

[도1]

muMVR_VH QVQLKESGPGLVAPSQSLSTCTVSGFSL [RYSVH]WVRQPPGKGLEWLG [MIWGGGSTDYNSALKS]
 AAV401.68 QVQLQESGPGLVKPSETLSLTCTVSGGSIS [SYYS]WIRQPPGKGLEWIG [YIYNGSTNYNPSLKS]
 huMVR.H1 QVQLQESGPGLVKPSETLSLTCTVSGGSIS [RYSVH]WIRQPPGKGLEWIG [MIWGGGSTDYNSALKS]
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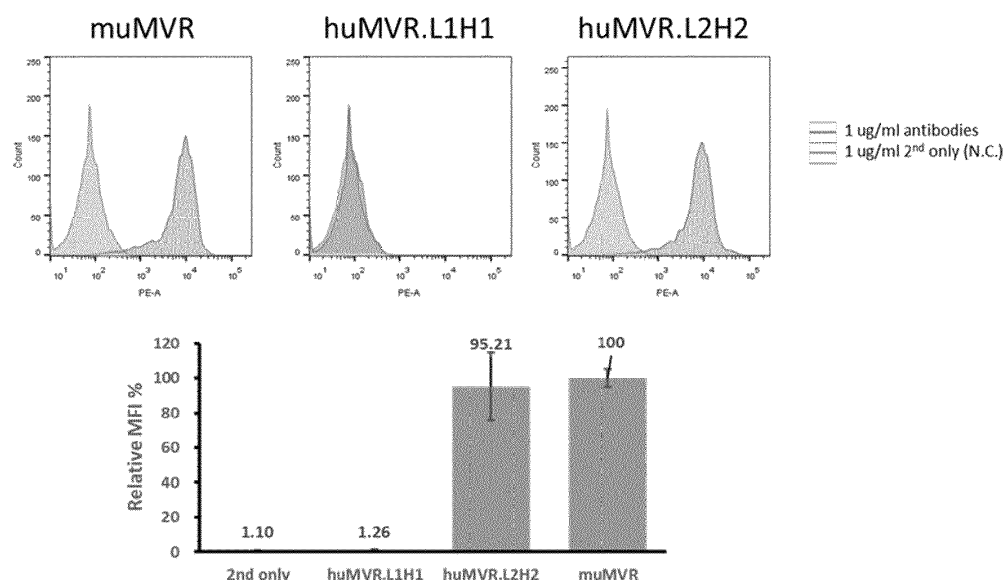
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[도2]

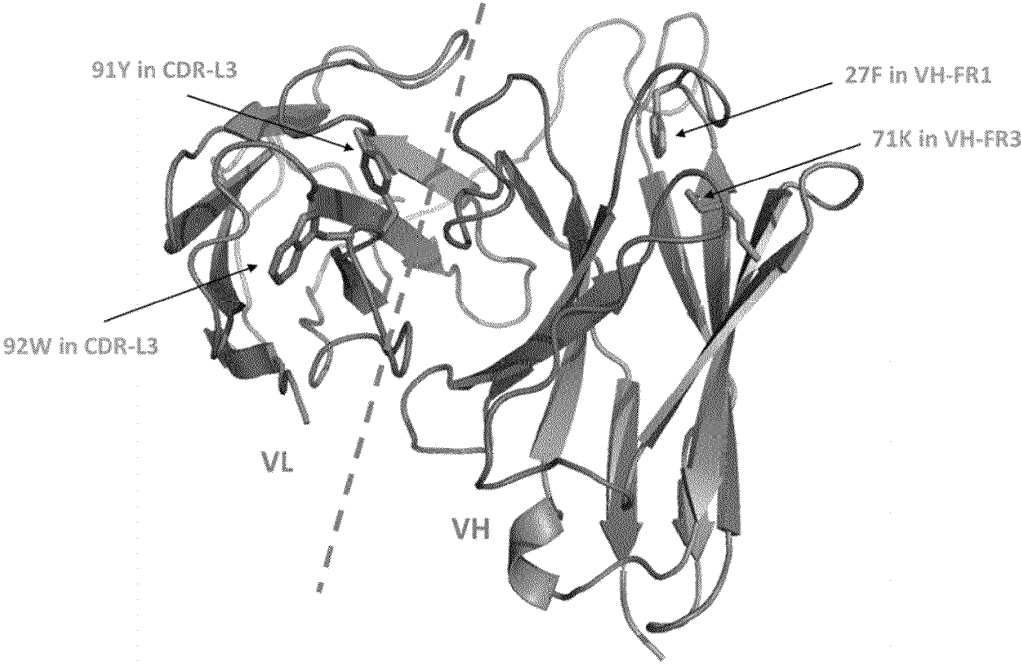
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 huMVR.L1 DIQMTQSPSSLSASVGDRTITC [RASDHINNWL]WYQQKPGKAPKLLLY [GATRLS]
 huMVR.L2 DIQMTQSPSSLSASVGDRTITC [KASDHINNWL]WYQQKPGKAPKLLIS [GATSLET]

muMVR_VL GVPSRFGSGSGKDYTLISLTQTEDVATYYC [QQYWSTPFT]FGSGTKLEIK
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 huMVR.L1 GVPSRFGSGSGTDYTLTISLQPEDFATYYC [QQYWSTPFT]FGGQTKVEIK
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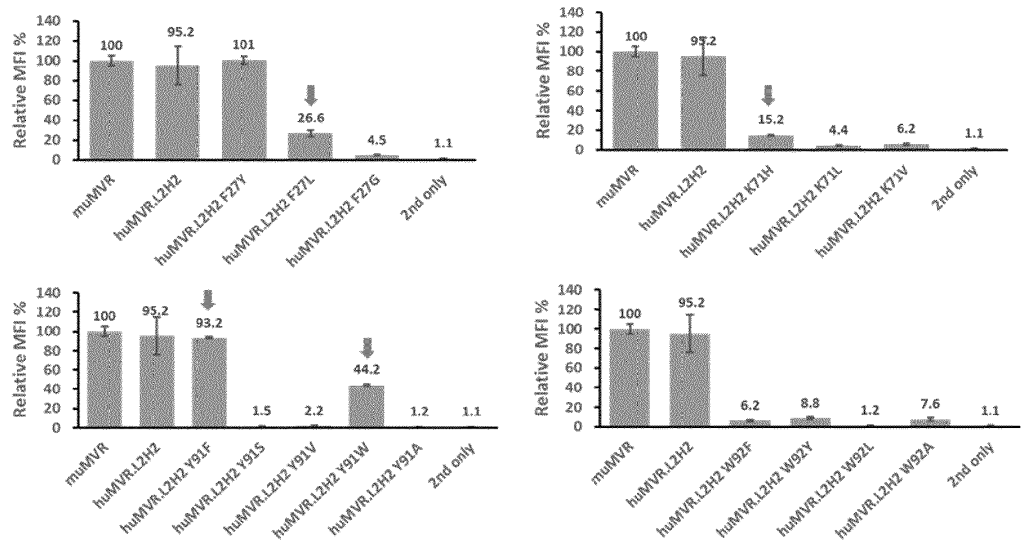
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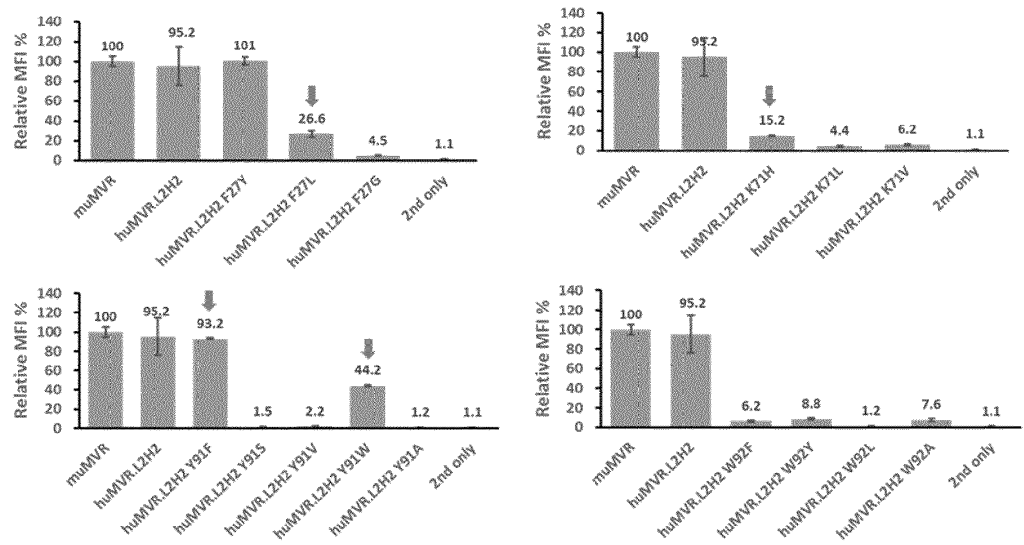
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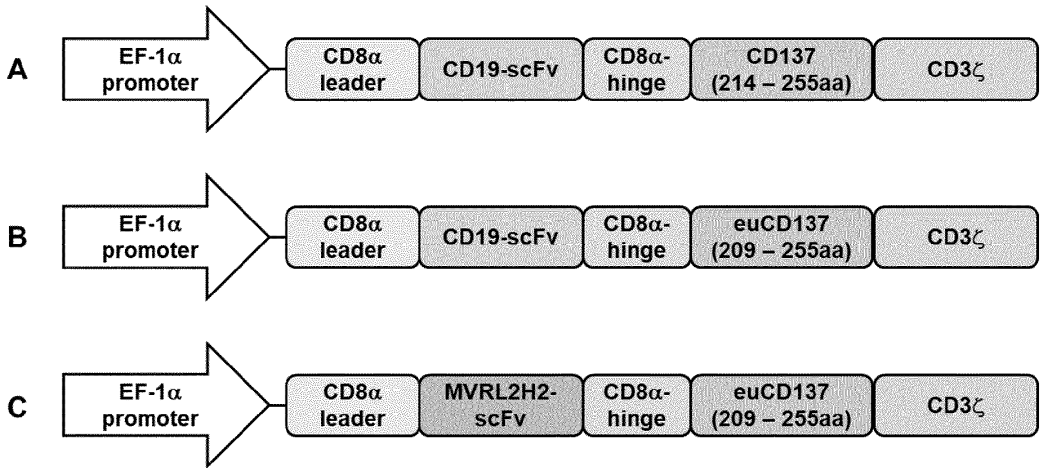
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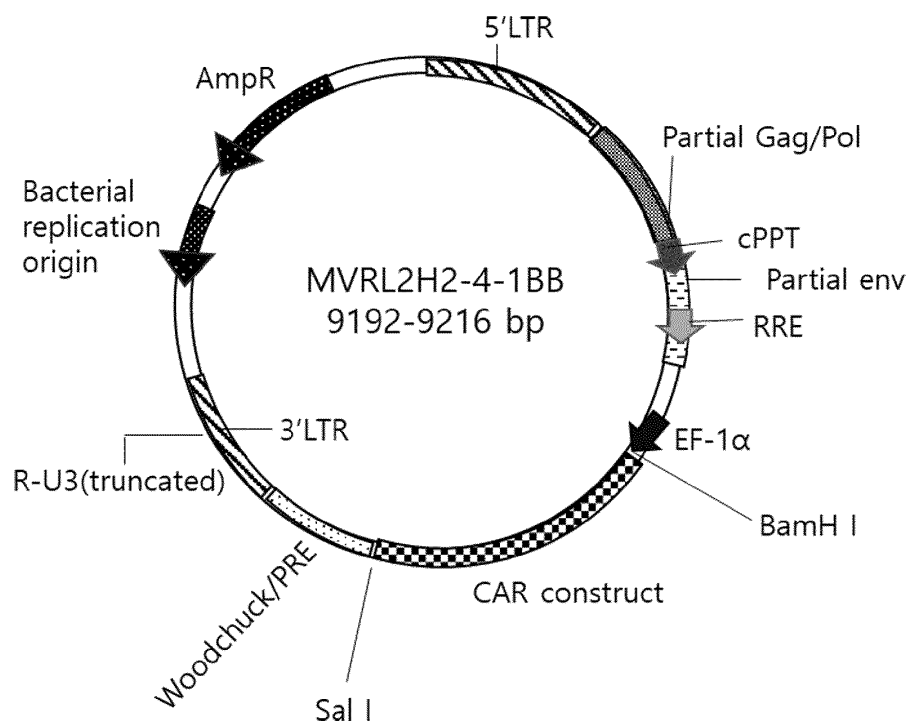
[圖5b]



[圖6a]



[도 6b]



[E7a]

7. Variable region of huMVR.H2 heavy chain

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NQVSLKLSSVTAADTAVYYCARNEGDITAGTWFAFWGQGTLTVSS

8. Variable region of huMVR.L2 Light chain

DIQMTQSPSSLSASVGDRVTITCKASDHINNWLAWYQQKPGKAPKLLISGATSLETGVPSRFSGSGSGKDYLTLIS
SLQPEDFATYYCQYWSTPFTFGQGTKVEIK

9. scFv of huMVR.L2H2

DIQMTQSPSSLSASVGDRVTITCKASDHINNWLAWYQQKPGKAPKLLISGATSLETGVPSRFSGSGSGKDYLTLIS
SLQPEDFATYYCQYWSTPFTFGQGTKVEIKGGGGSGGGSGGGGSQVQLQESGPGLVKPSSETLSLTCTVSGFSL
SRYSVHWIRQPPGKGLEWLGMIWGGGSTDYNSALKSRLTISKDNSKNQVSLKLSSVTAADTAVYYCARNEGDIT
AGTWFAFWGQGTLTVSS

10. Variable region of huMVR.H1 heavy chain

QVQLQESGPGLVKPSSETLSLTCTVSGGSISRYSVHWIRQPPGKGLEWIGMIWGGGSTDYNSALKSRVTISVDTSK
NQFSLKLSSVTAADTAVYYCARNEGDITAGTWFAFWGQGTLTVSS

11. Variable region of huMVR.L1 light chain

DIQMTQSPSSLSASVGDRVTITCRASDHINNWLAWYQQKPGKAPKLLYGATRLVPSRFSGSGSGDYLTLI
SSLQPEDFATYYCQYWSTPFTFGGQGTKVEIK

[7b]

12. scFv of huMVRL1H1

DIQMTQSPSSLSASVGDRVTITCRASDHINNWLAWYQQKPGKAPKLLYGATRLESGVPSRFSGSGSGTDYTLTI
SSLQPEDFATYYCQQYWSTPFTFGGGTKVEIKGGGSGGGGSGGGGSGVQLQESGPGLVKPSSETLSLTCTVSGG
SISRYSVHWIRQPPGKGLEWIGMIWGGGSTDYNSALKSRVTISVDTSKNQFSLKLSVTAADTAVYYCARNEGDT
TAGTWFAFWGQGTLVTVSS

13. 4-1BB signaling domain

KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL

14. euCD137

RFSVVKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL

[7c]

15. sequence of MVR.L2H2 CAR

GATATTCAGATGACCCAGTCCCCGAGCTCCCTGTCCGCCTCTGTGGGCGATAGGGTCACCATCACCTGCAAGG
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GCGGCGCCACCTCTCTGAAACCGGAGTCCCTTCTCGCTTCTCTGGTTCCGGATCTGGGAAGGATTACACTCT
GACCATCAGCAGTCTGCAGCCGGAAGACTTCGCAACTTATTACTGTCAGCAGTACTGGTCCACCCCTTCACC
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AAGGACAACCTCCAAGAACCAGGTGTCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACGGCCGTGATTAC
TGTGCGAGAAATGAGGGCGATACCACCGCCGGCACTTGGTTTGCCTATTGGGGCCAGGGAACCTGGTCACC
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AGATGGCTGTAGCTGCCGATTTCAGAAGAAGAAGAAGGAGGATGTGAACTG
AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGGTACAAGCAGGGCCAGAACCAGCTCTATAACGAGCT
CAATCTAGGACGAAGAGAGGAGTACGATGTTTTGGACAAGAGACGTGGCCGGGACCCTGAGATGGGGGGA
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ACAGTGAGATTGGGATGAAAGGCGAGCGCCGGAGGGGCAAGGGGCACGATGGCCTTTACCAGGGTCTCAG
TACAGCCACCAAGGACACCTACGACGCCCTTCACATGCAGGCCCTGCCCCCTCGCTAA

[7d]

16. sequence of MVR.L2H2 CAR_euCD137

GATATTCAGATGACCCAGTCCCCGAGCTCCCTGTCCGCCTCTGTGGGCGATAGGGTCACCATCACCTGCAAGG
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GCGGCGCCACCTCTCTGAAACCGGAGTCCCTTCTCGCTTCTCTGGTTCCGGATCTGGGAAGGATTACACTCT
GACCATCAGCAGTCTGCAGCCGGAAGACTTCGCAACTTATTACTGTCAGCAGTACTGGTCCACCCCTTCACC
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GGATCTCAGGTGCAGCTGCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACCTGC
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TGTGCGAGAAATGAGGGCGATACCACCGCCGGCACTTGGTTTGCCTATTGGGGCCAGGGAACCCTGGTCACC
GTCTCTCAACCACGACGCCAGCGCCGCGACCACCAACACCGGCGCCCAACATCGCTAGCCAGCCCCTGTCC
CTGCGCCCAGAGGCGTGCCGGCCAGCGCGGGGGGCGCAGTGCACACGAGGGGGCTGGACTTCGCCTGTG
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CAATCTAGGACGAAGAGAGGAGTACGATGTTTTGGACAAGAGACGTGGCCGGGACCCTGAGATGGGGGGA
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ACAGTGAGATTGGGATGAAAGGCGAGCGCCGGAGGGGCAAGGGGCACGATGGCCTTTACCAGGGTCTCAG
TACAGCCACCAAGGACACCTACGACGCCCTTCACATGCAGGCCCTGCCCCCTCGCTAA

[E7e]

17. sequence of CD19 CAR

GACATCCAGATGACACAGACTACATCCTCCCTGTCTGCCTCTCTGGGAGACAGAGTCACCATCAGTTGCAGGG
CAAGTCAGGACATTAGTAAATATTTAAATTGGTATCAGCAGAAACCAGATGGAAGTGTAAACTCCTGATCTAC
CATACTCAAGATTACACTCAGGAGTCCCATCAAGGTTCACTGGCAGTGGGTCTGGAACAGATTATTCTCTCAC
CATTAGCAACCTGGAGCAAGAAGATATTGCCACTTACTTTTGCCAACAGGGTAATACGCTTCCGTACACGTTT
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ACCACGACGCCAGCGCCGACCAACACCGGCGCCACCATCGCTAGCCAGCCCTGTCCCTGCGCCC
AGAGGCGTGCCGGCCAGCGCGGGGGGCGCAGTGACACAGAGGGGGCTGGACTTCGCTGTGATATCTAC
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[7f]

18. sequence of CD19 CAR_euCD137

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CAAGTCAGGACATTAGTAAATATTTAAATTGGTATCAGCAGAAACCAGATGGAAGTGTAACTCCTGATCTAC
CATACTCAAGATTACACTCAGGAGTCCCATCAAGGTTCAAGTGGCAGTGGGTCTGGAACAGATTATTCTCTCAC
CATTAGCAACCTGGAGCAAGAAGATATTGCCACTTACTTTTGCCAACAGGGTAATACGCTTCCGTACACGTTT
GGAGGGGGGACCAAGCTGGAGATCACAGGTGGCGGTGGCTCGGGCGGTGGTGGGTGGGTGGCGGCGGA
TCTGAGGTGAACTGCAGGAGTCAGGACCTGGCTGGTGGCGCCCTCACAGAGCCTGTCCGTACATGCACT
GTCTCAGGGGTCTCATTACCCGACTATGGTGTAAAGCTGGATTGCGCAGCCTCCACGAAAGGGTCTGGAGTGGC
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AACTCCAAGAGCCAAGTTTTCTTAAAAATGAACAGTCTGCAAAGTATGACACAGCCATTTACTACTGTGCCA
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AGAGGCGTGCCGGCCAGCGGCGGGGGGCGCAGTGACACAGAGGGGGCTGGACTTCGCTGTGATATCTAC
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[7g]

19. EF1a-promoter

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ccttgaatttgcctttttagtttgatcttggttcattctcaagcctcagacagtgttcaaagtttttcttccatttcaggtgtcgtga

[$\pm 7h$]20. CD8- α leader sequence

GGATCCATGGCCTTACCACTGACCGCCTTGCTCCTGCCGCTGGCCTTGCTGCTCCACGCCGCCAGGCCG

21. Flag

gactacaaggacgacgatgacaag

22. CD19scFv

GACATCCAGATGACACAGACTACATCCTCCCTGTCTGCCTCTCTGGGAGACAGAGTCACCATCAGTTGCAGGG
CAAGTCAGGACATTAGTAAATATTTAAATTGGTATCAGCAGAAACCAGATGGAAGTGTAAACTCCTGATCTAC
CATACATCAAGATTACACTCAGGAGTCCCATCAAGGTTCACTGGCAGTGGGTCTGGAACAGATTATTCTCTCAC
CATTAGCAACCTGGAGCAAGAAGATATTGCCACTTACTTTTGCCAACAGGGTAATACGCTTCCGTACACGTTT
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GTCTCAGGGGTCTCATTACCCGACTATGGTGAAGCTGGATTGCGCCAGCCTCCACGAAAGGGTCTGGAGTGGC
TGGGAGTAATATGGGGTAGTGAAACCACATACTATAATTCAGCTCTCAAATCCAGACTGACCATCATCAAGGAC
AACTCCAAGAGCCAAGTTTTCTTAAAAATGAACAGTCTGCAAAGTATGACACAGCCATTTACTACTGTGCCA
AACATTATTACTACGGTGGTAGCTATGCTATGGACTACTGGGGCCAAGGAACCTCAGTCACCGTCTCCTCA

23. CD8/Hinge/Transmembrane Sequence

ACCACGACGCCAGCGCCGCGACCAACACCGGCGCCACCATCGCTAGCCAGCCCCTGTCCCTGCGCCC
AGAGGCGTGCCGCGCAGCGCGGGGGGCGCAGTGACACGAGGGGGCTGGACTTCGCCTGTGATATCTAC
ATCTGGGCGCCCTTGGCGGGGACTTGTGGGGTCTTCTCCTGTCACTGGTTATCACCCCTTTACTGC

[도 7i]

24. CD3z

AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGGTACAAGCAGGGCCAGAACCAGCTCTATAACGAGCT
CAATCTAGGACGAAGAGAGGAGTACGATGTTTTGGACAAGAGACGTGGCCGGGACCCTGAGATGGGGGGA
AAGCCGAGAAGGAAGAACCCTCAGGAAGGCCTGTACAATGAACTGCAGAAAGATAAGATGGCGGAGGCCT
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25. Woodchuck/PRE

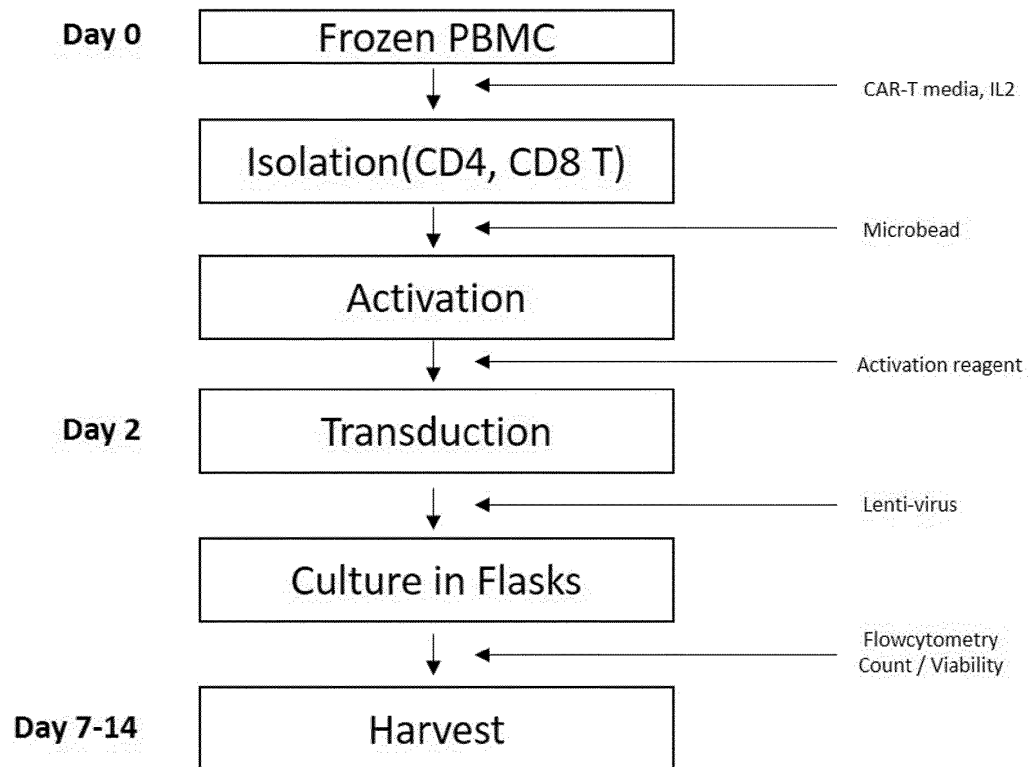
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26. R/region

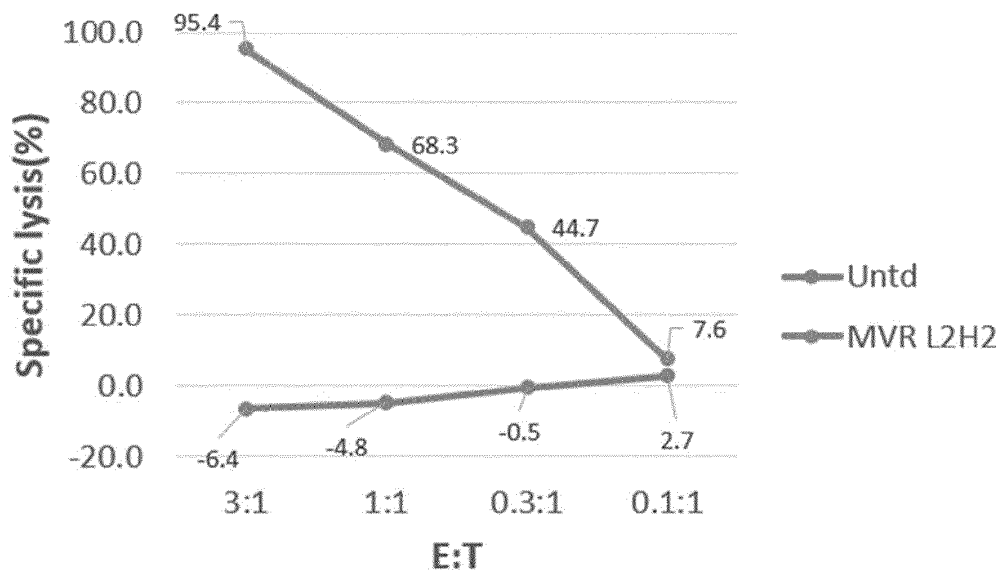
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[도8]

MVR CAR-T 세포 생산 공정

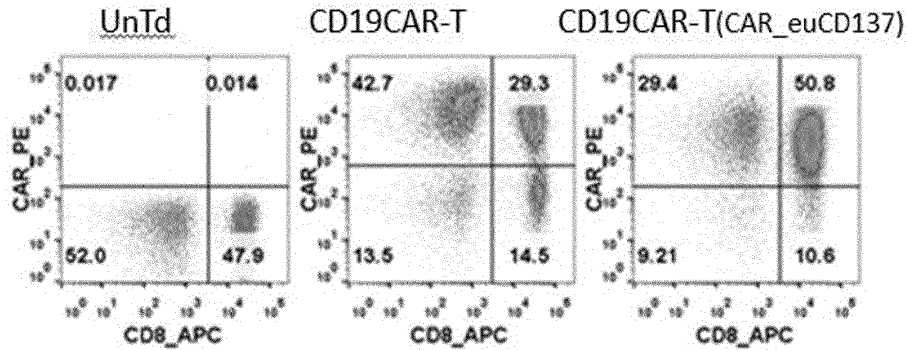


[도9]

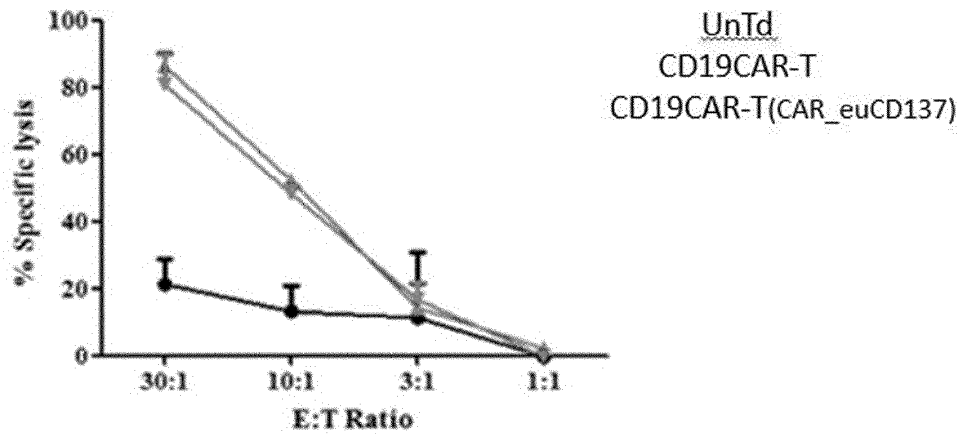


[510]

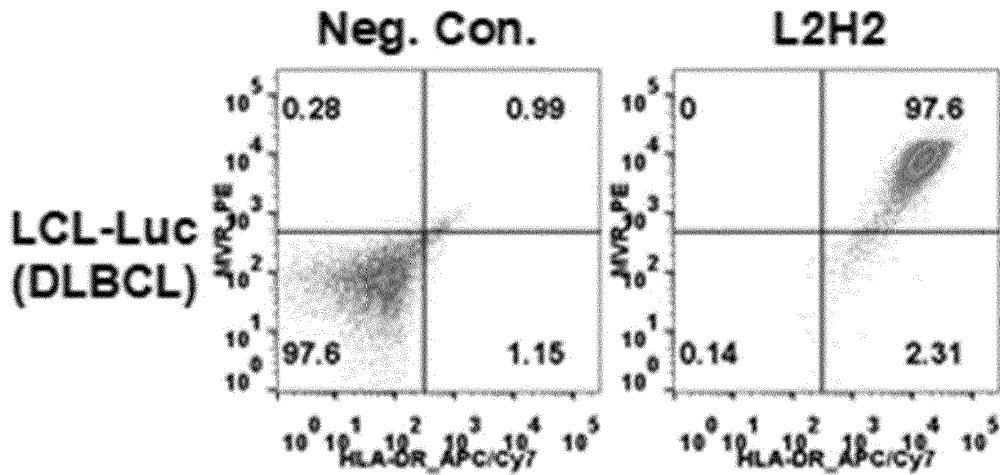
A. CAR expression (Day 14)



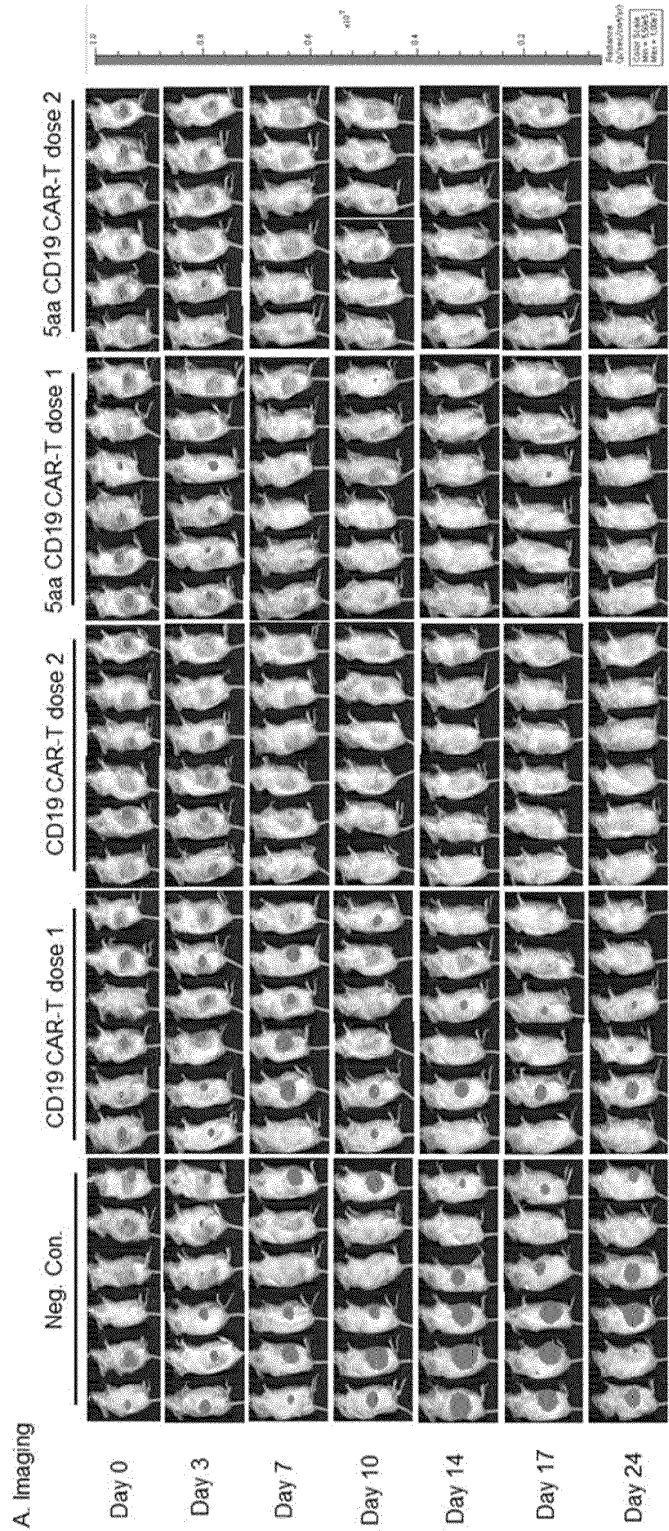
B. Killing activity (4 hr)



[511]

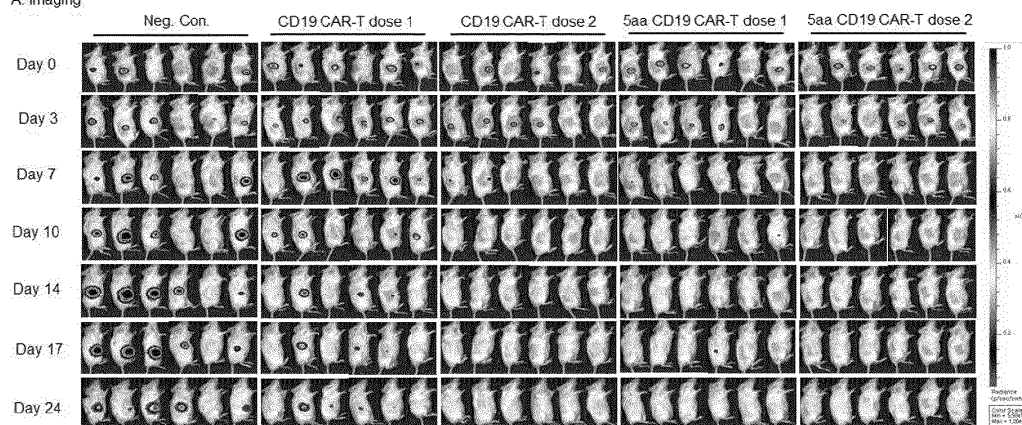


[Figure 12a]



[도 12b]

A. Imaging



B. Photon value

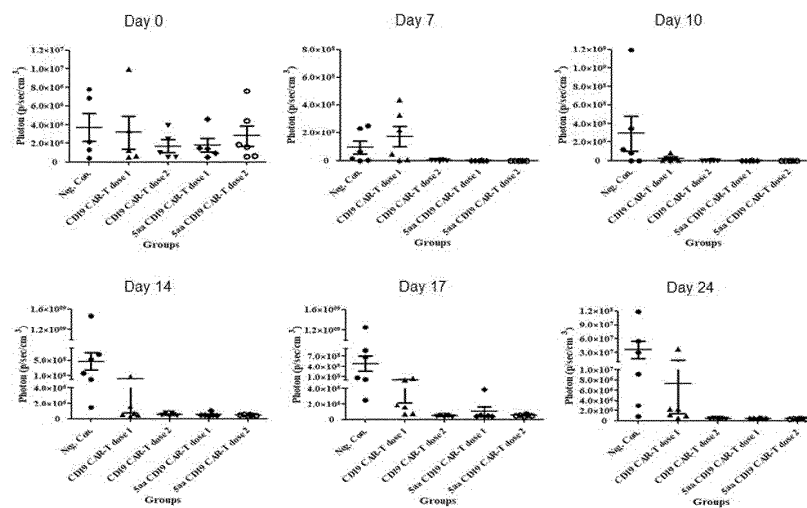


Figure 1 consists of four dot plots showing the percentage of CAR+ cells in the spleen at Days 8, 11, 15, and 18 post-infection. Each plot compares four groups: Neg. Con., CD19 CAR+ dose 1, CD19 CAR+ dose 2, and the 100x10⁶ CD19 CAR+ dose 2 group. The y-axis represents '% of CAR' from 0 to 60. The x-axis represents 'Groups'. Data points are shown as individual dots with horizontal bars indicating the mean and standard deviation. The percentage of CAR+ cells increases over time for all groups, with the 100x10⁶ CD19 CAR+ dose 2 group showing the highest percentages, reaching approximately 50% by Day 18.

Day 8

Group	NOD4 (%)	NOD8 (%)
Neg. Con.	~1	~1
CD13 CAR-T day 1	~1	~1
CD13 CAR-T day 2	~35	~35
Neg. CD13 CAR-T day 2	~35	~35

Day 11

Group	NOD4 (%)	NOD8 (%)
Neg. Con.	~1	~1
CD13 CAR-T day 1	~1	~1
CD13 CAR-T day 2	~35	~35
Neg. CD13 CAR-T day 2	~35	~35

Day 15

Group	NOD4 (%)	NOD8 (%)
Neg. Con.	~1	~1
CD13 CAR-T day 1	~1	~1
CD13 CAR-T day 2	~35	~35
Neg. CD13 CAR-T day 2	~35	~35

Day 18

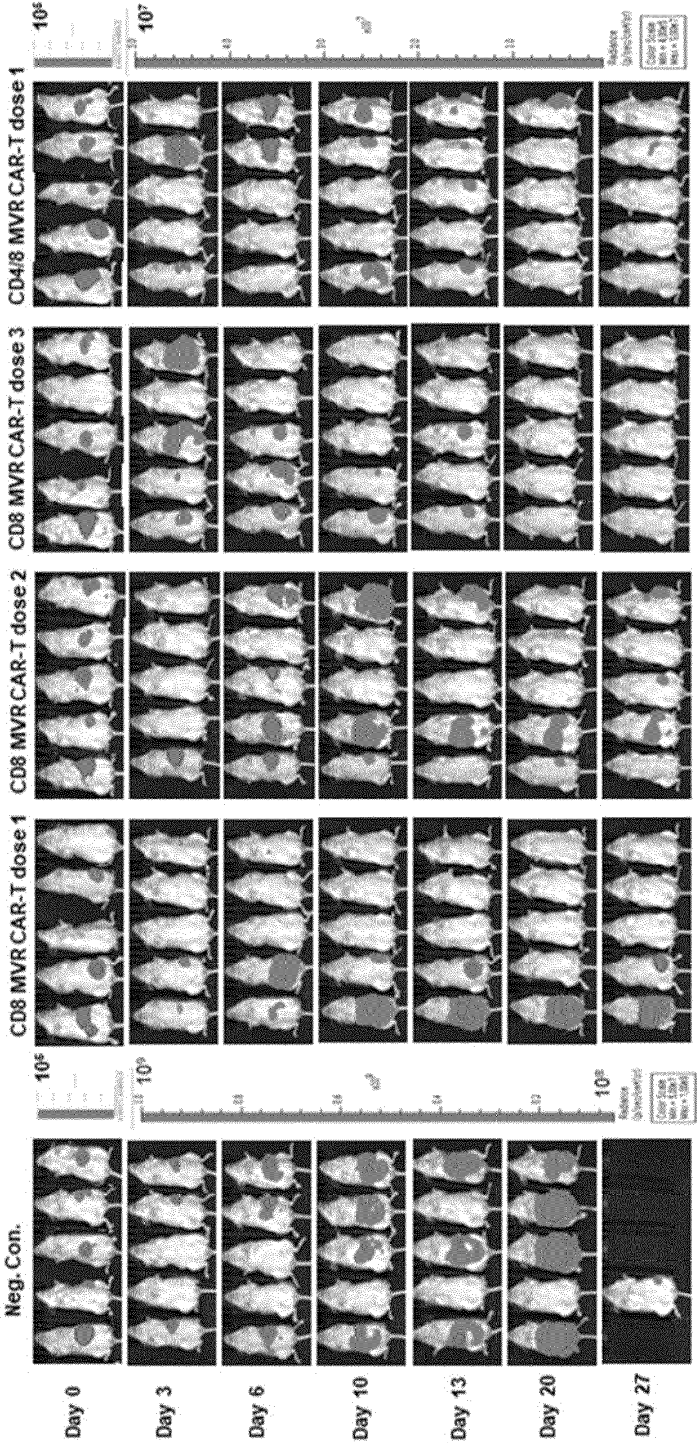
Group	NOD4 (%)	NOD8 (%)
Neg. Con.	~1	~1
CD13 CAR-T day 1	~1	~1
CD13 CAR-T day 2	~35	~35
Neg. CD13 CAR-T day 2	~35	~35

Day 25

Group	NOD4 (%)	NOD8 (%)
Neg. Con.	~1	~1
CD13 CAR-T day 1	~1	~1
CD13 CAR-T day 2	~35	~35
Neg. CD13 CAR-T day 2	~35	~35

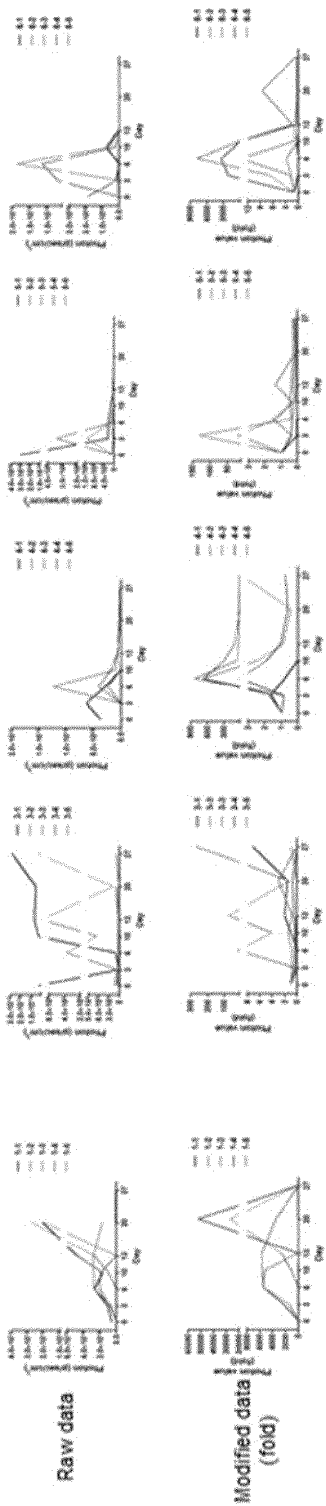
[도14a]

A. Imaging



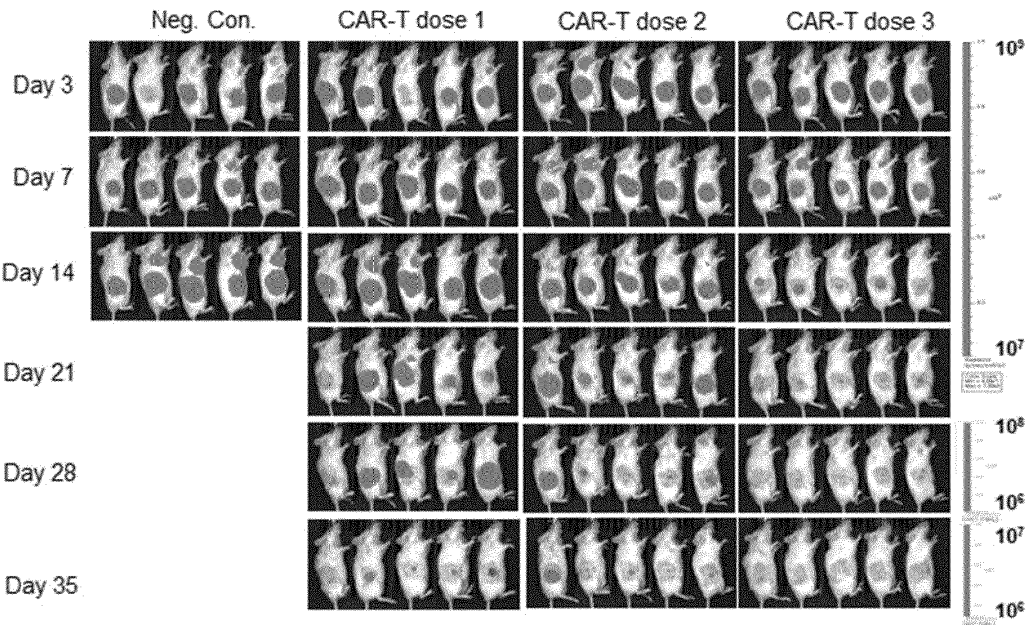
[도14b]

B. Photon value



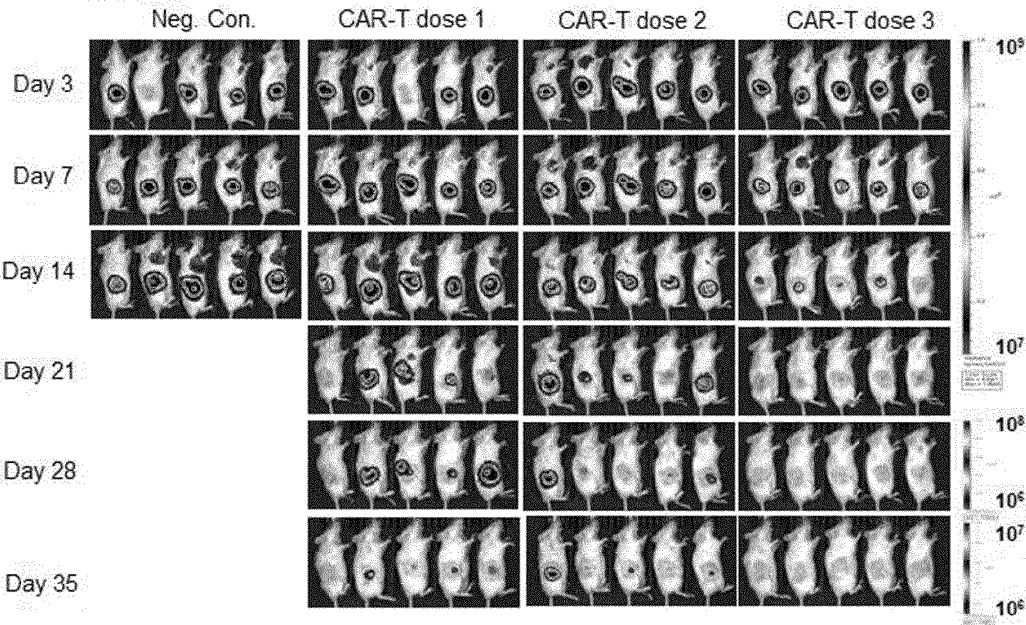
[515a]

A. IVIS imaging

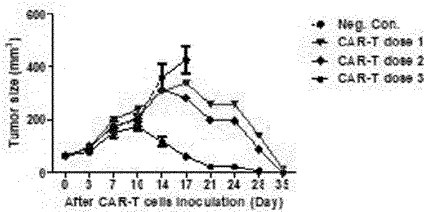


[515b]

A. IVIS imaging

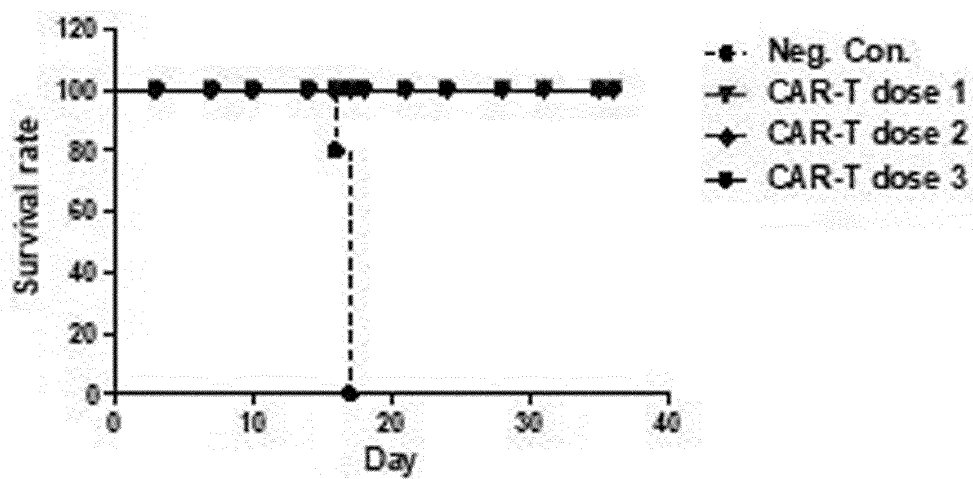


B. Tumor growth



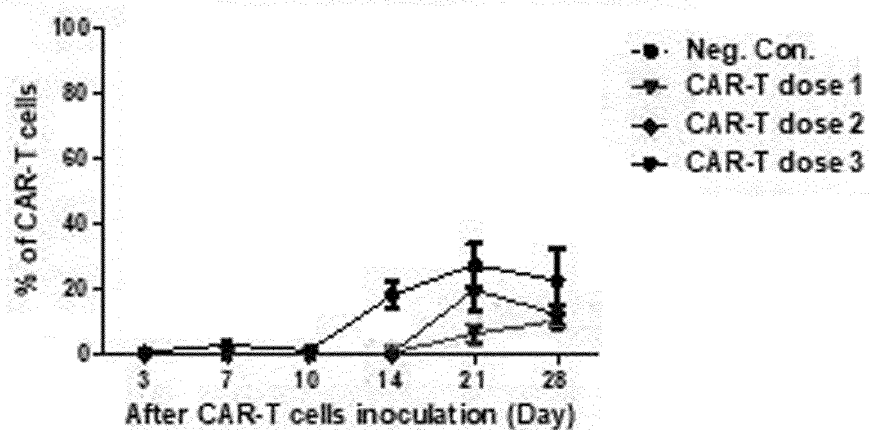
[E16]

Survival rate



[517]

A. % of CAR-T cells in mouse blood



B. Number of CAR-T cells in mouse blood

