

Figure 1A. Cytotoxic mechanism of classical CAR-expressing $\gamma\delta$ T cells

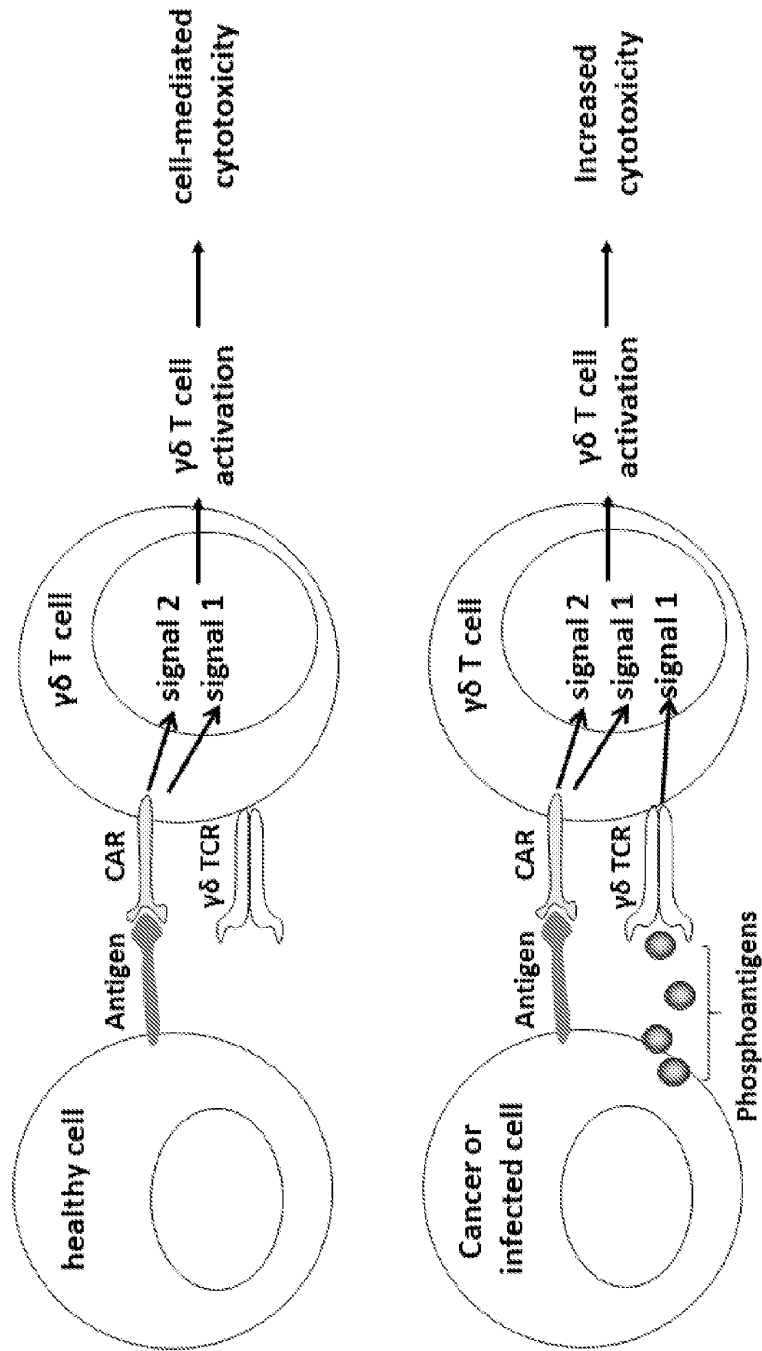


Figure 1B. Cytotoxic mechanism of co-stimulatory CAR-expressing $\gamma\delta$ T cells

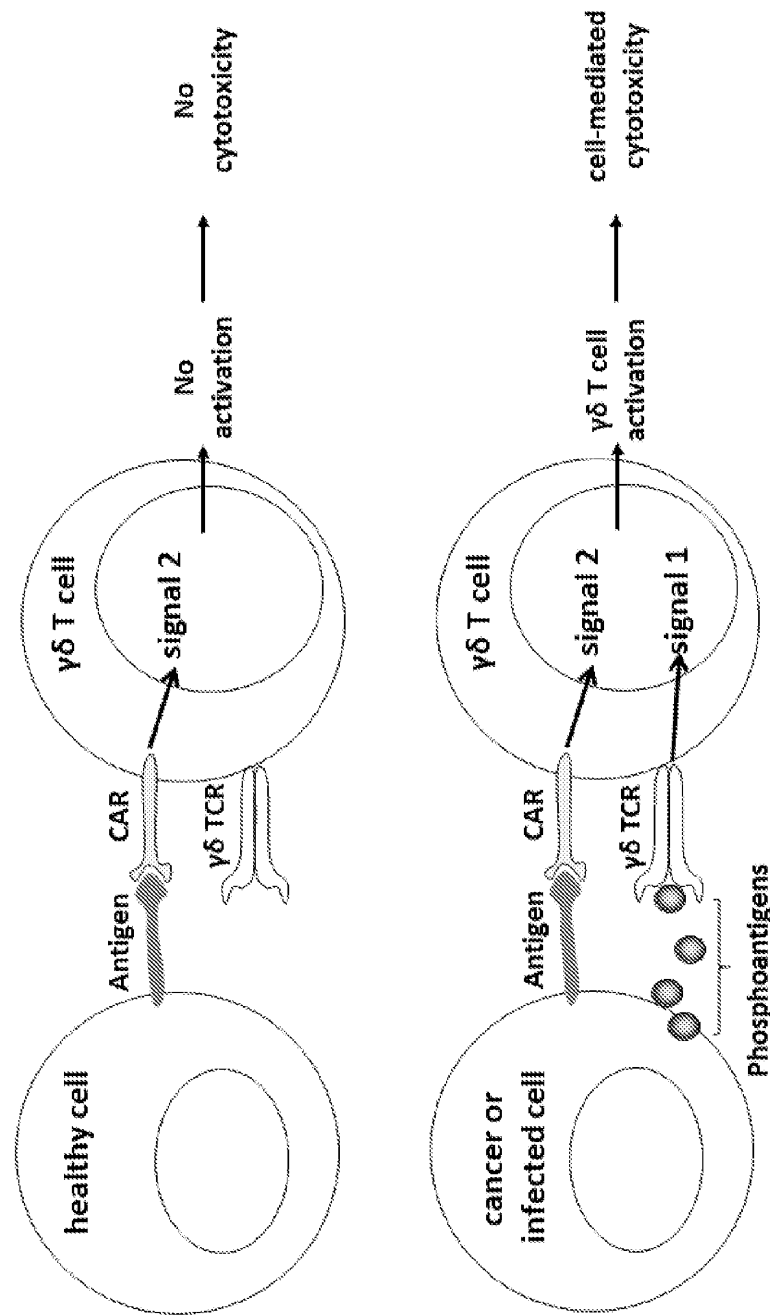


Figure 2. Illustrative comparison of classical and co-stimulatory CAR design

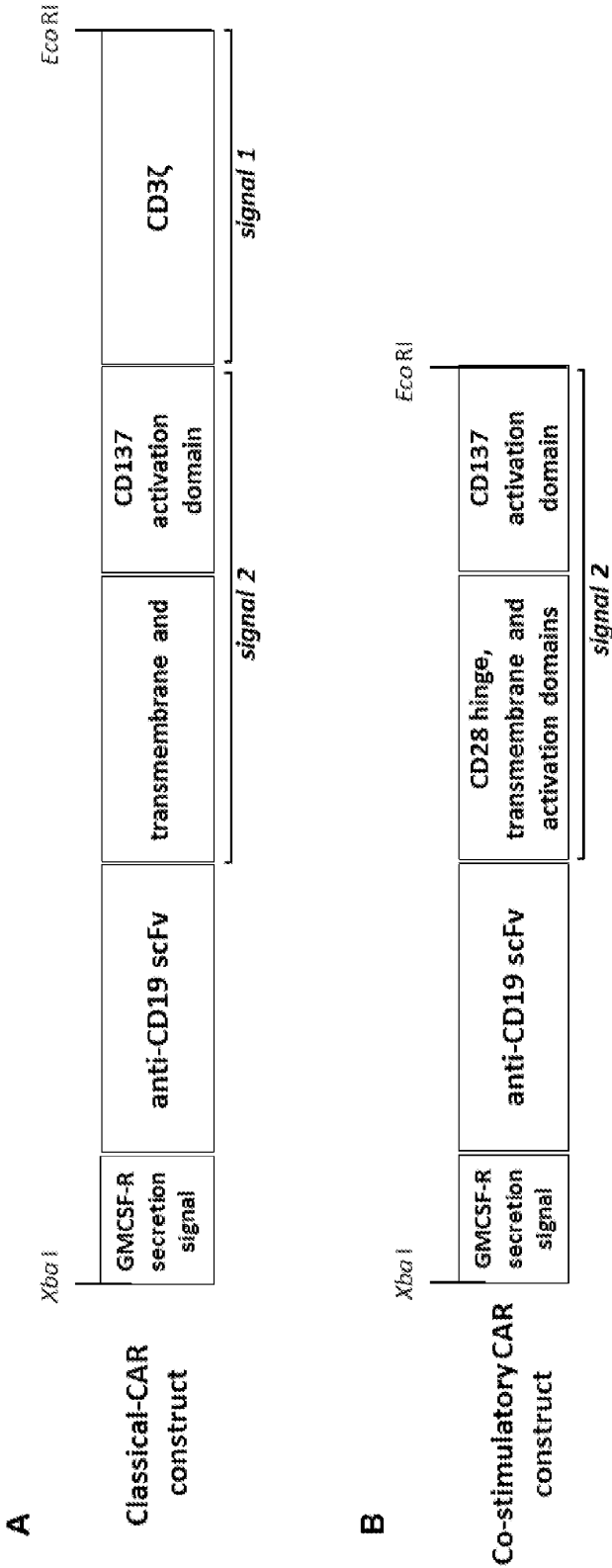


Figure 3A. Nucleic acid sequence of 'non-tuneable' / 'classical' CAR

ATGCTTCTCCTGGTGACAAGCCTTCTGCTCTGTGAGTTACCACACCCAGCAATTCCTCCTGATCCCAGACATCCAGATG
 ACACAGACTACATCCTCCCTGTCTGCCTCTCTGGGAGACAGAGTCACCATCAGTTGCAGGGCAAGTCAGGACATTAGT
 AAATATTTAAATTGGTATCAGCAGAAACCAGATGGAACTGTTAAACTCCTGATCTACCATACATCAAGATTACACTCA
 GGAGTCCCATCAAGGTTCAGTGGCAGTGGGTCTGGAACAGATTATTCTCTCACCATTAGCAACCTGGAGCAAGAAGAT
 ATTGCCACTTACTTTTGCCAAACAGGGTAATACGCTTCGTTACACGTTCCGAGGGGGACTAAGTTGGAATAACAGGC
 TCCACCTCTGGATCCGGCAAGCCCGGATCTGGCGAGGATCCACCAAGGGCGAGTGAAACTGCAGGAGTCAGGACCT
 GGCCTGTGGGCCCTCACAGAGCCTGTCCGTACATGCACTGTCTCAGGGGTCTCATTACCCGACTATGGTGTAAAGC
 TGGATTGCGCCAGCCTCCACGAAAGGGTCTGGAGTGGCTGGGAGTAATATGGGGTAGTGAAACCACATACTATAATTCA
 GCTCTCAAATCCAGACTGACCATCATCAAGGACAACCTCCAAGAGCCAAAGTTTCTTAAAAATGAACAGTCTGCAAACT
 GATGACACAGCCATTACTACTGTGCCAAACATTATTACTACGGTGGTAGCTATGCTATGGACTACTGGGGTCAAGGA
 ACCTCAGTCACCGTCTCTCAGCGGCCGCAATTGAAGTTATGTATCCTCCTCCTTACCTAGACAA TGAGAAGCAAT
 GGAAACCATTATCCATGTGAAAGGGAAACACCTTTGTCCAAAGTCCCCTATTTCCCGGACCTTCTAAGCCCTTTTGGGTG
 CTGGTGGTGGTTGGGGAGTCCTGGCTTGCTATAGCTTGCTAGTAACAGTGGCCTTTATTA TTTTCTGGGTGAGGAGT
 AAGAGGAGCAGGCTCCTGCACAGTGA CTACATGAACATGACTCCCGCCGCCCGGGCCCACTCTGTATA TATTCAAACAA
 CCTATGCCCCACACCGGACTTCGCAGCCTATCGCTCCAAACGGGGCAGAAAGAACTCTCTGTATA TATTCAAACAA
 CCATTTATGAGACCACTACAAACTACTCAAGAGGAAGATGGCTGTAGCTGCCGATTTCCAGAGAAGAAAGAGGAGGA
 TGTGAAC TGAGAGTGAA GTTCAGCAGGAGCGCAGACGCCCGCGTACCAGCAGGGCCAGAACCACTCTATAACGAG
 CTC AATCTAGGACGAAGAGAGGAGTACGATGTTTTGGACAAAGAGACGTGGCCGGGACCTTGAGATGGGGGAAAGCCG
 AGAAGGAAGAACCTCAGGAAGGCCCTGTACAATGAAC TGCAGAAAGATAAGATGGCGGAGGCCCTACAGTGAGATTGGG
 ATGAAAGGCGAGCGCGGAGGGGCAAGGGCACGATGGCCTTTACCAGGGTCTCAGTACAGCCACCAAGGACACCTAC
 GACGCCCTTCATGTCAGGGCCCTGCCCCCTCGCTAATGA (SEQ ID NO:1)

Figure 3B. Translated protein sequence of 'non-tuneable' / 'classical' CAR

<secretion signal> (SEQ ID NO: 2)
 MLLLVTSLLLCCLPAPAFLLIP

<Anti-CD19 scFv> (SEQ ID NO: 3)
 DIQMTQTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRHLHSGVPSRFSGSGTDYSLTISNL
 EQEDIAATYFCQQGNTLPYTFGGGKLEITGSTSGSKPGSGEGSTKGEVKLQESGGLVAPSQSLSVTCTVSGVSLPD
 YGVSWIRQPPRKGLEWLVGIWGSETTYNSALKSRLTIIKDNSKQVFLKMNSLQTDDTAIYYCAKHYYYGGSYAMDY
 WGQGTSVTVSSAAA

<CD28 hinge, transmembrane domain, co-stimulatory domain> (SEQ ID NO: 4)
 IEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPLPFGPSKPFWVLVVVGGVLACYSLVTVAFIIFWVRSKRSRLHSDY
 MNMTPRRPGPTRKHYQPYAPPRDFAAYRS

<CD137 (4-1BB) co-stimulatory domain> (SEQ ID NO: 5)
 KRGRKKLLYIFKQPFMRPVQITQEEDGCSCRFPEEEGGCEL

<CD3 zeta activation domain> (SEQ ID NO: 6)
 RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQDKMAEAYSEIGMKG
 ERRRGKGDHGLYQGLSTATKDTYDALHMQALPPR

Figure 4A. Nucleic acid sequence of 'TCR-tuneable' / 'co-stimulatory' CAR

ATGCTTCTCCTGGTGACAAGCCTTCTGCTCTGTGAGTTACCACACCCAGCATTCCTCCTGATCCAGACATCCAGATG
ACACAGACTACATCCTCCTGTCTGCTCTCTGGGAGACAGAGTCACCATCAGTTGCAGGGCAAGTCAGGACATTAGT
AAATATTTAAATTGGTATCAGCAGAAACCAGATGGAACTGTTAAACTCCTGATCTACCATACATCAAGATTACACTCA
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TCCACCTCTGGATCCGGCAAGCCCGGATCTGGCGAGGGATCCACCAAGGGCGAGGTGAAACTGCAGGAGTCAGGACCT
GGCCTGGTGGCCCTCACAGAGCCTGTCCGTACATGCATGCTCAGGGGTCTCATACCCGACTATGGGTAAAGC
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GCTCTCAAATCCAGACTGACCATCATCAAGGACAACTCCAAGAGCCAAAGTTTCTTAAAAATGAACAGTCTGCAAACT
GATGACACAGCCATTTACTACTGTGCCAAACATTATTACTACGGTGGTAGCTATGCTATGGACTACTGGGTCAAGGA
ACCTCAGTCACCGTCTCCTCAGCGGCCGCAATTGAAGTTATGTATCCTCCTCCTTACCTAGACAAATGAGAAGAGCAAT
GGAACCATATCCATGTGAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGGACCTTCTAAGCCCTTTTGGGTG
CTGGTGGTGGTTGGGGAGTCCTGGCTTGCTATAGCTTGCTAGTAACAGTGGCCTTATTATTCTGGGTGAGGAGT
AAGAGGAGCAGGCTCCTGCACAGTGACTACATGAACATGACTCCCGCCGCCCGGGCCCCACCCGCAAGCATTACCAG
CCCTATGCCCCACACGCGACTTCGCAGCCTATCGCTCCAAACGGGCGAGAAAGAACTCCTGTATATATTCAAACAA
CCATTTATGAGACCAGTACAACTACTCAAGAGGAAGATGGCTGTAGCTGCCGATTTCCAGAAGAAGAGAGGAGGA
TGTGAACGTGAATGA (SEQ ID NO: 7)

Figure 4B. Translated protein sequence of 'TCR-tuneable' / 'co-stimulatory' CAR

<Secretion signal> (SEQ ID NO: 8)
 MLLLVTSLLCELPHPAFLIP

<Anti-CD19 scFv> (SEQ ID NO: 9)
 DIQMTQTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRHSGVPSRFSGSGTDYSLTISNL
 EQEDIATYFCQQGNTLPYTFGGGKLEITGSTSGSGKPGSGEGSTKGEVKLQESGPGLVAPSQSLSVTCTVSGVSLPD
 YGVSWIRQPPRKGLEWLGVIWGSETTYNSALKSRLTIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGGSYAMDY
 WGQGTSVTVSSAA

<CD28 hinge, transmembrane domain, co-stimulatory domain> (SEQ ID NO: 10)
 IEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPLPFGPSKPFWLVVVGVLACYSLLVTVAFIIFWVRSKRSLHSDY
 MNMTPRRPGPTRKHYQPYAPPRDFAAYRS

<CD137 (4-1BB) activation / co-stimulatory domain> (SEQ ID NO: 11)
 KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEGGCEL

Figure 5. Primers used to detect CAR expression by quantitative PCR

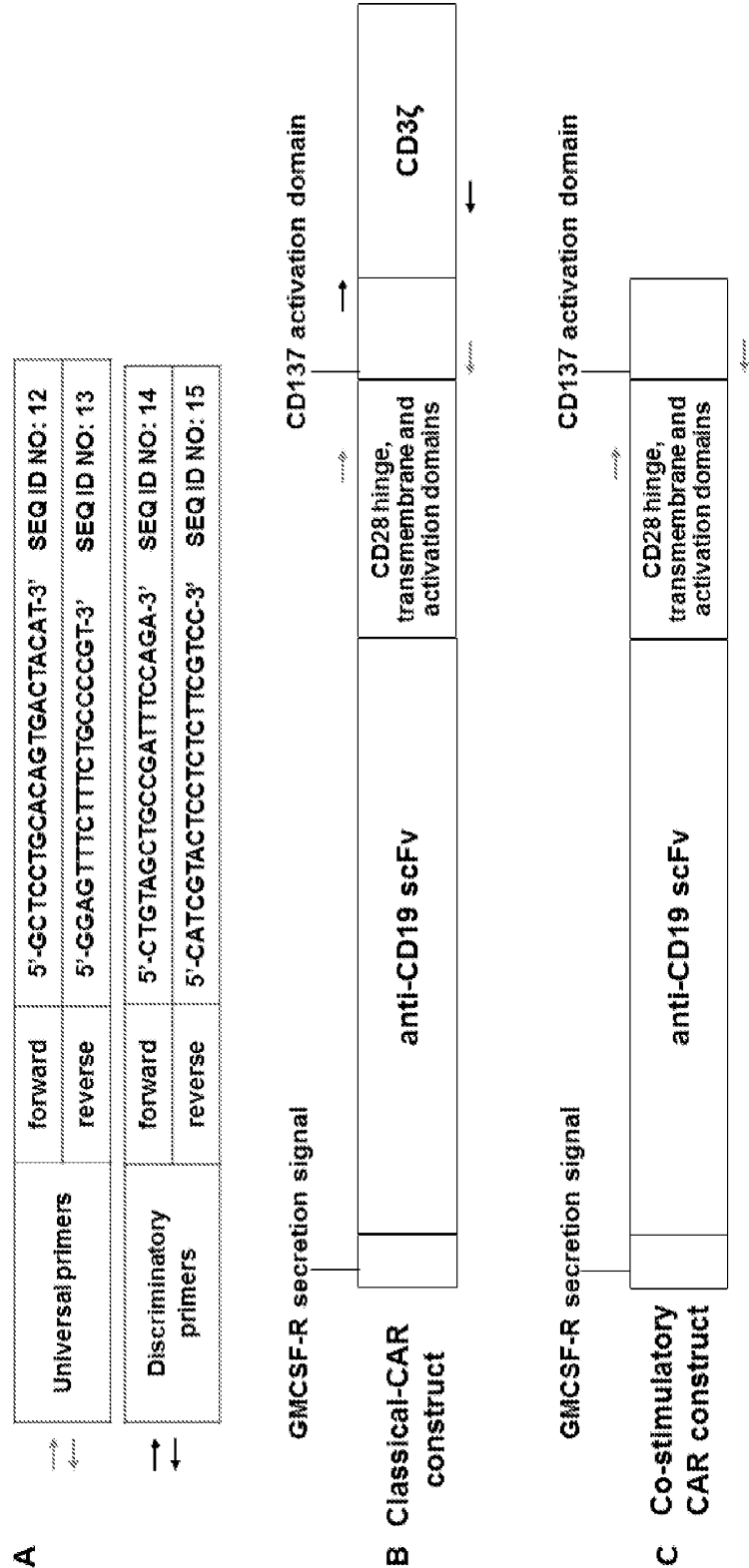


Figure 6. Quantitative detection of classical CAR and co-stimulatory CAR expression

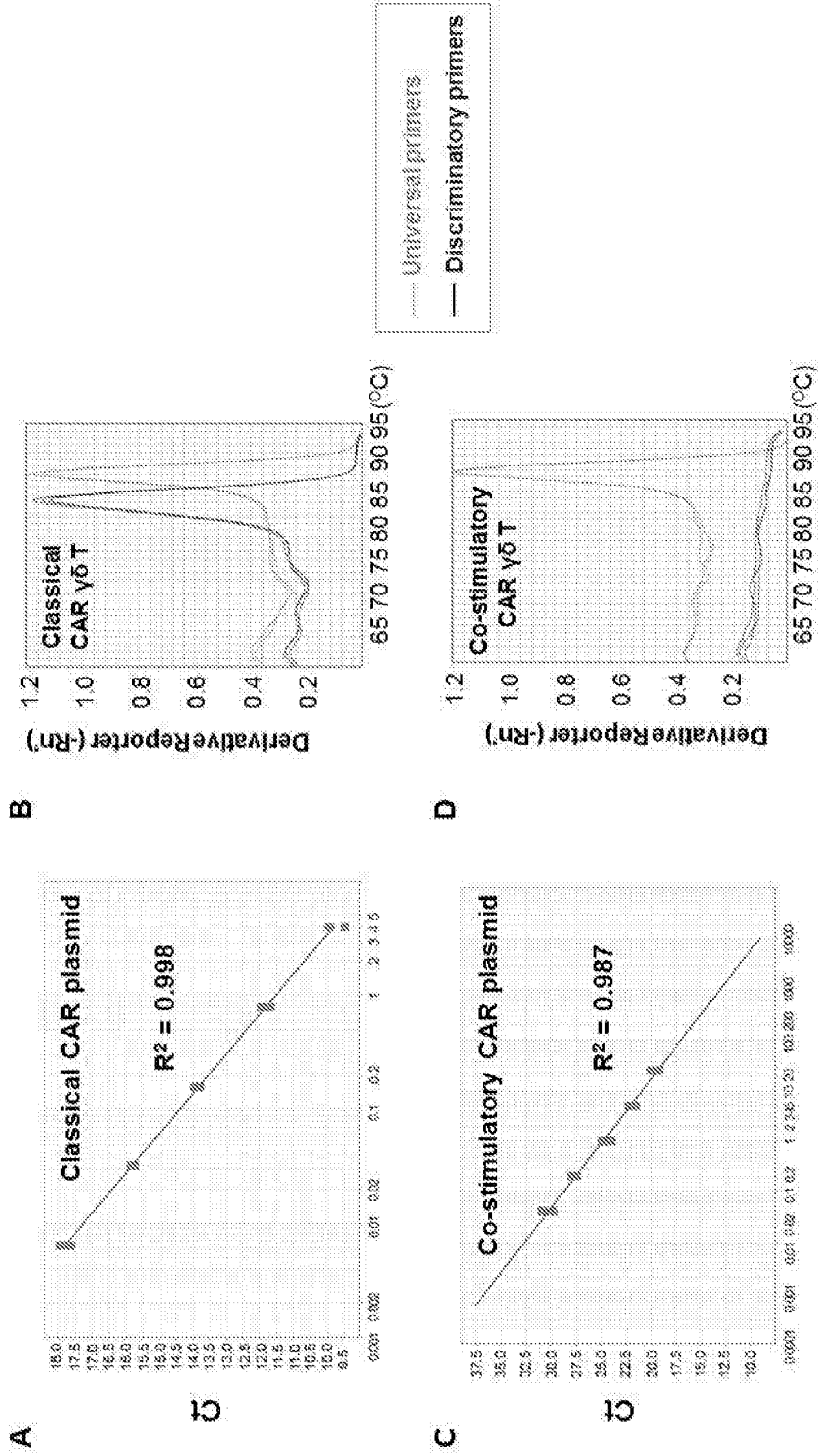


Figure 7. Potency of classical CAR $\gamma\delta$ T cells towards CD19 positive lymphoma cell lines

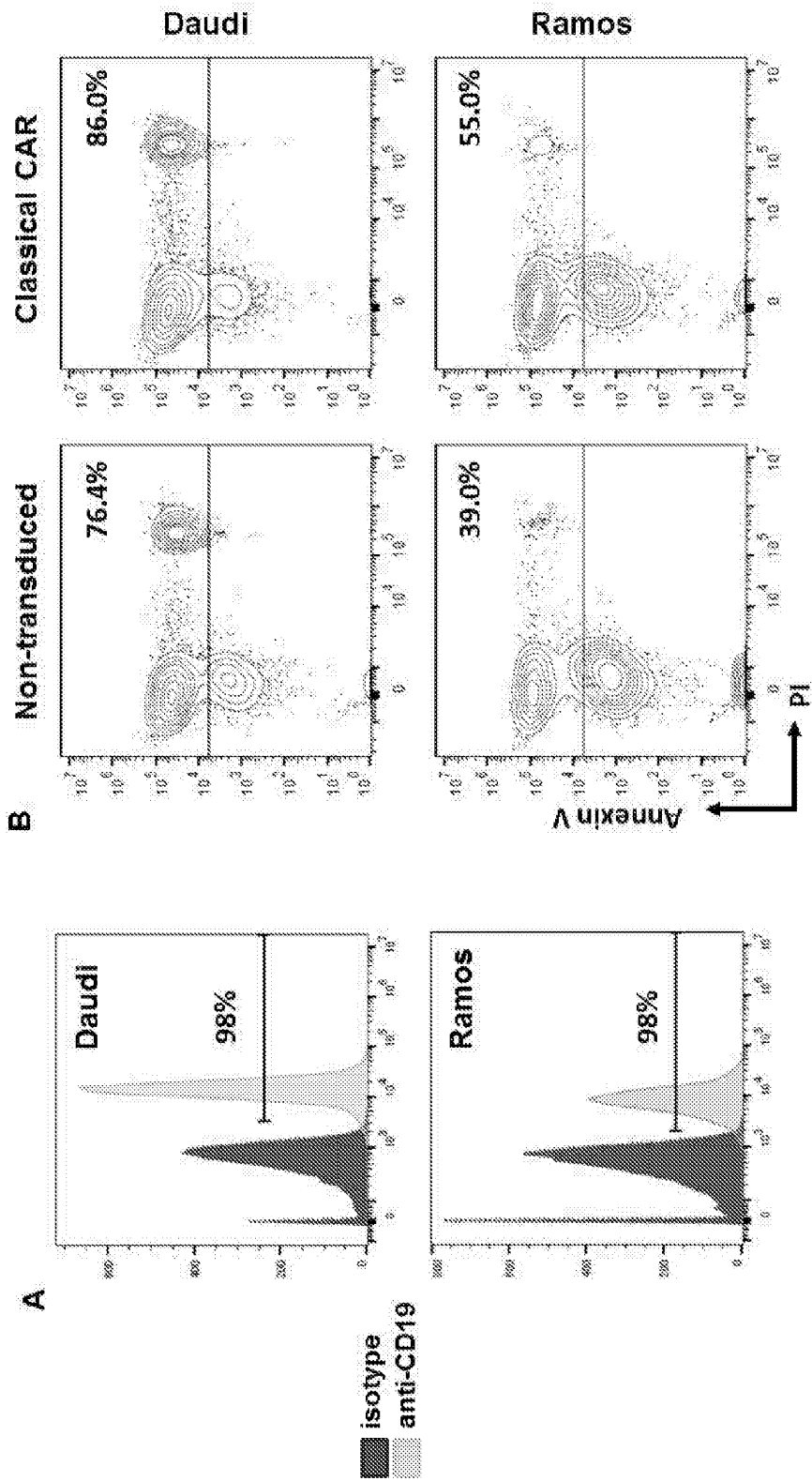


Figure 7.
(continued)

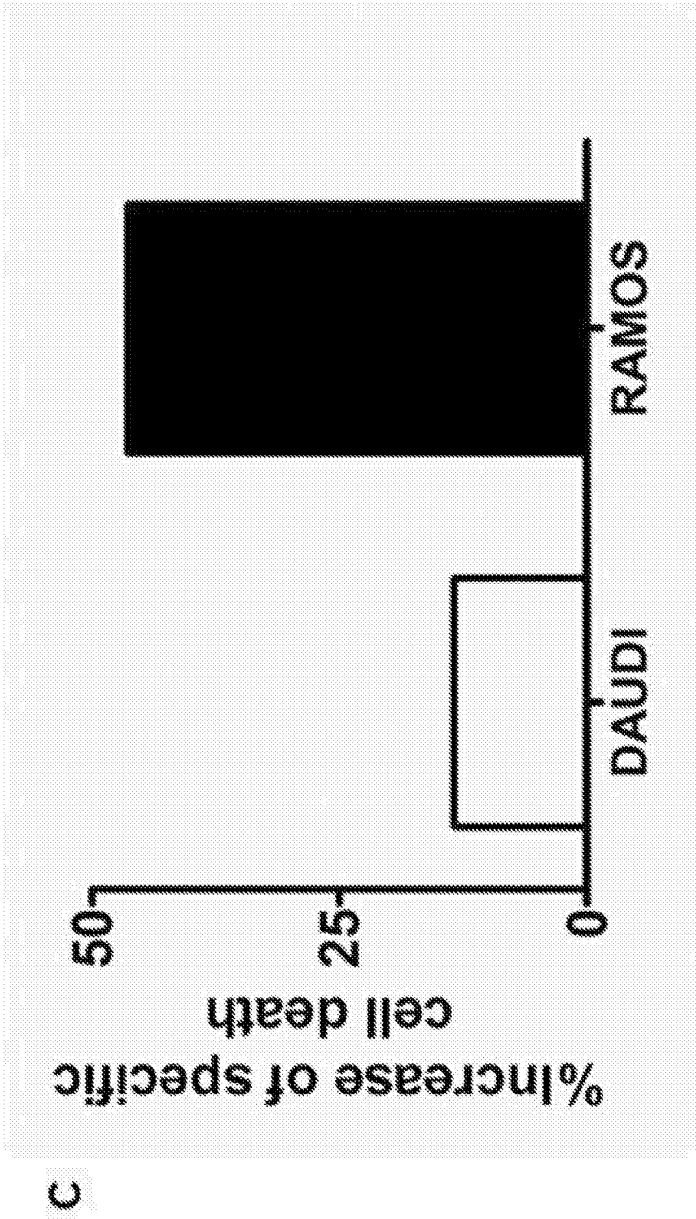


Figure 8. Potency of classical and costimulatory CAR $\gamma\delta$ T cells towards CD19 positive lymphoma cell lines

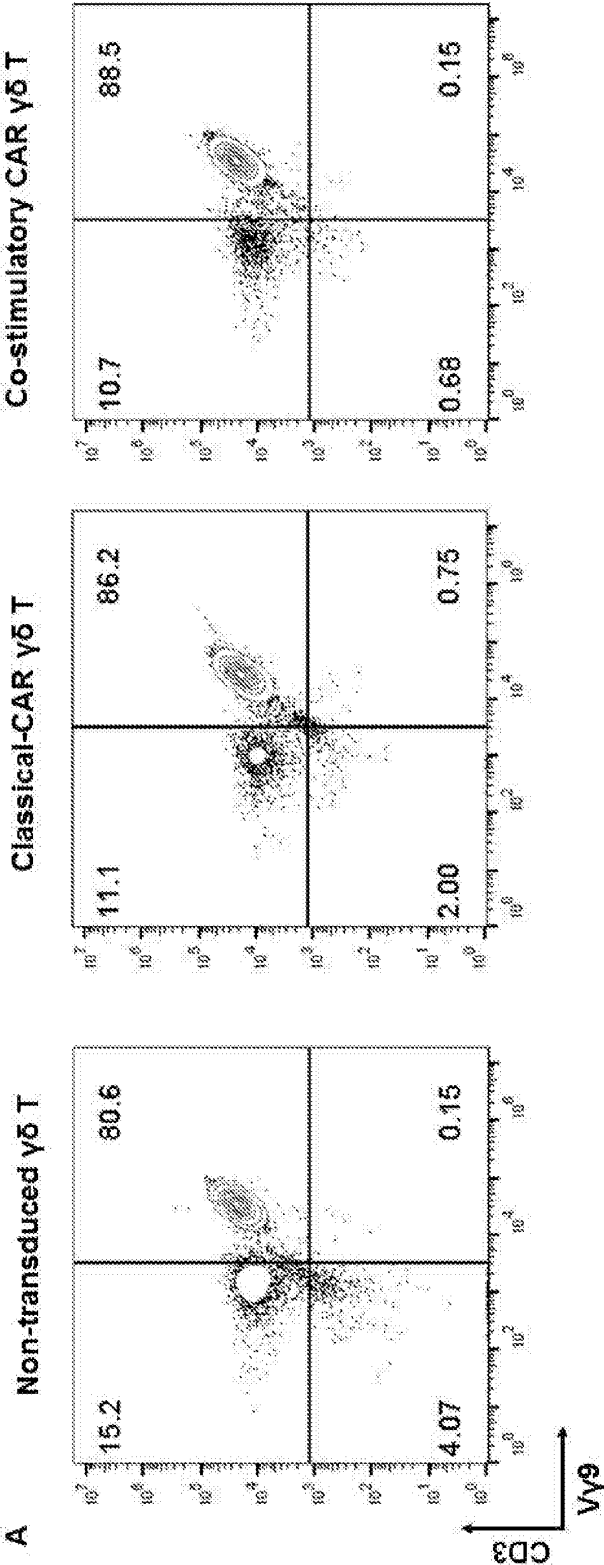
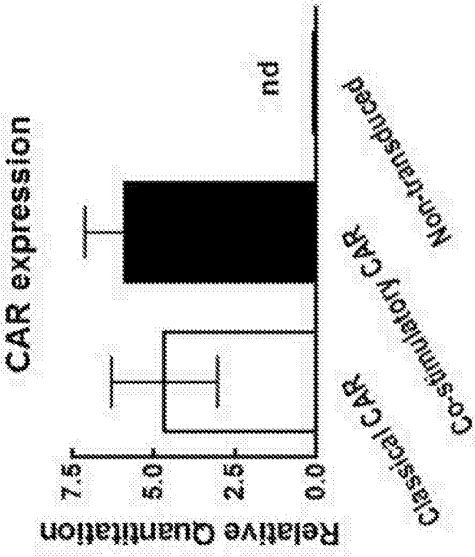
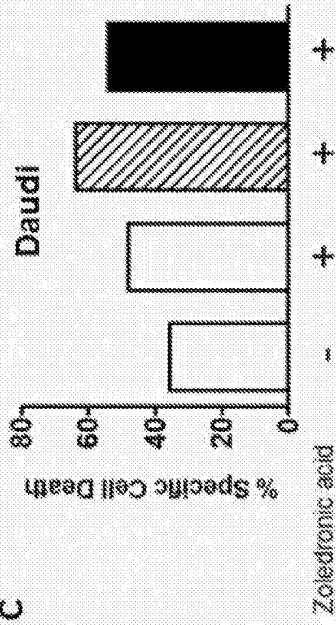


Figure 8. Continued

B



C



D

