

Figure 1

Wild Type EBV LMPA2 TCR TRAV12-3*01/TRAJ41*01/TRAC alpha chain amino acid sequence
(SEQ ID No: 2)

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      10      20      30
      *      *      *
Q K E V E Q D P G P L S V P E G A I V S L N C T Y S N S A F Q

      40      50      60
      *      *      *
Y F M W Y R Q Y S R K G P E L L M Y T Y S S G N K E D G R F T

      70      80      90
      *      *      *
A Q V D K S S K Y I S L F I R D S Q P S D S A T Y L C A M S A

      100     110     120
      *      *      *
E A N S G Y A L N F G K G T S L L V T P H I Q N P D P A V Y Q

      130     140     150
      *      *      *
L R D S K S S D K S V C L F T D F D S Q T N V S Q S K D S D V

      160     170     180
      *      *      *
Y I T D K T V L D M R S M D F K S N S A V A W S N K S D F A C

      190     200
      *      *
A N A F N N S I I P E D T F F P S P E S S
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Figure 2

Wild Type EBV LMPA2 TCR TRBV11-2*01/TRBD1/TRBJ2-7/TRBC beta chain amino acid sequence (SEQ ID No: 3)

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      10      20      30
      *      *      *
E A G V A Q S P R Y K I I E K R Q S V A F W C N P I S G H A T

      40      50      60
      *      *      *
L Y W Y Q Q I L G Q G P K L L I Q F Q N N G V V D D S Q L P K

      70      80      90
      *      *      *
D R F S A E R L K G V D S T L K I Q P A K L E D S A V Y L C A

      100     110     120
      *      *      *
S S L G G Y E Q Y F G P G T R L T V T E D L K N V F P P E V A

      130     140     150
      *      *      *
V F E P S E A E I S H T Q K A T L V C L A T G F Y P D H V E L

      160     170     180
      *      *      *
S W W V N G K E V H S G V S T D P Q P L K E Q P A L N D S R Y

      190     200     210
      *      *      *
C L S S R L R V S A T F W Q N P R N H F R C Q V Q F Y G L S E

      220     230     240
      *      *      *
N D E W T Q D R A K P V T Q I V S A E A W G R A D

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Figure 3

Reference TCR alpha chain – Wild type EBV LMPA2-specific TCR TRAV12-3*01/TRAJ41*01/TRAC alpha chain amino acid sequence, but with cysteine (bold and underlined) substituted for T162 (i.e. T48 of the TRAC constant region) (SEQ ID No: 4)

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      10      20      30
      *      *      *
Q K E V E Q D P G P L S V P E G A I V S L N C T Y S N S A F Q

      40      50      60
      *      *      *
Y F M W Y R Q Y S R K G P E L L M Y T Y S S G N K E D G R F T

      70      80      90
      *      *      *
A Q V D K S S K Y I S L F I R D S Q P S D S A T Y L C A M S A

      100     110     120
      *      *      *
E A N S G Y A L N F G K G T S L L V T P H I Q N P D P A V Y Q

      130     140     150
      *      *      *
L R D S K S S D K S V C L F T D F D S Q T N V S Q S K D S D V

      160     170     180
      *      *      *
Y I T D K C V L D M R S M D F K S N S A V A W S N K S D F A C

      190     200
      *      *
A N A F N N S I I P E D T F F P S P E S S
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Figure 4

Reference TCR beta chain – Wild type EBV LMPA2-specific TCR TRBV5-1*01/TRBD1/TRBJ2-7*01/TRBC2 beta chain amino acid sequence, but with cysteine (bold and underlined) substituted for S169 (i.e. S57 of the TRBC2 constant region) and with A187 substituted for C187 and D201 substituted for N201 (SEQ ID No: 5)

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      10      20      30
      *      *      *
E A G V A Q S P R Y K I I E K R Q S V A F W C N P I S G H A T

      40      50      60
      *      *      *
L Y W Y Q Q I L G Q G P K L L I Q F Q N N G V V D D S Q L P K

      70      80      90
      *      *      *
D R F S A E R L K G V D S T L K I Q P A K L E D S A V Y L C A

     100     110     120
      *      *      *
S S L G G Y E Q Y F G P G T R L T V T E D L K N V F P P E V A

     130     140     150
      *      *      *
V F E P S E A E I S H T Q K A T L V C L A T G F Y P D H V E L

     160     170     180
      *      *      *
S W W V N G K E V H S G V C T D P Q P L K E Q P A L N D S R Y

     190     200     210
      *      *      *
A L S S R L R V S A T F W Q D P R N H F R C Q V Q F Y G L S E

     220     230     240
      *      *      *
N D E W T Q D R A K P V T Q I V S A E A W G R A D
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Figure 5**Alpha chain amino acid sequence (SEQ ID Nos: 6-12)****a12 (SEQ ID No: 6)**

QKEVEQDPGPLSVPEGAIIVSLNCTYSNSAFQYFMWYRQYSRKGPPELLMYTYSSGNKEDGRFTAQVD
KSSKYISLFIRDSQPSDSATYLCAMSAEAHQPYRLNFGKGTSLLVTPHIQNPDPAVYQLRDSKSSDKS
VCLFTDFDSQTNVSQSKSDVYITDKCVLDMRSMDFKSNSAVAWSNKSDFACANAFNNSIIPEDTFFP
SPSS

a29 (SEQ ID No: 7)

QKEVEQDPGPLSVPEGAIIVSLNCTYSNSAFQYFMWYRQYSRKGPPELLMYLPGGGNKEDGRFTAQVD
KSSKYISLFIRDSQPSDSATYLCAMSAEAYGHYALNFGKGTSLLVTPHIQNPDPAVYQLRDSKSSDKS
VCLFTDFDSQTNVSQSKSDVYITDKCVLDMRSMDFKSNSAVAWSNKSDFACANAFNNSIIPEDTFFP
SPSS

a32 (SEQ ID No: 8)

QKEVEQDPGPLSVPEGAIIVSLNCTYSNSAFQYFMWYRQYSRKGPPELLMYQFQDGNKEDGRFTAQV
DKSSKYISLFIRDSQPSDSATYLCAMSAEAHQPYRLNFGKGTSLLVTPHIQNPDPAVYQLRDSKSSDK
SVCLFTDFDSQTNVSQSKSDVYITDKCVLDMRSMDFKSNSAVAWSNKSDFACANAFNNSIIPEDTFF
PSPSS

a37 (SEQ ID No: 9)

QKEVEQDPGPLSVPEGAIIVSLNCTYSNPHMAYFMWYRQYSRKGPPELLMYTYSSGNKEDGRFTAQVD
KSSKYISLFIRDSQPSDSATYLCAMSAEAYGHYALNFGKGTSLLVTPHIQNPDPAVYQLRDSKSSDKS
VCLFTDFDSQTNVSQSKSDVYITDKCVLDMRSMDFKSNSAVAWSNKSDFACANAFNNSIIPEDTFFP
SPSS

a38 (SEQ ID No: 10)

QKEVEQDPGPLSVPEGAIIVSLNCTYSNPHMAYFMWYRQYSRKGPPELLMYTYSSGNKEDGRFTAQVD
KSSKYISLFIRDSQPSDSATYLCAMSAEAHQPYRLNFGKGTSLLVTPHIQNPDPAVYQLRDSKSSDKS
VCLFTDFDSQTNVSQSKSDVYITDKCVLDMRSMDFKSNSAVAWSNKSDFACANAFNNSIIPEDTFFP
SPSS

a42 (SEQ ID No: 11)

QKEVEQDPGPLSVPEGAIIVSLNCTYSNPHMAYFMWYRQYSRKGPPELLMYQFQDGNKEDGRFTAQV
DKSSKYISLFIRDSQPSDSATYLCAMSAEAYGHYALNFGKGTSLLVTPHIQNPDPAVYQLRDSKSSDK
SVCLFTDFDSQTNVSQSKSDVYITDKCVLDMRSMDFKSNSAVAWSNKSDFACANAFNNSIIPEDTFF
PSPSS

a43 (SEQ ID No: 12)

QKEVEQDPGPLSVPEGAIIVSLNCTYSNPHMAYFMWYRQYSRKGPPELLMYQFQDGNKEDGRFTAQV
DKSSKYISLFIRDSQPSDSATYLCAMSAEAHQPYRLNFGKGTSLLVTPHIQNPDPAVYQLRDSKSSDK
SVCLFTDFDSQTNVSQSKSDVYITDKCVLDMRSMDFKSNSAVAWSNKSDFACANAFNNSIIPEDTFF
PSPSS

Figure 6**Beta chain amino acid sequence (SEQ ID No: 13)**

EAGVAQSPRYKIIKRQSVAFWCNPISGHATLYWYQQILGQGPKLLIQFVVAASVDDSQLPKDRFSAE
RLKGVDSTLKIQPAKLED SAVYLCASSLGGYEQYFGPGTRLTVTEDLKNVFPPEVAVFEPSEAEISHTQ
KATLVCLATGFYPDHVELSWWVNGKEVHSGVCTDPQPLKEQPALNDSRYALSSRLRVSATFWQDPR
NHFRCQVQFYGLSENDEWTQDRAKPVTQIVSAEAWGRAD

Figure 7**Reference TCR alpha chain (see Figure 3) DNA sequence (SEQ ID No: 14) (introduced cysteine is bold)**

atgcaaaaagaagttgaacaagatcctggaccactcagtgttccagagggagccatcgtttctctcaactgcact
tacagcaacagtgcttttcaatacttcatgtggtacagacagattccagaaaaggccctgagttgctgatgtac
acatactccagtggttaacaaagaagatggaaggtttacagcacaggctcgataaatccagcaagtatatctccttg
ttcatcagagactcacagcccagtgattcagccacctacctctgtgcaatgagcgcggaagcaaattccgggtat
gcactcaacttcggcaaaggcacctcgctgttgggtcacaccccatatccagaaccctgacctgacctgtaccag
ctgagagactctaagtcgagtgacaagtctgtctgcctattcaccgattttgattctcaacaaa**tgt**gtcaca
agtaaggattctgatgtgtatatcacagacaaatgtgtgctagacatgaggtctatggacttcaagagcaacagt
gctgtggcctggagcaacaaatctgactttgcatgtgcaaacgccttcaacaacagcattattccagaagacacc
ttcttccccagcccagaaagttcctaa

Reference TCR beta chain (see Figure 4) DNA sequence (SEQ ID No: 15) (introduced cysteine is bold)

atggaagctggagttgccagttctccagatataagattatagagaaaaggcagagtggtgctttttggtgcaat
cctatatctggccatgctaccctttactggtaccagcagatcctgggacagggcccaaagcttctgattcagttt
cagaataacggtgtagtggtgattcacagttgcctaaggatcgattttctgcagagaggctcaaaggagtagac
tccactctcaagatccagcctgcaaagcttgaggactcgccgtgtatctctgtgccagcagccttggcgggtac
gagcagtaacttcgggccgggcaccaggctcacgggtcacagaggacctgaaaaacgtgttcccacccgaggtcgct
gtgtttgagccatcagaagcagagatctcccacacccaaaaggccacactggtgtgcctggccaccggtttctac
cccgaccacgtggagctgagctggtgggtgaatgggaaggaggtgcacagtggggtc**tgc**acagaccgcagccc
ctcaaggagcagcccgcctcaatgactccagatacgctctgagcagccgctgagggctctcgccaccttctgg
caggacccccgcaaccattccgctgtcaagtccagttctacgggctctcggagaatgacgagtggaaccaggat
agggccaaacccgtcaccagatcgtcagcggcggaggcctggggtagagcagactaa

Figure 8

SEQ ID No: 16 - Amino acid sequence of an anti-CD3 scFv antibody fragment (bold type) fused via a linker namely GGGGS (underlined) at the N-terminus of a EBV LMP2A TCR beta chain. The EBV LMP2A TCR beta chain is SEQ ID No: 13:

XXQMTQSPSSLSASVGDRVTITCRASQDIRNYLNWYQQKPGKAPKLLIYYTSRLESGVPSRFSGSG
SGTDYTLTISSLQPEDFATYYCQQGNTLPWTFGQGTKVEIKGGGSGGGGSGGGGSGGGGSGGG
SEVQLVESGGGLVQPGGSLRLSCAASGYSFTGYTMNWVRQAPGKGLEWVALINPYKGVSTYNQKF
KDRFTISVDKSKNTAYLQMNSLRAEDTAVYYCARSGYGSDSDWYFDVWGQGT**LVTVSSGGGG****SEA**
GVAQSPRYKIIKRQSVAFWCNPISGHATLYWYQQILGQGPKLLIQFVVAASVDDSQLPKDRFSAERL
KGV DSTLKI QPAKLED SAVYLCASSLGGYE QYFGPGTRLT VTE DLKNVFPPEVAVFEPSEAEISHTQK
ATLVCLATGFYPDHVELSWWWNGKEVHSGVCTDPQPLKEQPALNDSRYALSSRLRVSATFWQDPRN
HFR CQVQFYGLSENDEWTQDRAKPVTQIVSAEAWGRAD

X at position 1 = D or A

X at position 2 = I or Q

Figure 9

Redirection of T cells by the different antiCD3 scfv EBV LMP2A high affinity TCR fusion proteins against the EBV LMP2A positive cell line IM9 and EBV LMP2A negative cell line colo205. Data for antiCD3scfv EBV LMP2A a29b1, a32b1, a37b1, a38b1, and a42b1 are shown



