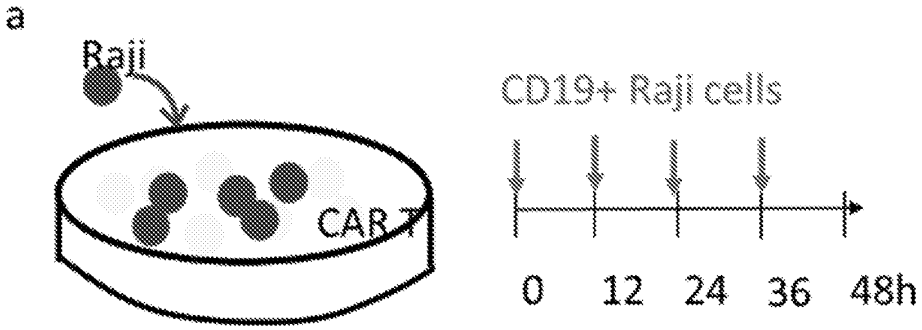

a
Raji
CAR T
CD19+ Raji cells
0
12
24
36
48h

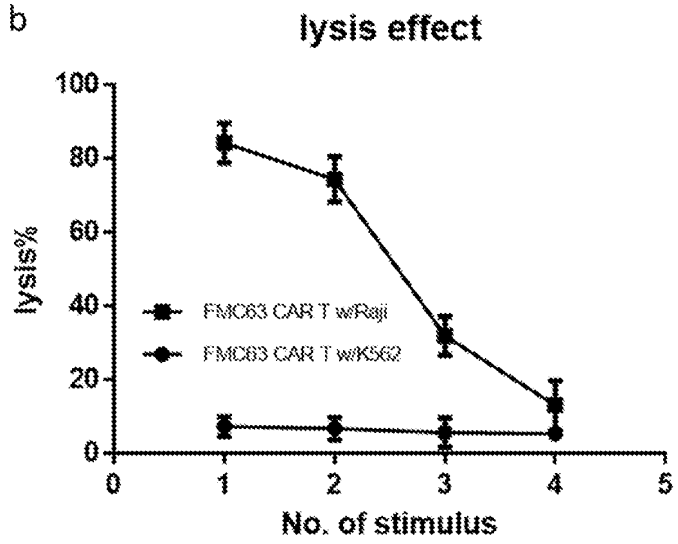

b
lysis effect
100
80
60
40
20
0
lysis%
FMC63 CAR T w/Raji
FMC63 CAR T w/K562
0
1
2
3
4
5
No. of stimulus

FIGURE 1

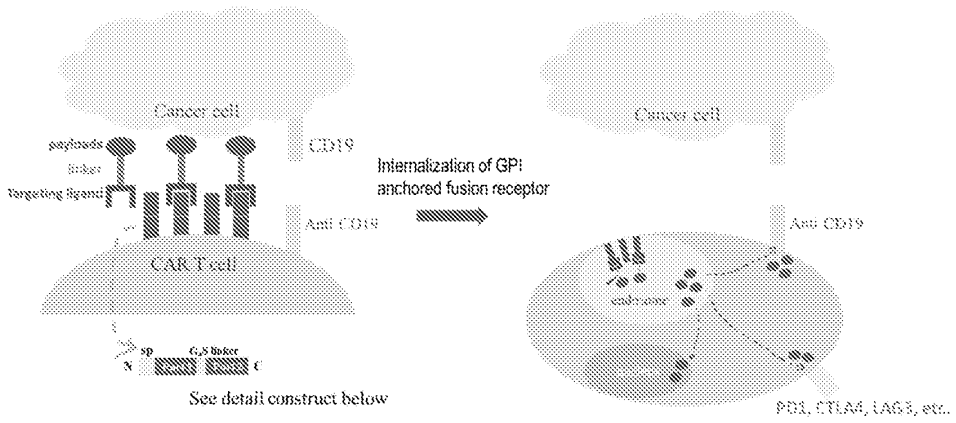

Cancer cell
CD19
Anti CD19
CAR T cell
See detail construct below
Internalization of GPI anchored fusion receptor
Cancer cell
Anti CD19
PD1, CTLA4, LAG3, etc.

FIGURE 2

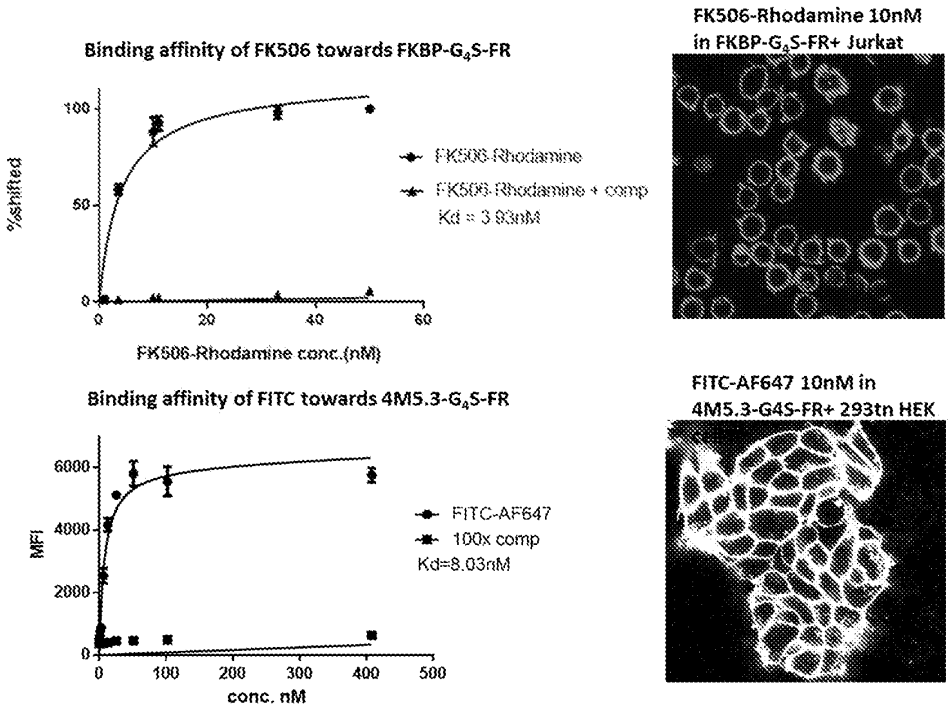
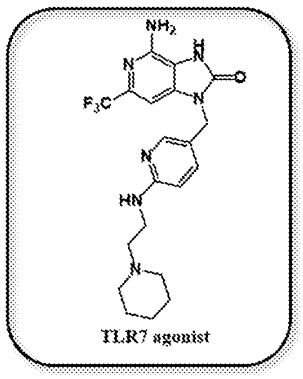

Binding affinity of FK506 towards FKBP-G4S-FR
%shifted
100
50
0
0
20
40
60
FK506-Rhodamine conc.(nM)
FK506-Rhodamine
FK506-Rhodamine + comp
Kd = 3.93nM
FK506-Rhodamine 10nM
in FKBP-G4S-FR+ Jurkat
Binding affinity of FITC towards 4M5.3-G4S-FR
MFI
6000
4000
2000
0
0
100
200
300
400
500
conc. nM
FITC-AF647
100x comp
Kd=8.03nM
FITC-AF647 10nM in
4M5.3-G4S-FR+ 293tn HEK

FIGURE 3

a



Chemical Formula: $C_{20}H_{24}F_3N_7O$
Molecular Weight: 435.46

b

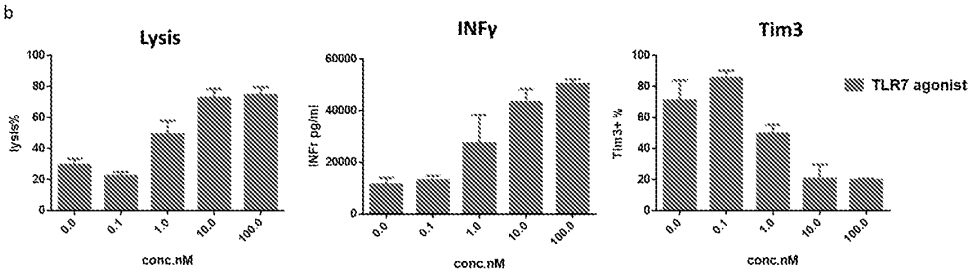


FIGURE 4

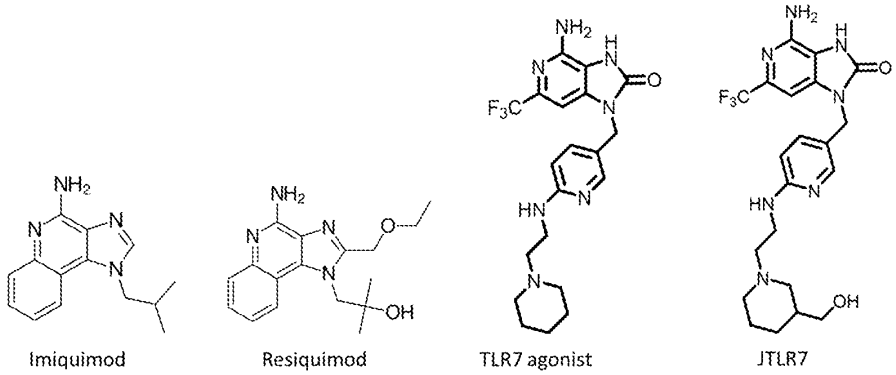

NH2
N
N
N
Imiquimod
NH2
N
N
O
N
OH
Resiquimod
NH2
H
N
N
O
F3C
N
HN
N
N
TLR7 agonist
NH2
H
N
N
O
F3C
N
HN
N
N
OH
JTLR7

FIGURE 5

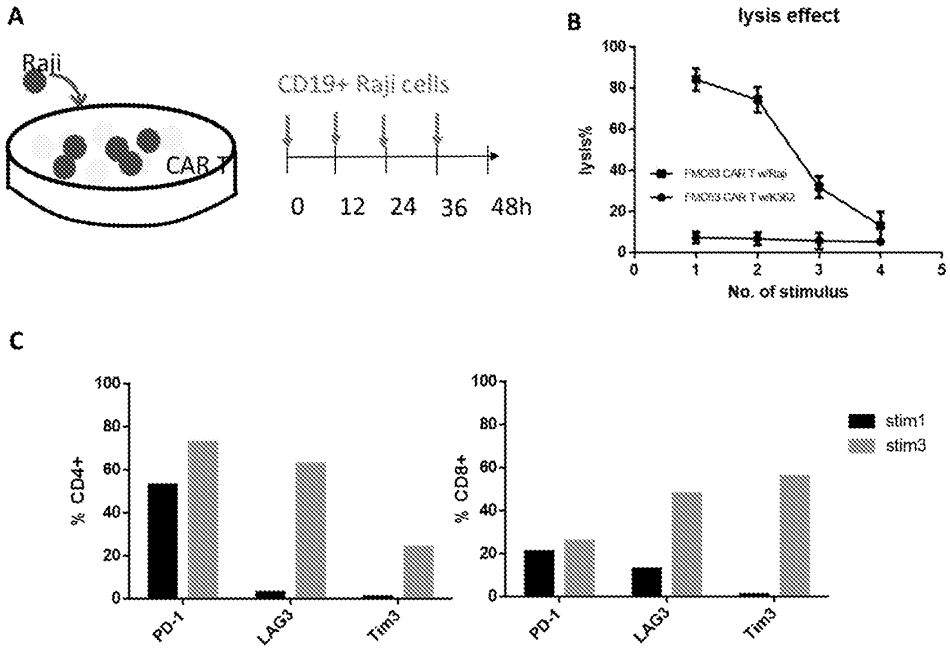

A
Raji
CAR T
CD19+ Raji cells
0 12 24 36 48h
B
lysis effect
lysis%
No. of stimulus
C
% CD4+
% CD8+
PD-1
LAG3
Tim3
stim1
stim3

FIGURE 6

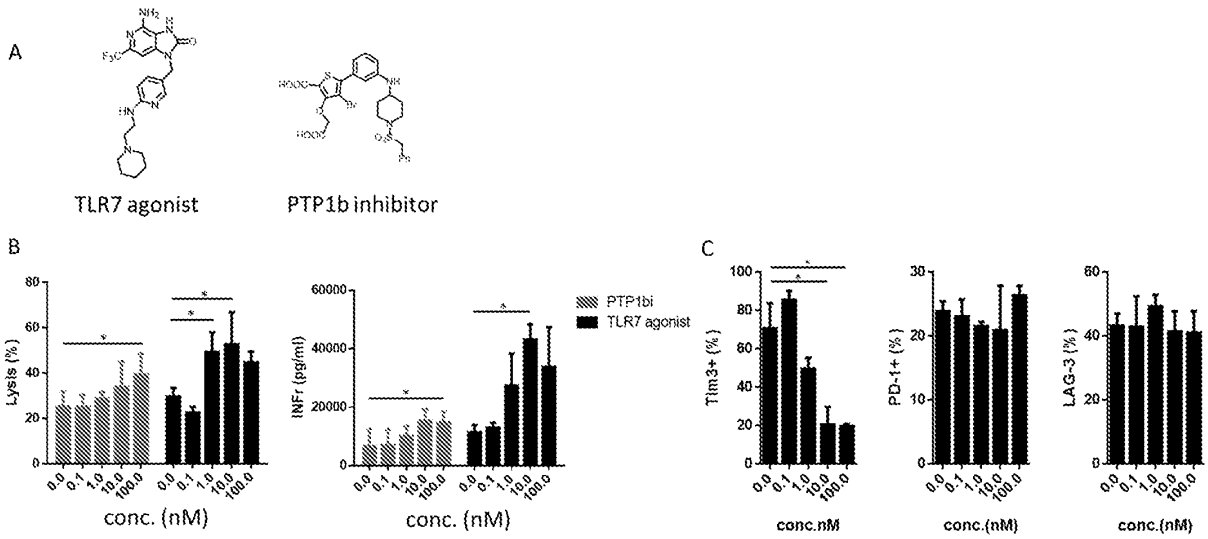

A
TLR7 agonist
PTP1b inhibitor
B
Lysis (%)
conc. (nM)
INFr (pg/ml)
conc. (nM)
PTP1bi
TLR7 agonist
C
Tim3+ (%)
conc.nM
PD-1+ (%)
conc.(nM)
LAG-3 (%)
conc.(nM)

FIGURE 7

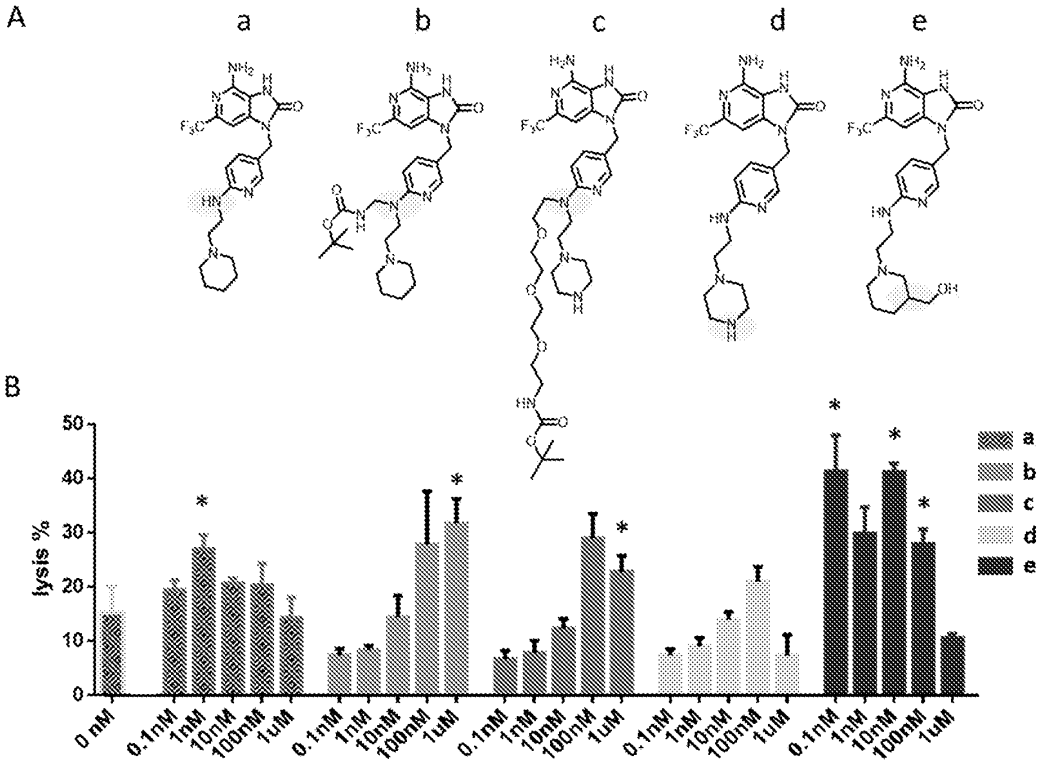

A
a
b
c
d
e
B
lysis %
50
40
30
20
10
0
0 nM
0.1nM
1nM
10nM
100nM
1uM
a
b
c
d
e

FIGURE 8

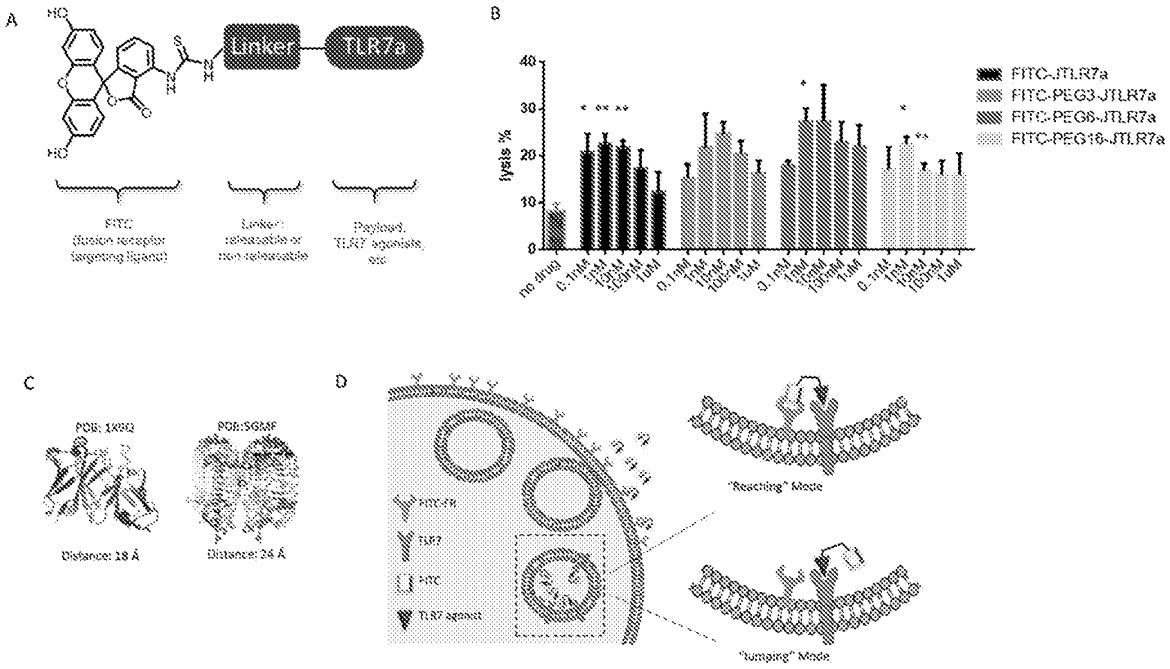

A
HO
HO
Linker
TLR7a
FITC
(fusion receptor
targeting ligand)
Linker:
releasable or
non-releasable
Payload,
TLR7 agonists,
etc
B
lysis %
40
30
20
10
0
FITC-JTLR7a
FITC-PEG3-JTLR7a
FITC-PEG6-JTLR7a
FITC-PEG16-JTLR7a
no drug
0.1nM
1nM
10nM
100nM
1uM
C
PDB: 1XBQ
PDB:5GMF
Distance: 18 Å
Distance: 24 Å
D
FITC-FR
TLR7
FITC
TLR7 agonist
"Reaching" Mode
"Jumping" Mode

FIGURE 9

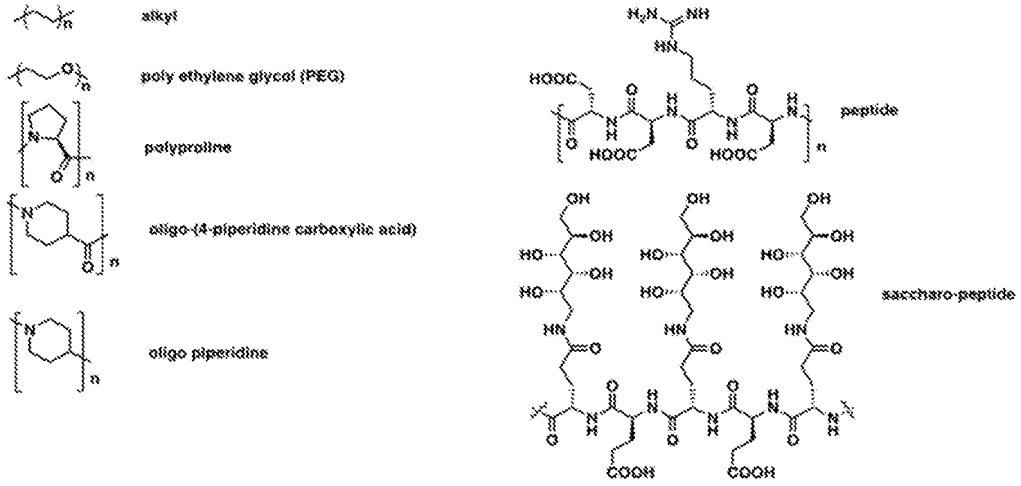

alkyl
poly ethylene glycol (PEG)
polyproline
oligo-(4-piperidine carboxylic acid)
oligo piperidine
peptide
saccharo-peptide

FIGURE 10