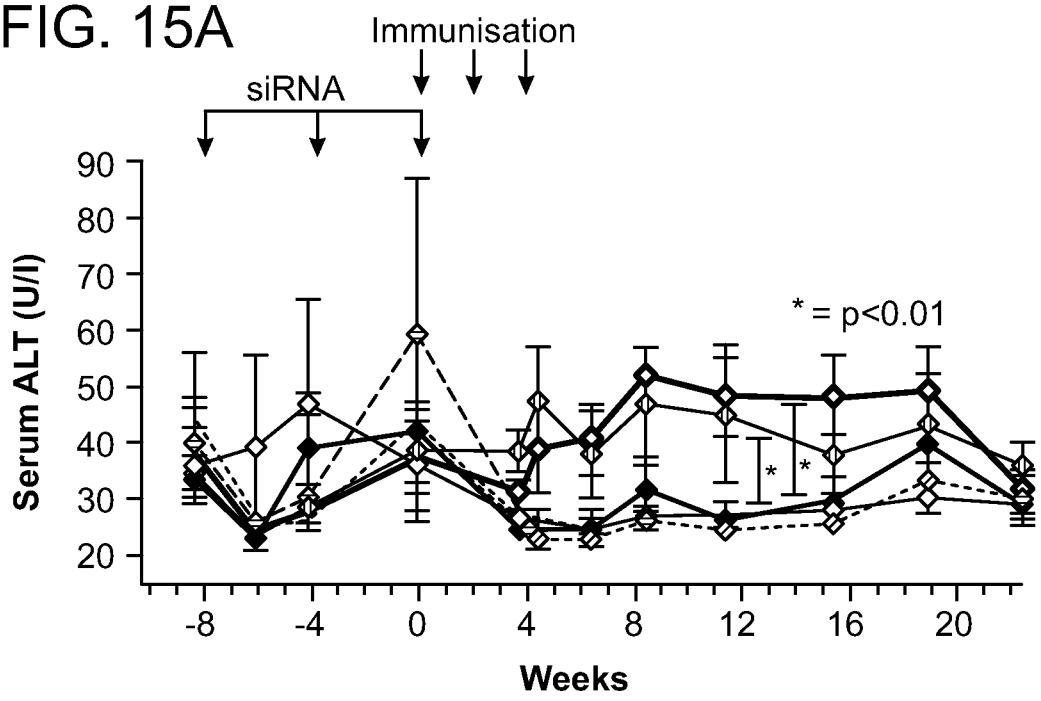


FIG. 15B

