Figure 1

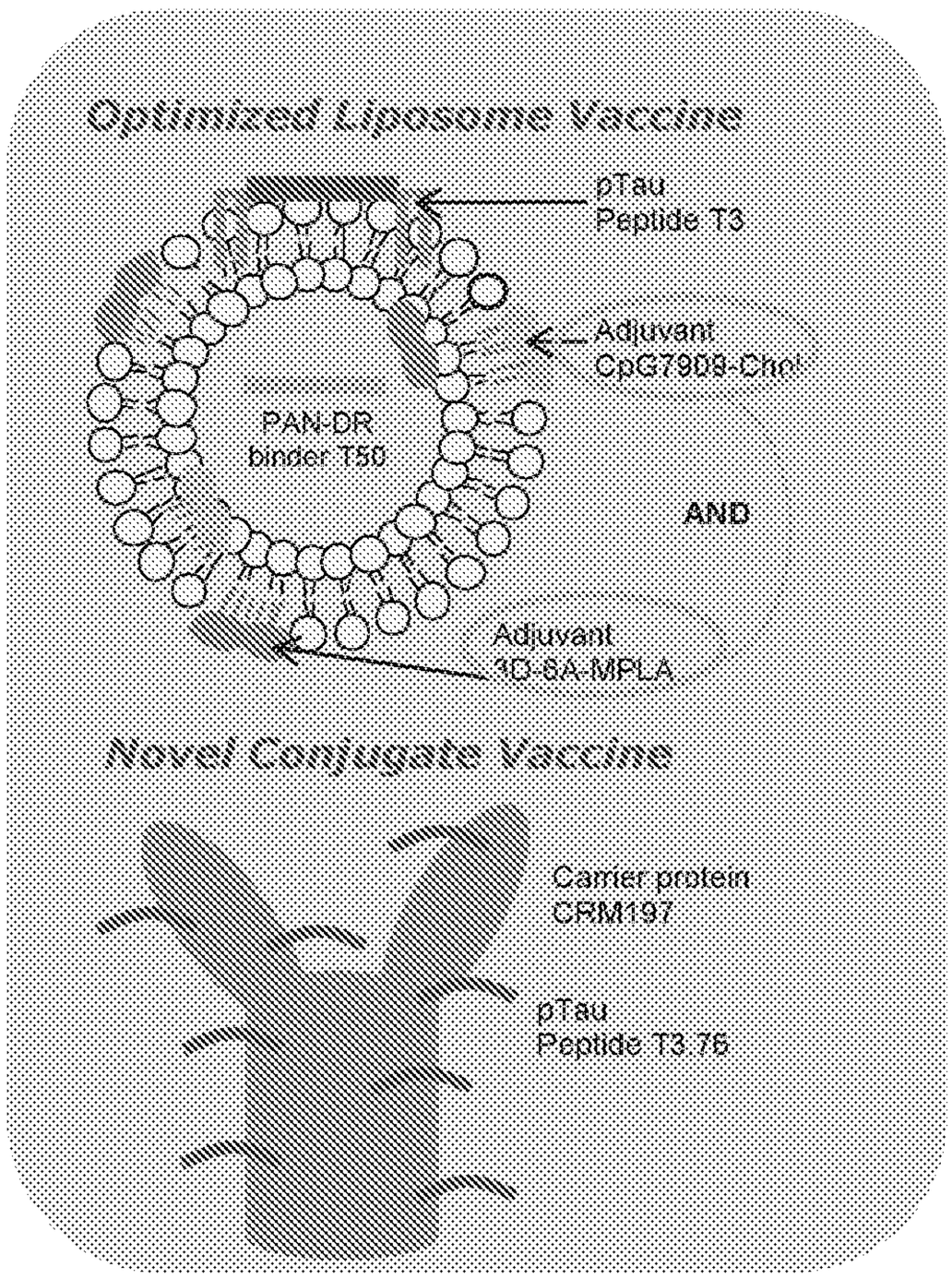

Optimized Liposome Vaccine
pTau
Peptide T3
Adjuvant
CpG7909-Chol
PAN-DR
binder T50
AND
Adjuvant
3D-6A-MPLA
Novel Conjugate Vaccine
Carrier protein
CRM197
pTau
Peptide T3 76

Figure 2

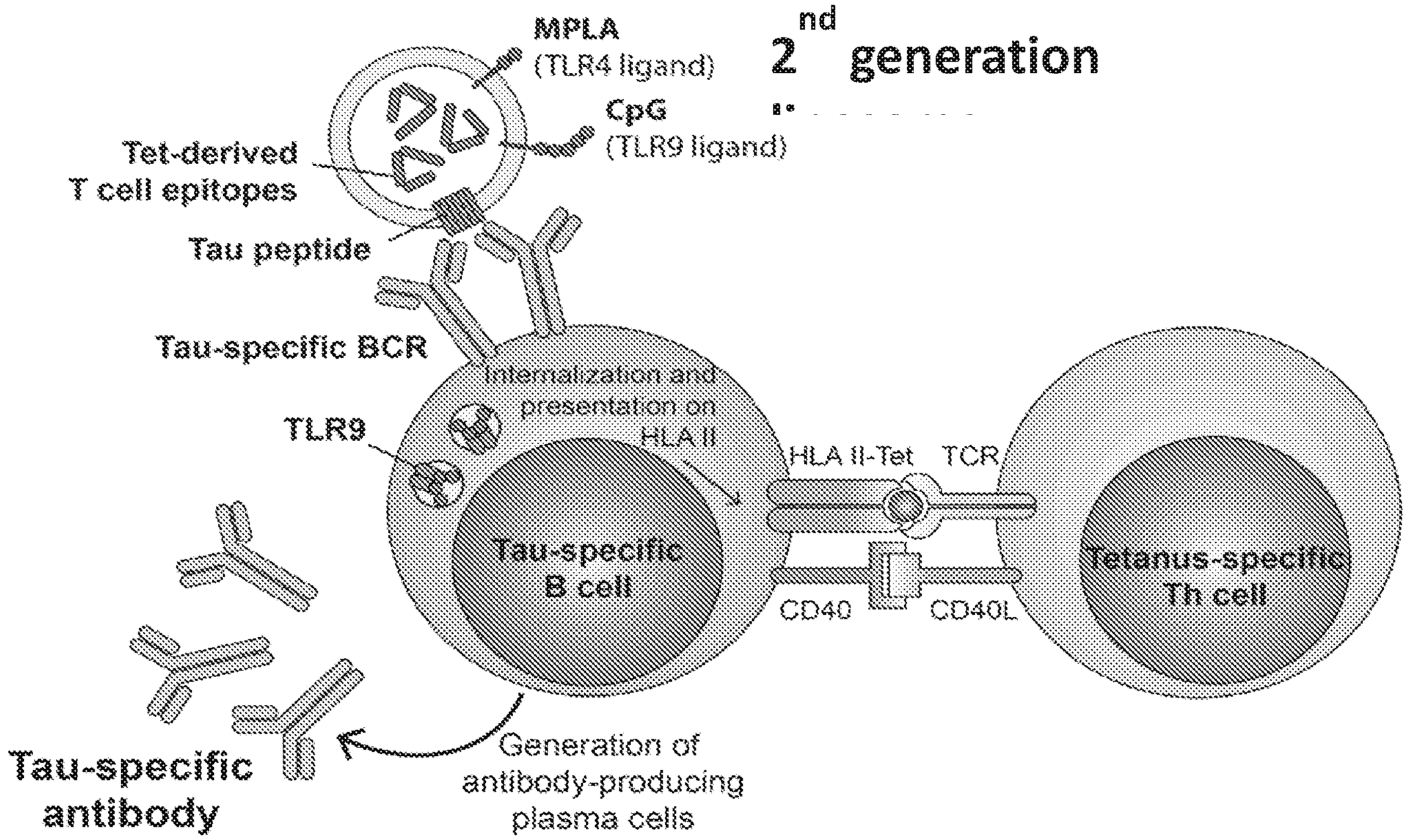

MPLA
(TLR4 ligand)
2nd generation
CpG
(TLR9 ligand)
Tet-derived
T cell epitopes
Tau peptide
Tau-specific BCR
Internalization and
presentation on
HLA II
TLR9
HLA II-Tet
TCR
Tau-specific
B cell
Tetanus-specific
Th cell
CD40
CD40L
Tau-specific
antibody
Generation of
antibody-producing
plasma cells

Figure 3

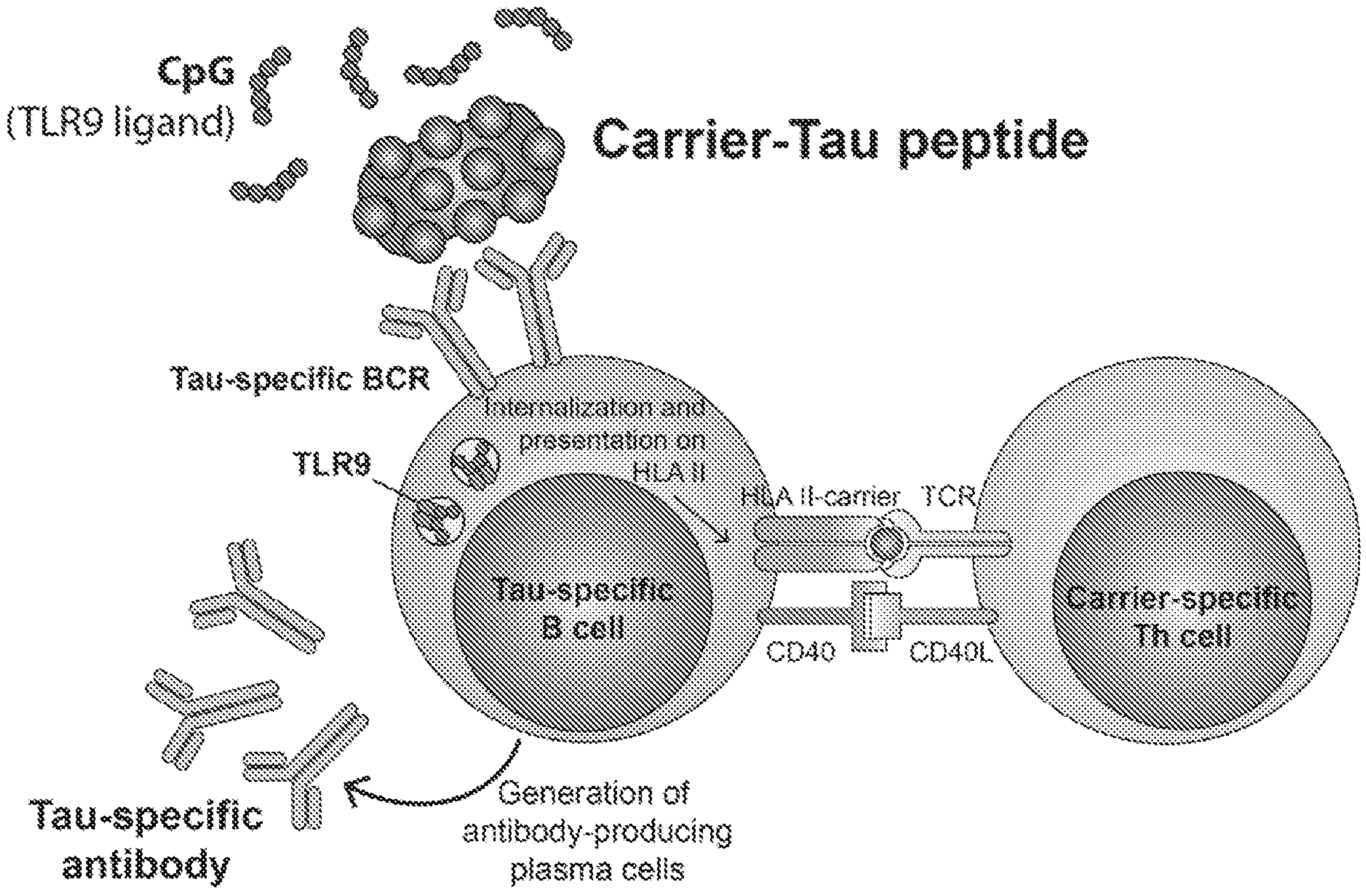

CpG
(TLR9 ligand)
Carrier-Tau peptide
Tau-specific BCR
TLR9
Internalization and presentation on HLA II
HLA II-carrier
TCR
Tau-specific B cell
CD40
CD40L
Carrier-specific Th cell
Tau-specific antibody
Generation of antibody-producing plasma cells

Figure 4

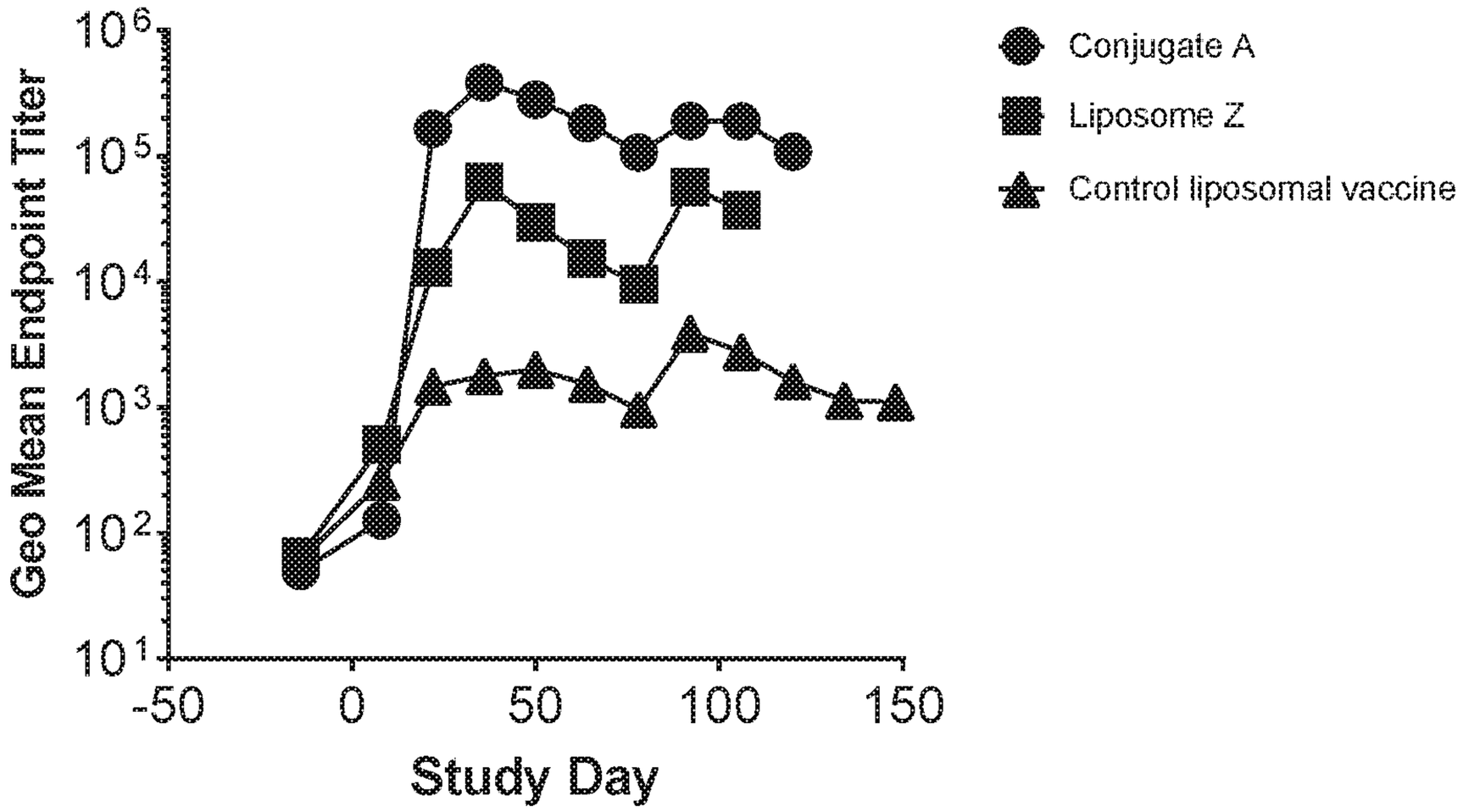

Geo Mean Endpoint Titer
10^6
10^5
10^4
10^3
10^2
10^1
-50
0
50
100
150
Study Day
Conjugate A
Liposome Z
Control liposomal vaccine

Figure 5

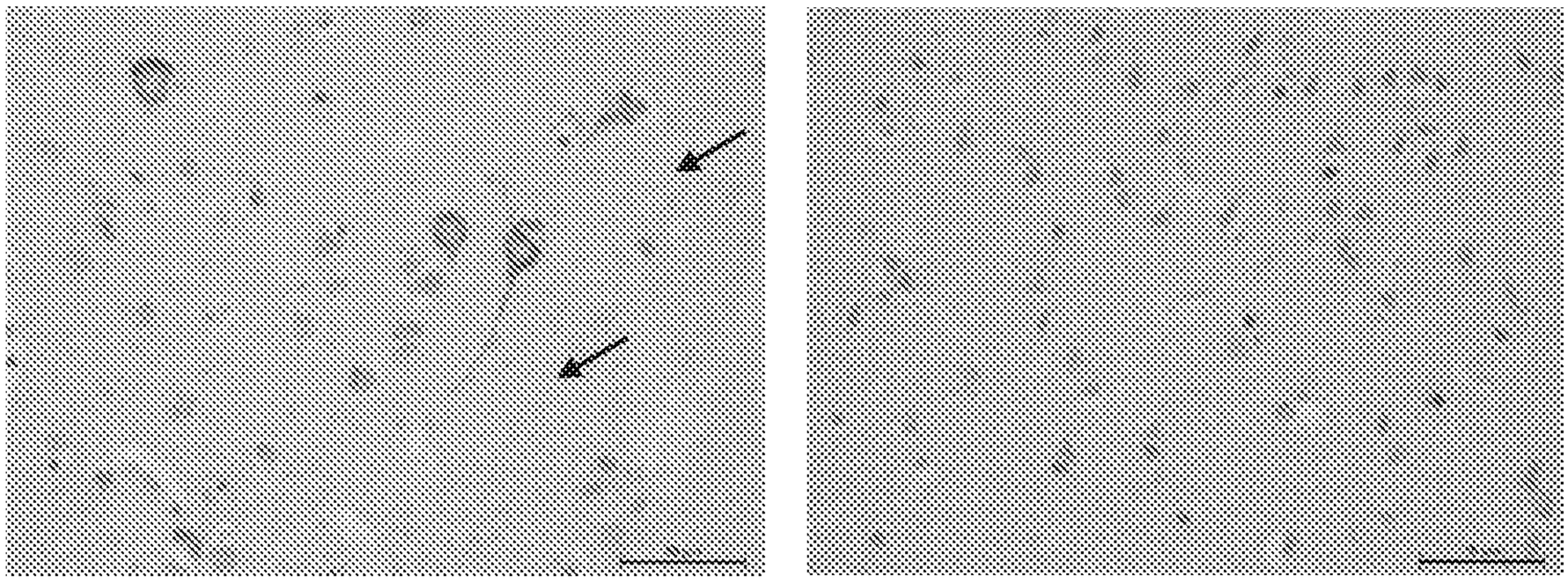


Figure 6

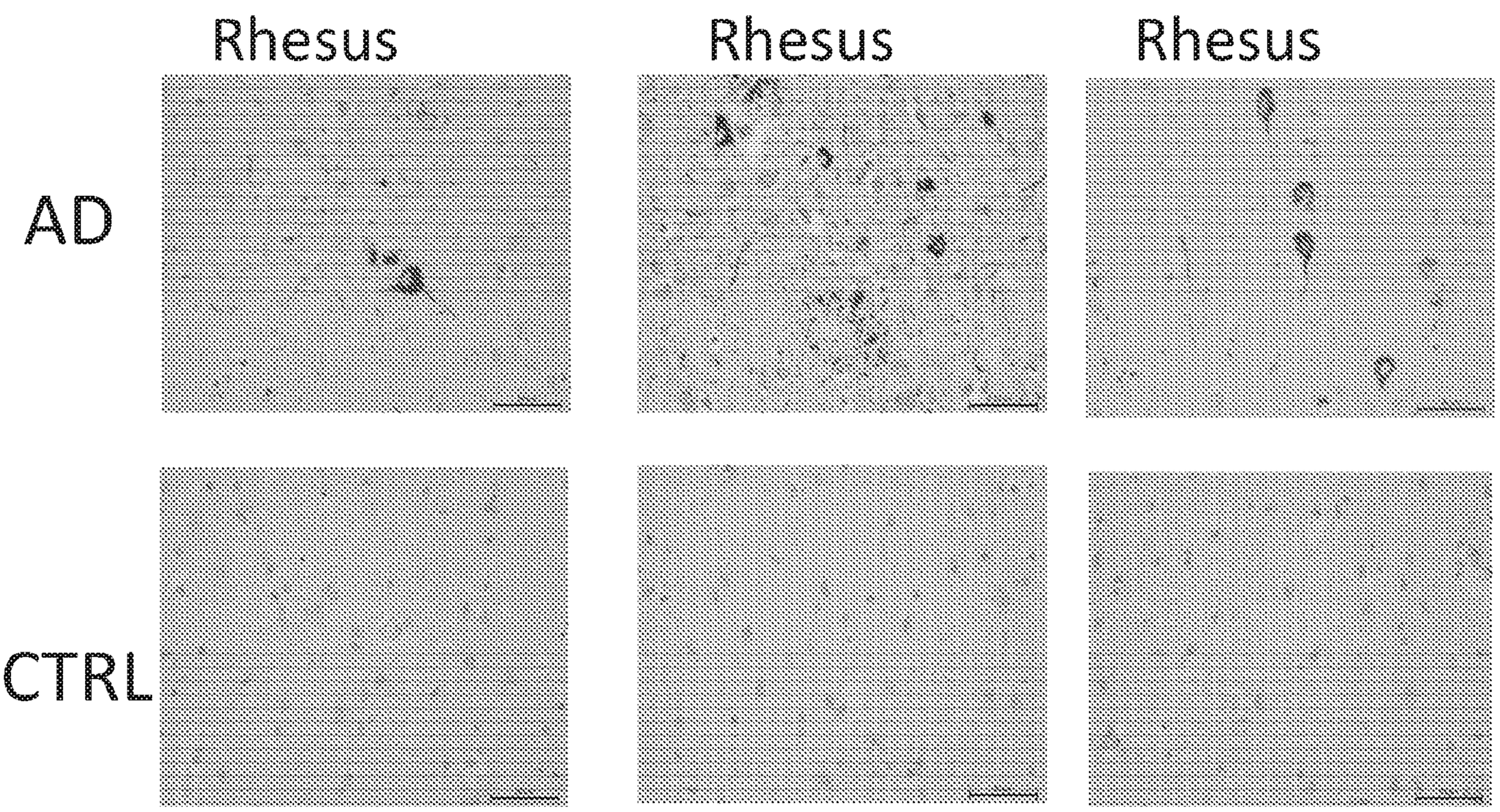


Figure 7

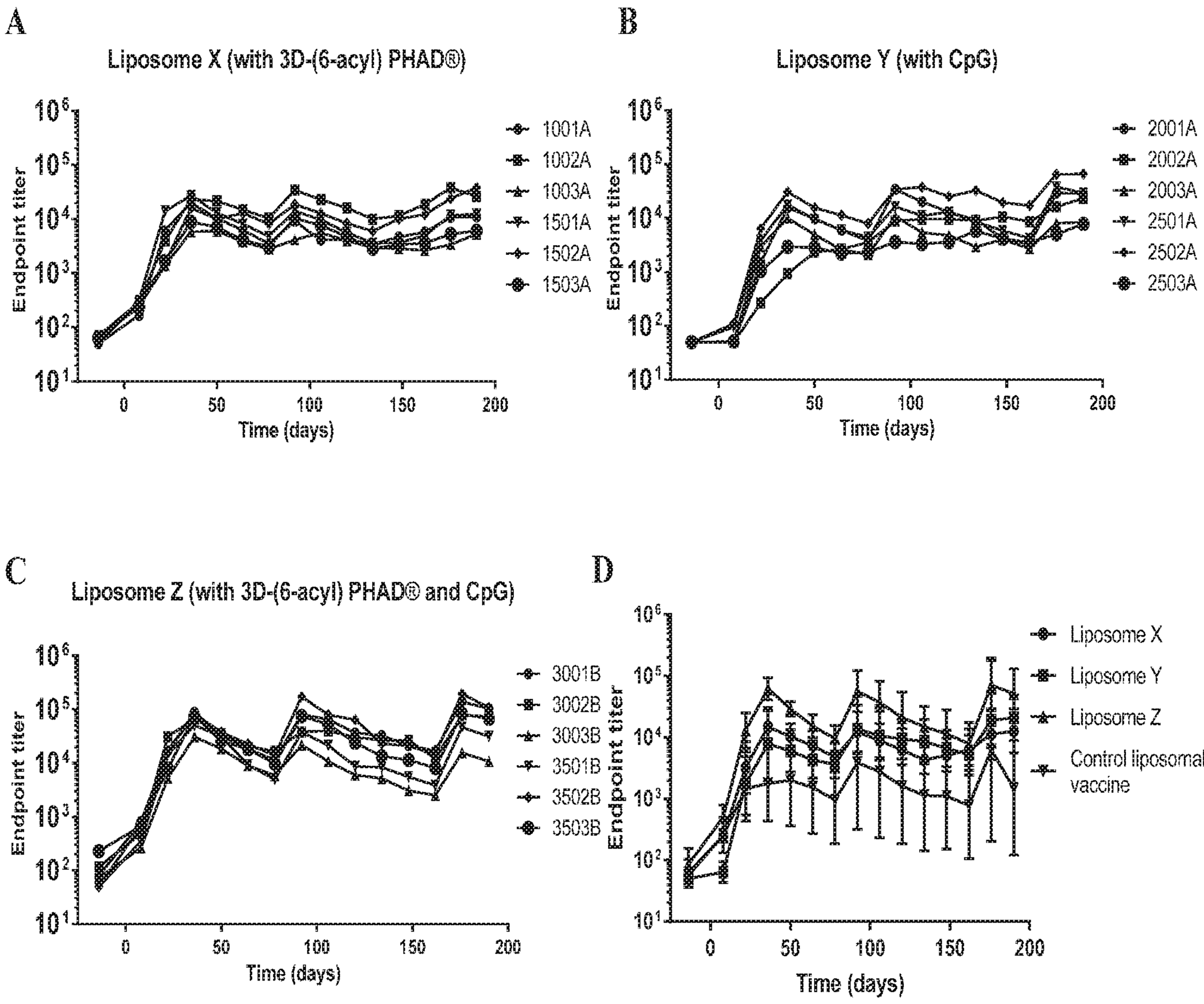

A
Liposome X (with 3D-(6-acyl) PHAD®)
Endpoint titer
Time (days)
1001A
1002A
1003A
1501A
1502A
1503A
B
Liposome Y (with CpG)
2001A
2002A
2003A
2501A
2502A
2503A
C
Liposome Z (with 3D-(6-acyl) PHAD® and CpG)
3001B
3002B
3003B
3501B
3502B
3503B
D
Liposome X
Liposome Y
Liposome Z
Control liposomal vaccine

Figure 8

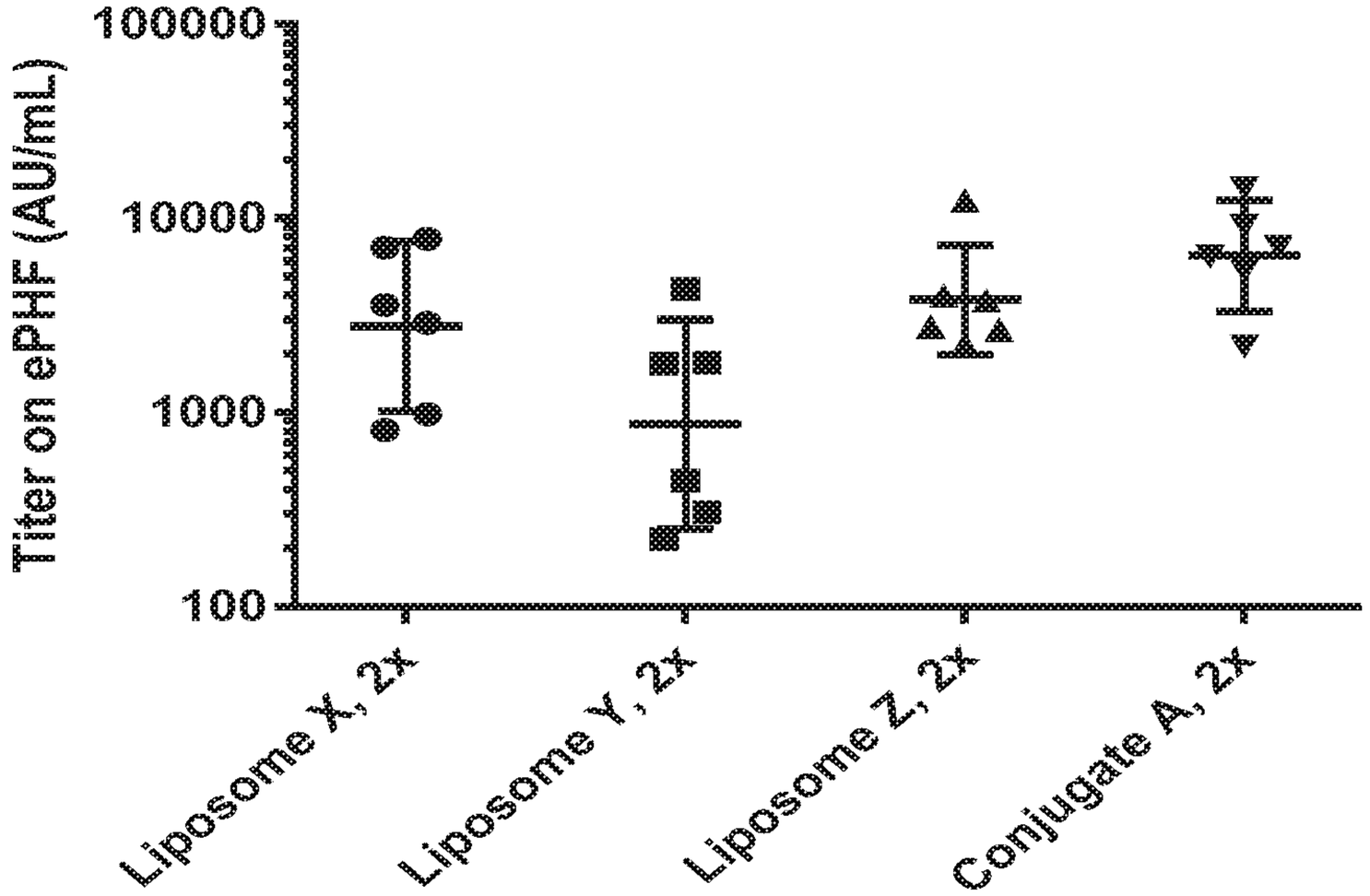
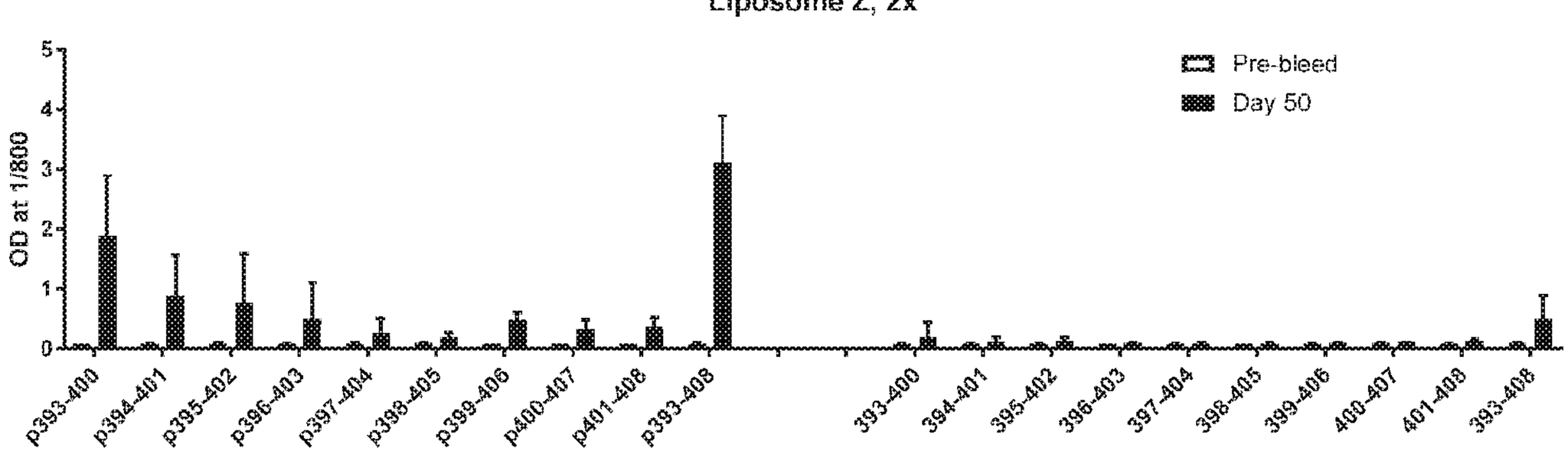

Titer on ePHF (AU/mL)
100000
10000
1000
100
Liposome X, 2x
Liposome Y, 2x
Liposome Z, 2x
Conjugate A, 2x

Figure 9

A


Liposome Z, 2x
Pre-bleed
Day 50
OD at 1/800
0
1
2
3
4
5
p393-400
p394-401
p395-402
p396-403
p397-404
p398-405
p399-406
p400-407
p401-408
p393-408
393-400
394-401
395-402
396-403
397-404
398-405
399-406
400-407
401-408
393-408

B

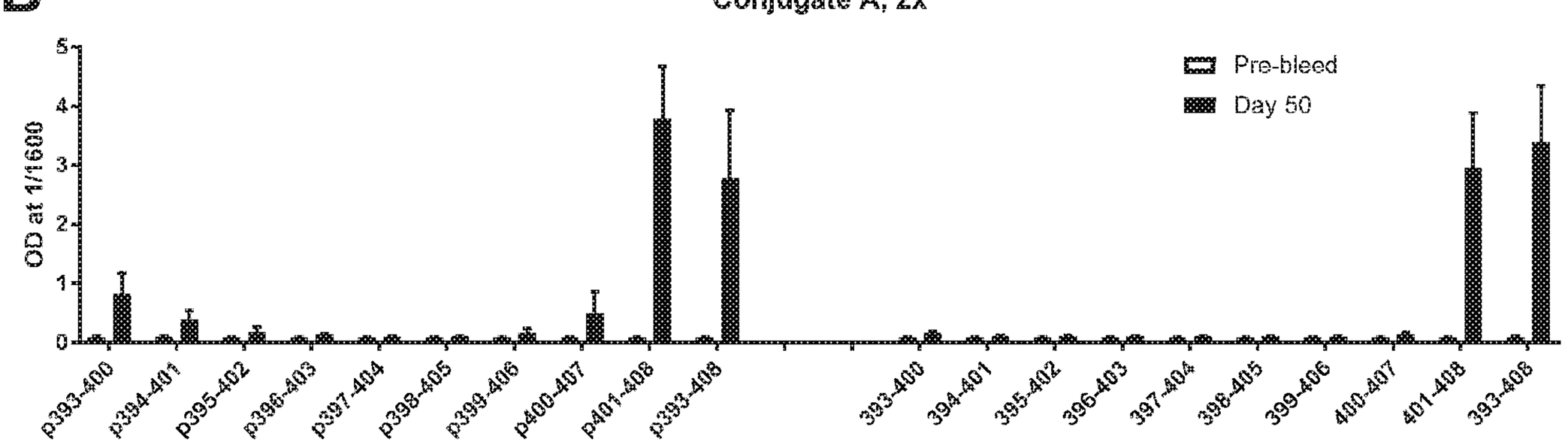

Conjugate A, 2x
Pre-bleed
Day 50
OD at 1/1600
0
1
2
3
4
5
p393-400
p394-401
p395-402
p396-403
p397-404
p398-405
p399-406
p400-407
p401-408
p393-408
393-400
394-401
395-402
396-403
397-404
398-405
399-406
400-407
401-408
393-408

Figure 10

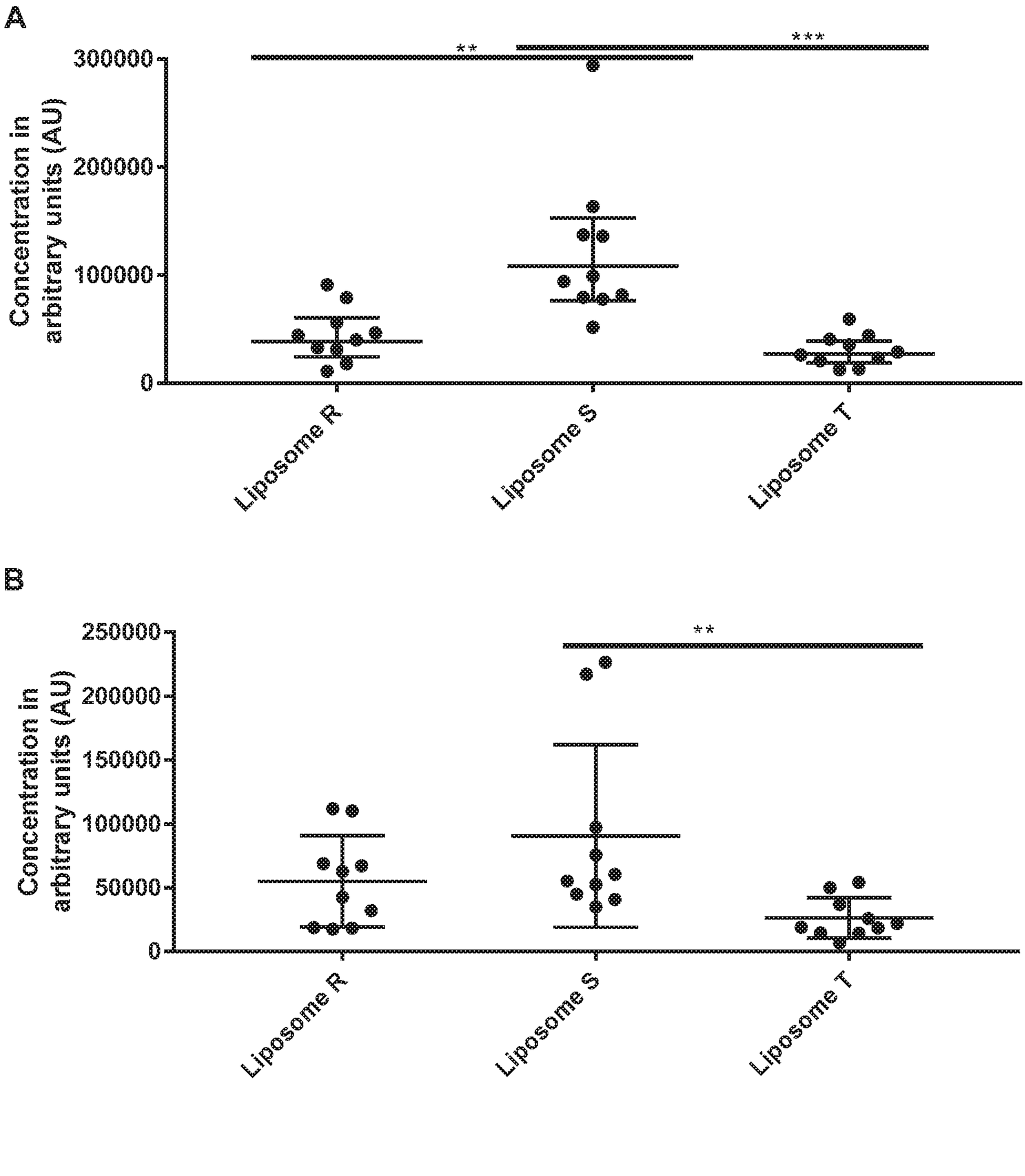

A
300000
200000
100000
0
Concentration in arbitrary units (AU)
**
***
Liposome R
Liposome S
Liposome T
B
250000
200000
150000
100000
50000
0
Concentration in arbitrary units (AU)
**
Liposome R
Liposome S
Liposome T

Figure 11

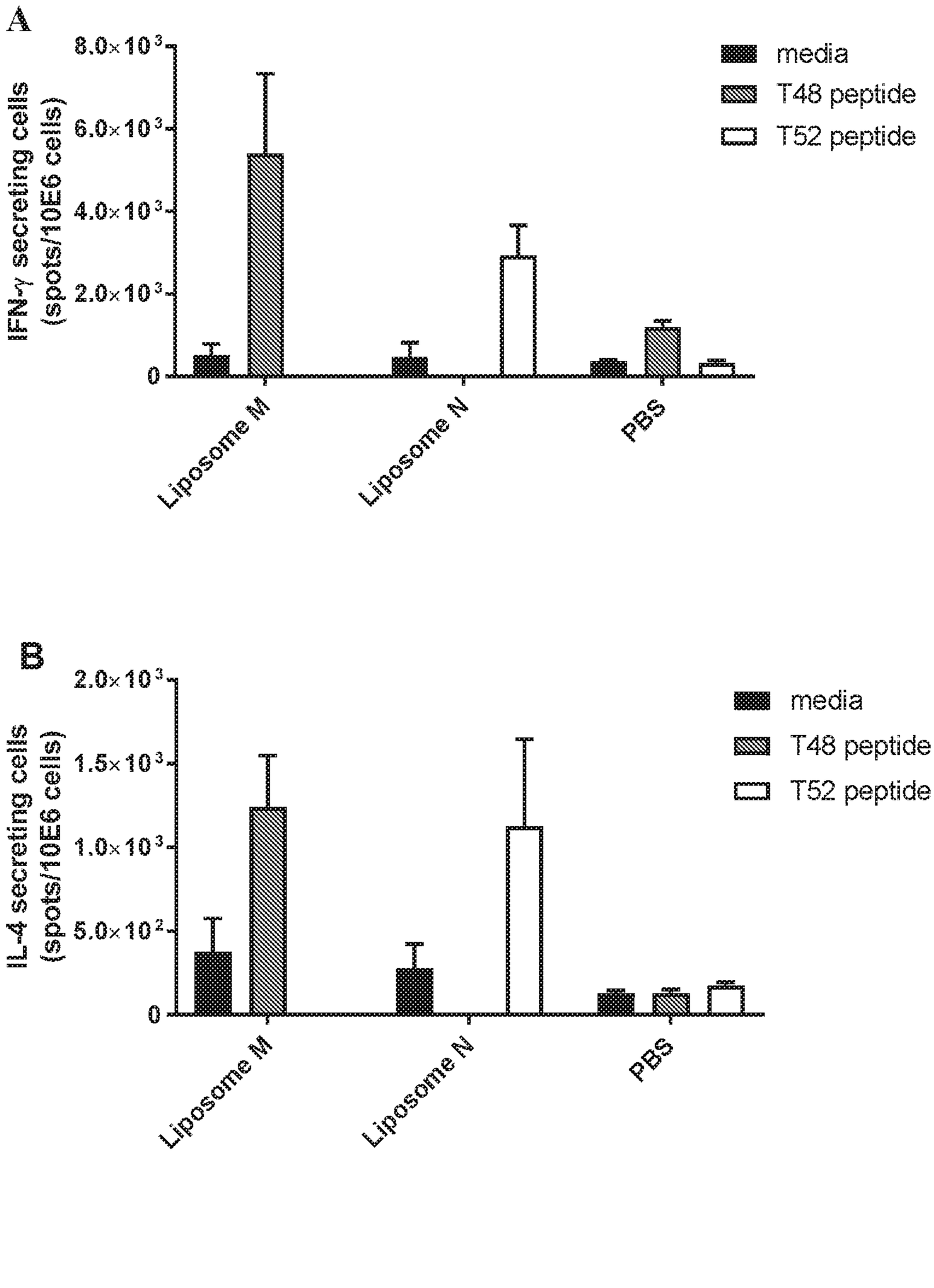

A
IFN-γ secreting cells (spots/10E6 cells)
8.0×10³
6.0×10³
4.0×10³
2.0×10³
0
media
T48 peptide
T52 peptide
Liposome M
Liposome N
PBS
B
IL-4 secreting cells (spots/10E6 cells)
2.0×10³
1.5×10³
1.0×10³
5.0×10²
0
media
T48 peptide
T52 peptide
Liposome M
Liposome N
PBS

Figure 12

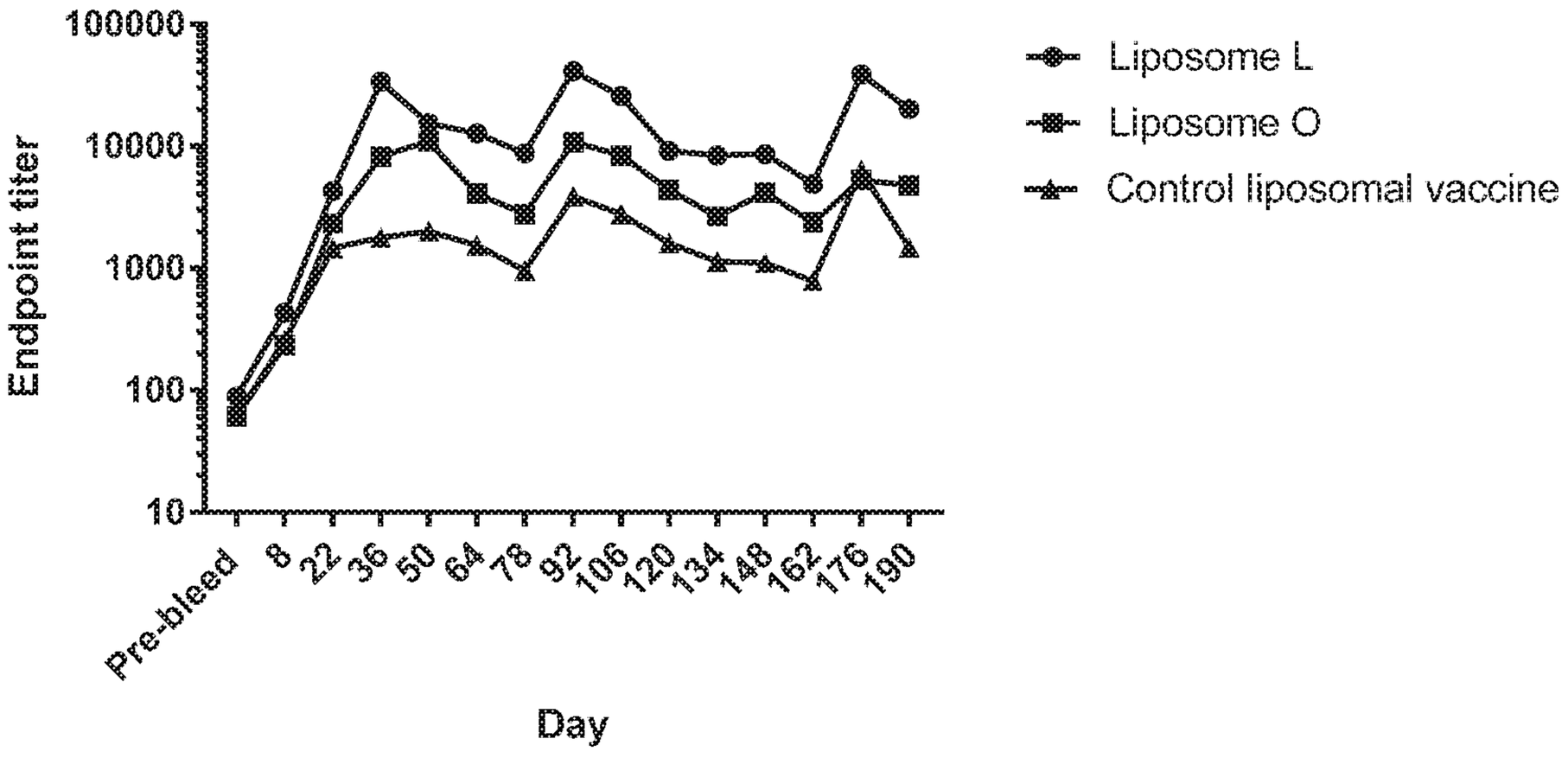

100000
10000
1000
100
10
Endpoint titer
Pre-bleed
8
22
36
50
64
78
92
106
120
134
148
162
176
190
Day
Liposome L
Liposome O
Control liposomal vaccine

Figure 13

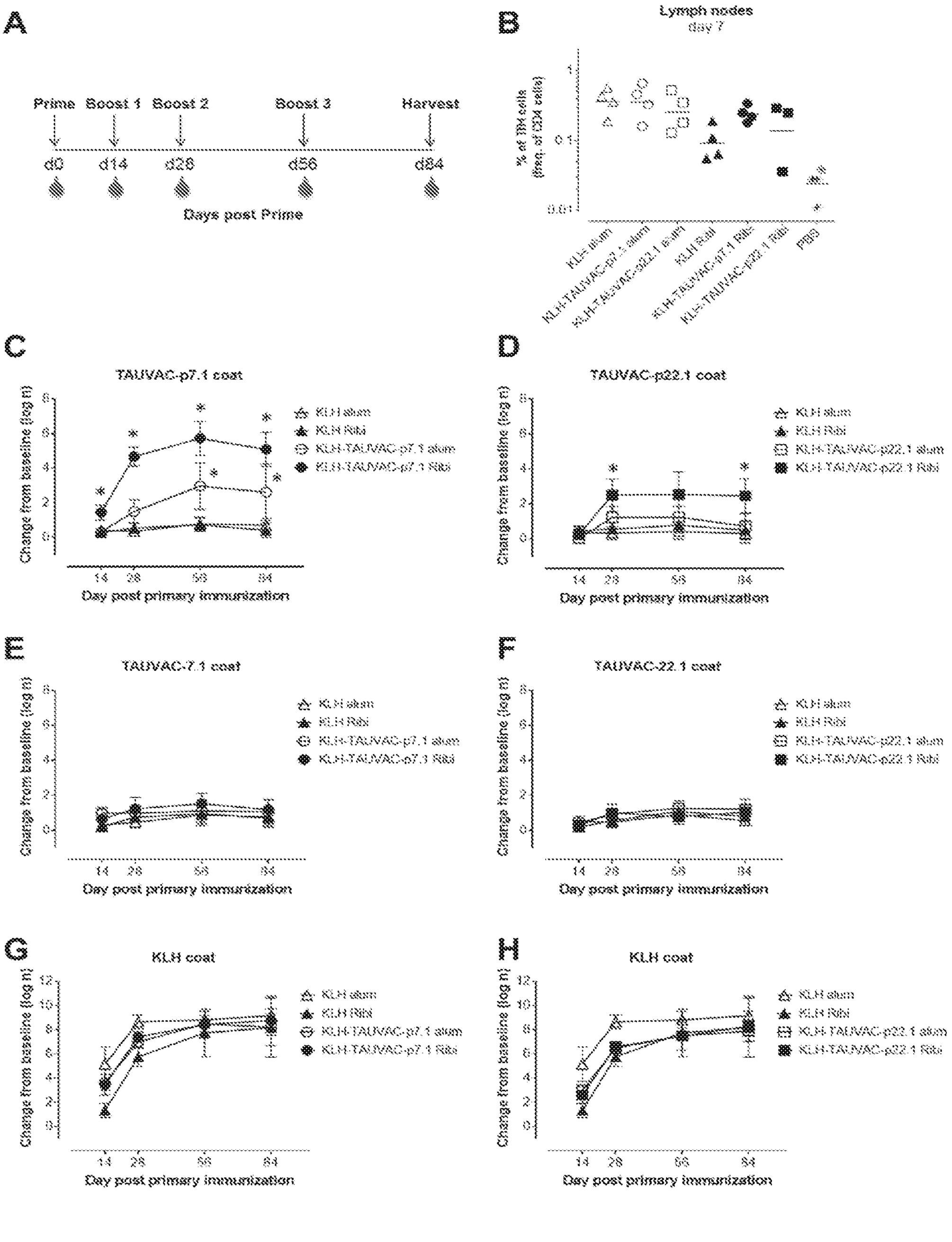

A
Prime
Boost 1
Boost 2
Boost 3
Harvest
d0
d14
d28
d56
d84
Days post Prime
B
Lymph nodes
day 7
% of IM cells
(freq. of CD4 cells)
KLH alum
KLH-TAUVAC-p7.1 alum
KLH-TAUVAC-p22.1 alum
KLH Ribi
KLH-TAUVAC-p7.1 Ribi
KLH-TAUVAC-p22.1 Ribi
PBS
C
TAUVAC-p7.1 coat
Change from baseline (log ELI)
KLH alum
KLH Ribi
KLH-TAUVAC-p7.1 alum
KLH-TAUVAC-p7.1 Ribi
14
28
56
84
Day post primary immunization
D
TAUVAC-p22.1 coat
Change from baseline (log ELI)
KLH alum
KLH Ribi
KLH-TAUVAC-p22.1 alum
KLH-TAUVAC-p22.1 Ribi
14
28
56
84
Day post primary immunization
E
TAUVAC-7.1 coat
Change from baseline (log ELI)
KLH alum
KLH Ribi
KLH-TAUVAC-p7.1 alum
KLH-TAUVAC-p7.1 Ribi
14
28
56
84
Day post primary immunization
F
TAUVAC-22.1 coat
Change from baseline (log ELI)
KLH alum
KLH Ribi
KLH-TAUVAC-p22.1 alum
KLH-TAUVAC-p22.1 Ribi
14
28
56
84
Day post primary immunization
G
KLH coat
Change from baseline (log ELI)
KLH alum
KLH Ribi
KLH-TAUVAC-p7.1 alum
KLH-TAUVAC-p7.1 Ribi
14
28
56
84
Day post primary immunization
H
KLH coat
Change from baseline (log ELI)
KLH alum
KLH Ribi
KLH-TAUVAC-p22.1 alum
KLH-TAUVAC-p22.1 Ribi
14
28
56
84
Day post primary immunization

Figure 14

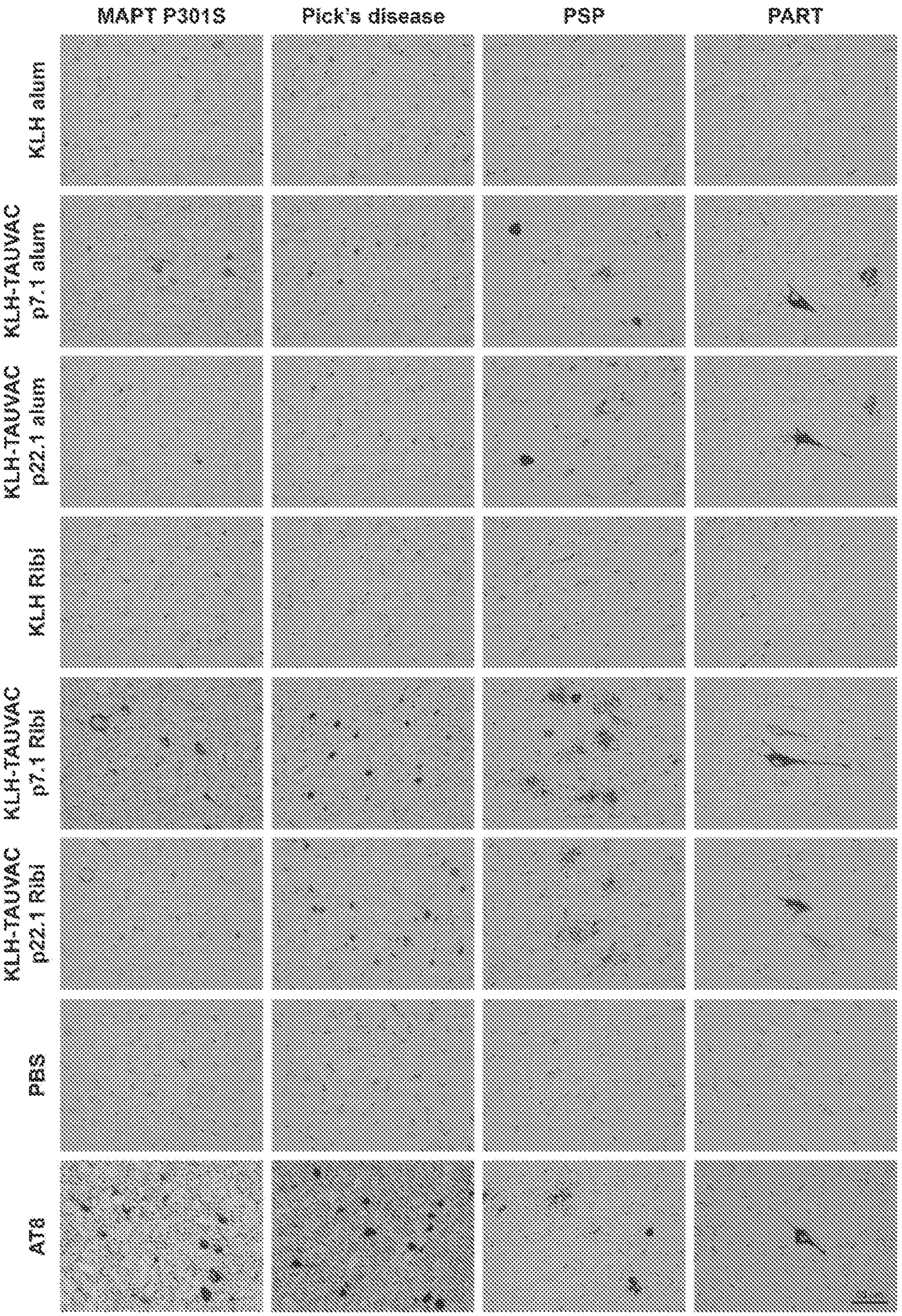

MAPT P301S
Pick's disease
PSP
PART
KLH alum
KLH Ribi
KLH-TAUVAC p22.1 alum
KLH-TAUVAC p7.1 alum
PBS
KLH-TAUVAC p22.1 Ribi
KLH-TAUVAC p7.1 Ribi
AT8

Figure 15

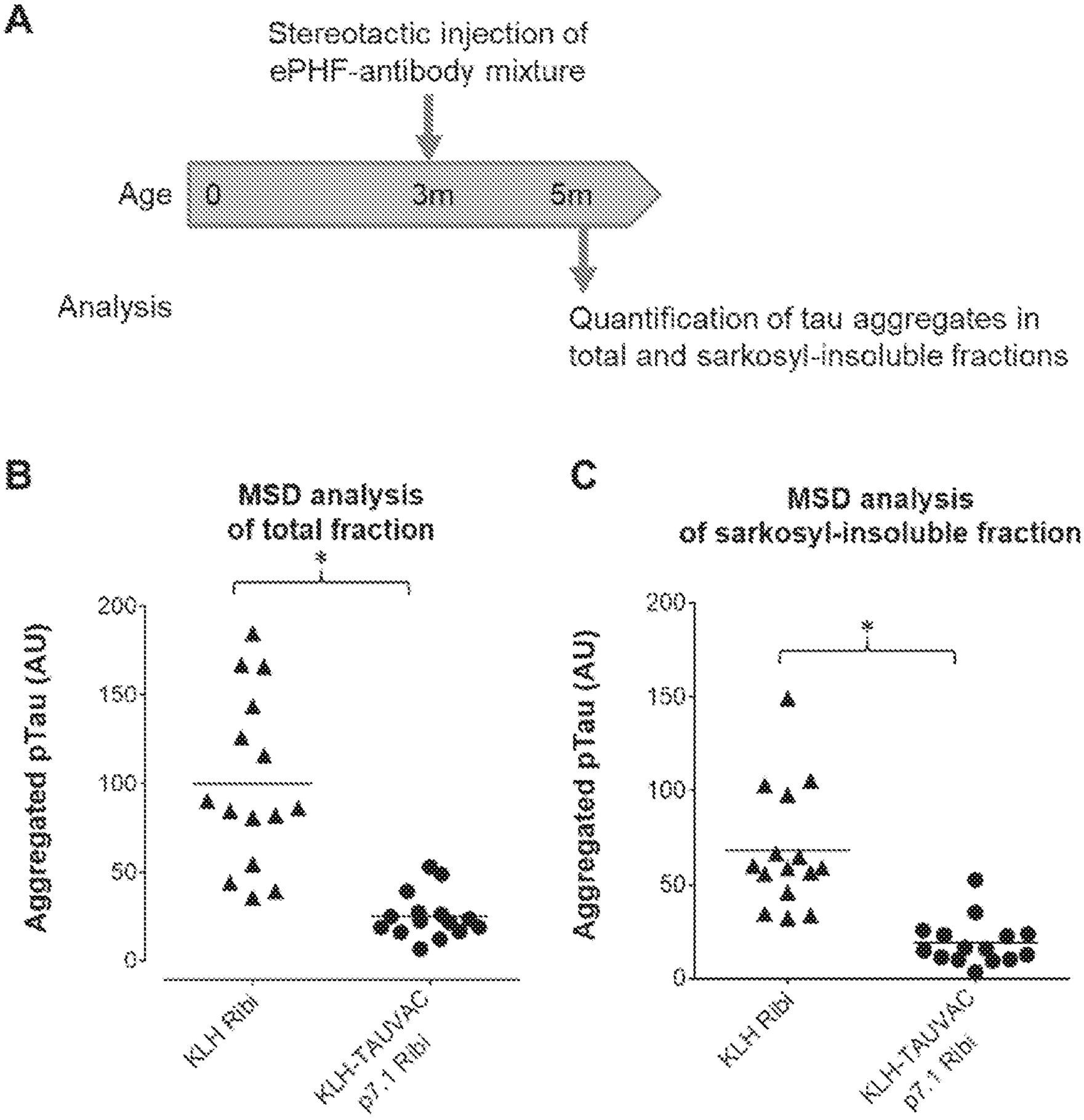

A
Stereotactic injection of
ePHF-antibody mixture
Age
0
3m
5m
Analysis
Quantification of tau aggregates in
total and sarkosyl-insoluble fractions
B
MSD analysis
of total fraction
Aggregated pTau (AU)
200
150
100
50
0
*
KLH-TAUVAC
p7.1 Ribi
C
MSD analysis
of sarkosyl-insoluble fraction
Aggregated pTau (AU)
200
150
100
50
0
*
KLH-TAUVAC
p7.1 Ribi

Figure 16

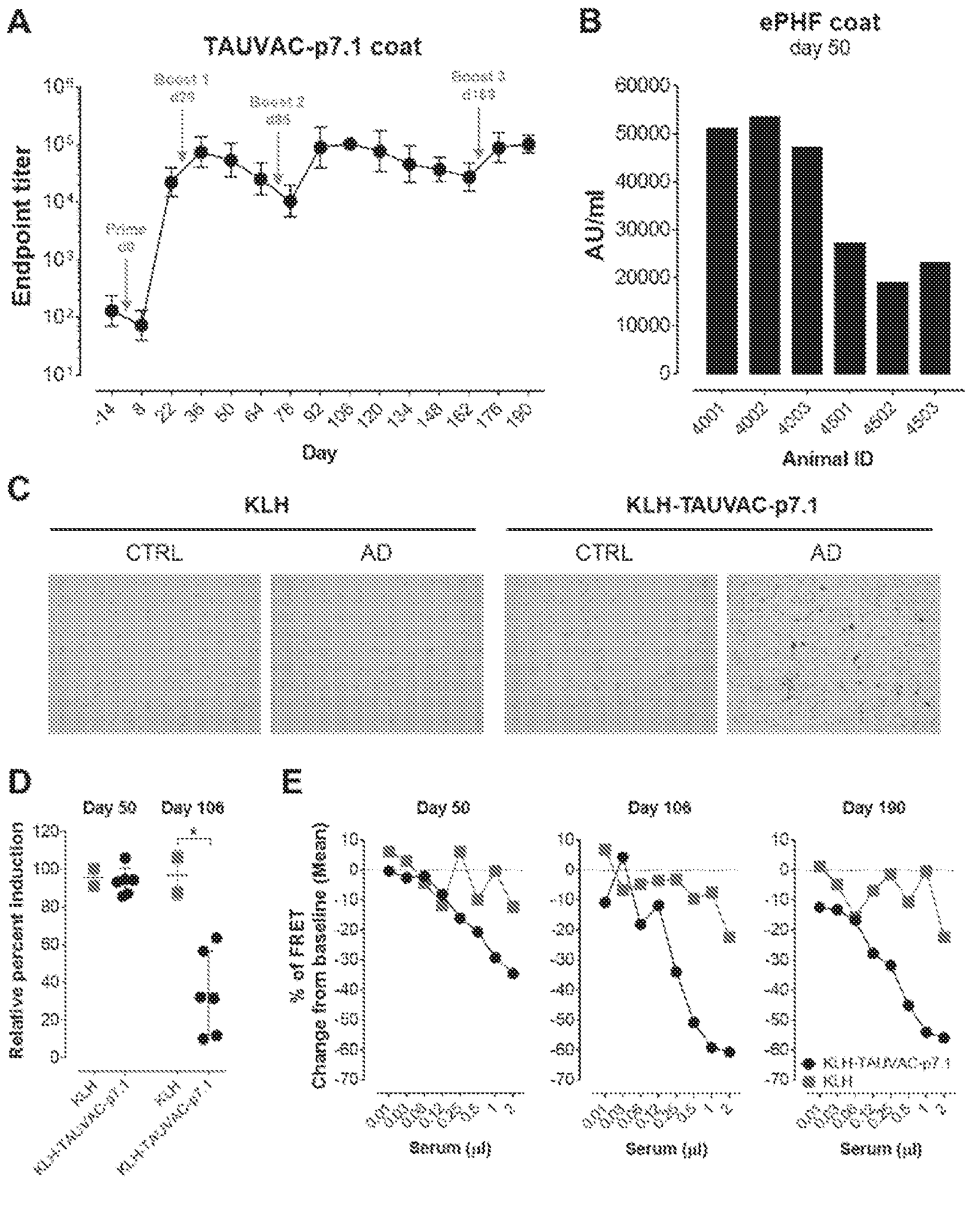
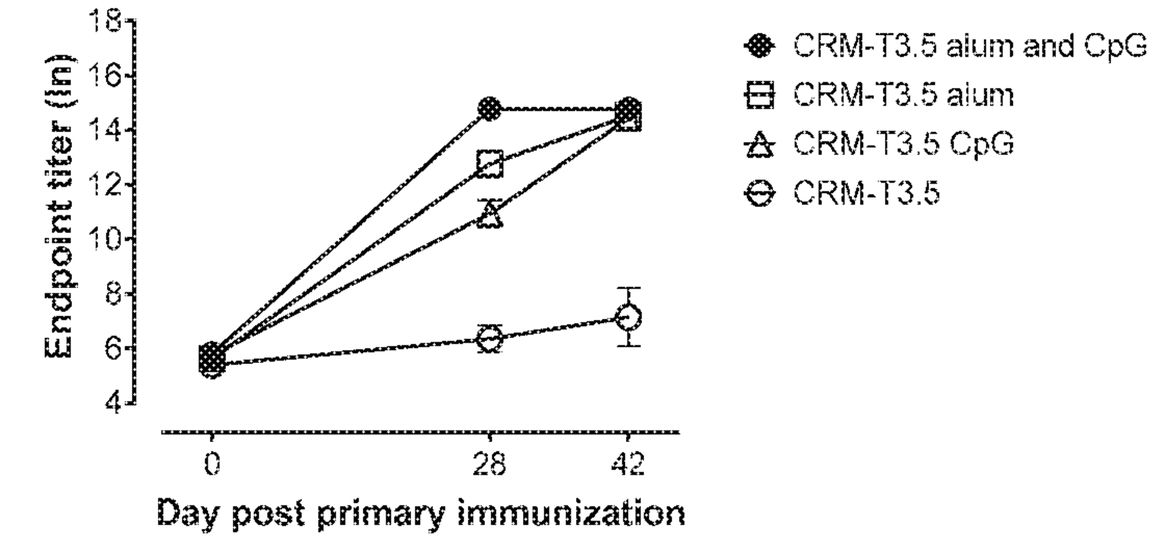

A
TAUVAC-p7.1 coat
Endpoint titer
Day
Prime d0
Boost 1 d28
Boost 2 d56
Boost 3 d168
B
ePHF coat
day 50
AU/ml
Animal ID
4001
4002
4003
4501
4502
4503
C
KLH
KLH-TAUVAC-p7.1
CTRL
AD
D
Day 50
Day 106
Relative percent induction
KLH
KLH-TAUVAC-p7.1
E
Day 50
Day 106
Day 190
% of FRET
Change from baseline (Mean)
Serum (µl)
KLH-TAUVAC-p7.1
KLH

Figure 17

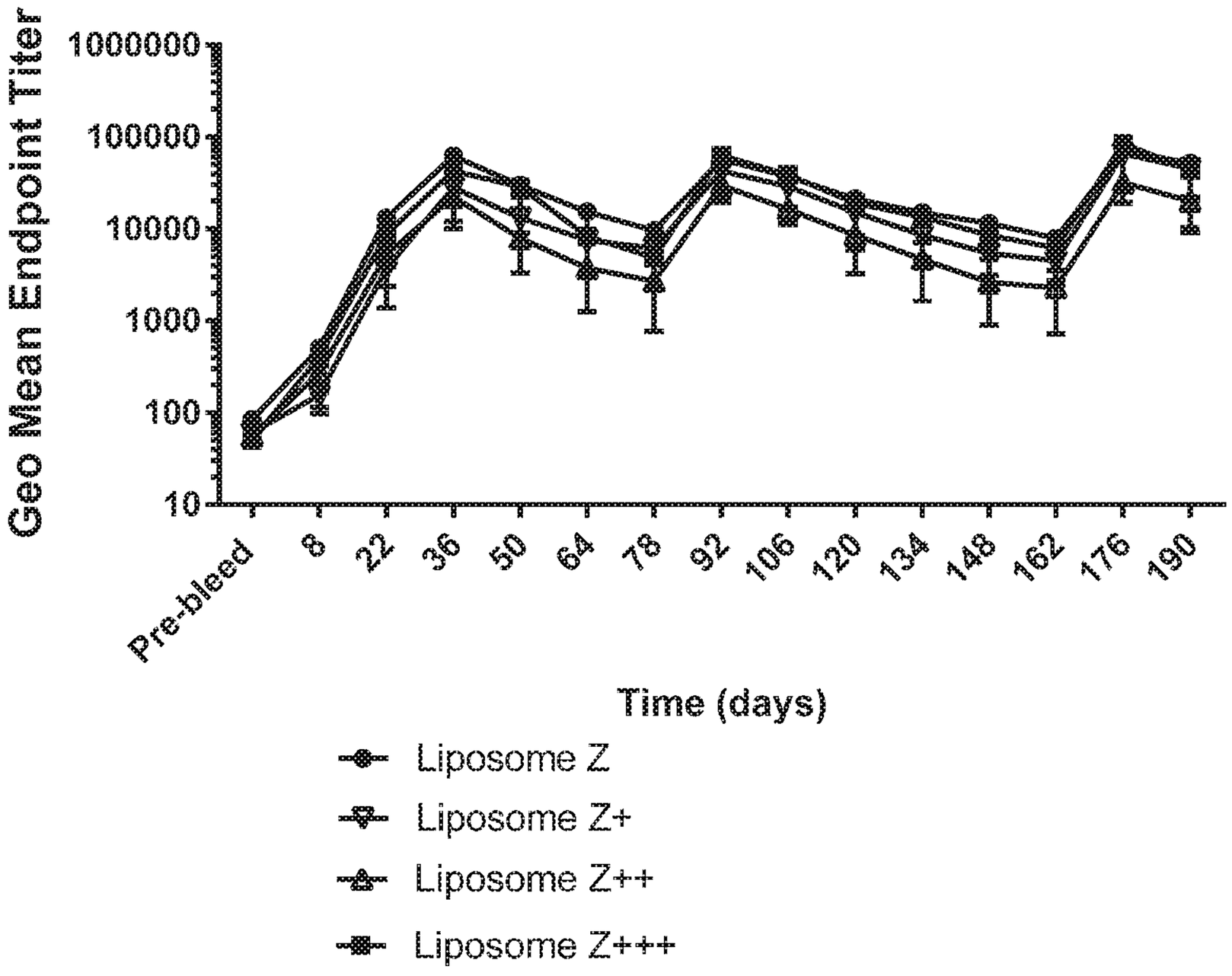


Group comparison

Group 1	Group 2	Unadj. p-value
Day 28		
CRM-T3.5 alum	CRM-T3.5	0.0022
CRM-T3.5 CpG	CRM-T3.5	0.0022
CRM-T3.5 alum and CpG	CRM-T3.5	0.0028
CRM-T3.5 alum and CpG	CRM-T3.5 alum	0.0029
CRM-T3.5 alum and CpG	CRM-T3.5 CpG	0.0038
Day 42		
CRM-T3.5 alum	CRM-T3.5	0.0075
CRM-T3.5 CpG	CRM-T3.5	0.0075
CRM-T3.5 alum and CpG	CRM-T3.5	0.0038
CRM-T3.5 alum and CpG	CRM-T3.5 alum	0.0740
CRM-T3.5 alum and CpG	CRM-T3.5 CpG	0.0740

Day 28		
CRM-T3.5 alum	CRM-T3.5	0.0022
CRM-T3.5 CpG	CRM-T3.5	0.1320
CRM-T3.5 alum and CpG	CRM-T3.5	0.0152
CRM-T3.5 alum and CpG	CRM-T3.5 alum	0.0649
CRM-T3.5 alum and CpG	CRM-T3.5 CpG	0.1584
Day 42		
CRM-T3.5 alum	CRM-T3.5	0.0022
CRM-T3.5 CpG	CRM-T3.5	0.0043
CRM-T3.5 alum and CpG	CRM-T3.5	0.0043
CRM-T3.5 alum and CpG	CRM-T3.5 alum	0.0609
CRM-T3.5 alum and CpG	CRM-T3.5 CpG	0.0497

Figure 18


Geo Mean Endpoint Titer
1000000
100000
10000
1000
100
10
Pre-bleed
8
22
36
50
64
78
92
106
120
134
148
162
176
190
Time (days)
Liposome Z
Liposome Z+
Liposome Z++
Liposome Z+++