Fig. 1

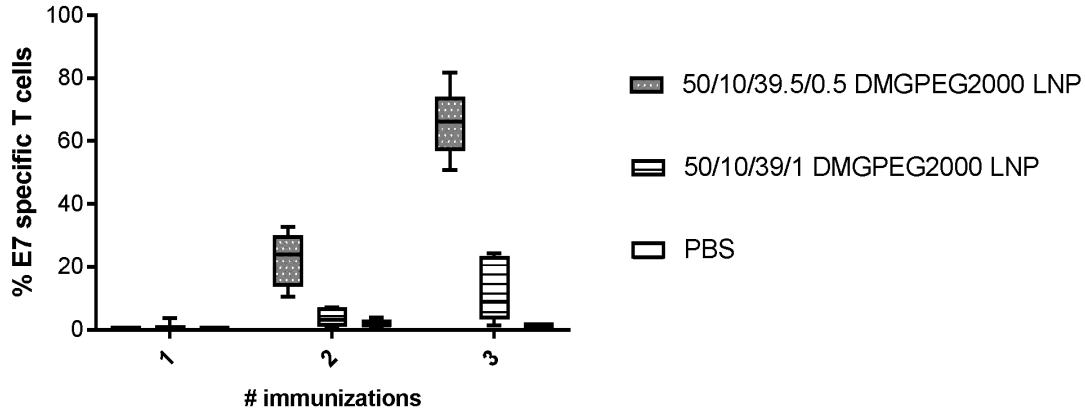


Fig. 2

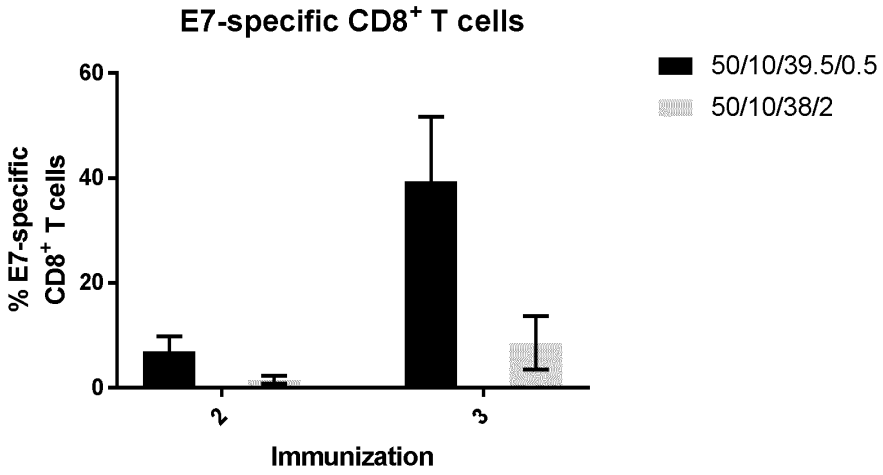


Fig. 3

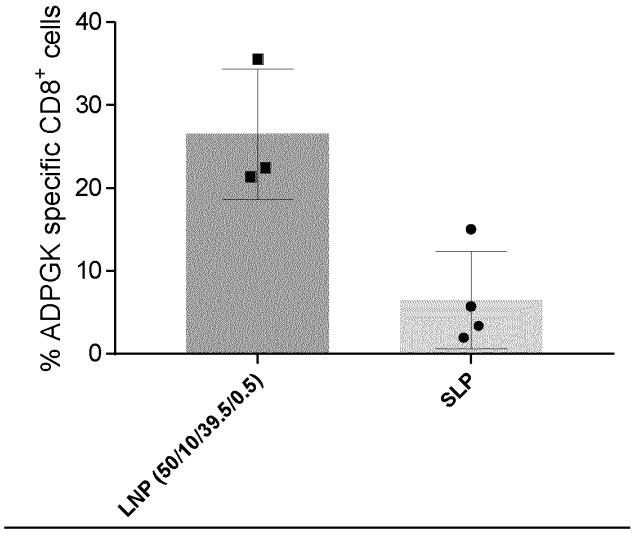
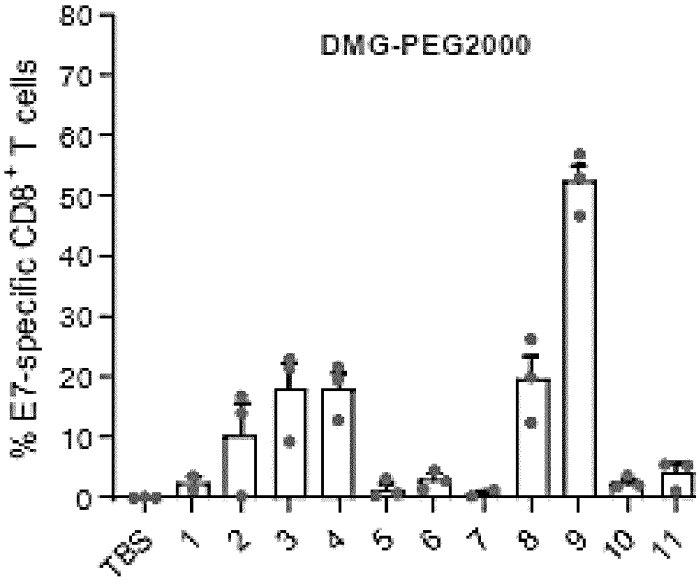
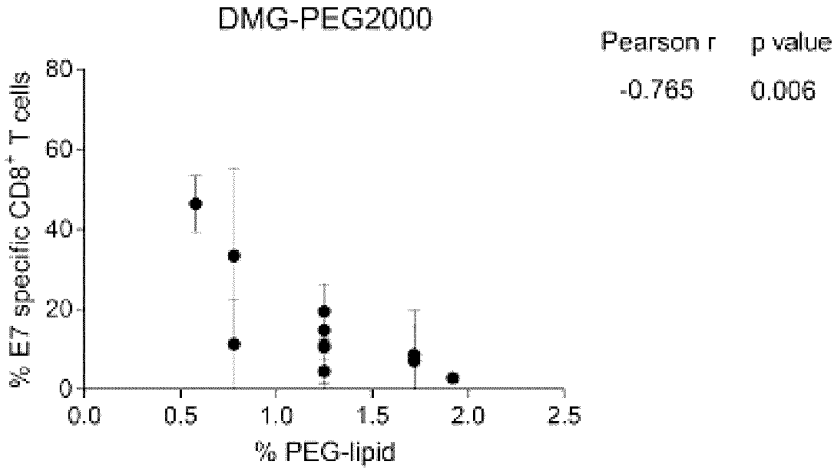


Fig. 4

A


DMG-PEG2000
% E7-specific CD8+ T cells
80
70
60
50
40
30
20
10
0
TBS
1
2
3
4
5
6
7
8
9
10
11

B


DMG-PEG2000
Pearson r
p value
-0.765
0.006
% E7 specific CD8+ T cells
80
60
40
20
0
0.0
0.5
1.0
1.5
2.0
2.5
% PEG-lipid

C

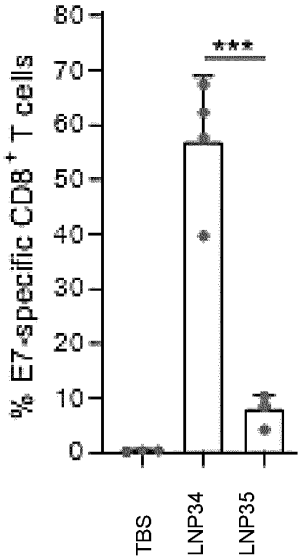

% E7-specific CD8+ T cells
80
70
60
50
40
30
20
10
0
***
TBS
LNP34
LNP35

Fig. 5

A

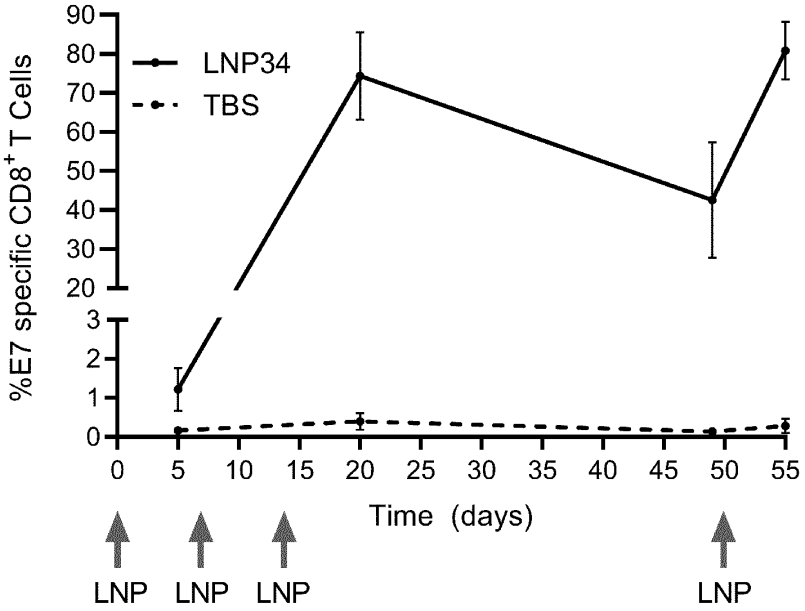
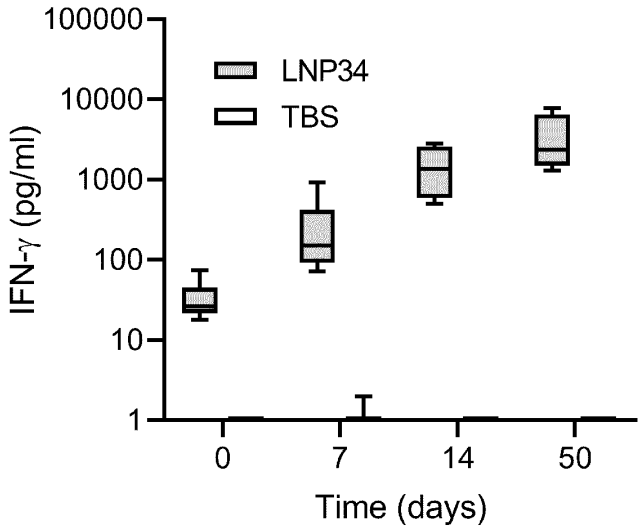

%E7 specific CD8+ T Cells
90
80
70
60
50
40
30
20
3
2
1
0
LNP34
TBS
0
5
10
15
20
25
30
35
40
45
50
55
Time (days)
LNP
LNP
LNP
LNP

Fig. 5

B


100000
10000
1000
100
10
1
IFN-γ (pg/ml)
LNP34
TBS
0
7
14
50
Time (days)

C.

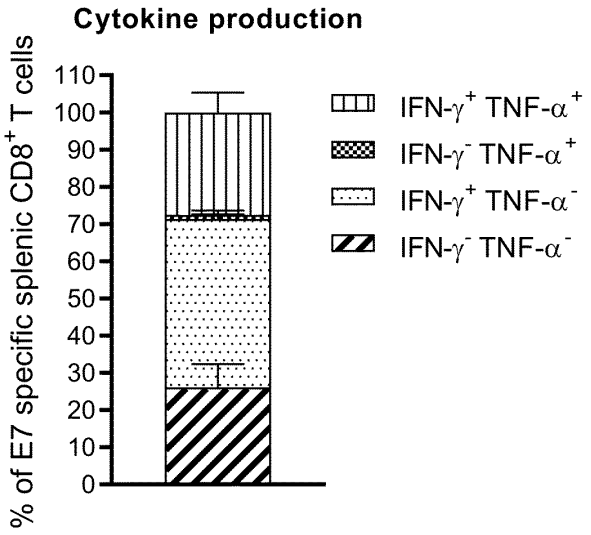
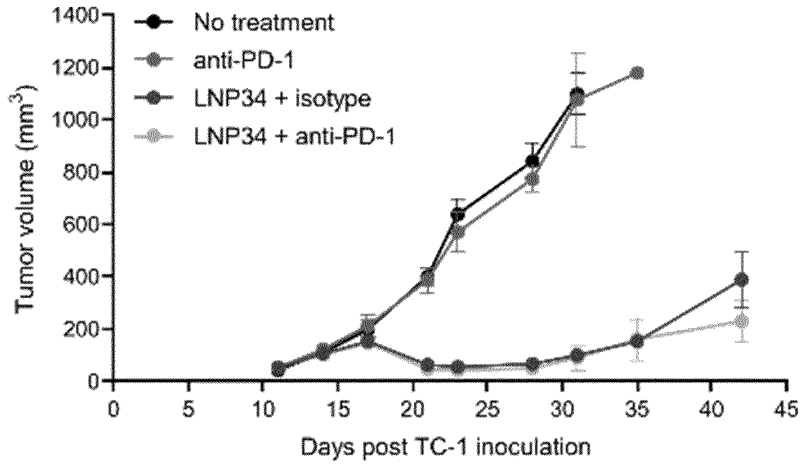

Cytokine production
% of E7 specific splenic CD8+ T cells
110
100
90
80
70
60
50
40
30
20
10
0
IFN-γ+ TNF-α+
IFN-γ- TNF-α+
IFN-γ+ TNF-α-
IFN-γ- TNF-α-

Fig. 5

D


No treatment
anti-PD-1
LNP34 + isotype
LNP34 + anti-PD-1
Tumor volume (mm3)
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
25
30
35
40
45
Days post TC-1 inoculation

E

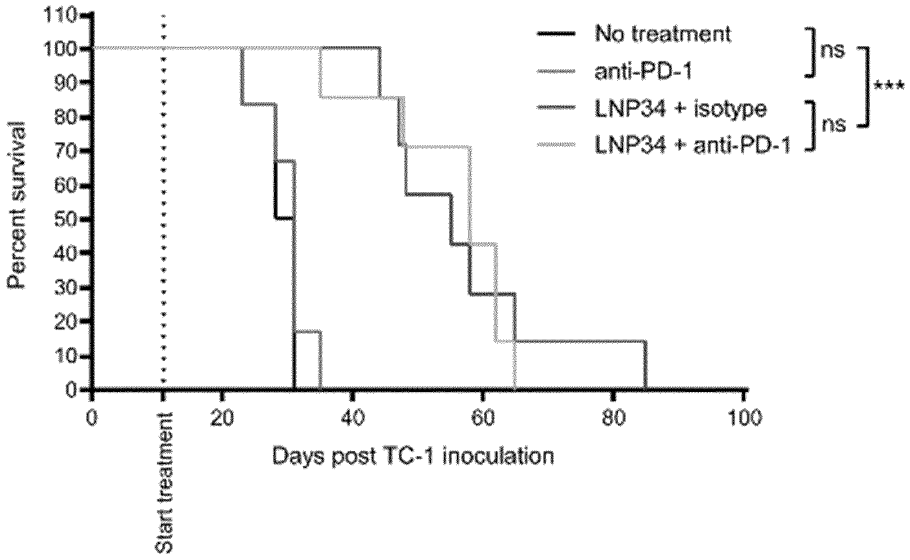
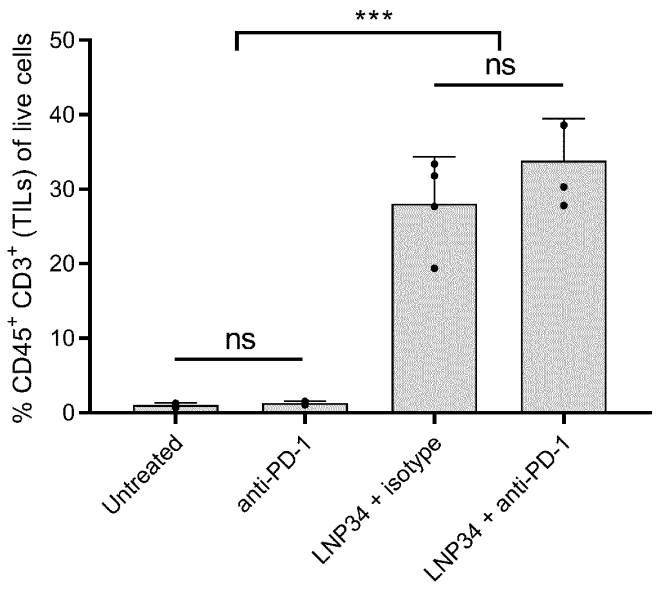

No treatment
anti-PD-1
LNP34 + isotype
LNP34 + anti-PD-1
ns
ns
***
Percent survival
110
100
90
80
70
60
50
40
30
20
10
0
0
20
40
60
80
100
Days post TC-1 inoculation
Start treatment

Fig. 5

F


***
ns
ns
% CD45+ CD3+ (TILs) of live cells
50
40
30
20
10
0
Untreated
anti-PD-1
LNP34 + isotype
LNP34 + anti-PD-1

G

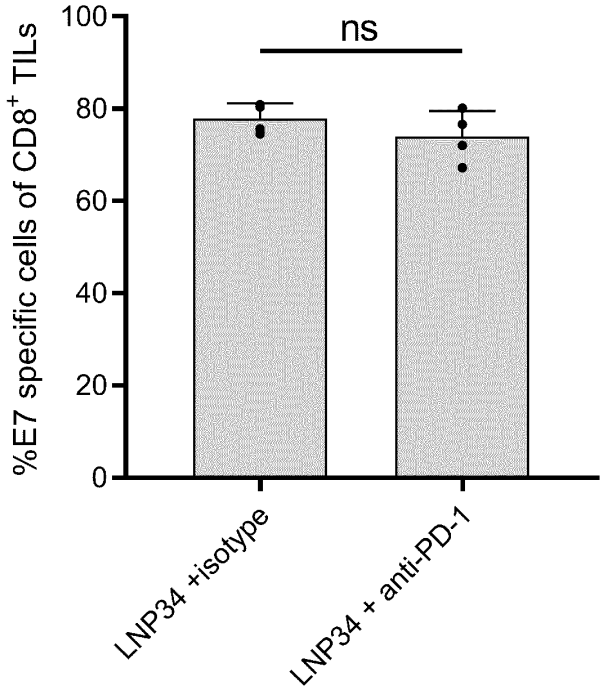
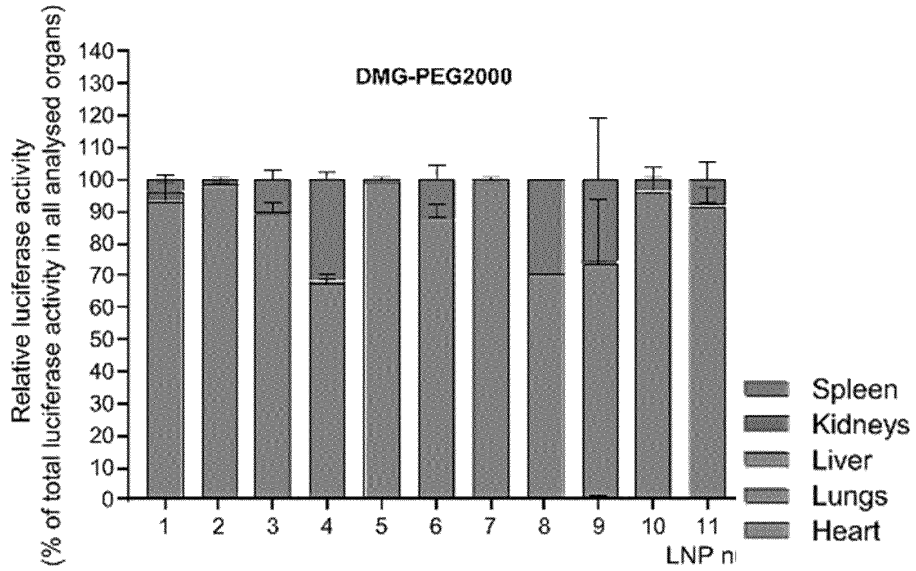

ns
%E7 specific cells of CD8+ TILs
100
80
60
40
20
0
LNP34 +isotype
LNP34 + anti-PD-1

Fig. 6

A


DMG-PEG2000
Relative luciferase activity
(% of total luciferase activity in all analysed organs)
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
1
2
3
4
5
6
7
8
9
10
11
LNP n
Spleen
Kidneys
Liver
Lungs
Heart

B

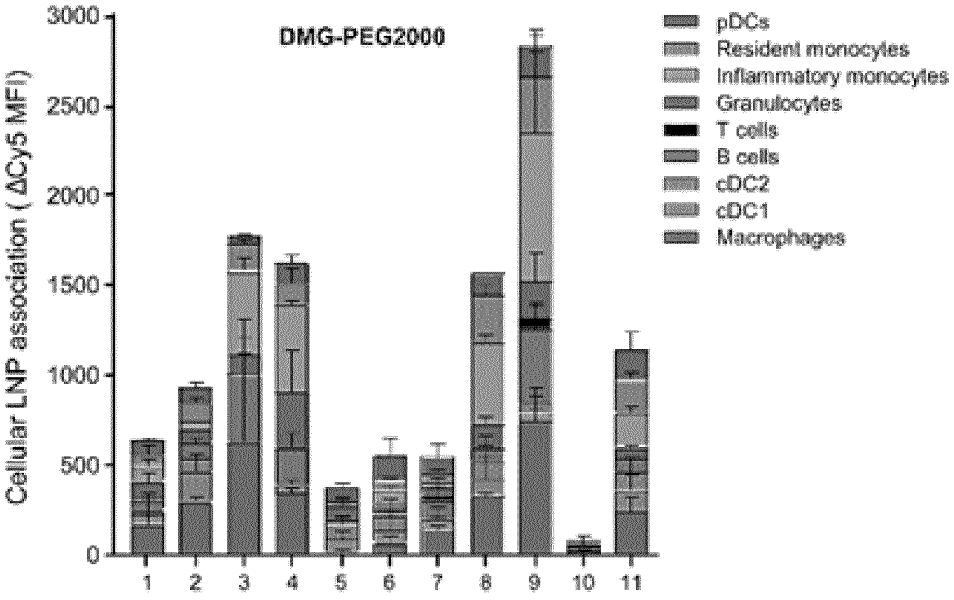
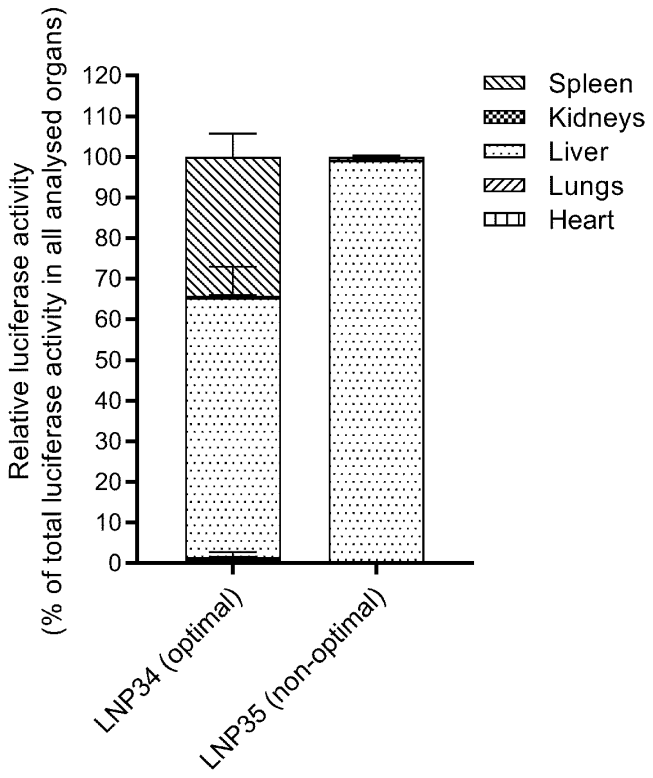

DMG-PEG2000
Cellular LNP association (ΔCy5 MFI)
3000
2500
2000
1500
1000
500
0
1
2
3
4
5
6
7
8
9
10
11
pDCs
Resident monocytes
Inflammatory monocytes
Granulocytes
T cells
B cells
cDC2
cDC1
Macrophages

Fig. 6

C


Relative luciferase activity
(% of total luciferase activity in all analysed organs)
120
110
100
90
80
70
60
50
40
30
20
10
0
Spleen
Kidneys
Liver
Lungs
Heart
LNP34 (optimal)
LNP35 (non-optimal)

D

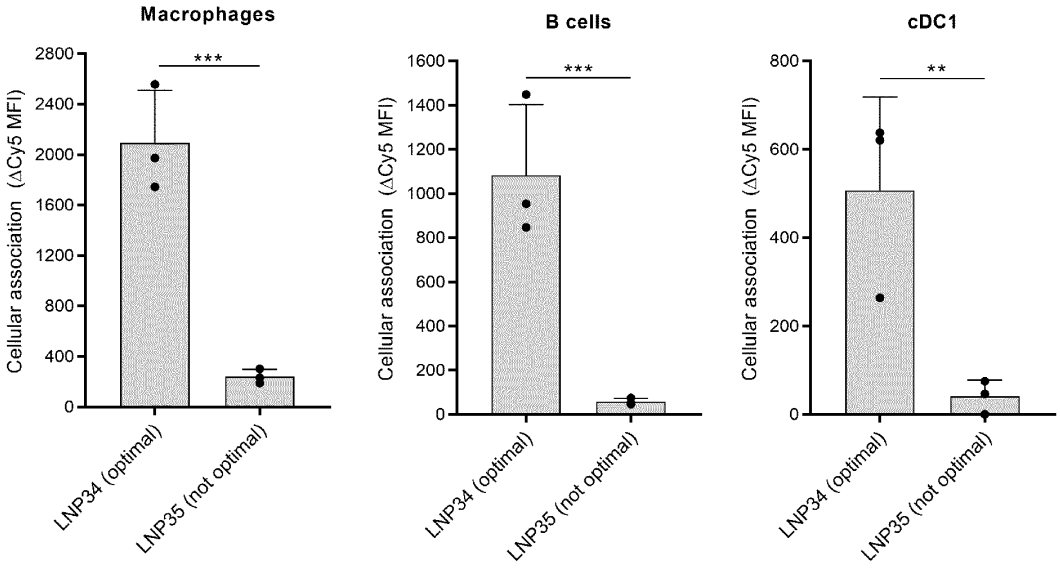
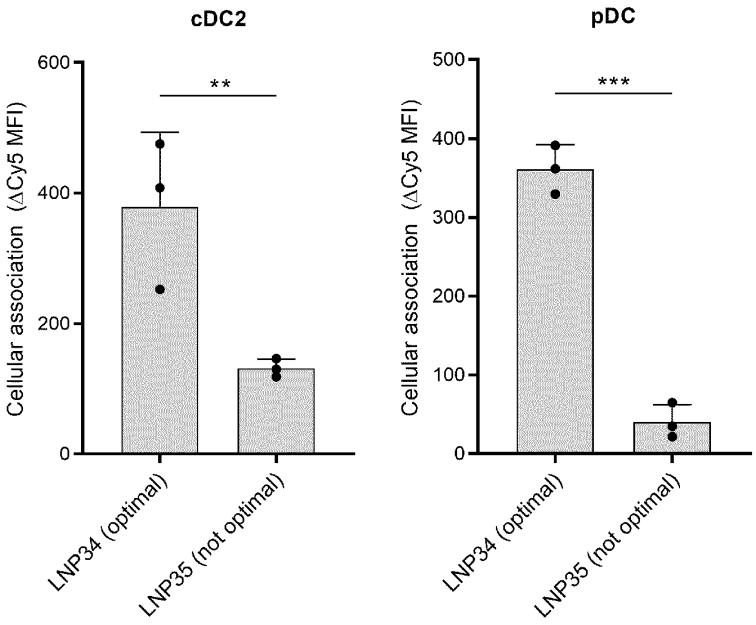
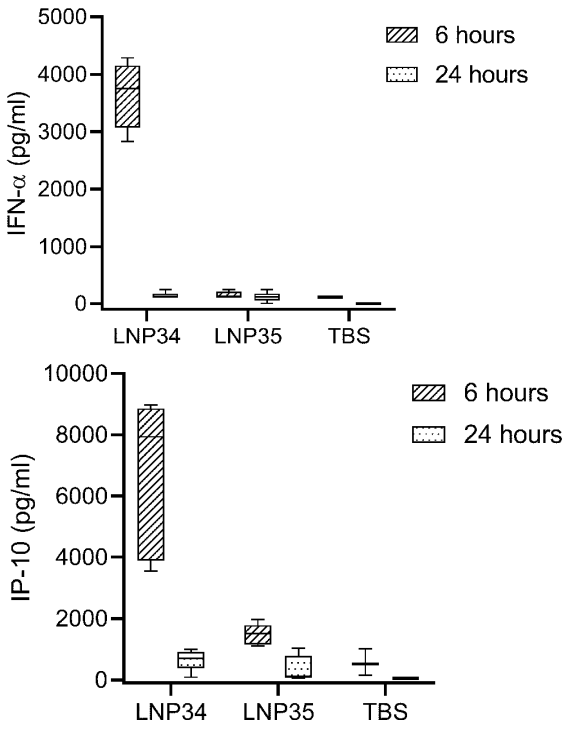

Macrophages
B cells
cDC1
Cellular association (ΔCy5 MFI)
***
***
**
2800
2400
2000
1600
1200
800
400
0
1600
1400
1200
1000
800
600
400
200
0
800
600
400
200
0
LNP34 (optimal)
LNP35 (not optimal)

Fig. 6D –cont.


cDC2
pDC
Cellular association (ΔCy5 MFI)
600
400
200
0
500
300
100
**
***
LNP34 (optimal)
LNP35 (not optimal)

E


IFN-α (pg/ml)
5000
4000
3000
2000
1000
0
6 hours
24 hours
LNP34
LNP35
TBS
IP-10 (pg/ml)
10000
8000
6000
4000
2000
0
6 hours
24 hours
LNP34
LNP35
TBS

F

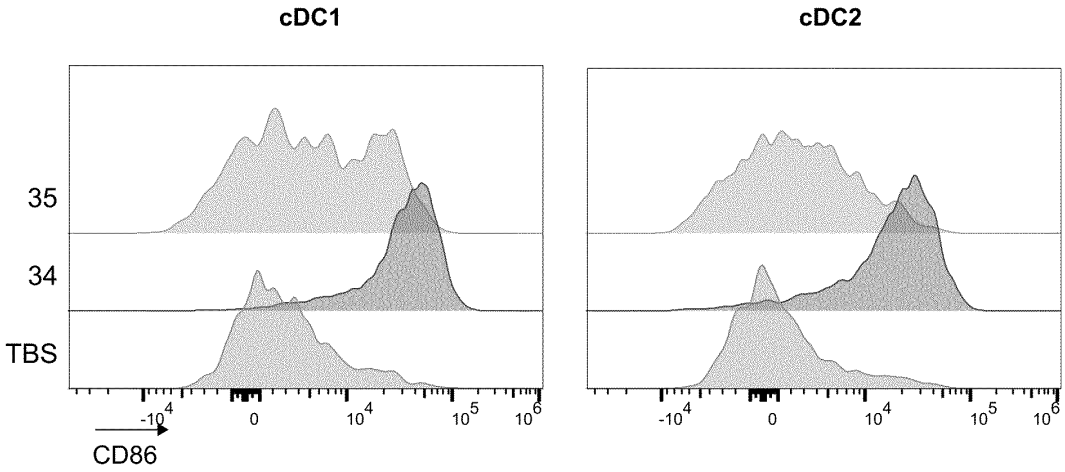
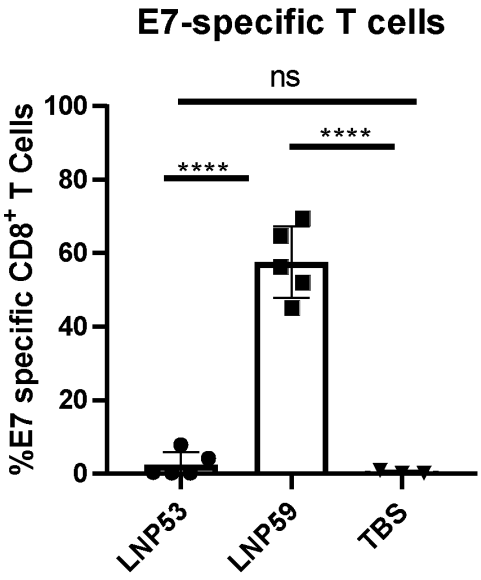

cDC1
cDC2
35
34
TBS
-10^4
0
10^4
10^5
10^6
CD86

Fig. 7


E7-specific T cells
ns
****
****
%E7 specific CD8+ T Cells
100
80
60
40
20
0
LNP53
LNP59
TBS