

LISTADO DE SECUENCIAS

<110> CRISPR THERAPEUTICS AG

<120> MÉTODOS Y COMPOSICIONES PARA TRATAR EL CÁNCER

<130> AC1992 PCT S3

<140> PCT/IB2019/000500

<141> 2019-05-10

<150> US 62/670,417

<151> 2018-05-11

<150> US 62/701,340

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<150> US 62/756,643

<151> 2018-11-07

<150> US 62/773,658

<151> 2018-11-30

<150> US 62/826,600

<151> 2019-03-29

<160> 180

<170> PatentIn version 3.5

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<223> u puede estar presente o ausente

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aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugcuuuu uuuu 114

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<220>
<223> Sintético: 4-1BB secuencia de nucleótidos

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actactcaag aggaagatgg ctgtagctgc cgatttccag aagaagaaga aggaggatgt 120

gaactg 126

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<211> 42
<212> PRT
<213> Secuencia artificial

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<223> Sintético: 4-1BB secuencia de aminoácidos

<400> 19

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
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Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Gly Gly Cys Glu Leu
35 40

<210> 20

<211> 40

<212> PRT

<213> Secuencia artificial

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<223> Sintético: CD28 secuencia de aminoácidos

<400> 20

Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro
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Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro
20 25 30

Arg Asp Phe Ala Ala Tyr Arg Ser
35 40

<210> 21

<211> 336

<212> ADN

<213> Secuencia artificial

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<223> Sintético: CD3-z secuencia de nucleótidos

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tataacgaac tgaatttggg acgccgcgag gagtatgacg tgcttgataa acgccggggg 120

agagacccgg aaatggggggg taaaccccga agaaagaatc cccaagaagg actctacaat	180
gaactccaga aggataagat ggcggaggcc tactcagaaa taggtatgaa gggcgaacga	240
cgacgggggaa aaggtcacga tggcctctac caaggggtga gtacggcaac caaagatacg	300
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<210> 22
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<220>
 <223> Sintético: CD3-z secuencia de aminoácidos

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Asp	Val	Leu	Asp	Lys	Arg	Arg	Gly	Arg	Asp	Pro	Glu	Met	Gly	Gly	Lys
		35					40					45			

Pro	Arg	Arg	Lys	Asn	Pro	Gln	Glu	Gly	Leu	Tyr	Asn	Glu	Leu	Gln	Lys
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Asp	Lys	Met	Ala	Glu	Ala	Tyr	Ser	Glu	Ile	Gly	Met	Lys	Gly	Glu	Arg
65					70					75					80

Arg	Arg	Gly	Lys	Gly	His	Asp	Gly	Leu	Tyr	Gln	Gly	Leu	Ser	Thr	Ala
				85					90					95	

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<223> Sintético: CD70 sgRNA (E1_T1)

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cguuaucaac uugaaaaagu ggcaccgagu cggugcuuuu 100

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<211> 100

<212> ARN

<213> Secuencia artificial

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<223> Sintético: CD70 sgRNA (E1_T3)

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<213> Secuencia artificial

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<223> Sintético: CD70 sgRNA (E1_T4)

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<212> ARN

<213> Secuencia artificial

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<223> Sintético: CD70 sgRNA (E1_T7)

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cguuaucaac uugaaaaagu ggcaccgagu cggugcuuuu 100

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<211> 100

<212> ARN

<213> Secuencia artificial

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<223> Sintético: CD70 sgRNA (E1_T8)

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cguuaucaac uugaaaaagu ggcaccgagu cggugcuuuu 100

<210> 28

<211> 100

<212> ARN

<213> Secuencia artificial

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<223> Sintético: CD70 sgRNA (E1_T10)

<400> 28

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cguuaucaac uugaaaaagu ggcaccgagu cggugcuuuu 100

<210> 29

<211> 100

<212> ARN

<213> Secuencia artificial

<220>

<223> Sintético: CD70 sgRNA (E3_T1)

<400> 29

cagcuacgua uccaucguga guuuuagagc uagaaauagc aaguuaaaau aaggcuaguc 60

cguuaucaac uugaaaaagu ggcaccgagu cggugcuuuu 100

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<211> 100

<212> ARN

<213> Secuencia artificial

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<223> Sintético: TRAC sgRNA

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agagcaacag ugcuguggcc guuuuagagc uagaaauagc aaguuaaaau aaggcuaguc 60

cguuaucaac uugaaaaagu ggcaccgagu cggugcuuuu 100

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<211> 100

<212> ARN

<213> Secuencia artificial

<220>

<223> Sintético: b2M sgRNA

<400> 31

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<223> Sintético: PD-1 sgRNA

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cguuaucaac uugaaaaagu ggcaccgagu cggugcuuuu 100

<210> 33

<211> 100

<212> ARN

<213> Secuencia artificial

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<223> Sintético: CD70 sgRNA (E1_T1)

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<222> (1)..(3)

<223> 2'-O-metil fosforotioato

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 <221> modified_base
 <222> (97)..(99)
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 <223> Sintético: CD70 sgRNA (E1_T3)

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<400> 34
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<210> 36
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<220>
 <221> modified_base
 <222> (97)..(99)
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<400> 36
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 cguaaucaac uugaaaaagu ggcaccgagu cggugcuuuu 100

<210> 37
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 <212> ARN
 <213> Secuencia artificial

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 <223> Sintético: CD70 sgRNA (E1_T8)

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 <222> (1)..(3)
 <223> 2'-O-metil fosforotioato

<220>
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 <222> (97)..(99)
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 <400> 37
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<210> 38
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 <223> Sintético: CD70 sgRNA (E1_T10)

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<220>
 <221> modified_base
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 <223> Sintético: b2M sgRNA

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<220>
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 <223> Sintético: PD-1 sgRNA

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<220>
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ccagtacaaa ctactcaaga ggaagatggc tgtagctgcc gatttccaga agaagaagaa	3300
ggaggatgtg aactgcgagt gaagttttcc cgaagcgcag acgctccggc atatcagcaa	3360
ggacagaatc agctgtataa cgaactgaat ttgggacgcc gcgaggagta tgacgtgctt	3420
gataaacgcc gggggagaga cccggaaatg gggggtaaac cccgaagaaa gaatcccca	3480
gaaggactct acaatgaact ccagaaggat aagatggcgg aggcctactc agaaataggt	3540
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gcaaccaaag atacgtacga tgactgcat atgcaggccc tgcctcccag ataataataa	3660
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gagaaaggta accacgtgcg gaccgaggct gcagcgtcgt cctccctagg aacccttagt	4560
gatggagttg gccactccct ctctgcgcgc tcgctcgctc actgaggccg ggcgacaaaa	4620

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cctgcagg	4688

<210> 44
 <211> 4364
 <212> ADN
 <213> Secuencia artificial

<220>
 <223> Sintético: CD70 LHA a RHA (CD70B scFV con 41BB)

<400> 44	
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tcctggtaat gtgatagatt tcccaactta atgccaacat accataaacc tcccattctg	180
ctaatgcccga gcctaagttg gggagaccac tccagattcc aagatgtaca gtttgctttg	240
ctgggccttt ttcccatgcc tgcctttact ctgccagagt tatattgctg gggttttgaa	300
gaagatccta ttaaataaaaa gaataagcag tattattaag tagccctgca tttcagggtt	360
ccttgagtgg caggccaggc ctggccgtga acgttcactg aaatcatggc ctcttgcca	420
agattgatag cttgtgcctg tccctgagtc ccagtccatc acgagcagct ggtttctaag	480
atgctatttc ccgtataaag catgagaccg tgacttgcca gcccacaga gcccgcct	540
tgtccatcac tggcatctgg actccagcct gggttggggc aaagaggga atgagatcat	600
gtcctaacc tgatcctctt gtcccacaga tatccagaac cctgaccctg ccgtgtacca	660
gctgagagac tctaaatcca gtgacaagtc tgtctgccta ttcaccgatt ttgattctca	720
aacaaatgtg tcacaaagta aggattctga tgtgtatatc acagacaaaa ctgtgctaga	780
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gagaaccgta tataagtgc gtagtcgccg tgaacgttct ttttcgcaac gggtttgccg	1020
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caagcgccgg	ggcagggact	gaaatggatg	gggtggataa	atacctacac	cggcgaacct	2220
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cttcagattg gaatgtgttt taactcaggg ttgagaaaac agctaccttc aggacaaaag	4260
tcagggaagg gctctctgaa gaaatgctac ttgaagatac cagccctacc aagggcaggg	4320
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<210> 45
 <211> 1527
 <212> ADN
 <213> Secuencia artificial

<220>
 <223> Sintético: CD70 secuencia de nucleótidos CAR (CD70B scFV con 41BB)

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gtgtcctgta aggcgtccgg ttatacgttc acgaactacg ggatgaattg ggttcgccaa	180
gcgccggggc agggactgaa atggatgggg tggataaata cctacaccgg cgaacctaca	240
tacgccgacg cttttaaagg gcgagtcact atgacgcgcg ataccagcat atccaccgca	300
tacatggagc tgtcccgact ccggtcagac gacacggctg tctactattg tgctcgggac	360
tatggcgatt atggcatgga ctactggggg cagggtacga ctgtaacagt tagtagtggt	420
ggaggcggca gtggcggggg gggaagcgga ggaggggggt ctggtgacat agttatgacc	480
caatccccag atagtttggc ggtttctctg ggcgagaggg caacgattaa ttgtcgcgca	540
tcaaagagcg tttcaacgag cggatattct tttatgcatt ggtaccagca aaaaccggga	600
caaccgccga agctgctgat ctacttggct tcaaactctg agtctggggg gccggaccga	660
ttttctggta gtggaagcgg aactgacttt acgctcacga tcagttcact gcaggctgag	720
gatgtagcgg tctattattg ccagcacagt agagaagtcc cctggacctt cggtaaggc	780
acgaaagtag aaattaaaag tgctgctgcc tttgtcccgg tatttctccc agccaaaccg	840
accacgactc ccgccccgcg ccctccgaca cccgctccca ccatcgctc tcaacctctt	900

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agtcttcgcc ccgaggcatg ccgacccgcc gccgggggtg ctgttcatac gaggggcttg      960
gacttcgctt gtgatattta catttgggct ccgttggcgg gtacgtgcgg cgtccttttg      1020
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ctcctgtata tattcaaaca accatttatg agaccagtac aaactactca agaggaagat      1140
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tcccgaagcg cagacgctcc ggcatatcag caaggacaga atcagctgta taacgaactg      1260
aatttgggac gccgcgagga gtatgacgtg cttgataaac gccggggggag agacccggaa      1320
atggggggta aaccccgaag aaagaatccc caagaaggac tctacaatga actccagaag      1380
gataagatgg cggaggccta ctcagaaata ggtatgaagg gcgaacgacg acggggaaaa      1440
ggtcacgatg gcctctacca agggttgagt acggcaacca aagatacgta cgatgcactg      1500
catatgcagg ccctgcctcc cagataa                                          1527

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<210> 46

<211> 508

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: secuencia de aminoácidos CD70 CAR (CD70B scFV con 41BB)

<400> 46

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Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1           5           10          15

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His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
          20          25          30

```

```

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
          35          40          45

```

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Thr Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln
          50          55          60

```

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Gly Leu Lys Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr

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65					70						75				80
Tyr	Ala	Asp	Ala	Phe	Lys	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	Thr	Ser
				85					90					95	
Ile	Ser	Thr	Ala	Tyr	Met	Glu	Leu	Ser	Arg	Leu	Arg	Ser	Asp	Asp	Thr
			100					105					110		
Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Asp	Tyr	Gly	Asp	Tyr	Gly	Met	Asp	Tyr
		115					120					125			
Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser
	130					135					140				
Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Asp	Ile	Val	Met	Thr
145					150					155					160
Gln	Ser	Pro	Asp	Ser	Leu	Ala	Val	Ser	Leu	Gly	Glu	Arg	Ala	Thr	Ile
				165					170					175	
Asn	Cys	Arg	Ala	Ser	Lys	Ser	Val	Ser	Thr	Ser	Gly	Tyr	Ser	Phe	Met
			180					185					190		
His	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro	Lys	Leu	Leu	Ile	Tyr
		195					200					205			
Leu	Ala	Ser	Asn	Leu	Glu	Ser	Gly	Val	Pro	Asp	Arg	Phe	Ser	Gly	Ser
	210					215					220				
Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Ala	Glu
225					230					235					240
Asp	Val	Ala	Val	Tyr	Tyr	Cys	Gln	His	Ser	Arg	Glu	Val	Pro	Trp	Thr
				245					250					255	
Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys	Ser	Ala	Ala	Ala	Phe	Val
			260					265					270		

Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg Pro
275 280 285

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
290 295 300

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
305 310 315 320

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
325 330 335

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Asn His Arg
340 345 350

Asn Arg Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
355 360 365

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
370 375 380

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
385 390 395 400

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
405 410 415

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
420 425 430

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
435 440 445

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
450 455 460

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys

465

470

475

480

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
485 490 495

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505

<210>	47
<211>	735
<212>	ADN
<213>	Secuencia artificial

<220>
<223> Sintético: CD70A scFv secuencia de nucleótidos

<400>	47						
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agccttcagg	ccgaagatgt	ggcgggtata	tactgccagc	attcaaggga	agttccttgg		300
acgttcggtc	agggcacgaa	agtggaaatt	aaaggcgggg	ggggatccgg	cgggggaggg		360
tctggaggag	gtggcagtg	tcaggtccaa	ctggtgcagt	ccggggcaga	ggtaaaaaaa		420
cccggcgcgt	ctgttaaggt	ttcatgcaag	gccagtggat	atactttcac	caattacgga		480
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tacaccggtg	aacctaccta	tgccgatgcc	tttaagggtc	gggttacgat	gacgagagac		600
acctccatat	caacagccta	catggagctc	agcagattga	ggagtgcga	tacggcagtc		660
tattactgtg	caagagacta	cggcgattat	ggcatggatt	actggggcca	gggcactaca		720
gtaaccgttt	ccagc						735

$\langle 210 \rangle$	48
$\langle 211 \rangle$	245
$\langle 212 \rangle$	PRT

<213> Secuencia artificial

<220>

<223> Sintético: CD70A scFv secuencia de aminoácidos

<400> 48

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Val Ser Thr Ser
20 25 30

Gly Tyr Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln His Ser Arg
85 90 95

Glu Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gln
115 120 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
130 135 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly
145 150 155 160

Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Lys Trp Met Gly
165 170 175

Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Ala Phe Lys
180 185 190

Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr Met
195 200 205

Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala
210 215 220

Arg Asp Tyr Gly Asp Tyr Gly Met Asp Tyr Trp Gly Gln Gly Thr Thr
225 230 235 240

Val Thr Val Ser Ser
245

<210> 49
<211> 735
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: CD70B scFv secuencia de nucleótidos

<400> 49
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ccggggcagg gactgaaatg gatgggggtgg ataaatacct acaccggcga acctacatac 180
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ggcgattatg gcatggacta ctgggggtcag ggtacgactg taacagttag tagtggtgga 360
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tccccagata gtttggcggt ttctctgggc gagagggcaa cgattaattg tcgcgcatca 480
aagagcgttt caacgagcgg atattctttt atgcattggt accagcaaaa acccggaaca 540
ccgccgaagc tgctgatcta cttggcttca aatcttgagt ctgggggtgcc ggaccgattt 600

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tctggtagtg gaagcggaac tgactttacg ctcacgatca gttcactgca ggctgaggat      660
gtagcgggtct attattgcc a gcacagtaga gaagtcccct ggaccttcgg tcaaggcacg      720
aaagtagaaa ttaaa                                     735
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$\langle 210 \rangle$	50
$\langle 211 \rangle$	245
$\langle 212 \rangle$	PRT
$\langle 213 \rangle$	Secuencia artificial

<220>
<223> Sintético: CD70B scFv secuencia de aminoácidos

<400> 50

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Ala Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Gly Asp Tyr Gly Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Asp Ile Val Met Thr Gln Ser Pro Asp Ser

130

135

140

Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser
 145 150 155 160

Lys Ser Val Ser Thr Ser Gly Tyr Ser Phe Met His Trp Tyr Gln Gln
 165 170 175

Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu
 180 185 190

Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
 195 200 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
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Tyr Cys Gln His Ser Arg Glu Val Pro Trp Thr Phe Gly Gln Gly Thr
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Lys Val Glu Ile Lys
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<211> 118

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: CD70 VH

<400> 51

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
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Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Lys Trp Met

35

40

45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Ala Phe
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Lys Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
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Ala Arg Asp Tyr Gly Asp Tyr Gly Met Asp Tyr Trp Gly Gln Gly Thr
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Thr Val Thr Val Ser Ser
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<400> 52

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Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Val Ser Thr Ser
 20 25 30

Gly Tyr Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Asp
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser

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<400> 53

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<400> 54

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<211> 4364

<212> ADN

<213> Secuencia artificial

<220>

<223> Sintético: BCMA RHA a LHA

<400> 55

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<213> Secuencia artificial

<220>
<223> Sintético: BCMA secuencia de nucleótidos CAR

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<212> PRT
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<223> Sintético: BCMA secuencia de aminoácidos CAR

<400> 57

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Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Asn
35 40 45

Thr Leu Thr Asn Tyr Val Ile His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Arg Leu Glu Trp Met Gly Tyr Ile Leu Pro Tyr Asn Asp Leu Thr Lys
65 70 75 80

Tyr Ser Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Arg Asp Lys Ser
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Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Thr Arg Trp Asp Trp Asp Gly Phe Phe Asp Pro

115

120

125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
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Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln
 145 150 155 160

Ser Pro Ala Thr Leu Ser Val Ser Pro Gly Glu Arg Ala Ser Ile Ser
 165 170 175

Cys Arg Ala Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr His Leu
 180 185 190

His Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
 195 200 205

Ser Val Ser Asn Arg Phe Ser Glu Val Pro Ala Arg Phe Ser Gly Ser
 210 215 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Glu Ser Glu
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Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Ala Ala Ala Phe Val
 260 265 270

Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg Pro
 275 280 285

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
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Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
 305 310 315 320

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
325 330 335

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Asn His Arg
340 345 350

Asn Arg Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
355 360 365

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
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Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
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Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
405 410 415

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
420 425 430

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
435 440 445

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
450 455 460

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
465 470 475 480

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
485 490 495

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505

<211> 735
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: BCMA secuencia de nucleótidos scFv

<400> 58
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cccgccaaa ggctggagtg gatgggctac atcctgccct acaacgacct gaccaagtac 180
agccagaagt tccagggcag ggtgaccatc accagggata agagcgcctc caccgcctat 240
atggagctga gcagcctgag gagcaggagc accgctgtgt actactgtac aaggtgggac 300
tgggacggct tctttgaccc ctggggccag ggcacaacag tgaccgtcag cagcggcggc 360
ggaggcagcg gcggcggcgg cagcggcggg ggcggaagcg aaatcgtgat gacccagagc 420
cccgccacac tgagcgtgag ccctggcgag agggccagca ttcctgcag ggctagccaa 480
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gctcccaggc tgctgatcta cagcgtgagc aacaggttct ccgaggtgcc tgccaggttt 600
agcggcagcg gaagcggcac cgactttacc ctgaccatca gcagcgtgga gtccgaggac 660
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aagctggaga tcaaa 735

<210> 59
<211> 245
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA secuencia de aminoácidos scFv

<400> 59

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Asn Thr Leu Thr Asn Tyr

20

25

30

Val Ile His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
 35 40 45

Gly Tyr Ile Leu Pro Tyr Asn Asp Leu Thr Lys Tyr Ser Gln Lys Phe
 50 55 60

Gln Gly Arg Val Thr Ile Thr Arg Asp Lys Ser Ala Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Thr Arg Trp Asp Trp Asp Gly Phe Phe Asp Pro Trp Gly Gln Gly Thr
 100 105 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
 130 135 140

Ser Val Ser Pro Gly Glu Arg Ala Ser Ile Ser Cys Arg Ala Ser Gln
 145 150 155 160

Ser Leu Val His Ser Asn Gly Asn Thr His Leu His Trp Tyr Gln Gln
 165 170 175

Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ser Val Ser Asn Arg
 180 185 190

Phe Ser Glu Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
 195 200 205

Phe Thr Leu Thr Ile Ser Ser Val Glu Ser Glu Asp Phe Ala Val Tyr
 210 215 220

Tyr Cys Ser Gln Thr Ser His Ile Pro Tyr Thr Phe Gly Gly Gly Thr
225 230 235 240

Lys Leu Glu Ile Lys
245

<210> 60
<211> 118
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA VH

<400> 60

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Asn Thr Leu Thr Asn Tyr
20 25 30

Val Ile His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Tyr Ile Leu Pro Tyr Asn Asp Leu Thr Lys Tyr Ser Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Arg Asp Lys Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Trp Asp Trp Asp Gly Phe Phe Asp Pro Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> 61
<211> 112
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA VL

<400> 61

Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Ser Ile Ser Cys Arg Ala Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Asn Thr His Leu His Trp Tyr Gln Gln Arg Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Ser Val Ser Asn Arg Phe Ser Glu Val Pro
50 55 60

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65 70 75 80

Ser Ser Val Glu Ser Glu Asp Phe Ala Val Tyr Tyr Cys Ser Gln Thr
85 90 95

Ser His Ile Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 62
<211> 15
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: CD70 VL CDR1 (Kabat)

<400> 62

Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser Phe Met His

1 5 10 15

<210> 63
<211> 11
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: CD70 VL CDR1 (Chothia)

<400> 63

Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser Phe
1 5 10

<210> 64
<211> 7
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: CD70 VL CDR2 (Kabat)

<400> 64

Leu Ala Ser Asn Leu Glu Ser
1 5

<210> 65
<211> 3
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: CD70 VL CDR2 (Chothia)

<400> 65

Leu Ala Ser
1

<210> 66
<211> 9
<212> PRT
<213> Secuencia artificial

<220>

<223> Sintético: CD70 VL CDR3 (Kabat)

<400> 66

Gln His Ser Arg Glu Val Pro Trp Thr

1 5

<210> 67

<211> 6

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: CD70 VL CDR3 (Chothia)

<400> 67

Ser Arg Glu Val Pro Trp

1 5

<210> 68

<211> 5

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: CD70 VH CDR1 (Kabat)

<400> 68

Asn Tyr Gly Met Asn

1 5

<210> 69

<211> 10

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: CD70 VH CDR1 (Chothia)

<400> 69

Gly Tyr Thr Phe Thr Asn Tyr Gly Met Asn

1 5 10

<210> 70
<211> 17
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: CD70 VH CDR2 (Kabat)

<400> 70

Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	Ala	Asp	Ala	Phe	Lys
1				5					10					15	

Gly

<210> 71
<211> 6
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: CD70 VH CDR2 (Chothia)

<400> 71

Asn	Thr	Tyr	Thr	Gly	Glu
1				5	

<210> 72
<211> 9
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: CD70 VH CDR3 (Kabat)

<400> 72

Asp	Tyr	Gly	Asp	Tyr	Gly	Met	Asp	Tyr
1				5				

<210> 73
<211> 14
<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: CD70 VH CDR3 (Chothia)

<400> 73

Cys	Ala	Arg	Asp	Tyr	Gly	Asp	Tyr	Gly	Met	Asp	Tyr	Trp	Gly
1				5					10				

<210> 74

<211> 16

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: BCMA VL CDR1 (Kabat)

<400> 74

Arg	Ala	Ser	Gln	Ser	Leu	Val	His	Ser	Asn	Gly	Asn	Thr	His	Leu	His
1				5					10					15	

<210> 75

<211> 16

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: BCMA VL CDR1 (Chothia)

<400> 75

Arg	Ala	Ser	Gln	Ser	Leu	Val	His	Ser	Asn	Gly	Asn	Thr	His	Leu	His
1				5					10					15	

<210> 76

<211> 5

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: BCMA VL CDR2 (Kabat)

<400> 76

Ser Val Ser Asn Arg

1 5

<210> 77
<211> 5
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA VL CDR2 (Chothia)

<400> 77

Ser Val Ser Asn Arg
1 5

<210> 78
<211> 9
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA VL CDR3 (Kabat)

<400> 78

Ser Gln Thr Ser His Ile Pro Tyr Thr
1 5

<210> 79
<211> 9
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA VL CDR3 (Chothia)

<400> 79

Ser Gln Thr Ser His Ile Pro Tyr Thr
1 5

<210> 80
<211> 5
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA VH CDR1 (Kabat)

<400> 80

Asn Tyr Val Ile His
1 5

<210> 81
<211> 7
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA VH CDR1 (Chothia)

<400> 81

Gly Asn Thr Leu Thr Asn Tyr
1 5

<210> 82
<211> 17
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA VH CDR2 (Kabat)

<400> 82

Tyr Ile Leu Pro Tyr Asn Asp Leu Thr Lys Tyr Ser Gln Lys Phe Gln
1 5 10 15

Gly

<210> 83
<211> 6
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA VH CDR2 (Chothia)

<400> 83

Leu Pro Tyr Asn Asp Leu
1 5

<210> 84
<211> 9
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA VH CDR3 (Kabat)

<400> 84

Trp Asp Trp Asp Gly Phe Phe Asp Pro
1 5

<210> 85
<211> 9
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: BCMA VH CDR3 (Chothia)

<400> 85

Trp Asp Trp Asp Gly Phe Phe Asp Pro
1 5

<210> 86
<211> 20
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: Secuencia objetivo TRAC

<400> 86
agagcaacag tgctgtggcc

20

<210> 87
<211> 4691
<212> ADN
<213> Secuencia artificial

<220>

<223> Sintético: anti-CD33 CAR rAAV

<400> 87

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aggggttcct gcggccgcac gcgtgagatg taaggagctg ctgtgacttg ctcaaggcct	180
tatatcgagt aaacggtagt gctggggcct agacgcaggt gttctgattt atagttcaaa	240
acctctatca atgagagagc aatctcctgg taatgtgata gatttcccaa cttaatgcca	300
acataccata aacctcccat tctgctaata cccagcctaa gttggggaga ccactccaga	360
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gccagcccca cagagccccg cccttggtcca tcaactggcat ctggactcca gcctgggttg	720
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<210> 88
 <211> 22
 <212> PRT
 <213> Secuencia artificial

<220>
 <223> Sintético: péptido señal

<400> 88

Met	Leu	Leu	Leu	Val	Thr	Ser	Leu	Leu	Leu	Cys	Glu	Leu	Pro	His	Pro
1				5					10					15	

Ala	Phe	Leu	Leu	Ile	Pro
				20	

<210> 89
 <211> 21
 <212> PRT
 <213> Secuencia artificial

<220>
 <223> Sintético: péptido señal

<400> 89

Met	Ala	Leu	Pro	Val	Thr	Ala	Leu	Leu	Leu	Pro	Leu	Ala	Leu	Leu	Leu
1				5					10					15	

His	Ala	Ala	Arg	Pro
			20	

<210> 90

<211> 84
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: CD8a dominio transmembrana

<400> 90

Phe Val Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr Pro Ala Pro
1 5 10 15

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
20 25 30

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
35 40 45

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
50 55 60

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Asn
65 70 75 80

His Arg Asn Arg

<210> 91
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E1_T1) espaciador

<400> 91

ucaccaagcc cgcgaccaau

20

<210> 92
<211> 20
<212> ARN
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<220>
<223> Sintético: CD70 sgRNA (E1_T3) espaciador

<400> 92
aucaccaagc ccgcgaccaa 20

<210> 93
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E1_T4) espaciador

<400> 93
cggugcggcg caggcccuau 20

<210> 94
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E1_T7) espaciador

<400> 94
gcuuuggucc cauuggucgc 20

<210> 95
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E1_T8) espaciador

<400> 95
gcccgcagga cgcacccaaua 20

<210> 96
<211> 20
<212> ARN
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<220>
<223> Sintético: CD70 sgRNA (E1_T10) espaciador

<400> 96
gugcauccag cgcuucgcac 20

<210> 97
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E3_T1) espaciador

<400> 97
cagcuacgua uccaucguga 20

<210> 98
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: TRAC espaciador

<400> 98
agagcaacag ugcuguggcc 20

<210> 99
<211> 20
<212> ARN
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<220>
<223> Sintético: b2M sgRNA espaciador

<400> 99
gcuacucucu cuuucuggcc 20

<210> 100
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: PD-1 sgRNA espaciador

<400> 100

cugcagcuuc uccaacacau 20

<210> 101
<211> 20
<212> SRN
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<220>
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<220>
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<222> (1)..(3)
<223> 2'-O-metil fosforotioato

<400> 101
ucaccaagcc cgcgaccaau 20

<210> 102
<211> 20
<212> ARN
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<220>
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<220>
<221> modified_base
<222> (1)..(3)
<223> 2'-O-metil fosforotioato

<400> 102
aucaccaagc ccgcgaccaa 20

<210> 103
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E1_T7) espaciador

<220>
<221> modified_base

<222> (1)..(3)
<223> 2'-O-metil fosforotioato

<400> 103
cggugcggcg caggcccuau 20

<210> 104
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E1_T8) espaciador

<220>
<221> modified_base
<222> (1)..(3)
<223> 2'-O-metil fosforotioato

<400> 104
gcuuuggucc cauuggucgc 20

<210> 105
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E1_T10) espaciador

<220>
<221> modified_base
<222> (1)..(3)
<223> 2'-O-metil fosforotioato

<400> 105
gcccgcagga cgcacccaaua 20

<210> 106
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E3_T10) espaciador

<220>
<221> modified_base
<222> (1)..(3)
<223> 2'-O-metil fosforotioato

<400> 106
gugcauccag cgcuucgcac 20

<210> 107
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E1_T3) espaciador

<220>
<221> modified_base
<222> (1)..(3)
<223> 2'-O-metil fosforotioato

<400> 107
cagcuacgua uccaucguga 20

<210> 108
<211> 20
<212> ARN
<213> Secuencia artificial

<220>
<223> Sintético: TRAC espaciador

<220>
<221> modified_base
<222> (1)..(3)
<223> 2'-O-metil fosforotioato

<400> 108
agagcaacag ugcuguggcc 20

<210> 109
<211> 20
<212> ARN

<213> Secuencia artificial

<220>

<223> Sintético: b2M sgRNA espaciador

<220>

<221> modified_base

<222> (1)..(3)

<223> 2'-O-metil fosforotioato

<400> 109

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20

<210> 110

<211> 20

<212> ARN

<213> Secuencia artificial

<220>

<223> Sintético: PD-1 sgRNA espaciador

<220>

<221> modified_base

<222> (1)..(3)

<223> 2'-O-metil fosforotioato

<400> 110

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20

<210> 111

<211> 23

<212> ADN

<213> Secuencia artificial

<220>

<223> Sintético: CD70 sgRNA (E1_T1) con PAM

<400> 111

tcaccaagcc cgcgaccaat ggg

23

<210> 112

<211> 23

<212> ADN

<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E1_T3) con PAM

<400> 112
atcaccaagc ccgcgaccaa tgg 23

<210> 113
<211> 23
<212> ADN
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<220>
<223> Sintético: CD70 sgRNA (E1_T4) con PAM

<400> 113
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<210> 114
<211> 23
<212> ADN
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<220>
<223> Sintético: CD70 sgRNA (E1_T7) con PAM

<400> 114
gctttggtcc cattggtcgc ggg 23

<210> 115
<211> 23
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E1_T8) con PAM

<400> 115
gcccgcagga cgcacccata ggg 23

<210> 116
<211> 23
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E1_T10) con PAM

<400> 116
gtgcatccag cgcttcgcac agg 23

<210> 117
<211> 23
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: CD70 sgRNA (E3_T1) con PAM

<400> 117
cagctacgta tccatcgtga tgg 23

<210> 118
<211> 23
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: TRAC sgRNA con PAM

<400> 118
agagcaacag tgctgtggcc tgg 23

<210> 119
<211> 23
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: b2M sgRNA con PAM

<400> 119
gctactctct ctttctggcc tgg 23

<210> 120
<211> 23
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: PD-1 sgRNA wcon PAM

<400> 120

ctgcagcttc tccaacacat cgg 23

<210> 121
<211> 120
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: CD28 secuencia de nucleótidos

<400> 121
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ccgacaagaa aacattacca accctatgcc ccccccacgag acttcgctgc gtacagggtcc 120

<210> 122
<211> 800
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: TRAC-LHA

<400> 122
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gggcttagac gcagggtgtt tgatttatag ttcaaaacct ctatcaatga gagagcaatc 120
tcctggtaat gtgatagatt tcccaactta atgccaacat accataaacc tcccattctg 180
ctaatgcccc gcctaagttg gggagaccac tccagattcc aagatgtaca gtttgctttg 240
ctgggccttt ttcccatgcc tgcctttact ctgccagagt tatattgctg gggttttgaa 300
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ccttgagtgg caggccaggc ctggccgtga acgttactg aaatcatggc ctcttgacca 420
agattgatag cttgtgcctg tccctgagtc ccagtccatc acgagcagct ggtttctaag 480
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tgtccatcac tggcatctgg actccagcct gggttggggc aaagaggga atgagatcat 600
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gctgagagac tctaaatcca gtgacaagtc tgtctgccta ttcaccgatt ttgattctca 720

aacaaatgtg tcacaaagta aggattctga tgtgtatatc acagacaaaa ctgtgctaga	780
catgagggtct atggacttca	800

<210> 123
 <211> 1178
 <212> ADN
 <213> Secuencia artificial

<220>
 <223> Sintético: promotor EF1-alfa

<400> 123	
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ggaggggtcg gcaattgaac cggcgcctag agaaggtggc gcggggtaaa ctgggaaagt	120
gatgtcgtgt actggctccg cctttttccc gaggggtgggg gagaaccgta tataagtgca	180
gtagtcgccg tgaacgttct ttttcgcaac gggtttgccg ccagaacaca ggtaagtgcc	240
gtgtgtgggt cccgcgggcc tggcctcttt acgggttatg gcccttgctg gccttgaatt	300
acttccactg gctgcagtac gtgattcttg atcccagact tcgggttgga agtgggtggg	360
agagttcgag gccttgctgct taaggagccc cttcgctcgc tgcttgagtt gaggcctggc	420
ctgggcgctg gggccgccgc gtgcgaatct ggtggcacct tcgcgcctgt ctcgctgctt	480
tcgataagtc tctagccatt taaaattttt gatgacctgc tgcgacgctt tttttctggc	540
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tctccttgga atttgccctt tttgagtttg gatcttggtt cattctcaag cctcagacag	1140
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<210> 124
 <211> 49
 <212> ADN
 <213> Secuencia artificial

<220>
 <223> Sintético: Señal poli(A) sintética

<400> 124	
aataaaatcg ctatccatcg aagatggatg tgtgttggtt ttttgtgtg	49

<210> 125
 <211> 804
 <212> ADN
 <213> Secuencia artificial

<220>
 <223> Sintético: TRACRHA

<400> 125	
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gacaccttct tccccagccc aggttaagggc agcttttggtg ccttcgcagg ctgtttcctt	120
gcttcaggaa tggccagggt ctgcccagag ctctgggtcaa tgatgtctaa aactcctctg	180
attggtgggtc tcggccttat ccattgccac caaaaccctc tttttactaa gaaacagtga	240
gccttggttct ggcagtccag agaatgacac gggaaaaaag cagatgaaga gaagggtggca	300
ggagaggggca cgtggcccag cctcagtctc tccaactgag ttcctgcctg cctgcctttg	360
ctcagactgt ttgcccccta ctgctcttct aggcctcatt ctaagcccct tctccaagtt	420
gcctctcctt atttctccct gtctgcaaaa aaatctttcc cagctcacta agtcagtctc	480
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ttgaagtgga ggaattaaaa agtcagatga ggggtgtgcc cagaggaagc accattctag	600
ttggggggagc ccatctgtca gctgggaaaa gtccaaataa cttcagattg gaatgtgttt	660
taactcaggg ttgagaaaac agctaccttc aggacaaaag tcagggaagg gctctctgaa	720

gaaatgctac ttgaagatac cagccctacc aagggcaggg agaggaccct atagaggcct 780
 gggacaggag ctcaatgaga aagg 804

<210> 126
 <211> 23
 <212> PRT
 <213> Secuencia artificial

<220>
 <223> Sintético: CD8a transmembrana

<400> 126

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
 1 5 10 15

Ser Leu Val Ile Thr Leu Tyr
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<210> 127
 <211> 65
 <212> ADN
 <213> Secuencia artificial

<220>
 <223> Sintético: cebador directo CD70

<400> 127
 tcgtcggcag cgtcagatgt gtataagaga cagcccaact tttccatctc aactcacccc 60
 aagtg 65

<210> 128
 <211> 53
 <212> ADN
 <213> Secuencia artificial

<220>
 <223> Sintético: cebador inverso CD70

<400> 128
 gtctcgtggg ctcggagatg tgtataagag acagcccctc ctgcgctagc gga 53

<210> 129

<211> 58
 <212> ADN
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 <220>
 <223> Sintético: CD70 Indel

 <400> 129
 cacaccacga ggcagatcac caagcccgcg caatgggacc aaagcagccc gcaggacg 58

<210> 130
 <211> 61
 <212> ADN
 <213> Secuencia artificial

 <220>
 <223> Sintético: CD70 Indel

 <400> 130
 cacaccacga ggcagatcac caagcccgcg aaccaatggg accaaagcag cccgcaggac 60

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<210> 131
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 <212> ADN
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 <400> 131
 cacaccacga ggcagatcac caatgggacc aaagcagccc gcaggacg 48

<210> 132
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 <212> ADN
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 <400> 132
 cacaccacga ggcagatcac caagcccgcg ccaatgggac caaagcagcc cgcaggacg 59

<210> 133

<211> 59
 <212> ADN
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 <220>
 <223> Sintético: CD70 Indel

 <400> 133
 cacaccacga ggcagatcac caagcccgca ccaatgggac caaagcagcc cgcaggacg 59

 <210> 134
 <211> 35
 <212> ADN
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 <220>
 <223> Sintético: CD70 Indel

 <400> 134
 cacaccacga ggcagatcac caagcccgca ggacg 35

 <210> 135
 <211> 4367
 <212> ADN
 <213> Secuencia artificial

 <220>
 <223> Sintético: Anti-CD33 CAR Donador LHA a RHA 41BB costim.

 <400> 135
 gagatgtaag gagctgctgt gacttgctca aggccttata tcgagtaaac ggtagtgctg 60
 gggcttagac gcagggtgttc tgatttatag ttcaaaacct ctatcaatga gagagcaatc 120
 tcctggtaat gtgatatagatt tcccaactta atgccaacat accataaacc tcccattctg 180
 ctaatgcccc gcctaagttg gggagaccac tccagattcc aagatgtaca gtttgctttg 240
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 gaagatccta ttaaataaaa gaataagcag tattattaag tagccctgca tttcagggtt 360
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tgtccatcac tggcatctgg actccagcct gggttggggc aaagagggaa atgagatcat	600
gtcctaaccc tgatcctctt gtccacaga tatccagaac cctgaccctg ccgtgtacca	660
gctgagagac tctaaatcca gtgacaagtc tgtctgccta ttcaccgatt ttgattctca	720
aacaaatgtg tcacaaagta aggattctga tgtgtatatc acagacaaaa ctgtgctaga	780
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<211> 1585

<212> ADN

<213> Secuencia artificial

<220>

<223> Sintético: Anti-CD33 CAR 41BB costim

<400> 136

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gagtcactat gagctgcaaa tccagtcaga gtgttttttt ctcaagtagc cagaagaact	180
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gtacccgcga atccggcgta ccggatcgat tcacgggatc tgggtcaggt actgatttca	300
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gaaagaaact cctgtatata ttcaaacaac catttatgag accagtacaa actactcaag	1140
aggaagatgg ctgtagctgc cgatttccag aagaagaaga aggaggatgt gaactgcgag	1200
tgaagttttc ccgaagcgca gacgctccgg catatcagca aggacagaat cagctgtata	1260
acgaactgaa tttgggacgc cgcgaggagt atgacgtgct tgataaacgc cgggggagag	1320
acccggaaaat ggggggtaaa ccccgaagaa agaatcccca agaaggactc tacaatgaac	1380
tccagaagga taagatggcg gaggcctact cagaaatagg tatgaagggc gaacgacgac	1440
ggggaaaagg tcacgatggc ctctaccaag ggttgagtac ggcaacaaaa gatacgtacg	1500
atgcactgca tatgcaggcc ctgcctccca gataataata aaatcgctat ccatcgaaga	1560
tggatgtgtg ttggtttttt gtgtg	1585

<210> 137

<211> 246

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: Anti-CD33 scFv enlazador

<400> 137

Glu Ile Val Leu Thr Gln Ser Pro Gly Ser Leu Ala Val Ser Pro Gly
1 5 10 15

Glu Arg Val Thr Met Ser Cys Lys Ser Ser Gln Ser Val Phe Phe Ser
20 25 30

Ser Ser Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Ile Pro Gly Gln
35 40 45

Ser Pro Arg Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Pro Glu Asp Leu Ala Ile Tyr Tyr Cys His Gln
85 90 95

Tyr Leu Ser Ser Arg Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Val Val Lys Pro Gly Ala
130 135 140

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
145 150 155 160

Tyr Ile His Trp Ile Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Val
165 170 175

Gly Val Ile Tyr Pro Gly Asn Asp Asp Ile Ser Tyr Asn Gln Lys Phe
180 185 190

Gln Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Thr Thr Ala Tyr
195 200 205

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
210 215 220

Ala Arg Glu Val Arg Leu Arg Tyr Phe Asp Val Trp Gly Gln Gly Thr
225 230 235 240

Thr Val Thr Val Ser Ser
245

<210> 138
<211> 738
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: Anti-CD33 scFv

<400> 138
gaaatcgtcc tcacacaatc cccgggggagc ctcgcagtca gtcctgggga acgagtcact 60
atgagctgca aatccagtca gagtgttttt ttctcaagta gccagaagaa ctacctcgca 120
tggtaccaac aaataccggg gcaatctccc cgcttgctta tatactgggc aagtaccgcg 180
gaatccggcg taccggatcg attcacggga tctgggtcag gtactgattt cactttgact 240
atcagctctg ttcagcctga agatttggca atttactact gtcaccaata cttgagtagc 300
cgaactttcg gccagggcac gaagctcgaa atcaaggcg gagggggagg ttctggtggg 360
ggcggttctg gcggtggagg aagccaagta cagttgcaac agccaggggc ggaggtcgta 420
aaacctgggg cgtctgtcaa gatgagctgt aaagcaagtg gatacacctt cacctcctac 480
tatatacatt ggattaagca aactccgggt caggggctgg aatgggttgg cgttatatac 540
cccgggaacg atgatatac atacaaccaa aaatttcaag gcaaggcgac tctgactgcc 600
gataagagta gcacaacagc ttacatgcag ctttcttccc tgaccagcga agattcagca 660
gtttactact gcgctcggga agtgcgctg cgatactttg atgtctgggg tcaaggaact 720

acagttactg tatcaagc

738

<210> 139

<211> 509

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: Anti-CD33 CAR 41BB costim.

<400> 139

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Leu Thr Gln Ser Pro Gly Ser Leu
20 25 30

Ala Val Ser Pro Gly Glu Arg Val Thr Met Ser Cys Lys Ser Ser Gln
35 40 45

Ser Val Phe Phe Ser Ser Ser Gln Lys Asn Tyr Leu Ala Trp Tyr Gln
50 55 60

Gln Ile Pro Gly Gln Ser Pro Arg Leu Leu Ile Tyr Trp Ala Ser Thr
65 70 75 80

Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr
85 90 95

Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Pro Glu Asp Leu Ala Ile
100 105 110

Tyr Tyr Cys His Gln Tyr Leu Ser Ser Arg Thr Phe Gly Gln Gly Thr
115 120 125

Lys Leu Glu Ile Lys Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
130 135 140

Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Val

145		150		155		160									
Val	Lys	Pro	Gly	Ala	Ser	Val	Lys	Met	Ser	Cys	Lys	Ala	Ser	Gly	Tyr
				165					170					175	
Thr	Phe	Thr	Ser	Tyr	Tyr	Ile	His	Trp	Ile	Lys	Gln	Thr	Pro	Gly	Gln
			180					185					190		
Gly	Leu	Glu	Trp	Val	Gly	Val	Ile	Tyr	Pro	Gly	Asn	Asp	Asp	Ile	Ser
		195					200					205			
Tyr	Asn	Gln	Lys	Phe	Gln	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Lys	Ser
	210					215					220				
Ser	Thr	Thr	Ala	Tyr	Met	Gln	Leu	Ser	Ser	Leu	Thr	Ser	Glu	Asp	Ser
225					230					235					240
Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Glu	Val	Arg	Leu	Arg	Tyr	Phe	Asp	Val
				245					250					255	
Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ser	Ala	Ala	Ala	Phe
			260					265					270		
Val	Pro	Val	Phe	Leu	Pro	Ala	Lys	Pro	Thr	Thr	Thr	Pro	Ala	Pro	Arg
		275					280					285			
Pro	Pro	Thr	Pro	Ala	Pro	Thr	Ile	Ala	Ser	Gln	Pro	Leu	Ser	Leu	Arg
	290					295					300				
Pro	Glu	Ala	Cys	Arg	Pro	Ala	Ala	Gly	Gly	Ala	Val	His	Thr	Arg	Gly
305					310					315					320
Leu	Asp	Phe	Ala	Cys	Asp	Ile	Tyr	Ile	Trp	Ala	Pro	Leu	Ala	Gly	Thr
				325					330					335	
Cys	Gly	Val	Leu	Leu	Leu	Ser	Leu	Val	Ile	Thr	Leu	Tyr	Cys	Asn	His
			340					345					350		

Arg Asn Arg Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
355 360 365

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
370 375 380

Cys Arg Phe Pro Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
385 390 395 400

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
405 410 415

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
420 425 430

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
435 440 445

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
450 455 460

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
465 470 475 480

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
485 490 495

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
500 505

<210> 140

<211> 118

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: VH CDRs de anticuerpo anti-CD33

<400> 140

Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Val Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Tyr Ile His Trp Ile Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Val
35 40 45

Gly Val Ile Tyr Pro Gly Asn Asp Asp Ile Ser Tyr Asn Gln Lys Phe
50 55 60

Gln Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Thr Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Val Arg Leu Arg Tyr Phe Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> 141

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: VL CDR del anticuerpo antiCD33

<400> 141

Glu Ile Val Leu Thr Gln Ser Pro Gly Ser Leu Ala Val Ser Pro Gly
1 5 10 15

Glu Arg Val Thr Met Ser Cys Lys Ser Ser Gln Ser Val Phe Phe Ser
20 25 30

Ser Ser Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Ile Pro Gly Gln
35 40 45

Ser Pro Arg Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Pro Glu Asp Leu Ala Ile Tyr Tyr Cys His Gln
85 90 95

Tyr Leu Ser Ser Arg Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 142
<211> 5
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: VH CDR1 (Kabat) de anticuerpo anti-CD33

<400> 142

Ser Tyr Tyr Ile His
1 5

<210> 143
<211> 17
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: VH CDR2 (Kabat) de anticuerpo anti-CD33

<400> 143

Val Ile Tyr Pro Gly Asn Asp Asp Ile Ser Tyr Asn Gln Lys Phe Gln
1 5 10 15

Gly

<210> 144
<211> 9
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: VH CDR3 (Kabat) de anticuerpo anti-CD33

<400> 144

Glu Val Arg Leu Arg Tyr Phe Asp Val
1 5

<210> 145
<211> 17
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: VL CDR1 (Kabat & Chothia) de anticuerpo anti-CD33

<400> 145

Lys Ser Ser Gln Ser Val Phe Phe Ser Ser Ser Gln Lys Asn Tyr Leu
1 5 10 15

Ala

<210> 146
<211> 7
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: VL CDR2 (Kabat & Chothia) del anticuerpo anti-CD33

<400> 146

Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 147

<211> 8
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: VL CDR3 (Kabat & Chothia) del anticuerpo anti-CD33

<400> 147

His Gln Tyr Leu Ser Ser Arg Thr
1 5

<210> 148
<211> 1518
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: Anti-CD19 CAR CD8[tm]-CD28[dominio
co-estimuladorio]-CD3z)

<400> 148

atgcttcttt tggttacgtc tctgttgctt tgcgaacttc ctcacccagc gttcttgctg	60
atccccgata ttcagatgac tcagaccacc agtagcttgt ctgcctcact gggagaccga	120
gtaacaatct cctgcagggc aagtcaagac attagcaaat acctcaattg gtaccagcag	180
aagcccgcgc gaacggtaaa actcctcatc tatcatacgt caagggtgca ttccggagta	240
ccgtcacgat tttcagggtc tgggagcgga actgactatt ctttgactat ttcaaacctc	300
gagcaggagg acattgcgac atatttttgt caacaaggta ataccctccc ttacactttc	360
ggaggaggaa ccaaactcga aattaccggg tccaccagtg gctctgggaa gcctggcagt	420
ggagaagggt ccactaaagg cgagggtgaag ctccaggaga gcggccccgg tctcgttgcc	480
cccagtcaaa gcctctctgt aacgtgcaca gtgagtgggt tatcattgcc tgattatggc	540
gtctcctgga taaggcagcc cccgcgaaag ggtcttgaat ggcttgggggt aatatggggc	600
tcagagacaa cgtattataa ctccgctctc aaaagtcgct tgacgataat aaaagataac	660
tccaagagtc aagttttcct taaaatgaac agtttgaga ctgacgatac cgctatatat	720
tattgtgcta aacattatta ctacggcggg agttacgca tggattattg ggggcagggg	780
acttctgtca cagtcagtag tgctgctgcc tttgtcccgg tatttctccc agccaaaccg	840

accacgactc ccgccccgcg ccctccgaca cccgctccca ccatcgcttc tcaacctctt 900
 agtcttcgcc ccgaggcatg ccgacccgcc gccgggggtg ctgttcatac gaggggcttg 960
 gacttcgctt gtgatattta catttgggct ccgttggcgg gtacgtgcgg cgtccttttg 1020
 ttgtcactcg ttattacttt gtattgtaat cacaggaatc gctcaaagcg gagtaggttg 1080
 ttgcattccg attacatgaa tatgactcct cgccggcctg ggccgacaag aaaacattac 1140
 caaccctatg cccccccacg agacttcgct gcgtacaggt cccgagtga gttttcccg 1200
 agcgcagacg ctccggcata tcagcaagga cagaatcagc tgtataacga actgaatttg 1260
 ggacgccgcg aggagtatga cgtgcttgat aaacgccggg ggagagaccc ggaaatgggg 1320
 ggtaaaccac gaagaaagaa tccccaaagaa ggactctaca atgaactcca gaaggataag 1380
 atggcggagg cctactcaga aataggtatg aagggcgaac gacgacgggg aaaaggtcac 1440
 gatggcctct accaagggtt gagtacggca accaaagata cgtacgatgc actgcatatg 1500
 caggccctgc ctcccaga 1518

<210> 149
 <211> 506
 <212> PRT
 <213> Secuencia artificial

<220>
 <223> Sintético: amino-ácidos Anti-CD19 CAR CD8[tm]-CD28[dominio
 co-estimuladorio]-CD3z)

<400> 149

Met Leu Leu Leu Val Thr Ser Leu Leu Leu Cys Glu Leu Pro His Pro
 1 5 10 15

Ala Phe Leu Leu Ile Pro Asp Ile Gln Met Thr Gln Thr Thr Ser Ser
 20 25 30

Leu Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser
 35 40 45

Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly

50

55

60

Thr Val Lys Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Val
65 70 75 80

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
85 90 95

Ile Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln
100 105 110

Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
115 120 125

Thr Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser
130 135 140

Thr Lys Gly Glu Val Lys Leu Gln Glu Ser Gly Pro Gly Leu Val Ala
145 150 155 160

Pro Ser Gln Ser Leu Ser Val Thr Cys Thr Val Ser Gly Val Ser Leu
165 170 175

Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu
180 185 190

Glu Trp Leu Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser
195 200 205

Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln
210 215 220

Val Phe Leu Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr
225 230 235 240

Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr
245 250 255

Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ala Ala Phe Val
260 265 270

Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg Pro
275 280 285

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
290 295 300

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
305 310 315 320

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
325 330 335

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Asn His Arg
340 345 350

Asn Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met
355 360 365

Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala
370 375 380

Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser Arg Val Lys Phe Ser Arg
385 390 395 400

Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn
405 410 415

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
420 425 430

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
435 440 445

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala

450

455

460

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
 465 470 475 480

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
 485 490 495

Ala Leu His Met Gln Ala Leu Pro Pro Arg
 500 505

<210> 150

<211> 735

<212> ADN

<213> Secuencia artificial

<220>

<223> Sintético: Anti-CD19 scFv

<400> 150

gatattcaga tgactcagac caccagtagc ttgtctgcct cactgggaga ccgagtaaca 60
 atctcctgca gggcaagtca agacattagc aaatacctca attggtacca gcagaagccc 120
 gacggaacgg taaaactcct catctatcat acgtcaaggt tgcattccgg agtaccgtca 180
 cgattttcag gttctgggag cggaactgac tattccttga ctatttcaaa cctcgagcag 240
 gaggacattg cgacatattt ttgtcaacaa ggtaataccc tcccttacac tttcggagga 300
 ggaaccaaac tcgaaattac cgggtccacc agtggctctg ggaagcctgg cagtggagaa 360
 ggttcacta aaggcgaggt gaagctccag gagagcggcc ccggtctcgt tgccccagt 420
 caaagcctct ctgtaacgtg cacagtgagt ggtgtatcat tgcctgatta tggcgtctcc 480
 tggataaggc agccccgcg aaagggtctt gaatggcttg gggtaatatg gggctcagag 540
 acaacgtatt ataactccgc tctcaaaagt cgcttgacga taataaaaga taactccaag 600
 agtcaagttt tccttaaaat gaacagtttg cagactgacg ataccgtat atattattgt 660
 gctaaacatt attactacgg cggtagttac gcgatggatt attgggggca ggggacttct 720
 gtcacagtca gtagt 735

<210> 151

<211> 245

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: secuencia de aminoácidos del enlazador CD19 scFv

<400> 151

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Ser Thr Ser Gly
100 105 110

Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr Lys Gly Glu Val Lys
115 120 125

Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser
130 135 140

Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser
145 150 155 160

Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile
165 170 175

Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu
180 185 190

Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn
195 200 205

Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr
210 215 220

Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
225 230 235 240

Val Thr Val Ser Ser
245

<210> 152
<211> 120
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: Anti-CD19 VH

<400> 152

Glu Val Lys Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

Ser Leu Ser Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Leu Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 153

<211> 107

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: Anti-CD19 VL

<400> 153

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr
100 105

<210> 154
<211> 18
<212> PRT
<213> Secuencia artificial

<220>
<223> Sintético: enlazador scFv Anti-CD19

<400> 154

Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr
1 5 10 15

Lys Gly

<210> 155
<211> 4682
<212> ADN
<213> Secuencia artificial

<220>
<223> Sintético: anti-CD19 CAR rAAV

<400> 155
cctgcaggca gctgcgcgct cgctcgctca ctgaggccgc ccgggcgctc ggcgaccttt 60
ggctgccccg cctcagtgag cgagcgagcg cgcagagagg gaggggccaa ctccatcact 120
agggggttcct gcggccgcac gcgtgagatg taaggagctg ctgtgacttg ctcaaggcct 180
tatatcgagt aaacggtagt gctggggcctt agacgcaggt gttctgattt atagttcaaa 240
acctctatca atgagagagc aatctcctgg taatgtgata gatttcccaa cttaatgcca 300
acataccata aacctcccat tctgctaata cccagcctaa gttggggaga ccaactccaga 360
ttccaagatg tacagtttgc tttgctgggc ctttttccca tgcctgcctt tactctgcca 420
gagttatatt gctgggggttt tgaagaagat cctattaaat aaaagaataa gcagtattat 480
taagtagccc tgcatttcag gtttccttga gtggcaggcc aggccctggcc gtgaacgttc 540

actgaaatca tggcctcttg gccaaagattg atagcttgtg cctgtccctg agtcccagtc	600
catcacgagc agctgggtttc taagatgcta tttcccgtat aaagcatgag accgtgactt	660
gccagcccca cagagccccg cccttgtcca tctactggcat ctggactcca gcctgggttg	720
gggcaaagag ggaaatgaga tcatgtccta accctgatcc tcttgtccca cagatatcca	780
gaaccctgac cctgccgtgt accagctgag agactctaaa tccagtgaca agtctgtctg	840
cctattcacc gatttttgatt ctcaaacaaa tgtgtcacia agtaaggatt ctgatgtgta	900
tatcacagac aaaactgtgc tagacatgag gtctatggac ttcaggctcc ggtgcccgtc	960
agtgggcaga gcgcacatcg cccacagtcc ccgagaagtt ggggggaggg gtcggcaatt	1020
gaaccggtgc ctagagaagg tggcgcgggg taaactggga aagtgatgtc gtgtactggc	1080
tccgcctttt tcccaggggt ggggggagaa cgtatataag tgcagtagtc gccgtgaacg	1140
ttctttttcg caacgggttt gccgccagaa cacaggtaag tgccgtgtgt ggttcccgcg	1200
ggcctggcct ctttacgggt tatggccctt gcgtgccttg aattacttcc actggctgca	1260
gtacgtgatt cttgatcccg agcttcgggt tggaaagtggg tgggagagtt cgaggccttg	1320
cgcttaagga gccccttcgc ctcgtgcttg agttgaggcc tggcctgggc gctggggccg	1380
ccgcgtgcga atctggtggc accttcgcgc ctgtctcgct gctttcgata agtctctagc	1440
catttaaaat tttttagtgac ctgctgcgac gctttttttc tggcaagata gtcttgtaaa	1500
tgcgggccaa gatctgcaca ctggtatttc ggtttttggg gccgcgggcg gcgacggggc	1560
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<211> 20

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<223> Sintético: CD70 sgRNA (E1_T4)

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<223> Sintético: CD70 sgRNA (E1_T7)

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<210> 161

<211> 20

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<220>
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<400> 161
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<210> 162
 <211> 20
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<220>
 <223> Sintético: CD70 sgRNA (E1_T10)

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<210> 163
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<400> 163
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<210> 164
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<400> 164
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<210> 165
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<220>
 <223> Sintético: PD-1 sgRNA

<400> 165
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<210> 166
<211> 11
<212> PRT
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<220>
<223> Sintético: anti-CD19 VL CDR1 (Kabat)

<400> 166

Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn
1 5 10

<210> 167
<211> 7
<212> PRT
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<220>
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<400> 167

His Thr Ser Arg Leu His Ser
1 5

<210> 168
<211> 9
<212> PRT
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<220>
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<400> 168

Gln Gln Gly Asn Thr Leu Pro Tyr Thr
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<210> 169
<211> 5
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<223> Sintético: anti-CD19 VH CDR1 (Kabat)

<400> 169

Asp Tyr Gly Val Ser
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<210> 170

<211> 16

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: anti-CD19 VH CDR2 (Kabat)

<400> 170

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<210> 171

<211> 12

<212> PRT

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<220>

<223> Sintético: anti-CD19 VH CDR3 (Kabat)

<400> 171

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr
1 5 10

<210> 172

<211> 11

<212> PRT

<213> Secuencia artificial

<220>

<223> Sintético: anti-CD19 VL CDR1 (Chothia)

<400> 172

Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn

1 5 10

<210> 173
<211> 7
<212> PRT
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<400> 173

His Thr Ser Arg Leu His Ser
1 5

<210> 174
<211> 9
<212> PRT
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<400> 174

Gln Gln Gly Asn Thr Leu Pro Tyr Thr
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<210> 175
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<212> PRT
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<400> 175

Gly Val Ser Leu Pro Asp Tyr
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<210> 176
<211> 5
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<400> 176

Trp Gly Ser Glu Thr
1 5

<210> 177
<211> 12
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<400> 177

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr
1 5 10

<210> 178
<211> 7
<212> PRT
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<400> 178

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 179
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<212> PRT
<213> Secuencia artificial

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<400> 179

Tyr Pro Gly Asn Asp Asp
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<210> 180

<211> 9

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<223> Sintético: anti-CD33 VH CDR3 (Chothia)

<400> 180

Glu Val Arg Leu Arg Tyr Phe Asp Val

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5