

SEQUENCE LISTING

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<120> CD22-TARGETED CHIMERIC ANTIGEN RECEPTOR, PREPARATION METHOD
THEREFOR AND APPLICATION THEREOF

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<151> 2020-04-16

<160> 16

<170> PatentIn version 3.5

<210> 1

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> Heavy chain variable domain

<400> 1

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Asn Phe Thr Ser Tyr
20 25 30

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

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

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

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

Ala Thr Pro Thr Tyr Tyr Phe Gly Ser Val Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 2
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Light chain variable domain

<400> 2

Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys
1 5 10 15

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

Leu His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile
35 40 45

Lys Tyr Ala Ser Gln Ser Phe Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

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

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

<210> 3
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy chain variable domain

<400> 3

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

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

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

Gly Arg Ile Ile Pro Ile Leu Gly Met Ala Ile Tyr Ala Pro Lys Phe
50 55 60

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

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

Ala Arg Ala Pro Thr Tyr Trp Gly Ser Lys Asp Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 4

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Light chain variable domain

<400> 4

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

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

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

Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Phe Pro Tyr
85 90 95

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

<210> 5
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy chain variable domain

<400> 5

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Ser Ile Tyr
20 25 30

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

Ser Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val
50 55 60

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

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

Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr

100

105

110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 6

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Light chain variable domain

<400> 6

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

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

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

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

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

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

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

<210> 7

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Heavy chain variable domain

<400> 7

Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln Thr Leu Ser
1 5 10 15

Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn Ser Ala Ala
20 25 30

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

Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala Val Ser Val
50 55 60

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

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

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

Gln Gly Thr Met Val Thr Val Ser
115 120

<210> 8

<211> 105

<212> PRT

<213> Artificial Sequence

<220>

<223> Light chain variable domain

<400> 8

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

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Thr Ile Trp Ser Tyr Leu
20 25 30

Asn Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Asn Leu Leu Ile Tyr

35

40

45

Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Arg
 50 55 60

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

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Ile Pro Gln Thr
 85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile
 100 105

<210> 9
 <211> 21
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Signal peptide

<400> 9

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> 10
 <211> 55
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hinge region

<400> 10

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
50 55

<210> 11
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<223> Transmembrane region

<400> 11

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 Cys
20

<210> 12
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> Co-stimulatory signaling molecule

<400> 12

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

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> 13
<211> 113
<212> PRT

<213> Artificial Sequence

<220>

<223> CD3? signaling sequence

<400> 13

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
1 5 10 15

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
20 25 30

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

Pro Gln Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
50 55 60

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
65 70 75 80

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

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
100 105 110

Arg

<210> 14

<211> 497

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric antigen receptor

<400> 14

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 Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Glu Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr
35 40 45

Asn Phe Thr Ser Tyr Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys
50 55 60

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

Tyr Ser Pro Ser Phe Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser
85 90 95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
100 105 110

Ala Met Tyr Tyr Cys Ala Thr Pro Thr Tyr Tyr Phe Gly Ser Val Ala
115 120 125

Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly
130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val
145 150 155 160

Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys Val
165 170 175

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser Leu His Trp
180 185 190

Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys Tyr Ala
195 200 205

Ser Gln Ser Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
210 215 220

Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala

225		230		235		240									
Ala	Ala	Tyr	Tyr	Cys	His	Gln	Ser	Ser	Ser	Leu	Pro	Tyr	Thr	Phe	Gly
				245					250					255	
Gln	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Phe	Val	Pro	Val	Phe	Leu	Pro	Ala
			260					265					270		
Lys	Pro	Thr	Thr	Thr	Pro	Ala	Pro	Arg	Pro	Pro	Thr	Pro	Ala	Pro	Thr
		275					280					285			
Ile	Ala	Ser	Gln	Pro	Leu	Ser	Leu	Arg	Pro	Glu	Ala	Cys	Arg	Pro	Ala
	290					295					300				
Ala	Gly	Gly	Ala	Val	His	Thr	Arg	Gly	Leu	Asp	Phe	Ala	Cys	Asp	Ile
305					310					315					320
Tyr	Ile	Trp	Ala	Pro	Leu	Ala	Gly	Thr	Cys	Gly	Val	Leu	Leu	Leu	Ser
			325						330					335	
Leu	Val	Ile	Thr	Leu	Tyr	Cys	Lys	Arg	Gly	Arg	Lys	Lys	Leu	Leu	Tyr
			340					345					350		
Ile	Phe	Lys	Gln	Pro	Phe	Met	Arg	Pro	Val	Gln	Thr	Thr	Gln	Glu	Glu
		355					360					365			
Asp	Gly	Cys	Ser	Cys	Arg	Phe	Pro	Glu	Glu	Glu	Glu	Gly	Gly	Cys	Glu
	370					375					380				
Leu	Arg	Val	Lys	Phe	Ser	Arg	Ser	Ala	Asp	Ala	Pro	Ala	Tyr	Gln	Gln
385					390					395					400
Gly	Gln	Asn	Gln	Leu	Tyr	Asn	Glu	Leu	Asn	Leu	Gly	Arg	Arg	Glu	Glu
				405					410					415	
Tyr	Asp	Val	Leu	Asp	Lys	Arg	Arg	Gly	Arg	Asp	Pro	Glu	Met	Gly	Gly
		420						425					430		
Lys	Pro	Arg	Arg	Lys	Asn	Pro	Gln	Glu	Gly	Leu	Tyr	Asn	Glu	Leu	Gln
		435					440					445			

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
450 455 460

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
465 470 475 480

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
485 490 495

Arg

<210> 15
<211> 498
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric antigen receptor

<400> 15

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 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Pro Ser Gly Asp
35 40 45

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

Gly Leu Glu Trp Met Gly Arg Ile Ile Pro Ile Leu Gly Met Ala Ile
65 70 75 80

Tyr Ala Pro Lys Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
85 90 95

Thr Asn Thr Ala Phe Met Asp Leu Thr Ser Leu Tyr Phe Glu Asp Thr

100	105	110															
Ala Val Tyr Tyr Cys Ala Arg Ala Pro Thr Tyr Trp Gly Ser Lys Asp																	
115	120	125															
Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly																	
130	135	140															
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ile																	
145	150	155															
Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg																	
	165	170															
Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Gly Leu Ala																	
	180	185															
Trp Tyr Gln Gln Lys Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Asp																	
	195	200															
Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly																	
	210	215															
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp																	
225	230	235															
Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Phe Pro Tyr Thr Phe																	
	245	250															
Gly Gln Gly Thr Lys Leu Glu Ile Lys Phe Val Pro Val Phe Leu Pro																	
	260	265															
Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro																	
	275	280															
Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro																	
	290	295															
Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp																	
305	310	315															

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

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

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
355 360 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
370 375 380

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

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
405 410 415

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
420 425 430

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
435 440 445

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
450 455 460

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
465 470 475 480

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
485 490 495

Pro Arg

<210> 16
<211> 15
<212> PRT

<213> Artificial Sequence

<220>

<223> Linker peptide

<400> 16

Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser
1				5					10					15