

## Supplementary Figure S1. Amino acid sequences of the CARs.

a) The CD4-35-17b CAR includes the following features:

	<u>a.a. #</u>	<u>functional elements</u>
<b>CD4 segment</b>	1-208;	<u>signal peptide, D1D2</u>
<b>35 a.a. linker</b>	209-243; (G4S) <sub>7</sub>	
<b>17b scFv</b>	244-495; <b>V<sub>H</sub></b> , (G4S) <sub>3</sub> , <b>V<sub>L</sub></b>	
<b>spacer</b>	496-498;	AAA tripeptide
<b>CD28 segment</b>	499-605;	<u>extracellular hinge, TM, intracellular signaling</u>
<b>CD3-zeta segment</b>	606-717;	<u>intracellular signaling</u>

1 **MVRGVPFRHLLLVLQLALLPAATQGKKVVLGKKGDTVELTCTASQKKSIQ**  
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**FHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRSLWDQGNFPLI** IKNLK  
**IEDSDTYICEVEDQKEEVQLLVFGLTANS** DTHLLQGQSLTLTLESPPGSS  
**PSVQCRSPRGKNIQGGKTL** VSQLELQDSGTWTCTVLQNQKKVEFKIDIV  
**VLA**FQKASGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSQVQLLES  
GAEVKKPGSSVKVSCKASGDTFIRYSFTWVRQAPGQGLEWMGRIITILDV  
AHYAPHLQGRVTITADKSTSTVYLELRNLRSDDTAVYFCAGVYEADEG  
EYDNNNGFLKHVGQGTLVTVTSGGGSGGGSGGGSELELTQSPATLSVS  
PGERATLSCRASESVSSDLAWYQQKPGQAPRLLIYGASTRATGVPARFSG  
SGSGAEFTLTISSLQSEDFAVYYCQQYNNWP~~PRYTFGQGTRLEIKA~~AAAIE  
VMYPPP~~YLDNEKSNGTIIHVKGKHLCP~~SPLFPGPSKPFWVLVVVGVLAC  
YSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRRPGPTRKHYQPYAPPDF  
AA~~YRSRVKF~~SRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEM  
GGKPRRKNPQEGLYNELQKD~~KMAEAYSEIGMK~~GERRRGKGHDGLYQGLST  
ATKDTYDALHMQALPPR

b) CD4-10-17b CAR includes the following features:

	<u>a.a. #</u>	<u>functional elements</u>
<b>CD4 segment</b>	1-208;	<u>signal peptide</u> , D1D2
<b>10 a.a. linker</b>	209-218; (G4S) <sub>2</sub>	
<b>17b scFv</b>	219-470; <b>V<sub>H</sub></b> , (G4S) <sub>3</sub> , <b>V<sub>L</sub></b>	
<b>spacer</b>	471-473; AAA tripeptide	
<b>CD28 segment</b>	474-580; extracellular hinge, <u>TM</u> , intracellular signaling	
<b>CD3-zeta segment</b>	581-692; intracellular signaling	

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MVRGVPFRHLLLVLQLALLPAATQGKKVVLGKKGDTVELTCTASQKKSIQ  
FHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRLWDQGNFPLIINKNLK  
IEDSDTYICEVEDQKEEVQLLVFGLTANSDDTHLLQGQSLTLTLESPPGSS  
PSVQCRSPRGKNIQGGKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIV  
VLAFAQKASGGGGSGGGGSQVQLLESQAEVKPGSSVKVSKASGDTFIRY  
SFTWVRQAPGQGLEWMGRIITILDVAHYAPHLQGRVTITADKSTSTVYLE  
LRNLRSDDTAVYFCAGVYEGERADEGEYEDNNNGFLKHWGQGTLVTVTSGGGG  
SGGGGSGGGGSELELTQSPATLSVSPGERATLSCRASESVSSDLAWYQQK  
PGQAPRLLIYGASTRATGVPARFSGSGSGAEFTLTISLQSEDFAVYYCQ  
QYNNWPPRYTFGQGTRLEIKAAAIEVMYPPPYLDNEKSGNTIIHVKGKHL  
CPSPPLFPGPSKPFWVLVVVGGVLACYSSLVTVAIFIIFWVRSKRSRLLHSD  
YMNMTPRRPGPTRKHYPYAPPDFAAAYRSRVKFSSRSADAPAYQQGQNQL  
YNELNLRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA  
YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

c) The CD4 CAR includes the following features:

	<u>a.a. #</u>	<u>functional elements</u>
<b>CD4 segment</b>	1-208;	<u>signal peptide</u> , D1D2
<b>spacer</b>	209-211;	AAA tripeptide
<b>CD28 segment</b>	212-318;	<u>extracellular hinge</u> , <u>TM</u> , intracellular signaling
<b>CD3-zeta segment</b>	319-430;	intracellular signaling

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MVRGVPFRLLLVLQLALLPAATQGKKVVLGKKGDTVELTCTASQKKSIQ  
FHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRSLWDQGNFPLIIKNLK  
IEDSDTYICEVEDQKEEVQLLVFGLTANSDTHLLQGQSLTLESPPGSS  
PSVQCRSPRGKNIQGGKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIV  
VLAFAQKASAAAIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPLFPGPSKP  
FWVLVVVGVLACYLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRPGPT  
RKYQPYAPPRDFAAYRSRVKFSRSADAPAYQQGQNQLYNELNLGREEY  
DVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERR  
GKGHDGLYQGLSTATKDTYDALHMQALPPR

d) The CD4-35-DDY3 CAR includes the following features:

	<u>a.a. #</u>	<u>functional elements</u>
<b>CD4 segment</b>	1-208;	<u>signal peptide</u> , D1D2
<b>35 a.a. linker</b>	209-243; (G4S),	
<b>DDY scFv</b>	244-486; <b>V<sub>H</sub></b> , (G4S) <sub>3</sub> , <b>V<sub>L</sub></b>	
<b>spacer</b>	487-489; AAA tripeptide	
<b>CD28 segment</b>	490-593; extracellular hinge, <u>TM</u> , intracellular signaling	
<b>CD3-zeta segment</b>	594-708; intracellular signaling	

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MVRGVFRHLLLVLQLALLPAATQGKKVVLGKKGDTVELTCTASQKKSIQ  
FHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRLWDQGNFPLIINKNLK  
IEDSDTYICEVEDQKEEVQLLVFGLTANSNDTHLLQGQSLTLTLESPPGSS  
PSVQCRSPRGKNIQGGKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIV  
VLAFFQKASGGGGSGGGGSGGGGSGGGSGGGGGGGGGGGGGGGGGGGGGSEVQLVQS  
GAEVKKPGATVKISCKVSGYTFTDYYMHWVQQAPGKGLEWMGLVDPEDGE  
TIYAEKFQGRVTITADTSTDAYMELSSLRSEDTAVYYCATERTDYWGQG  
TLVTVSSGGGGSGGGSGGGSEIVLTQSPLSVTPGEPASISCRSSQS  
LLSDDGNTYLDWYLQKPGQSPQLLIYEVSNRFSGVPDFSGSGSGTDFT  
LKISRVEAEDVGVYYCMQSIQLPWTFGQGTKLEIKRAAAIEVMYPPPYLD  
NEKSNGTIIHVKGKHLCPSPLFPGPSKPFWVLVVVGVLACYSLLVTVAF  
IIFWVRSKRSRLLHSDYMNMTPRRPGPTRKHYQPYAPPRDFAAYRSRVKE  
SRSADAPAYQQQNQLYNELNLGREEYDVLDRGRDPEMGGKPRRKNP  
QEGLYNELQDKMAEAYSEIGMKGERRGKGDGLYQGLSTATKDTYDAL  
HMQALPPR

e) The 139 CAR includes the following features:

	<u>a.a. #</u>	<u>functional elements</u>
<b>signal peptide</b>	1-22;	
<b>139 scFv</b>	23-262; <b>V<sub>H</sub></b> , “128 linker”, <b>V<sub>L</sub></b>	
<b>spacer</b>	263-265; AAA tripeptide	
<b>CD28 segment</b>	266-372; <b>extracellular hinge</b> , <b>TM</b> , intracellular signaling	
<b>CD3-zeta segment</b>	373-484; <b>intracellular signaling</b>	

1 **MVLLVTSLLLCELPHAFLLIPDIQMTQSPSSLSASVGDRVТИTCRASQG**  
IRNNLAWYQQKPGKAPKRLIYAASNLIQSGVPSRFTGSGSGTEFTLIVSSL  
QPEDFATYYCLQHHSYPLTSGGTVKEIKRTGSTSGSGKPGSGEVQV  
LESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGS  
GGSTNYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAGSSGWSE  
YWGQGTLVTVSSAAAIEVMYPPPYLDNEKSNGTIIHVKGKHLCP SPLFPG  
**PSKPFWVLVVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTPRR**  
PGPTRKHYQPYAPPRDFAAAYRSRVKF SRSADAPAYQQGQNQLYNELNLGR  
REEYDVL DKKRRGRDPEMGGKPRRKNPQEGLYNELQKD KMAEAYSEIGMKG  
ERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR