

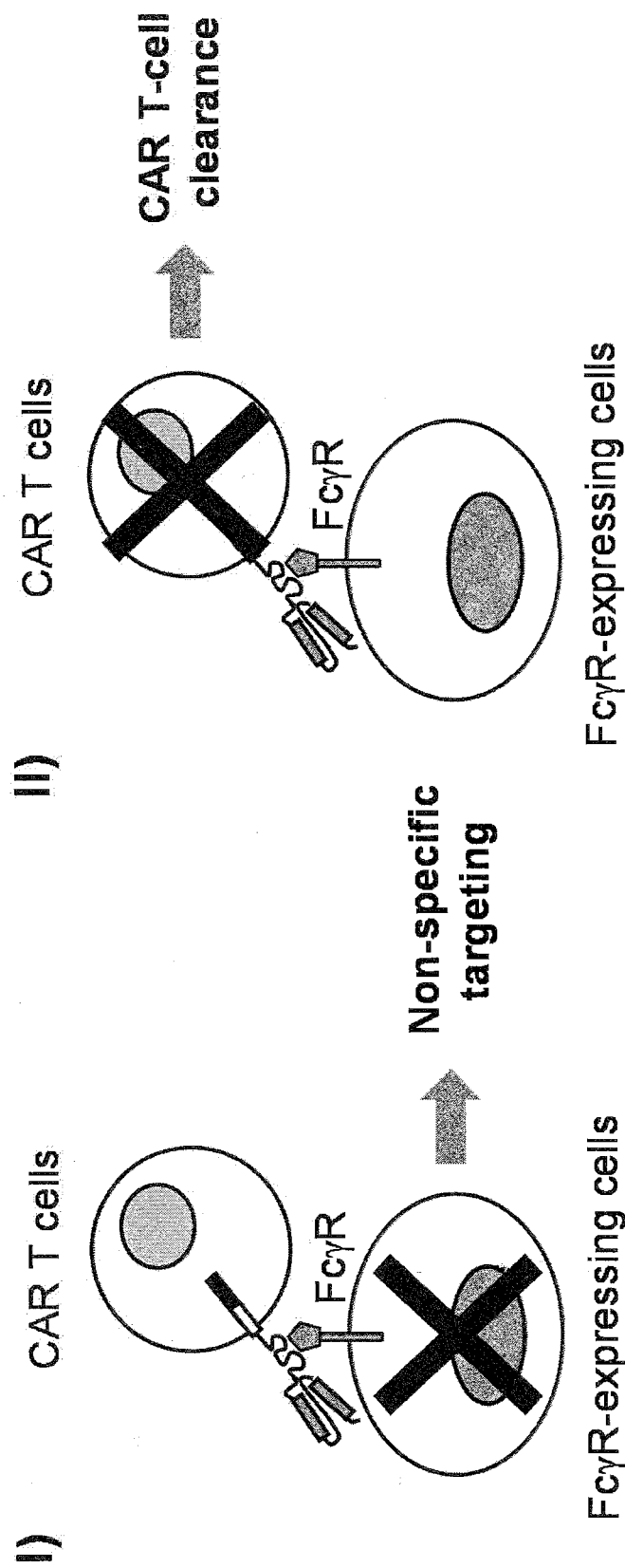


FIG. 1A

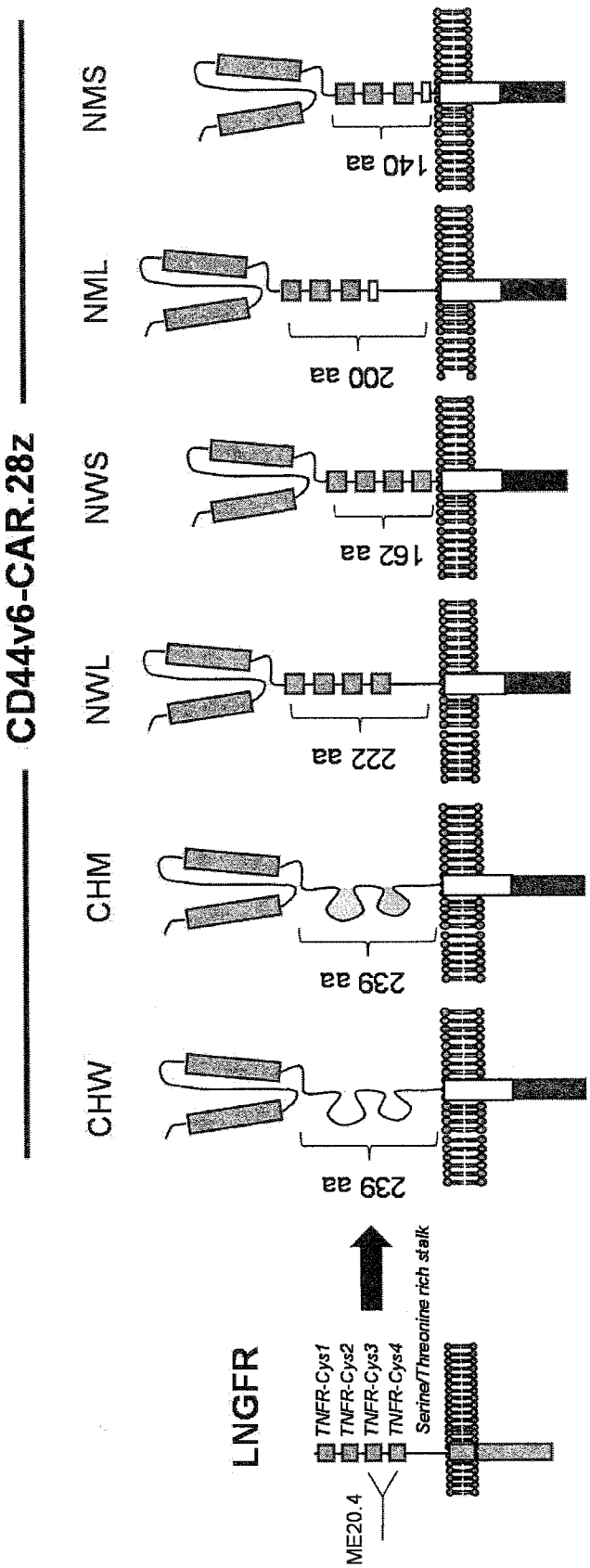


FIG. 1B

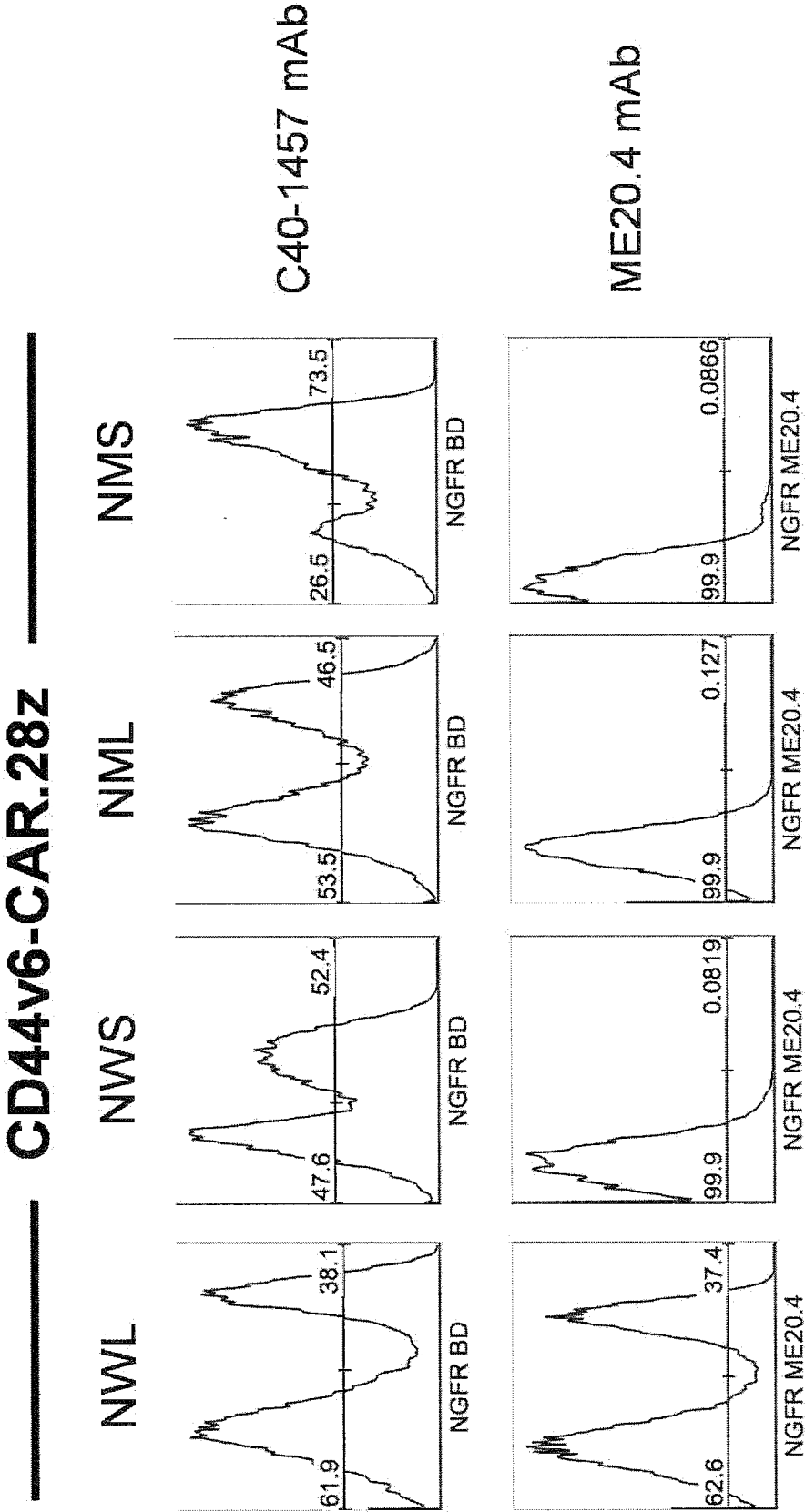


FIG. 2A

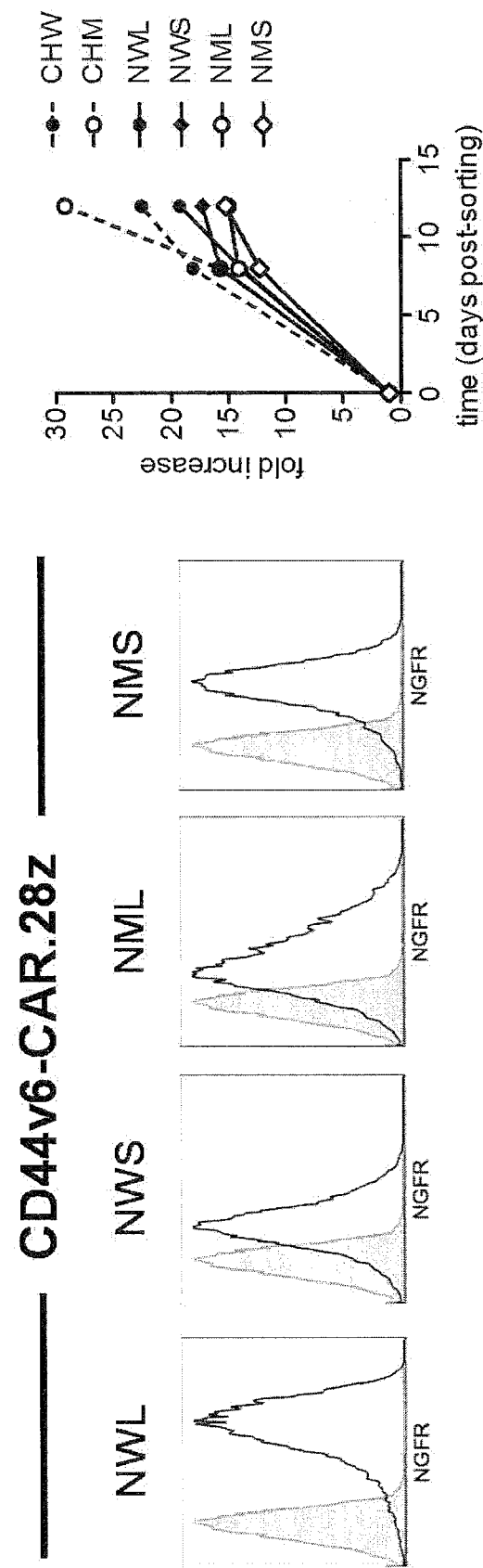


FIG. 2B

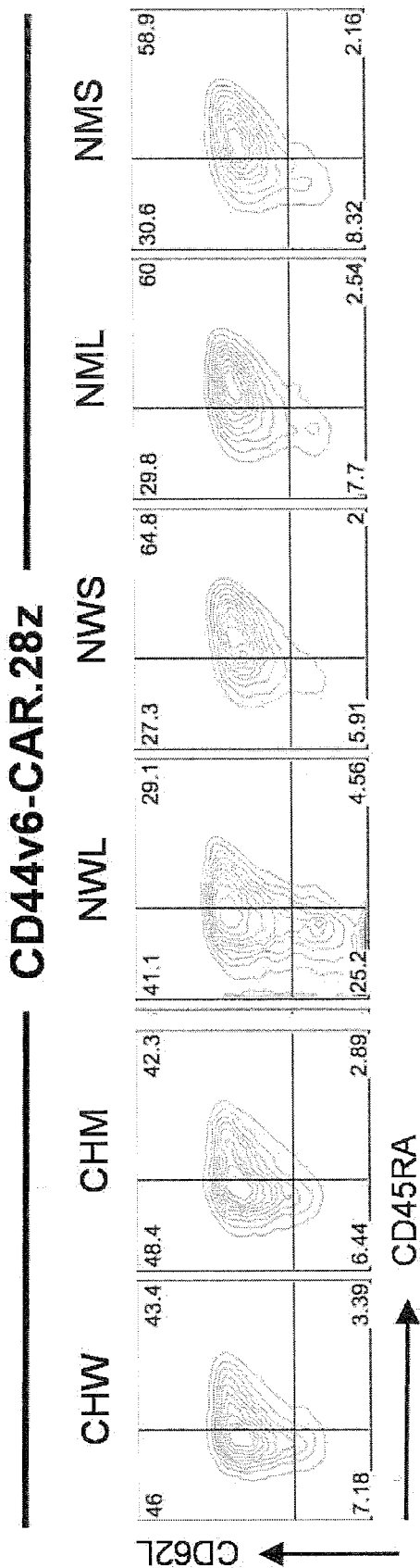


FIG. 2C

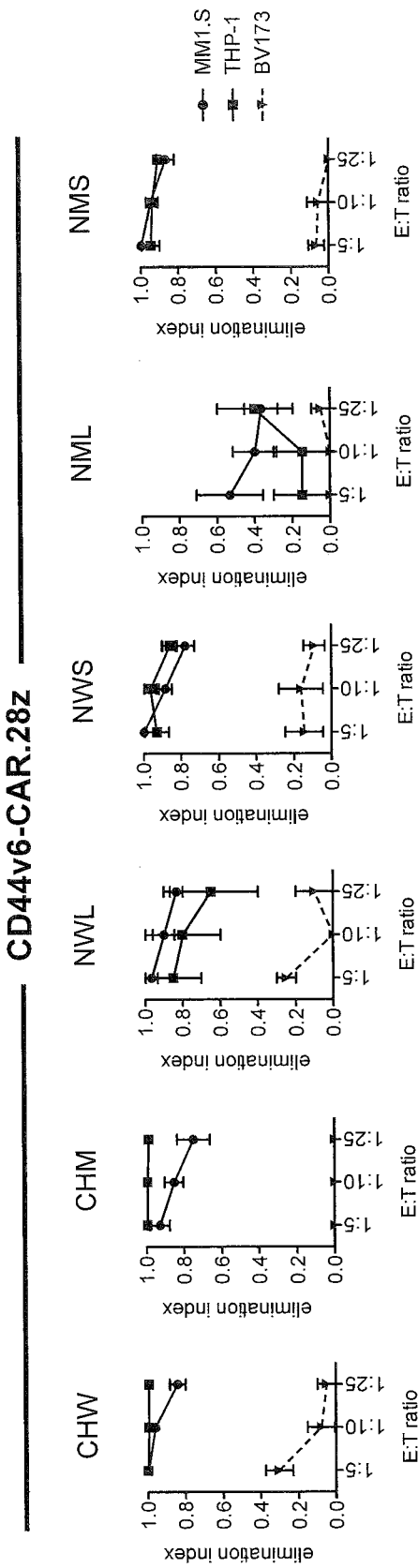


FIG. 3A

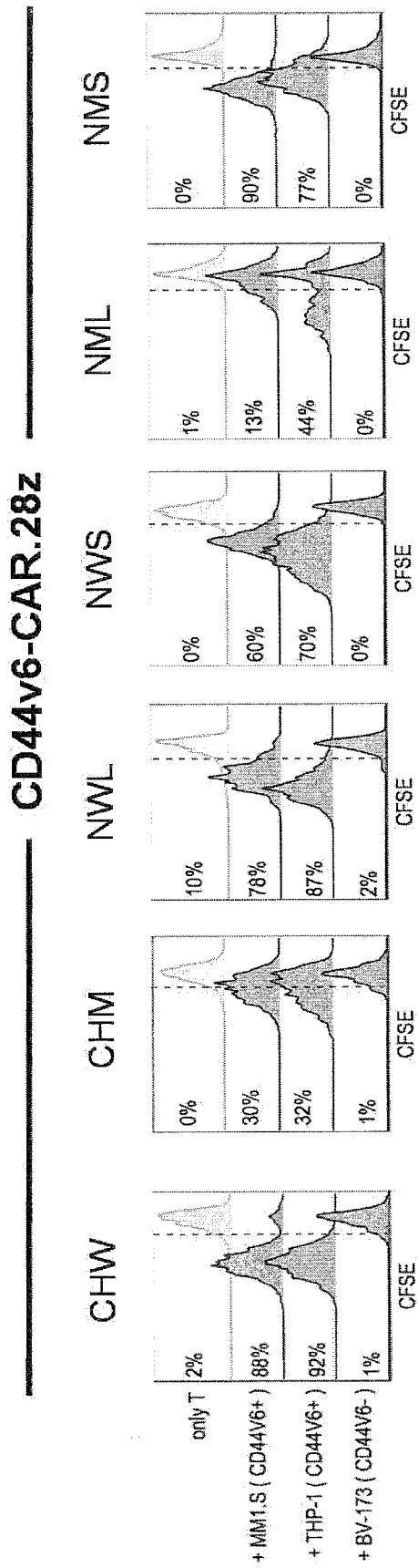
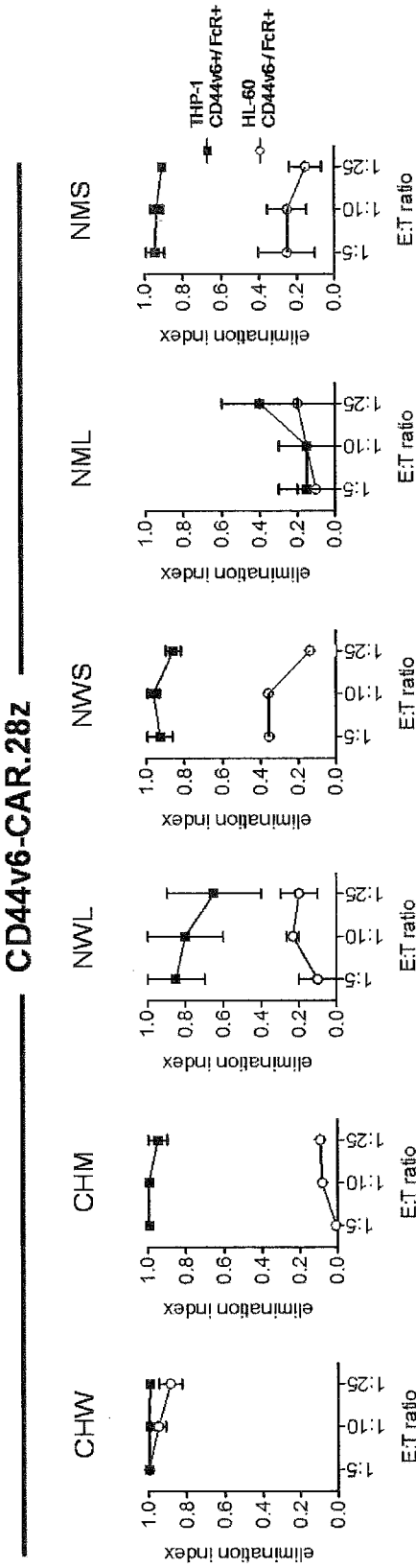


FIG. 3B

A



B

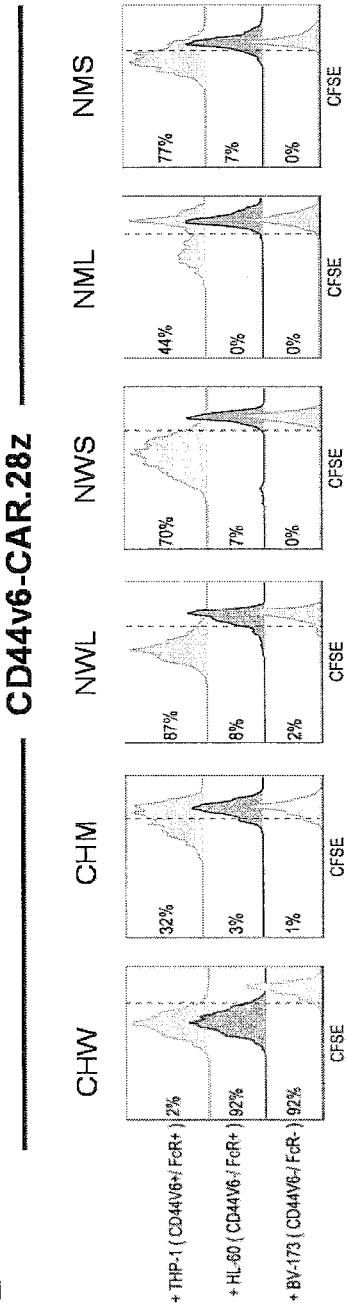


FIG. 4

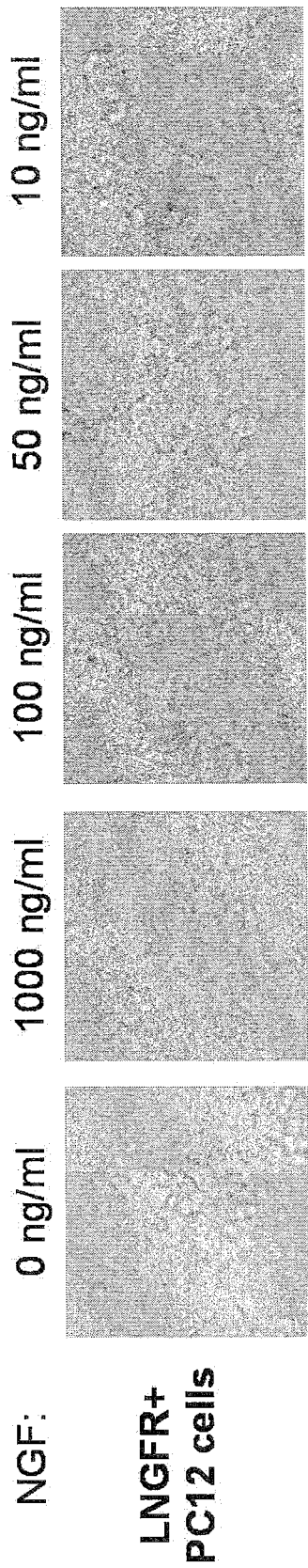


FIG. 5A

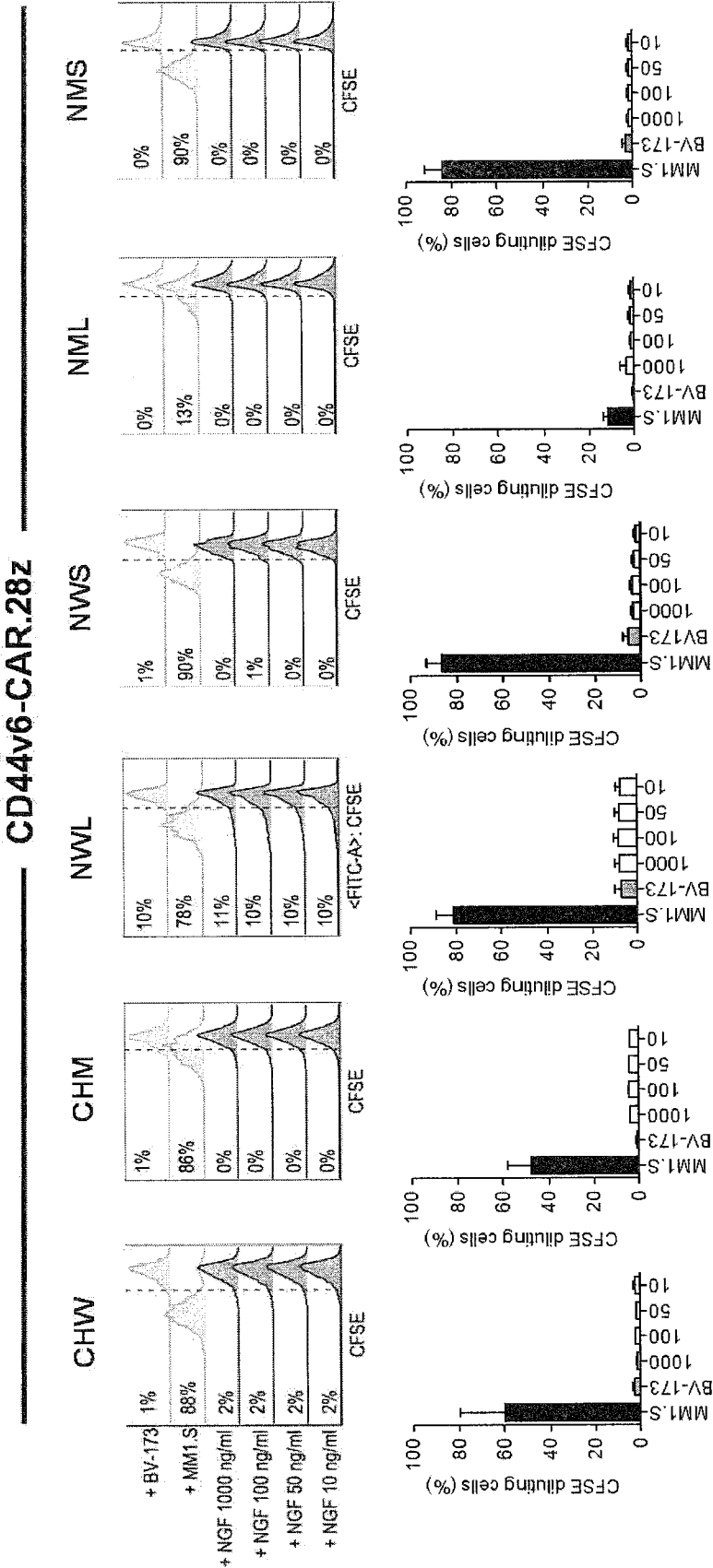


FIG. 5B

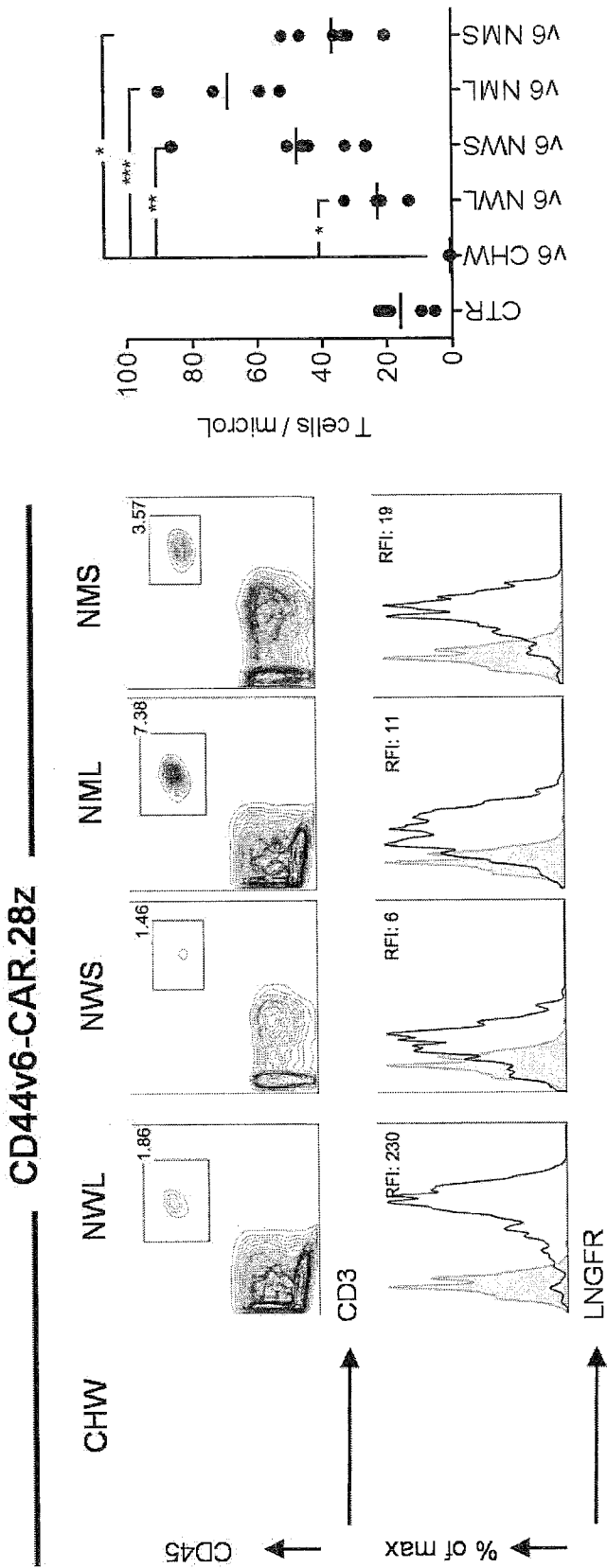
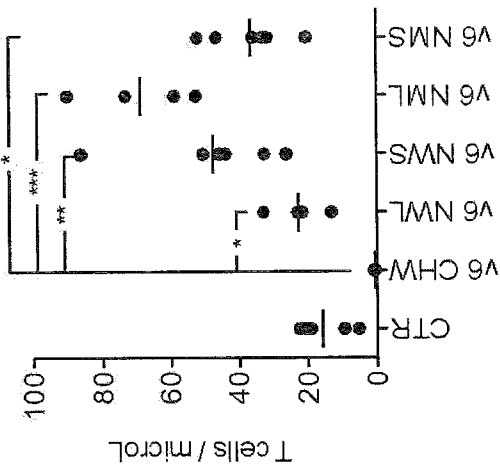


FIG. 6A



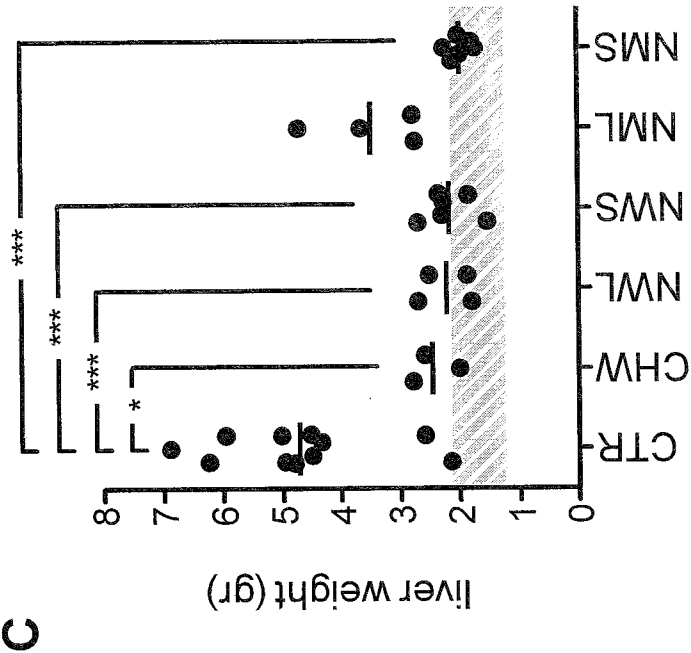
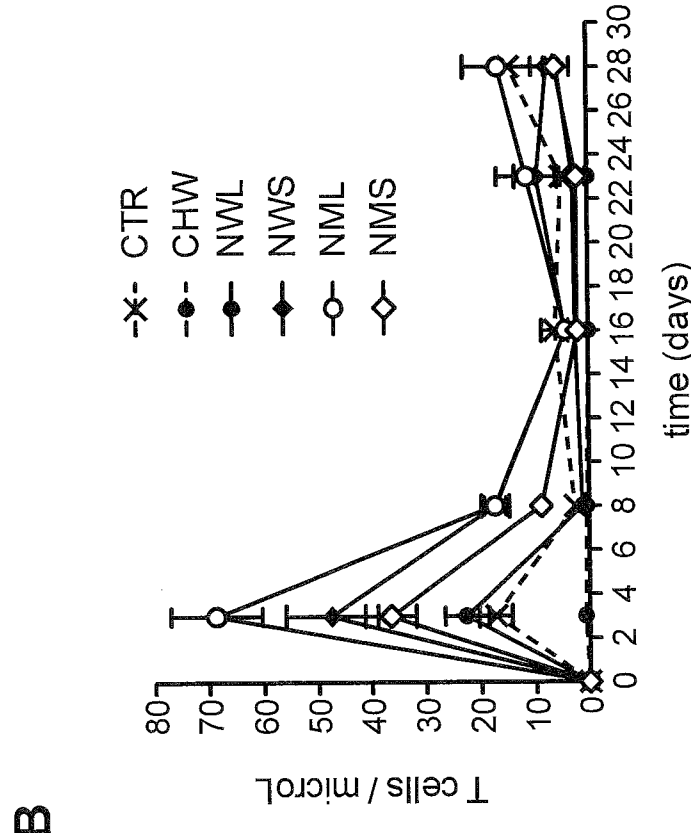


FIG. 6B-C

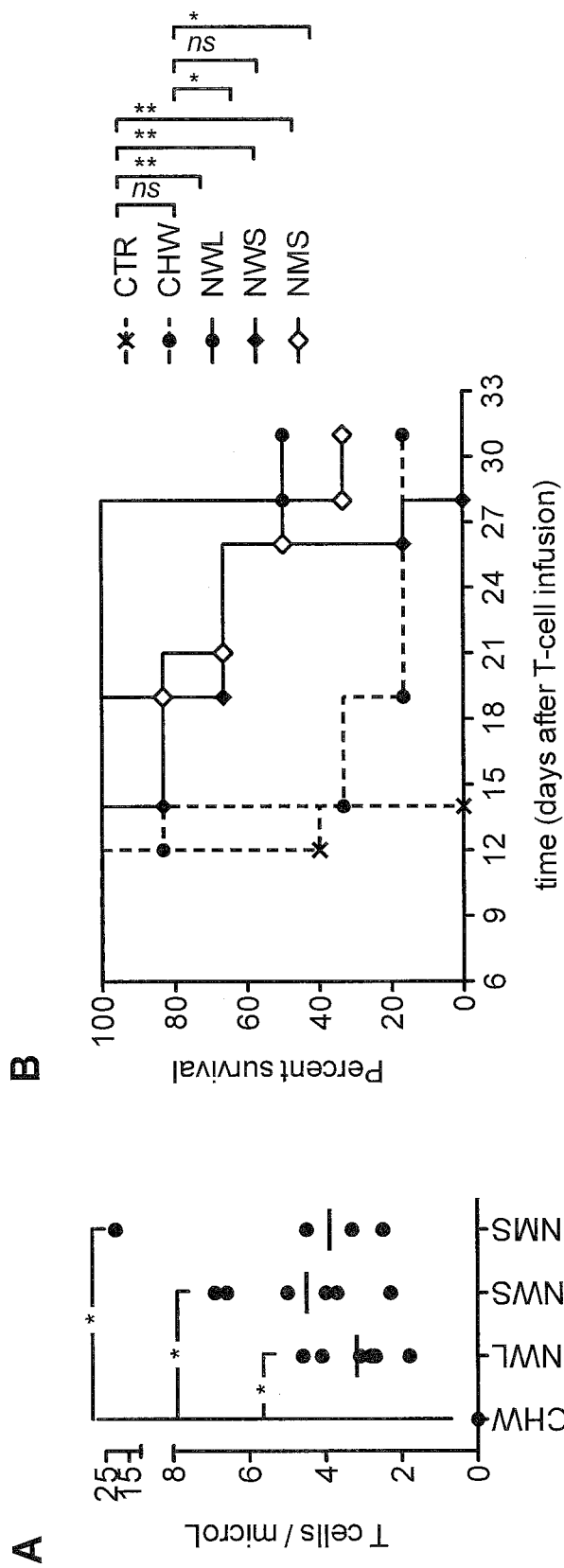


FIG. 7

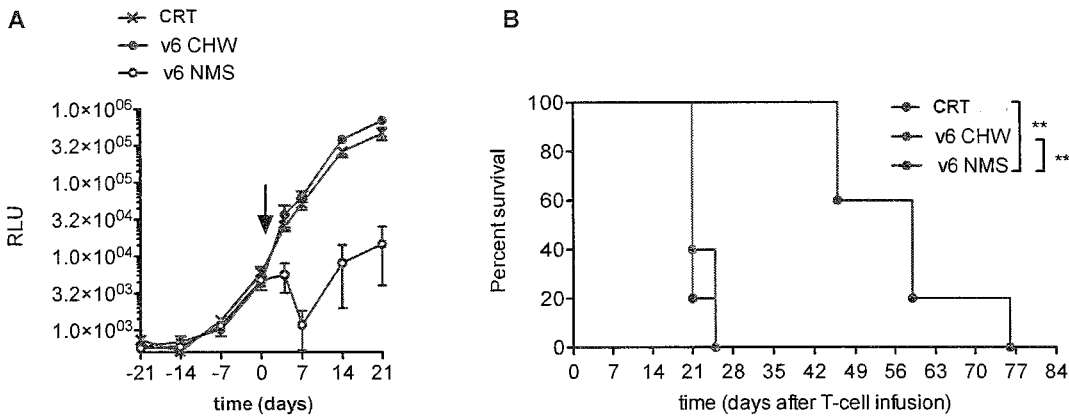


Figure 7BIS

10 20 30 40 50 60  
MGAGATGRAM DGPRLLLLLL LGVSLGGAKE ACPTGLYTHS GECCKACNLG EGVAQPCGAN  
70 80 90 100 110 120  
QTVCEPCLDS VTFSDVVSAT EPCKPCTECV GLQSMSAPCV EADDAVCRCA YGYYQDETTG  
130 140 150 160 170 180  
RCEACRVCEA GSGLVFSCQD KQNTVCEECP DGTYSDEANH VDPCLPCTVC EDTERQLREC  
190 200 210 220 230 240  
TRWADAECEE IPGRWITRST PPEGSDSTAP STQEPPEAPPE QDLIASTVAG VVTTVMGSSQ  
250 260 270 280 290 300  
PVVTRGTTDN LIPVYCSILA AVVVGLVAYI AFKRWNSCKQ NKQGANSRPV NQTPPPEGEK  
310 320 330 340 350 360  
LHSDSGISVD SQSLHDQQPH TQTASGQALK GDGGLYSSLP PAKREEVEKL LNGSAGDTWR  
370 380 390 400 410 420  
HLAGELGYQP EHIDSFTHEA CPVRALLASW ATQDSATLDA LLAALRRIQR ADLVESLCSE

STATSPV

FIG. 8 (SEQ ID NO:14)

FIG. 9 - CD44v6CAR.28z (SEQ ID NO: 15)

**Nucleotides**

ATGGAAGCCCCTGCCAGCTGCTGTTCTGCTGCTGCTGTGGCTGCCCGACAC  
CACCGGCGAGATCGTGCTGACACAGAGCCCCGCCACCCTGTCTCTGAGCCCTG  
GCGAGAGAGCCACCCTGAGCTGTAGCGCCAGCAGCAGCATCAACTACATCTAC  
TGGCTGCAGCAGAAGCCCGGCCAGGCCCCCAGAATCCTGATCTACCTGACCAG  
CAACCTGGCCAGCGGCGTGCCCGCCAGATTTTCTGGCAGCGGCAGCGGCACCG  
ACTTCACCCTGACCATCAGCAGCCTGGAACCCGAGGACTTCGCCGTGTACTAC  
TGCCTGCAGTGGTCCAGCAACCCCTGACCTTCGGCGGAGGCACCAAGGTGGA  
AATCAAGCGGGGTGGTGGTGGTTCTGGTGGTGGTGGTTCTGGCGGCGGCGGCT  
CCGGTGGTGGTGGATCTGAGGTGCAGCTGGTGGAAAGCGGCGGAGGCCTGGTC  
AAGCCTGGCGGCAGCCTGAGACTGAGCTGTGCCGCCAGCGGCTTCACCTTCAG  
CAGCTACGACATGAGCTGGGTCCGACAGGCTCCAGGCAAGGGACTGGAATGGG  
TGTCACCATCAGCAGCGGCGGCAGCTACACCTACTACCTGGACAGCATCAAG  
GGCCGGTTTACCATCAGCCGGGACAACGCCAAGAACAGCCTGTACCTGCAGAT  
GAACAGCCTGCGGGCCGAGGACACCGCCGTCTACTACTGTGCCCGGCAGGGCC  
TCGACTACTGGGGCAGAGGCACCCTGGTCACCCTGTCCAGCGGGGATCCCGCC  
GAGCCCAAATCTCCTGACAAACTCACATGCCACCCGTGCCCAGCACCTGA  
ACTCCTGGGGGGACCGTCAGTCTTCTCTTCCCCCAAACCCAAGGACACCC  
TCATGATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCAC  
GAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAA  
TGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCA  
GCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGC  
AAGGTCTCCAACAAAGCCCTCCAGCCCCCATCGAGAAAACCATCTCCAAAGC  
CAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATG  
AGCTGACCAAGAACCAGGTACGCTGACCTGCCTGGTCAAAGGCTTCTATCCC  
AGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAACCGGAGAACTACAA  
GACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTCTACAGCAAGC  
TCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTG  
ATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCC  
GGGTAAAAAAGATCCCAAATTTTGGGTGCTGGTGGTGGTTGGTGGAGTCTTGG  
CTTGCTATAGCTTGCTAGTAACAGTGGCCTTTATTATTTTCTGGGTGAGGAGT  
AAGAGGAGCAGGCTCCTGCACAGTGACTACATGAACATGACTCCCCGCCGCC  
CGGGCCCACCCGCAAGCATTACCAGCCCTATGCCCCACCACGCGACTTCGCAG  
CCTATCGCTCCAGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTACCAG  
CAGGGCCAGAACCAGCTCTATAACGAGCTCAATCTAGGACGAAGAGAGGAGTA  
CGATGTTTTGGACAAGAGACGTGGCCGGGACCCCTGAGATGGGGGGAAAGCCGA  
GAAGGAAGAACCCTCAGGAAGGCCTGTACAATGAACTGCAGAAAGATAAGATG  
GCGGAGGCCTACAGTGAGATTGGGATGAAAGGCGAGCGCCGGAGGGGCAAGGG  
GCACGATGGCCTTTACCAGGGTCTCAGTACAGCCACCAAGGACACCTACGACG  
CCCTTCACATGCAGGCCCTGCCCCCTCGCTAA

**Protein (SEQ ID NO: 16)**

MEAPAQLLFLLLLWLDPDTTGEIVLTQSPATLSLSPGERATLSCSASSSINYIY  
WLQQKPGQAPRILIYLTSLNLSGVPARFSGSGSGTDFTLTISSELPEDFAVYY  
CLQWSSNPLTFGGGTKEIKRGGGSGGGSGGGSGGGGSEVQLVESGGGLV  
KPGGSLRLSCAASGFTFSSYDMSWVRQAPGKGLEWVSTISSGGSYTYYLDSIK

GRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARQGLDYWGRGTLVTVSSGDPA  
EPKSPDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH  
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHODWLNGKEYKC  
KVSNKALPAPIEKTISKAKGOPREPOVYTLPPSRDELTKNOVSLTCLVKGFYP  
SDIAVEWESNGOPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQOQGNVFSCSV  
MHEALHNHYTQKSLSLSPGKKDPKFWVLVVVGVLACYSLLVTVAFIIFWVRS  
KRSRLHSDYMNMTPRRPGPTRKHYPYAPPRDFAAYRSRVKFSRSADAPAYQ  
QGQNQLYNELNLGRREEYDVLDKRRGRDPGEMGGKPRRKNPQEGLYNELQKDKM  
AEAYSEIGMKGERRRRGKGGHDGLYQGLSTATKDTYDALHMQALPPR

Features :

**SCFV**

CH2CH3

CD28

*zeta chain*

FIG. 10 - CD44v6-CAR28z with spacer LNGFR wild-type long (NWL)

## Protein sequence

MEAPAQLLFLLLLWLPDTTGEIVLTQSPATLSLSPGERATLSCSASSS  
 INYIYWLQQKPGQAPRILIYLTSLASGVPARFSGSGSGTDFTLTISL  
 EPEDFAVYYCLQWSSNPLTFGGGTKVEIKRGGGGSGGGGSGGGGS  
 GGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTFSSYDMSWVRQA  
 PGKGLEWVSTISSGGSYTTYLDSIKGRFTISRDNANKNSLYLQMNSLRA  
 EDTAVYYCARQGLDYWGRGTLVTVSSGDPKEACPTGLYTHSGECCK  
ACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGL  
QSMSAPCVEADDAVCRCAYGYQQDETTGRCEACRVCEAGSGLVFSC  
QDKQNTVCEECPDGTYSDEANHVDPCLPCTVCEDTERQLRECTRWA  
DAECEIIPGRWITRSTPPEGSDSTAPSTQEPEAPPEQDLIASTVAGVV  
TTVMGSSQPVVTRGTTDNPKFWVLVVGGVLACYSLLVTVAFIIFWVR  
SKRSRLHSDYMNMTPRRPGPTRKHYPYAPPRDFAAYRSRVKFSR  
 SADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPKQR  
 RKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGHDGLYQGLSTA  
 TKDTYDALHMQALPPR

**Legend****CD44v6-specific single-chain fragment**

LNGFR (sequence taken from the UNIPROT database (P08138, TNR16\_HUMAN, position 29-250)

**CD28** (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220).

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-143)

FIG. 11 - CD44v6-CAR28z with spacer LNGFR wild-type short (NWS)

Protein sequence

MEAPAQLLFLLLLWLPDTTGEIVLTQSPATLSLSPGERATLSCSASSS  
 INYIYWLQQKPGQAPRILIYLTSNLASGVPARFSGSGSGTDFTLTISL  
 EPEDFAVYYCLQWSSNPLTFGGGTKVEIKRGGGGSGGGGSGGGGS  
 GGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTFSSYDMSWVRQA  
 PGKGLEWVSTISSGGSYTYLDSIKGRFTISRDNAKNSLYLQMNSLRA  
 EDTAVYYCARQGLDYWGRGTLVTVSSGDPKEACPTGLYTHSGECCK  
ACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGL  
QSMSAPCVEADDAVCRCAYGYYQDETTGRCEACRVCEAGSGLVFSC  
QDKQNTVCEECPDGTYSDEANHVDPCLPCTVCEDTERQLRECTRWA  
DAECEEPKFWVLVVVGGVLACYSLLVTVAFIIFWVRSKRSRLHSDY  
MNMTPRRPGPTRKHYPYAPPRDFAAYRSRVKFSRSADAPAYQQG  
 QNQLYNELNLGRREEYDVLDKRRGRDPGEMGGKPQRRKNPQEGLYNE  
 LQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQ  
 ALPPR

**Legend****CD44v6-specific single-chain fragment**

LNGFR (sequence taken from the UNIPROT database (P08138, TNR16\_HUMAN, position 29-190).

CD28 (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220).

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-143)

FIG. 12 - CD44v6-CAR28z with spacer LNGFR mutated long (NML)

## Protein sequence

MEAPAQLLFLLLLWLPDTTGEIVLTQSPATLSLSPGERATLSCSASSS  
 INYIYWLQQKPGQAPRILIYLTSNLASGVPARFSGSGSGTDFTLTISSL  
 EPEDFAVYYCLQWSSNPLTFGGGKTKVEIKRGGGGSGGGGSGGGGS  
 GGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTFSSYDMSWVRQA  
 PGKGLEWVSTISSGGSYTYLDSIKGRFTISRDNKNSLYLQMNSLRA  
 EDTAVYYCARQGLDYWGRTLVTVSSGDPKEACPTGLYTHSGECCK  
ACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGL  
QSMSAPCVEADDAVCRCAYGYQQDETTGRCEACRVCEAGSGLVFSC  
QDKQNTVCEECPDGTYSDEAARAADAECEEIPGRWITRSTPPEGSDS  
TAPSTQEPEAPPEQDLIASTVAGVVTTVMGSSQPVVTRGTTDNPKFW  
VLVVVGGVLACYSLLVTVAFIIFWVRSKRSLHSDYMNMTPRRPGP  
TRKHYPYAPPRDFAAYRSRVKFSR SADAPAYQQGQNQLYNELNLG  
 RREEYDVLDKRRGRDPEMGGKPQRRKNPQEGLYNELQKDKMAEAYS  
 EIGMKGERRRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

Legend**CD44v6-specific single-chain fragment**

LNGFR (sequence taken from the UNIPROT database (P08138, TNR16\_HUMAN, position 29-250). **Bold**: aminoacids that, in the mutated version, has been substituted to the original residues (deleted aa: NHVDPCLPCTVCEDTERQLRECTRW))

**CD28** (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220).

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-143)

FIG. 13 - CD44v6-CAR28z with spacer LNGFR mutated short (NMS)

Protein sequence

MEAPAQLLFLLLLWLPD TTGEIVLTQSPATLSLSPGERATLSCSASSS  
 INYIYWLQQKPGQAPRIL IYLT SNLASGV PARFSGSGSGTDFTLTIS SL  
 EPEDFAVYYCLQWSSNPLTFGGG TKVEIKRGGGGSGGGGSGGGGS  
 GGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTFSSYDMSWVRQA  
 PGKGLEWVSTISSGGSYTYYLDSIKGRFTISRDN AKNSLYLQMNSLRA  
 EDTAVYYCARQGLDYWGRGTLVTVSSGDP PKEACPTGLYTHSGECCK  
ACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGL  
QSMSAPCVEADDAVCRCAYGY YQDETTGRCEACRVCEAGSGLVFSC  
QDKQNTVCEECPDGTYSDEAARAADAECEE PKFWVLVVGGVLACY  
SLLVTVAFIIFWVRSKRSRL LHSDYMNMTPRRPGPTRKHYPYAPPR  
DFAAYRSRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRR  
 GRDPEMGGKPQRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRG  
 KGH DGLYQGLSTATKDTYDALHMQALPPR

**Legend****CD44v6-specific single-chain fragment**

LNGFR (sequence taken from the UNIPROT database (P08138, TNR16\_HUMAN, position 29-190). **Bold**: amino acids that, in the mutated version, has been substituted to the original residues (deleted aa: NHVDPCLPCTVCEDTERQLRECTRW)).

**CD28** (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220)).

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-14))

FIG. 14 - CD44v6-CAR28z with spacer LNGFR wild-type long (NWL)

## Protein sequence

MEAPAQLLFLLLLWLPD TTGEIVLTQSPATLSLSPGERATLSCSASSS  
 INYIYWLQQKPGQAPRILIYLT SNLASGVPARFSGSGSGTDFTLTISL  
 EPEDFAVYYCLQWSSNPLTFGGG TKVEIKRGGGGSGGGGSGGGGS  
 GGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTFSSYDMSWVRQA  
 PGKGLEWVSTISSGGSYTYYLDSIKGRFTISRDN AKNSLYLQMNSLRA  
 EDTAVYYCARQGLDYWGRGTLVTVSSGDP KEACPTGLYTHSGECCK  
ACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGL  
QSMSAPCVEADDAVCRCAYGY YQDETTGRCEACRVCEAGSGLVFSC  
QDKQNTVCEECPDGTYSDEANHVDPCLPCTVCEDTERQLRECTRWA  
DAECEEEIPGRWITRSTPPEGSDSTAPSTQEPEAPPEQDLIASTVAGVV  
TTVMGSSQPVVTRGTTDNPK **FWVLVVGGVLACYSLLVTVAFIIFWVR**  
**SKRSRLHSDYMNMTPRRPGPTRKHYPYAPPRDFAAYRS**RVKFSR  
 SADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRK  
 NPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATK  
 DTYDALHMQALPPR

**Legend****CD44v6-specific single-chain fragment**

LNGFR (sequence taken from the UNIPROT database (P08138, TNR16\_HUMAN, position 29-250))

CD28 (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220)).

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-143, without Q at position 80))

FIG. 15 - CD44v6-CAR28z with spacer LNGFR wild-type short (NWS)

Protein sequence

MEAPAQLLFLLLLWLPDTTGEIVLTQSPATLSLSPGERATLSCSASSS  
 INIYIWLQQKPGQAPRILIYLTSLNASGVPARFSGSGSGTDFTLTISL  
 EPEDFAVYYCLQWSSNPLTFGGGGTKVEIKRGGGGSGGGGSGGGGS  
 GGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTFSSYDMSWVRQA  
 PGKGLEWVSTISSGGSYTYLDSIKGRFTISRDNAKNSLYLQMNSLRA  
 EDTAVYYCARQGLDYWGRGTLVTVSSGDPKEACPTGLYTHSGECCK  
ACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGL  
QSMSAPCVEADDAVCRCAYGYQQDETTGRCEACRVCEAGSGLVFSC  
QDKQNTVCEECPDGTYSDEANHVDPCLPCTVCEDTERQLRECTRWA  
DAECEEPKFWVLVVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSDY  
MNMTPRRPGPTRKHYPYAPPRDFAAYRSRVKFSRSADAPAYQQG  
 QNQLYNELNLGRREEYDVLDKRRGRDPGEMGGKPRRKNPQEGLYNEL  
 QKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA  
 LPPR

**Legend****CD44v6-specific single-chain fragment**

LNGFR (sequence taken from the UNIPROT database (P08138, TNR16\_HUMAN, position 29-190).

CD28 (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220).

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-143, without Q at position 80))

FIG. 16 - CD44v6-CAR28z with spacer LNGFR mutated long (NML)

Protein sequence

**MEAPAQLLFLLLLWLPD**TTGEIVLTQSPATLSLSPGERATLSCSASSS  
 INYIYWLQQKPGQAPRILIYLTSNLASGVPARFSGSGSGTDFTLTISL  
 EPEDFAVYYCLQWSSNPLTFGGG**TKVEIKRGGGGSGGGGSGGGGS**  
**GGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTFSSYDMSWVRQA**  
**PGKGLEWVSTISSGGSYTYLDSIKGRFTISRDN**AKNSLYLQMNSLRA  
**EDTAVYYCARQGLDYWGRGTLVT**VSSGDPKEACPTGLYTHSGECCK  
ACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGL  
QMSAPCVEADDAVCRCAYGYQQDETTGRCEACRVCEAGSGLVFSC  
QDKQNTVCEECPDGTYSDEA**ARA**ADAECEEIPGRWITRSTPPEGSDS  
TAPSTQEPEAPPEQDLIASTVAGVVTTVMGSSQPVVTRGTTDNPK**FW**  
VLVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGP  
TRKHYPYAPPRDFAAYRS**RVKFSRSADAPAYQQGQNQLYNELNLG**  
 RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSE  
 IGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

**Legend****CD44v6-specific single-chain fragment**

LNGFR (sequence taken from the UNIPROT database (P08138, TNR16\_HUMAN, position 29-250). **Bold**: aminoacids that, in the mutated version, has been substituted to the original residues (deleted aa: NHVDPCLPCTVCEDTERQLRECTRW))

**CD28** (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220).

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-143, without Q at position 80))

FIG. 17 - CD44v6-CAR28z with spacer LNGFR mutated short (NMS)

Protein sequence

**MEAPAQLLFLLLLWLP**DTTGEIVLTQSPATLSLSPGERATLSCSASSS  
 INYIYWLQQKPGQAPRILIYLTSNLASGVPARFSGSGSGTDFTLTISL  
 EPEDFAVYYCLQWSSNPLTFGGG**TKVEIKRGGGGSGGGGSGGGGS**  
 GGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTFSSYDMSWVRQA  
 PGKGLEWVSTISSGGSYTYYLDSIKGRFTISRDN**AKNSLYLQMNSLRA**  
 EDTAVYYCARQGLDYWGRGTLVTVSSG**DPKEACPTGLYTHSGECCK**  
ACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGL  
QSMSAPCVEADDAVCRCAYGYQQDETTGRCEACRVCEAGSGLVFSC  
QDKQNTVCEECPDGTYSDEA**ARAADAECEEPKFWVLVVVGGVLACY**  
**SLLVTVAFIIFWVR**SKRSRLLHSDYMNMT**PRRPGPTRKHYPYAPPR**  
**DFAAYRS**RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRR  
 GRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGK  
 GHDGLYQGLSTATKDTYDALHMQALPPR

**Legend****CD44v6-specific single-chain fragment**

LNGFR (sequence taken from the UNIPROT database (P08138, TNR16\_HUMAN, position 29-190). **Bold**: amino acids that, in the mutated version, have been substituted to the original residues (deleted aa: NHVDPCLPCTVCEDTERQLRECTRW)).

**CD28** (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220)).

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-143, without Q at position 80))

Figure 18 - CD44v6-4GS2-CAR28z with spacer LNGFR wild-type long (NWL)

## Protein sequence

MEAPALLFLLLLWLPDTTGEIVLTQSPATLSLSPGERATLSCSASSSINYIYWLQ  
 QKPGQAPRILYLTSLASGVPARFSGSGSGTDFTLTISSELPEDFAVYYCLQWSS  
 NPLTFGGGTKEIKRGGGGSGGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTF  
 SSYDMSWVRQAPGKGLEWVSTISSGGSYTYLDSIKGRFTISRDNKNSLYLQMN  
 SLRAEDTAVYYCARQGLDYWGRGTLVTVSSGDPKEACPTGLYTHSGECCACNL  
GEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGLQSMSAPCVEAD  
DAVCRCA YGYYQDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEECPDGTYSDE  
ANHVDPLPCTVCEDTERQLRECTRWADAECEEIPGRWITRSTPPEGSDSTAPST  
QEPEAPPEQDLIASTVAGVVTTVMGSSQPVVTRGTTDNPKFWVLVVVGGVLACYS  
LLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKHYPYAPPRDFAAYRSRV  
 KFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQ  
 EGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL  
 PPR

## Legend

**CD44v6-4GS2:** a CD44v6-specific single-chain fragment (SEQ. ID NO 31)

LNGFR (sequence taken from the UNIPROT database (P08138, TNFR16\_HUMAN, position 29-250))

**CD28** (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220))

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-143, without Q at position 80))

Figure 19 - CD44v6-4GS2-CAR28z with spacer LNGFR wild-type short (NWS)

## Protein sequence

MEAPAQLLFLLLLWLPDTTGEIVLTQSPATLSLSPGERATLSCSASSSINYIYWLG  
 QKPGQAPRILIYLTSLASGVPARFSGSGSGTDFTLTSSLEPEDFAVYYCLQWSS  
 NPLTFGGGKVEIKRGGGGSGGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTF  
 SSYDMSWVRQAPGKGLEWVSTISSGGSYTYLDSIKGRFTISRDNKNSLYLQMN  
 SLRAEDTAVYYCARQGLDYWGRGTLTVSSGDPKEACPTGLYTHSGECKACNL  
 GEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGLQSMSAPCVEAD  
 DAVCRCAYGYYQDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEECPDGTYSDE  
 ANHVDPCLPCTVCEDTERQLRECTRWADAEEEPKFWVLVVGGVLACYSLLV  
 VAFIIFWVRSKRSRLHSDYMNMTPRRPGPTRKHYPYAPPRDFAAYRSRVKFSR  
 SADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLY  
 NELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

## Legend

**CD44v6-4GS2:** a CD44v6-specific single-chain fragment (SEQ ID NO 31)

LNGFR (sequence taken from the UNIPROT database (P08138, TNR16\_HUMAN, position 29-190).

**CD28** (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220)

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-143, without Q at position 80)

Figure 20 - CD44v6-4GS2-CAR28z with spacer LNGFR mutated long (NML)

Protein sequence

MEAPAQLLFLLLLWLPDTTGEIVLTQSPATLSLSPGERATLSCSASSSINYIYWLQ  
 QKPGQAPRILYLTSLASGVPARFSGSGSGTDFTLTISSELPEDFAVYYCLQWSS  
 NPLTFGGGTKVEIKRGGGGSGGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTF  
 SSYDMSWVRQAPGKGLEWVSTISSGGSYTYLDSIKGRFTISRDNKNSLYLQMN  
 SLRAEDTAVYYCARQGLDYWGRGTLVTVSSGDPKEACPTGLYTHSGECCACNL  
GEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGLQSMSAPC  
VEADDAVCRCAYGYYQDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEECPDGTYSDE  
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MGSSQPVVTRGTTDNPKFWVLVVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSD  
YMNMTPRRPGPTRKHYPYAPPRDFAAYRSRVKFSRSADAPAYQQGQNQLYNE  
 LNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGM  
 KGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

**Legend****CD44v6-4GS2: a CD44v6-specific single-chain fragment (SEQ ID NO 31)**

LNGFR (sequence taken from the UNIPROT database (P08138, TNFR16\_HUMAN, position 29-250). **Bold**: aminoacids that, in the mutated version, has been substituted to the original residues (deleted aa: NHVDPCLPCTVCEDTERQLRECTRW))

**CD28** (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220).

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-143, without Q at position 80))

**Figure 21 - CD44v6-4GS2-CAR28z with spacer LNGFR mutated short (NMS)**

Protein sequence

**MEAPAQLLFLLLLWLPDTTGEIVLTQSPATLSLSPGERATLSCSASSSINYIYWLG**  
**QKPGQAPRILIYLTSNLASGVPARFSGSGSGTDFTLTISSLEPEDFAVYYCLQWSS**  
**NPLTFGGGTKVEIKRGGGGSGGGGSEVQLVESGGGLVKPGGSLRLSCAASGFTF**  
**SSYDMSWVRQAPGKGLEWVSTISSGGSYTYLDSIKGRFTISRDNKNSLYLQMN**  
**SLRAEDTAVYYCARQGLDYWGRGTLTVSSGDP**KEACPTGLYTHSGECKACNL  
GEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCPKPCTECVGLQSMSAPCVEAD  
DAVCRCAYGYYQDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEECPDGTYSDE  
AAAAADAECEEPKFWVLVVVGGLACYSLLVTVAFIIFWVRSKRSRLLHSDYMMN  
**TPRRPGPTRKHYPYAPPRDFAAYRS**RVKFSSRSADAPAYQQGQNQLYNELNLGR  
REEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERI  
GKGHDGLYQGLSTATKDTYDALHMQALPPR

**Legend****CD44v6-4GS2: a CD44v6-specific single-chain fragment (SEQ ID NO 31)**

LNGFR (sequence taken from the UNIPROT database (P08138, TNR16\_HUMAN, position 29-190). **Bold**: amino acids that, in the mutated version, has been substituted to the original residues (deleted aa: NHVDPCLPCTVCEDTERQLRECTRW).

**CD28** (sequence taken from the UNIPROT database (P10747, CD28\_HUMAN, position 153-220).

*CD3 zeta-chain* (sequence taken from the UNIPROT database (P20963, CD3Z\_HUMAN, position 31-143, without Q at position 80)

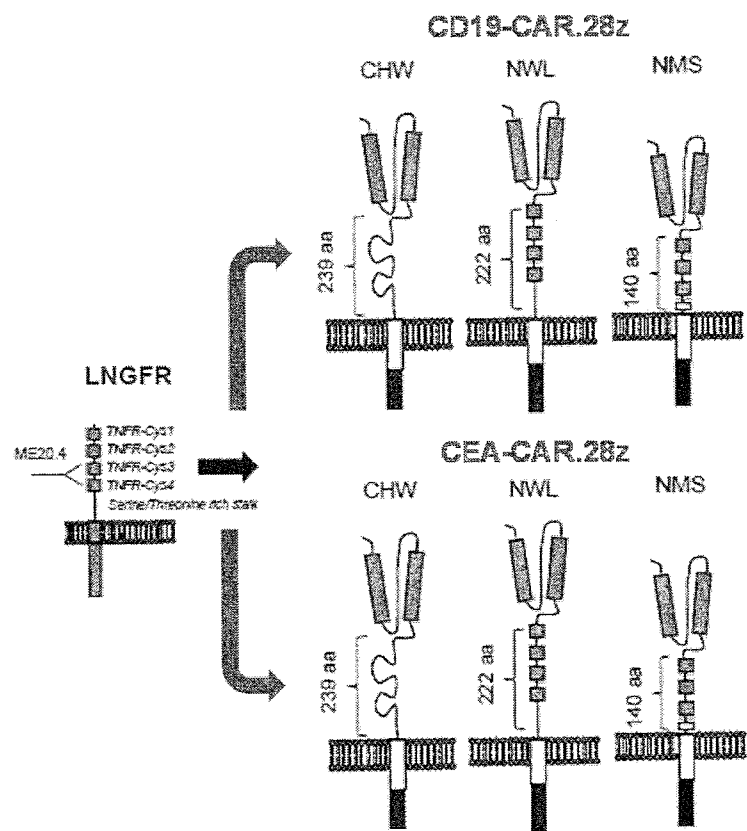


Figure 22

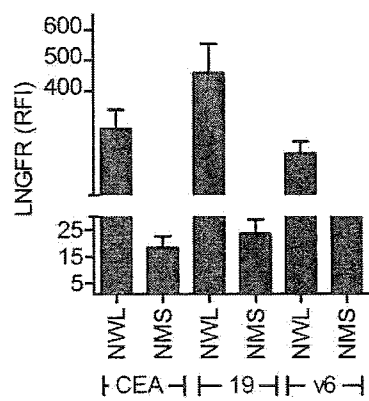


Figure 23

A

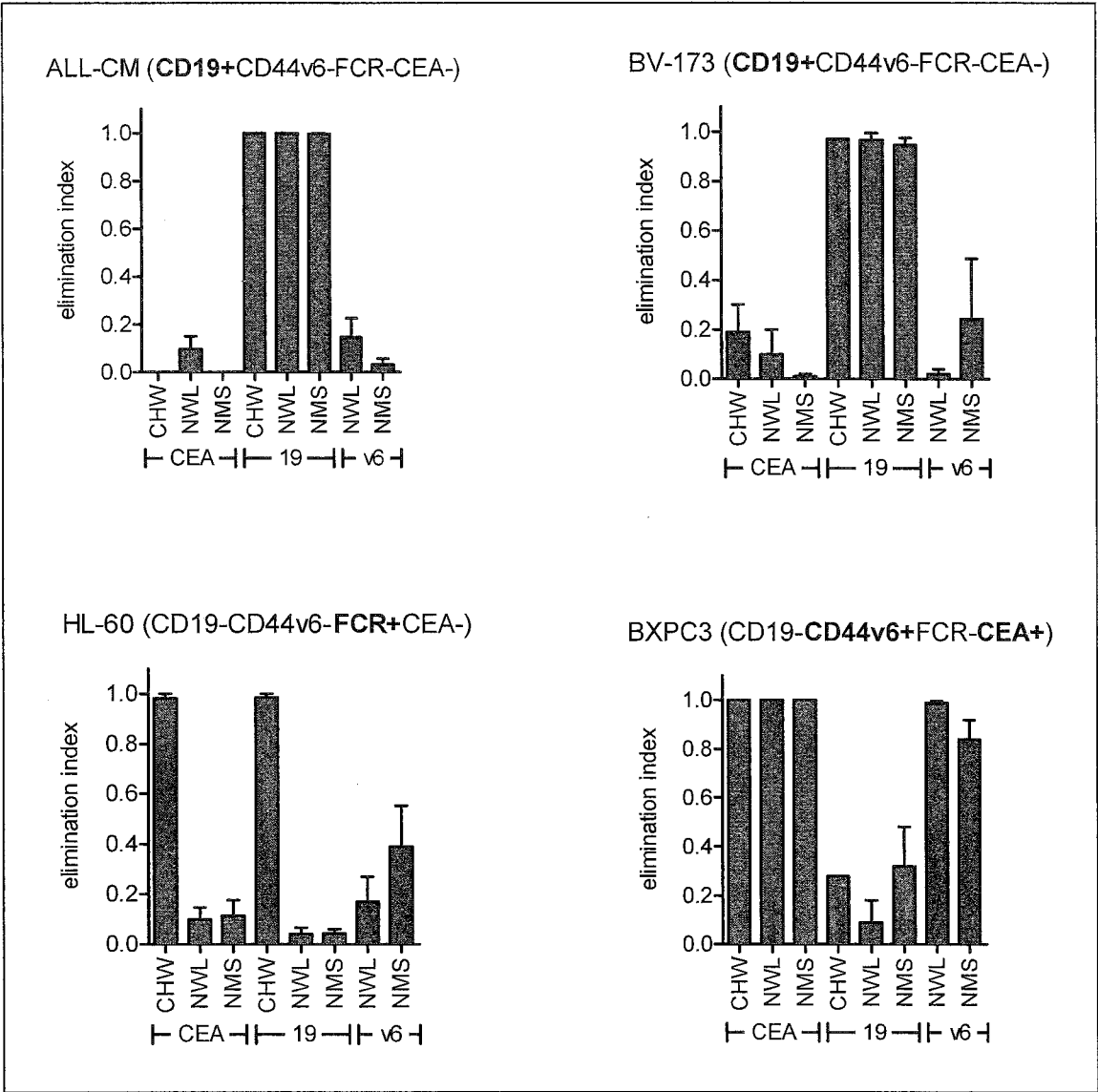


Figure 24

B

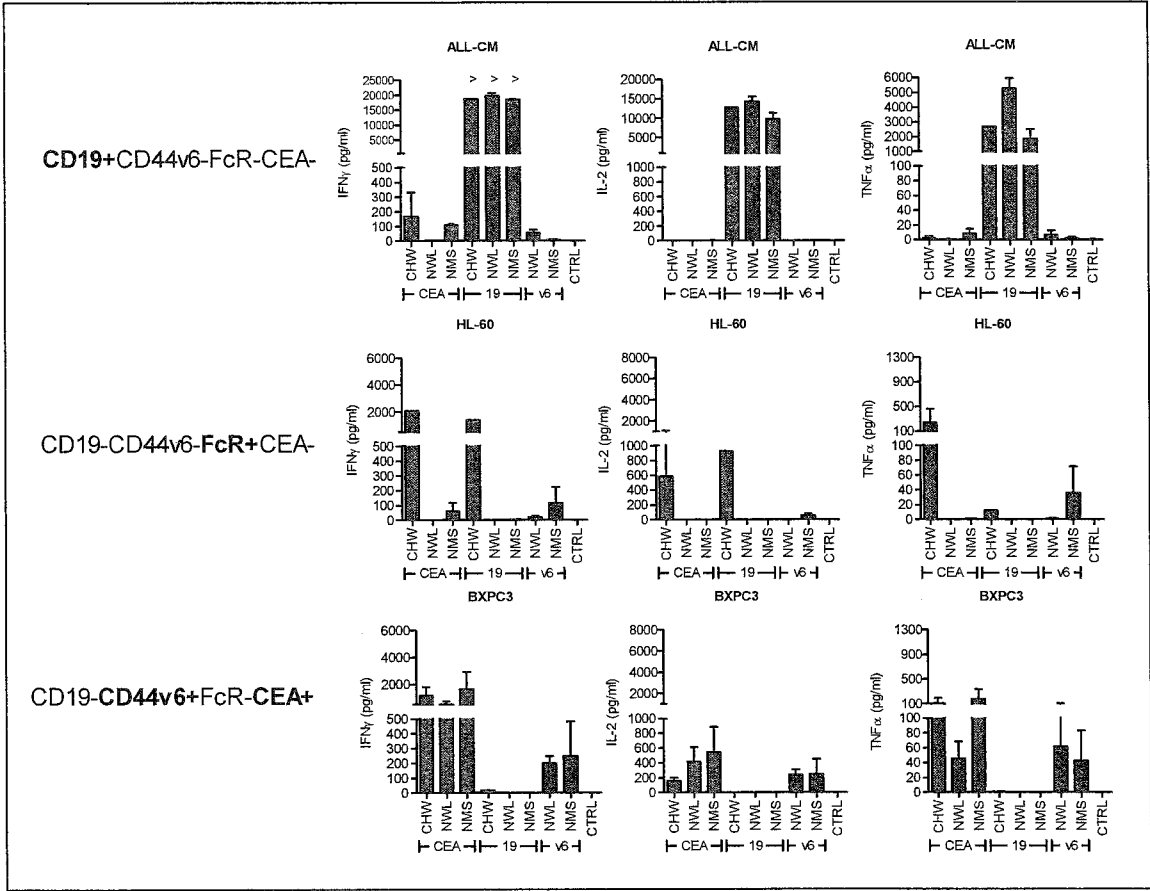


Figure 24

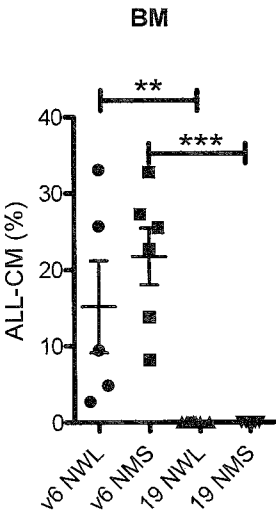


Figure 25

Figure 26

CD44v6-4GS2-CAR.28Z NGFR WILD TYPE LONG (V6 NWL) dna.gb

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Figure 27

CD44V6-4GS2-CAR.28Z NGFR WILD TYPE SHORT (V6 NWS) dna.gb

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**Figure 28**

CD44v6-4GS2-CAR.28Z NGFR MUTATED LONG (V6 NML) dna.gbb

[illegible]

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Figure 29

CD44v6-4GS2-CAR.28Z NGFR MUTATED SHORT (V6 NMS) dna.gb

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