

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 20

<211> 218

<212> PRT

<213> 人工序列

<220>

<223> K09A-L-17 LC 全长

<400> 20

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

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

[0015]

Gly Tyr Ser Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
35 40 45

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

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

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

Asp Leu Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln

115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

[0016]

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 21
<211> 447
<212> PRT
<213> 人工序列

<220>
<223> 重链

<400> 21

Gln Val Gln Leu Val Gln Ser Gly Val 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

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

Gly Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn Glu Lys Phe
50 55 60

Lys Asn Arg Val Thr Leu Thr Thr Asp Ser Ser Thr Thr Thr Ala Tyr
65 70 75 80

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

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

[0017] Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
130 135 140

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

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys

	195	200	205
	Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro		
	210	215	220
	Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val		
	225	230	235 240
	Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr		
	245	250	255
	Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu		
	260	265	270
[0018]	Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys		
	275	280	285
	Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser		
	290	295	300
	Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys		
	305	310	315 320
	Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile		
	325	330	335
	Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro		
	340	345	350
	Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu		
	355	360	365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
435 440 445

[0019] <210> 22
<211> 218
<212> PRT
<213> 人工序列

<220>
<223> 肽链

<400> 22

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

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

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

Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala

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 Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Ser Arg		
85	90	95
Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg		
100	105	110
Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln		
115	120	125
Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr		
[0020] 130	135	140
Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser		
145	150	155 160
Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr		
165	170	175
Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys		
180	185	190
His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro		
195	200	205
Val Thr Lys Ser Phe Asn Arg Gly Glu Cys		
210	215	

<210> 23
 <211> 440
 <212> PRT
 <213> 人工序列

<220>
 <223> 重链

<400> 23

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

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
 20 25 30

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

[0021]

Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
 50 55 60

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

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

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
 100 105 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser
 115 120 125

Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp

	130	135	140	
	Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr			
	145	150	155	160
	Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr			
	165	170	175	
	Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys			
	180	185	190	
	Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp			
	195	200	205	
[0022]	Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala			
	210	215	220	
	Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro			
	225	230	235	240
	Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val			
	245	250	255	
	Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val			
	260	265	270	
	Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln			
	275	280	285	
	Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln			
	290	295	300	

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly
305 310 315 320

Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
325 330 335

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr
340 345 350

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
355 360 365

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
370 375 380

[0023] Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
385 390 395 400

Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe
405 410 415

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
420 425 430

Ser Leu Ser Leu Ser Leu Gly Lys
435 440

<210> 24
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> 轻链

<400> 24

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

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

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

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

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

[0024]

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 25
<211> 290
<212> PRT
<213> 人工序列

[0025] <220>
<223> Precurs 或 人 PD-L1

<400> 25

Met Arg Ile Phe Ala Val Phe Ile Phe Met Thr Tyr Trp His Leu Leu
1 5 10 15

Asn Ala Phe Thr Val Thr Val Pro Lys Asp Leu Tyr Val Val Glu Tyr
20 25 30

Gly Ser Asn Met Thr Ile Glu Cys Lys Phe Pro Val Glu Lys Gln Leu
35 40 45

Asp Leu Ala Ala Leu Ile Val Tyr Trp Glu Met Glu Asp Lys Asn Ile
50 55 60

Ile Gln Phe Val His Gly Glu Glu Asp Leu Lys Val Gln His Ser Ser

	65	70	75	80
	Tyr Arg Gln Arg Ala Arg Leu Leu Lys Asp Gln Leu Ser Leu Gly Asn			
	85		90	95
	Ala Ala Leu Gln Ile Thr Asp Val Lys Leu Gln Asp Ala Gly Val Tyr			
	100	105		110
	Arg Cys Met Ile Ser Tyr Gly Gly Ala Asp Tyr Lys Arg Ile Thr Val			
	115	120		125
	Lys Val Asn Ala Pro Tyr Asn Lys Ile Asn Gln Arg Ile Leu Val Val			
	130	135		140
[0026]	Asp Pro Val Thr Ser Glu His Glu Leu Thr Cys Gln Ala Glu Gly Tyr			
	145	150	155	160
	Pro Lys Ala Glu Val Ile Trp Thr Ser Ser Asp His Gln Val Leu Ser			
	165	170		175
	Gly Lys Thr Thr Thr Thr Asn Ser Lys Arg Glu Glu Lys Leu Phe Asn			
	180	185		190
	Val Thr Ser Thr Leu Arg Ile Asn Thr Thr Thr Asn Glu Ile Phe Tyr			
	195	200		205
	Cys Thr Phe Arg Arg Leu Asp Pro Glu Glu Asn His Thr Ala Glu Leu			
	210	215		220
	Val Ile Pro Glu Leu Pro Leu Ala His Pro Pro Asn Glu Arg Thr His			
	225	230	235	240

Leu Val Ile Leu Gly Ala Ile Leu Leu Cys Leu Gly Val Ala Leu Thr
245 250 255

Phe Ile Phe Arg Leu Arg Lys Gly Arg Met Met Asp Val Lys Lys Cys
260 265 270

Gly Ile Gln Asp Thr Asn Ser Lys Lys Gln Ser Asp Thr His Leu Glu
275 280 285

Glu Thr
290

<210> 26
<211> 113
<212> PRT
<213> 人工序列

[0027] <220>
<223> 重链可变

<400> 26

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

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
20 25 30

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

Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
50 55 60

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

65	70	75	80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys			
	85	90	95

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser			
100	105	110	

Ser

<210> 27
 <211> 107
 <212> PRT
 <213> 人工序列

[0028] <220>
 <223> 轻链可变

<400> 27

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

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

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

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

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

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

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

<210> 28
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 重链 CDR1

<400> 28

Asn Ser Gly Met His
1 5

[0029]

<210> 29
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> 重链 CDR2

<400> 29

Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 30

<211> 4
<212> PRT
<213> 人工序列

<220>
<223> 重链 CDR3

<400> 30

Asn Asp Asp Tyr
1

<210> 31
<211> 11
<212> PRT
<213> 人工序列

<220>
<223> 轻链 CDR1

[0030] <400> 31

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1 5 10

<210> 32
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 轻链 CDR2

<400> 32

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 33
<211> 9

<212> PRT
<213> 人工序列

<220>
<223> 轻链 CDR3

<400> 33

Gln Gln Ser Ser Asn Trp Pro Arg Thr
1 5

<210> 34
<211> 8
<212> PRT
<213> 人工序列

<220>
<223> CDR

<400> 34

[0031]

Gly Phe Thr Phe Ser Asp Asn Trp
1 5

<210> 35
<211> 10
<212> PRT
<213> 人工序列

<220>
<223> CDR

<400> 35

Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr
1 5 10

<210> 36
<211> 6
<212> PRT

<213> 人工序列

<220>

<223> CDR

<400> 36

Thr Ala Gln Phe Ala Tyr

1 5

<210> 37

<211> 6

<212> PRT

<213> 人工序列

<220>

<223> CDR

<400> 37

[0032] Glu Asn Ile Tyr Gly Gly

1 5

<210> 38

<211> 3

<212> PRT

<213> 人工序列

<220>

<223> CDR

<400> 38

Gly Ala Thr

1

<210> 39

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> CDR

<400> 39

Gln Asn Val Leu Arg Ser Pro Phe Thr

1 5

<210> 40

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> CDR

<400> 40

Gln Asn Val Leu Ser Arg His Pro Gly

[0033] 1 5

<210> 41

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> CDR

<400> 41

Gln Asn Val Leu Ser Ser Arg Pro Gly

1 5

<210> 42

<211> 115

<212> PRT

<213> 人工序列

<220>

<223> 重链可变

<400> 42

Glu Val Lys Leu Asp Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Pro Met Lys Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Ser Asp Asn
20 25 30

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Asp
50 55 60

[0034] Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ser
65 70 75 80

Val Tyr Leu Gln Met Asn Asn Leu Arg Gly Glu Asp Met Gly Ile Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ala
115

<210> 43

<211> 106

<212> PRT

<213> 人工序列

<220>

<223> 轻链可变

<400> 43

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

Glu Thr Val Thr Ile Thr Cys Gly Thr Ser Glu Asn Ile Tyr Gly Gly
20 25 30

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

Phe Gly Ala Thr Asn Leu Ala Asp Gly Met Ser Ser Arg Phe Ser Gly
50 55 60

[0035] Ser Gly Ser Gly Arg Gln Tyr Ser Leu Lys Ile Ser Ser Leu His Pro
65 70 75 80

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

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

<210> 44

<211> 115

<212> PRT

<213> 人工序列

<220>

<223> 重链可变

<400> 44

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

1	5	10	15
Ser Met Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Asn	20	25	30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu	35	40	45
Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Asp	50	55	60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser	65	70	75
Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr	85	90	95
Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr	100	105	110
Val Ser Ser	115		

[0036]

<210> 45
 <211> 107
 <212> PRT
 <213> 人工序列

<220>
 <223> 轻链可变

<400> 45

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

Asp Arg Val Thr Ile Thr Cys Arg Thr Ser Glu Asn Ile Tyr Gly Gly
20 25 30

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

Tyr Gly Ala Thr Asn Leu Ala Ser Gly Met Ser Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Lys Ile Ser Ser Leu His Pro
65 70 75 80

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

[0037] Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 46
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 重链可变

<400> 46

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

Ser Met Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Asn
20 25 30

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Ala
50 55 60

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

Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

[0038]

Val Ser Ser
115

<210> 47
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 轻链可变

<400> 47

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 Thr Ser Glu Asn Ile Tyr Gly Gly
20 25 30

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

Tyr Gly Ala Thr Asn Leu Ala Ser Gly Val Ser Ser Arg Phe Ser Gly
50 55 60

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

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

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

[0039] <210> 48
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 重链可变

<400> 48

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 Thr Phe Ser Asp Asn
20 25 30

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Glu Tyr Ala Ala

50

55

60

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

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

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

[0040]

<210> 49
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 轻链可变

<400> 49

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 Glu Asn Ile Tyr Gly Gly
20 25 30

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

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

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

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

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

<210> 50
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 重链可变

[0041]

<400> 50

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

Ser Met Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Asn
20 25 30

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Ala
50 55 60

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

Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 51
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 轻链可变

[0042]

<400> 51

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 Thr Ser Glu Asn Ile Tyr Gly Gly
20 25 30

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

Tyr Gly Ala Thr Asn Leu Ala Ser Gly Val Ser Ser Arg Phe Ser Gly
50 55 60

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

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

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

<210> 52
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 重链可变

<400> 52

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

[0043]

Ser Met Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Asn
20 25 30

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Ala
50 55 60

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

Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr

100

105

110

Val Ser Ser

115

<210> 53

<211> 107

<212> PRT

<213> 人工序列

<220>

<223> 轻链可变

<400> 53

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

1 5 10 15

[0044] Asp Arg Val Thr Ile Thr Cys Arg Thr Ser Glu Asn Ile Tyr Gly Gly

20 25 30

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

35 40 45

Tyr Gly Ala Thr Asn Leu Ala Ser Gly Val Ser Ser Arg Phe Ser Gly

50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro

65 70 75 80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln Asn Val Leu Ser Ser Arg Pro

85 90 95

Gly Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys

100 105

<210> 54
 <211> 115
 <212> PRT
 <213> 人工序列

<220>
 <223> 鼠重链可变

<400> 54

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

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

Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Ile
 35 40 45

[0045]

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

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

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

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

Val Ser Ala
 115

<210> 55
 <211> 126
 <212> PRT
 <213> 人工序列

<220>
 <223> 鼠轻链可变

<400> 55

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

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser
 20 25 30

Asn Phe Ala Asn Trp Val Gln Glu Lys Pro Asp His Leu Phe Thr Ser
 35 40 45

[0046]

Leu Ile Gly Gly Thr Asn Asn Arg Ala Pro Gly Val Pro Ala Arg Phe
 50 55 60

Ser Gly Ser Leu Ile Gly Asp Lys Ala Ala Leu Thr Ile Thr Gly Ala
 65 70 75 80

Gln Thr Glu Asp Glu Ala Ile Tyr Phe Cys Ala Leu Trp Tyr Ser Asn
 85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro
 100 105 110

Lys Ser Ser Pro Ser Val Thr Leu Phe Gln Gly Gln Phe Cys
 115 120 125

<210> 56
<211> 8
<212> PRT
<213> 人工序列

<220>
<223> CDR

<400> 56

Gly Tyr Ser Phe Thr Gly Tyr Thr
1 5

<210> 57
<211> 5
<212> PRT
<213> 人工序列

<220>
[0047] <223> CDR

<220>
<221> MISC_特征
<222> (4)..(4)
<223> X = Met, Val, Leu, Ile, Gly, Ala, Ser, 或 Thr

<400> 57

Gly Tyr Thr Xaa Asn
1 5

<210> 58
<211> 8
<212> PRT
<213> 人工序列

<220>
<223> CDR

<220>
<221> MISC_特征
<222> (6)..(6)
<223> X = Asn, Asp, 或 Glu

<220>
<221> MISC_特征
<222> (8)..(8)
<223> X = Thr, Asp, Glu, Gly, 或 Ala

<400> 58

Ile Asn Pro Tyr Asn Xaa Ile Xaa
1 5

<210> 59
<211> 17
<212> PRT
<213> 人工序列

[0048] <220>
<223> CDR

<220>
<221> MISC_特征
<222> (7)..(7)
<223> X = Asn 或 Asp

<220>
<221> MISC_特征
<222> (9)..(9)
<223> X = Thr, Asp, Glu, Gly, 或 Ala

<220>
<221> MISC_特征
<222> (12)..(12)
<223> X = Ala 或 Asn

<220>
<221> MISC_特征
<222> (16)..(16)

<223> X = Gln 或 Met

<400> 59

Leu Ile Asn Pro Tyr Asn Xaa Ile Xaa Asn Tyr Xaa Gln Lys Phe Xaa
1 5 10 15

Gly

<210> 60

<211> 6

<212> PRT

<213> 人工序列

<220>

<223> CDR

<400> 60

[0049]

Leu Asp Tyr Arg Ser Tyr
1 5

<210> 61

<211> 8

<212> PRT

<213> 人工序列

<220>

<223> CDR

<400> 61

Ala Arg Leu Asp Tyr Arg Ser Tyr
1 5

<210> 62

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> CDR

<400> 62

Thr Gly Ala Val Thr Thr Ser Asn Phe
1 5

<210> 63

<211> 14

<212> PRT

<213> 人工序列

<220>

<223> CDR

<220>

[0050] <221> MISC_特征

<222> (13)..(13)

<223> X = Pro 或 Ala

<400> 63

Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Phe Xaa Asn
1 5 10

<210> 64

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> CDR

<220>

<221> MISC_特征

<222> (5)..(5)

<223> X = Lys 或 Arg

<220>

<221> MISC_特征

<222> (7)..(7)

<223> X = 除 Met 或 Cys 以外的任何氨基酸

<220>

<221> MISC_特征

<222> (7)..(7)

<223> X = Ser 或 Pro

<400> 64

Gly Thr Asn Asn Xaa Ala Xaa

1 5

<210> 65

<211> 8

[0051] <212> PRT

<213> 人工序列

<220>

<223> CDR

<220>

<221> MISC_特征

<222> (3)..(3)

<223> X = Trp 或除 Met 或 Cys 以外的任何氨基酸

<220>

<221> MISC_特征

<222> (8)..(8)

<223> X = Trp 或除 Met 或 Cys 以外的任何氨基酸

<400> 65

Ala Leu Xaa Tyr Ser Asn His Xaa

1 5

<210> 66
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> CDR

<220>
<221> MISC_特征
<222> (3)..(3)
<223> X = Trp 或除 Met 或 Cys 以外的任何氨基酸

<220>
<221> MISC_特征
<222> (8)..(8)
<223> X = Trp 或除 Met 或 Cys 以外的任何氨基酸

<400> 66

[0052]

Ala Leu Xaa Tyr Ser Asn His Xaa Val
1 5

<210> 67
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 重链可变

<400> 67

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

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

Thr Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

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

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

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

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

[0053] Val Ser Ala
115

<210> 68
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 重链可变

<400> 68

Gln Val Gln Leu Val Glu 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 Ser Phe Thr Gly Tyr
20 25 30

Thr Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile

	35	40	45
Gly Leu Ile Asn Pro Tyr Asn Asn Ile Thr Asn Tyr Ala Gln Lys Phe			
50	55	60	
Gln Gly Arg Val Thr Phe Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr			
65	70	75	80
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Gly Val Tyr Phe Cys			
85	90	95	
Ala Arg Leu Asp Tyr Arg Ser Tyr Trp Gly Gln Gly Thr Leu Val Thr			
100	105	110	
Val Ser Ala			
115			

[0054]

<210> 69
 <211> 115
 <212> PRT
 <213> 人工序列

<220>
 <223> 重链可变

<400> 69

Gln Val Gln Leu Val Glu 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 Ser Phe Thr Gly Tyr
20 25 30

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

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

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

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

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

Val Ser Ala
115

[0055]

<210> 70
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 重链可变

<400> 70

Gln Val Gln Leu Val Glu 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 Ser Phe Thr Gly Tyr
20 25 30

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

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

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

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

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

Val Ser Ala
 115

[0056]

<210> 71
 <211> 115
 <212> PRT
 <213> 人工序列

<220>
 <223> 重链可变

<220>
 <221> MISC_特征
 <222> (11)..(11)
 <223> X = Val 或 Leu

<220>
 <221> MISC_特征
 <222> (18)..(18)
 <223> X = Val 或 Met

<220>
 <221> MISC_特征
 <222> (20)..(20)

<223> X = Val 或 Ile

<220>

<221> MISC_特征

<222> (34)..(34)

<223> X = Met, Val, Leu, Ile, Gly, Ala, Ser 或 Thr

<220>

<221> MISC_特征

<222> (38)..(38)

<223> X = Arg 或 Lys

<220>

<221> MISC_特征

<222> (56)..(56)

<223> X = Asn, Asp, 或 Glu

<220>

<221> MISC_特征

<222> (58)..(58)

<223> X = Thr, Asp, Glu, Gly, 或 Ala

[0057]

<220>

<221> MISC_特征

<222> (61)..(61)

<223> X = Ala 或 Asn

<220>

<221> MISC_特征

<222> (65)..(65)

<223> X = Gln 或 Met

<220>

<221> MISC_特征

<222> (67)..(67)

<223> X = Gln 或 Met

<220>

<221> MISC_特征

<222> (68)..(68)

<223> X = Val 或 Ala

<220>

<221> MISC_特征
 <222> (74).. (74)
 <223> X =Thr 或 Lys

<220>
 <221> MISC_特征
 <222> (87).. (87)
 <223> X =Arg 或 Thr

<220>
 <221> MISC_特征
 <222> (91).. (91)
 <223> X = The 或 Ser

<400> 71

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

[0058] Ser Xaa Lys Xaa Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
 20 25 30

Thr Xaa Asn Trp Val Xaa Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Leu Ile Asn Pro Tyr Asn Xaa Ile Xaa Asn Tyr Xaa Gln Lys Phe
 50 55 60

Xaa Gly Xaa Xaa Thr Phe Thr Val Asp Xaa Ser Ile Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Arg Leu Xaa Ser Asp Asp Xaa Gly Val Tyr Phe Cys
 85 90 95

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

Val Ser Ala
115

<210> 72
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 轻链可变

<400> 72

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

[0059]

Asn Phe Ala Asn Trp Val Gln Glu Lys Pro Gly Gln Ala Phe Arg Ser
35 40 45

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

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

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

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 73
 <211> 109
 <212> PRT
 <213> 人工序列

<220>
 <223> 轻链可变

<400> 73

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
 20 25 30

Asn Phe Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Ser
 35 40 45

[0060]

Leu Ile Gly Gly Thr Asn Asn Lys Ala Ser Trp Thr Pro Ala Arg Phe
 50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
 65 70 75 80

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

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105

<210> 74
 <211> 109
 <212> PRT
 <213> 人工序列

- <220>
<223> 轻链可变
- <220>
<221> MISC_特征
<222> (35)..(35)
<223> X = Pro 或 Ala
- <220>
<221> MISC_特征
<222> (40)..(40)
<223> X = Gln 或 Glu
- <220>
<221> MISC_特征
<222> (46)..(46)
<223> X = Pro 或 Phe
- [0061] <220>
<221> MISC_特征
<222> (56)..(56)
<223> X =Lys, Arg 或除 Met 或 Cys 以外的任何氨基酸
- <220>
<221> MISC_特征
<222> (58)..(58)
<223> X =Ser 或 Pro
- <220>
<221> MISC_特征
<222> (60)..(60)
<223> X =Thr 或 Val
- <220>
<221> MISC_特征
<222> (89)..(89)
<223> X =Tyr 或 Phe
- <220>
<221> MISC_特征
<222> (93)..(93)
<223> X = Trp 或除 Met 或 Cys 以外的任何氨基酸

<220>

<221> MISC_特征

<222> (98)..(98)

<223> X = Trp 或除 Met 或 Cys 以外的任何氨基酸

<400> 74

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Phe Xaa Asn Trp Val Gln Xaa Lys Pro Gly Gln Ala Xaa Arg Ser
35 40 45

Leu Ile Gly Gly Thr Asn Asn Xaa Ala Xaa Trp Xaa Pro Ala Arg Phe
50 55 60

[0062]

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

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

His Xaa Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 75

<211> 115

<212> PRT

<213> 人工序列

<220>

<223> 重链可变

<400> 75

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

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

Thr Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

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

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

[0063]

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

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

Val Ser Ala
115

<210> 76

<211> 109

<212> PRT

<213> 人工序列

<220>

<223> 轻链可变

<400> 76

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Phe Ala Asn Trp Val Gln Glu Lys Pro Gly Gln Ala Phe Arg Ser
35 40 45

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

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

[0064]

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

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 77

<211> 115

<212> PRT

<213> 人工序列

<220>

<223> 重链可变

<400> 77

Gln Val Gln Leu Val Glu 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 Ser Phe Thr Gly Tyr
20 25 30

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

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

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

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

[0065]

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

Val Ser Ala
115

<210> 78
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 轻链可变

<400> 78

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Phe Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Ser
35 40 45

Leu Ile Gly Gly Thr Asn Asn Lys Ala Ser Trp Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

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

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

[0066]

<210> 79
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 重链可变

<400> 79

Gln Val Gln Leu Val Glu 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 Ser Phe Thr Gly Tyr
20 25 30

Thr Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile

35 40 45

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

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

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

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

Val Ser Ala
115

[0067]

<210> 80
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 轻链可变

<400> 80

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Phe Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Ser
35 40 45

Leu Ile Gly Gly Thr Asn Asn Lys Ala Ser Trp Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

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

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 81
<211> 115
<212> PRT
<213> 人工序列

[0068]

<220>
<223> 重链可变

<400> 81

Gln Val Gln Leu Val Glu 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 Ser Phe Thr Gly Tyr
20 25 30

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

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

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

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

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

Val Ser Ala
115

<210>	82
<211>	109
<212>	PRT
<213>	人工序列

[0069]

〈223〉 轻链可变

<400> 82

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Phe Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Ser
35 40 45

Leu Ile Gly Gly Thr Asn Asn Lys Ala Ser Trp Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

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

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 83
<211> 448
<212> PRT
<213> 人工序列

<220>
<223> 重链

<400> 83

[0070]

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

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

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

Thr Phe Ile Ser Tyr Asp Gly Asn Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys

	85	90	95
	Ala Arg Thr Gly Trp Leu Gly Pro Phe Asp Tyr Trp Gly Gln Gly Thr		
	100	105	110
	Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro		
	115	120	125
	Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly		
	130	135	140
	Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn		
	145	150	155 160
[0071]	Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln		
	165	170	175
	Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser		
	180	185	190
	Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser		
	195	200	205
	Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr		
	210	215	220
	His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser		
	225	230	235 240
	Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg		
	245	250	255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro		
260	265	270
Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala		
275	280	285
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val		
290	295	300
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr		
305	310	315 320
Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr		
325	330	335
[0072] Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu		
340	345	350
Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys		
355	360	365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser		
370	375	380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp		
385	390	395 400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser		
405	410	415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala		
420	425	430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 84
<211> 215
<212> PRT
<213> 人工序列

<220>
<223> 轻链

<400> 84

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

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

[0073]

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

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

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

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

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

120

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190

[0074] Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
195 200 205

Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 85
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> CDR

<400> 85

Ser Tyr Thr Met His
1 5

<210> 86

<211> 17
<212> PRT
<213> 人工序列

<220>
<223> CDR

<400> 86

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

Gly

<210> 87
<211> 9
<212> PRT
<213> 人工序列

[0075]

<220>
<223> CDR

<400> 87

Thr Gly Trp Leu Gly Pro Phe Asp Tyr
1 5

<210> 88
<211> 12
<212> PRT
<213> 人工序列

<220>
<223> CDR

<400> 88

Arg Ala Ser Gln Ser Val Gly Ser Ser Tyr Leu Ala
1 5 10

<210> 89
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> CDR

<400> 89

Gly Ala Phe Ser Arg Ala Thr
1 5

<210> 90
<211> 9
<212> PRT
<213> 人工序列

[0076] <220>
<223> CDR

<400> 90

Gln Gln Tyr Gly Ser Ser Pro Trp Thr
1 5

<210> 91
<211> 118
<212> PRT
<213> 人工序列

<220>
<223> 重链可变

<400> 91

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

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

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

Thr Phe Ile Ser Tyr Asp Gly Asn Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

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

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

[0077] Ala Arg Thr Gly Trp Leu Gly Pro Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 92
<211> 108
<212> PRT
<213> 人工序列

<220>
<223> 轻链可变

<400> 92

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

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

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

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

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

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

[0078] Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 93
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 可变重链

<220>
<221> MISC_特征
<222> (18)..(18)
<223> x = Leu, Val, Ile 或 Ala

<400> 93

Glu Val Lys Leu Asp Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Pro Xaa Lys Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Ser Asp Asn
20 25 30

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Asp
50 55 60

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

Val Tyr Leu Gln Met Asn Asn Leu Arg Gly Glu Asp Met Gly Ile Tyr
85 90 95

[0079]

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ala
115

<210> 94
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 可变重链

<400> 94

Glu Val Lys Leu Asp Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

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

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Asp
50 55 60

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

Val Tyr Leu Gln Met Asn Asn Leu Arg Gly Glu Asp Met Gly Ile Tyr
85 90 95

[0080] Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ala
115

<210> 95
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 可变重链

<220>
<221> MISC_特征
<222> (18)..(18)
<223> X = Leu, Val, Ile 或 Ala

<400> 95

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

Ser Xaa Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Asn
20 25 30

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Asp
50 55 60

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

[0081] Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 96
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 可变重链

<400> 96

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

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

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Asp
50 55 60

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

[0082] Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 97
<211> 115
<212> PRT
<213> 人工序列

<220>
<223> 可变重链

<220>
<221> MISC_特征

<222> (18)..(18)

<223> X = Leu, Val, Ile 或 Ala

<400> 97

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

Ser Xaa Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Asn
20 25 30

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Ala
50 55 60

[0083] Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 98

<211> 115

<212> PRT

<213> 人工序列

<220>

<223> 可变重链

<400> 98

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

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

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Ala
50 55 60

[0084] Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 99

<211> 115

<212> PRT

<213> 人工序列

<220>

<223> 可变重链

<220>

<221> MISC_特征

<222> (18)..(18)

<223> X = Leu, Val, Ile 或 Ala

<400> 99

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

Ser Xaa Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Asn
20 25 30

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

[0085] Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Ala
50 55 60

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

Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 100

<211> 115

<212> PRT

<213> 人工序列

<220>

<223> 可变重链

<400> 100

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

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

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

[0086] Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Ala
50 55 60

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

Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 101

<211> 115

<212> PRT

<213> 人工序列

<220>

<223> 可变重链

<220>

<221> MISC_特征

<222> (18)..(18)

<223> X = Leu, Val, Ile 或 Ala

<400> 101

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

Ser Xaa Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Asn
20 25 30

[0087] Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Ala
50 55 60

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

Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 102
 <211> 115
 <212> PRT
 <213> 人工序列

<220>
 <223> 可变重链

<400> 102

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

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

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

[0088]

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Ala
 50 55 60

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

Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
 85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
 100 105 110

Val Ser Ser
 115

<210> 103
 <211> 115
 <212> PRT
 <213> 人工序列

<220>
 <223> 轻链可变

<400> 103

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

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

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

[0089]

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Ala
 50 55 60

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

Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
 85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
 100 105 110

Val Ser Ser
 115

<210> 104
 <211> 122
 <212> PRT
 <213> 人工序列

<220>
 <223> 重链可变

<400> 104

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

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

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

[0090]

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

Met Asp Lys Ala Thr Leu Thr Ala Asp Lys Ala Ser Thr Thr Ala Tyr
 65 70 75 80

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

Ala Arg Ser Gly Trp Leu Val His Gly Asp Tyr Tyr Phe Asp Tyr Trp
 100 105 110

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

<210> 105

<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 轻链可变

<400> 105

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

Glu Lys Val Thr Met Thr Cys Lys Ser Ser Gln Ser Leu Leu His Thr
20 25 30

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

[0091] Ser Pro Lys 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 Ala Glu Asp Leu Ala Val Tyr Tyr Cys Lys Gln
85 90 95

Ser Tyr Asp Val Val Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 106
<211> 122
<212> PRT
<213> 人工序列

<220>

<223> 重链可变

<400> 106

Gln Val His Leu Gln Gln Ser Gly Ala Glu Leu Ala 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

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

[0092] Gly Tyr Ile Asn Pro Ser Ser Gly Tyr His Glu Tyr Asn Gln Lys Phe
50 55 60

Ile Asp Lys Ala Thr Leu Thr Ala Asp Arg Ser Ser Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Ser Gly Trp Leu Ile His Gly Asp Tyr Tyr Phe Asp Phe Trp
100 105 110

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

hPD-1.08A 轻链 CDR1 (SEQ ID NO:1)

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

hPD-1.08A 轻链 CDR2 (SEQ ID NO:2)

Leu Ala Ser Asn Leu Glu Ser

hPD-1.08A 轻链 CDR3 (SEQ ID NO:3)

Gln His Ser Trp Glu Leu Pro Leu Thr

hPD-1.08A 重链 CDR1 (SEQ ID NO:4)

Ser Tyr Tyr Leu Tyr

hPD-1.08A 重链 CDR2 (SEQ ID NO:5)

Gly Val Asn Pro Ser Asn Gly Gly Thr Asn Phe Ser Glu Lys Phe Lys Ser

hPD-1.08A 重链 CDR3 (SEQ ID NO:6)

Arg Asp Ser Asn Tyr Asp Gly Gly Phe Asp Tyr

图1

hPD-1.09A 轻链 CDR1 (SEQ ID NO:7)

Arg Ala Ser Lys Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu His

hPD-1.09A 轻链 CDR2 (SEQ ID NO:8)

Leu Ala Ser Tyr Leu Glu Ser

hPD-1.09A 轻链 CDR3 (SEQ ID NO:9)

Gln His Ser Arg Asp Leu Pro Leu Thr

hPD-1.09A 重链 CDR1 (SEQ ID NO:10)

Asn Tyr Tyr Met Tyr

hPD-1.09A 重链 CDR2 (SEQ ID NO:11)

Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn Glu Lys Phe Lys Asn

hPD-1.09A 重链 CDR3 (SEQ ID NO:12)

Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr

图2

109A-H 重链可变区 (SEQ ID NO:13)

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

409A-H 重链全长 (SEQ ID NO:14)

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

图3

K09A-L-11 轻链可变区 (SEQ ID NO:15)

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

K09A-L-16 轻链可变区 (SEQ ID NO:16)

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

K09A-L-17 轻链可变区 (SEQ ID NO:17)

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
Glu Pro Ala Ser Ile Ser Cys Arg Ala Ser Lys Gly Val Ser Thr Ser
Gly Tyr Ser Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
Gln Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Asp
Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Lys Ile Ser
Arg Val Glu Ala Glu Asp Val Gly Leu Tyr Tyr Cys Gln His Ser Arg
Asp Leu Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys

图4

K09A-L-11 轻链全长 (SEQ ID NO:18)

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Gly Val Ser Thr Ser
Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Ser Arg
Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

K09A-L-16 轻链全长 (SEQ ID NO:19)

Glu Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
Glu Pro Ala Ser Ile Ser Cys Arg Ala Ser Lys Gly Val Ser Thr Ser
Gly Tyr Ser Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
Gln Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Asp
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln His Ser Arg
Asp Leu Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

图5A

K09A-L-17 轻链全长 (SEQ ID NO:20)

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

图5B

派姆单抗

重链 (SEQ ID NO:21)

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QVQLVQSGVE VKKPGASVKV SCKASGYTFT NYMYWVRQA PGQGLEWMQG 50
INPSNGGTNF NEKFKNRVTL TIDSSTTTAY MELKSLQFDD TAVYYCARD 100
YRFDMGFDMY GQGTITVTVSS ASTKGPSVFP LAPCSRSTSE STAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTKT 200
YTCNVDHKPS NTKVDKRVES KYGPPCPPCP APEFLGGPSV FLFPPKPKDT 250
LMISRTPEVT CVVVDVSQED PEVQFNWYVD GVEVHNAKTK PREEQFNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYT 350
LPPSQEEMTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS 400
DGSFFLYSRL TVDKSRWQEG NVFSCSVME ALHNHYTQKS LSLSLGK 447

```

轻链 (SEQ ID NO:22)

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EIVLTQSPAT LSLSPGERAT LSCRASKGVS TSGYSYLHWY QOKPGQAPRL 50
LIYLASYLES GVPARFSGSG SGTDFTLTIS SLEPEDFAVY YQCHSRDLPL 100
TFGGGTKVEI KRTVAAPSVF IFPPSDEQLK SGTASVVCLL NNFYPREAKV 150
QWKVDNALQS GNSQESVTEQ DSKDSTYSLS STLTLKADY EKHKVYACEV 200
THQGLSSPVT KSFNRGEC 219

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图6

纳武单抗

重链 (SEQ ID NO:23)

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QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAV 50
IWYDGSKRYYADSVKGRFTISRDN SKNTLFLQMNSLRAEDTAVYYCATND 100
DYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPV 150
TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVPSSSLGKTYTCNV DH 200
KPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTP 250
EVTCTVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT 300
VLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEE 350
MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLY 400
SRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLK 440

```

轻链 (SEQ ID NO:24)

```

EIVLTQSPATLSLSPGERATLSORASQSVSYLAWYQQKPQAPRLLIYD 50
ASNRTGIPA RFGSGSGTDFTLTSSLEPEDFAVYYCQQSSNWPRTFGQ 100
GTKVEIKRTV AAPSVFIFPPSDEQLKSGTASVCLLNIFYPREAKVQWKV 150
DNALQSGNSQESVTEQDSKSTYSLSSLTLSKADYEKHKVYACEVTHQG 200
LSSPVTKSFN RGECC 214

```

图7

研究设计

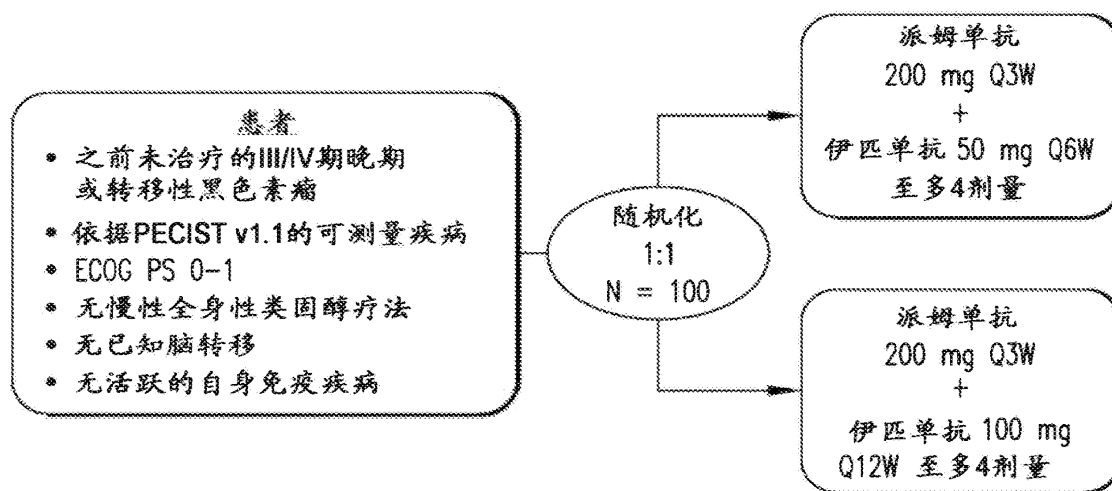


图8

患者适格标准

包含	不包含
• 年龄 > 18 岁 • 之前组织学上未治疗或细胞学上确认不可切除的III或IV期黑色素瘤不适用于局部疗法 • 基于RECIST v1.1, > 1个可测量的损伤 • 提供肿瘤样本（存档的或新获得的活组织检查）用于在中心实验室通过IHC确定PD-L1的状态 • ECOG性能状态0或1 • 足够的器官功能	• 葡萄膜或眼黑色素瘤 • 在首次研究剂量的4周内的先前全身性抗癌疗法 • 不允许在先化疗或靶向小分子疗法, 包括BRAF或MEK抑制剂 • 在过去两年需要全身性治疗的活跃的自身免疫疾病 • 免疫缺陷史或正在接受全身类固醇疗法 (>10 毫克/天强的松或等同) 或首次研究剂量前7天内其他免疫抑制疗法 • 已知的活跃中枢神经系统转移和/或癌性脑膜炎（先前治疗过的稳定脑转移是允许的） • 需要类固醇的非感染性肺炎史或当前肺炎 • 已知HIV或乙肝或丙肝病毒感染史

图9

伊匹单抗

重链 (SEQ ID NO:83)

QVQLVESGGG VVQPGRSLRL SCAASGFTFS SYTMHWVRQA PGKGLEWVTF
ISYDGNKYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAIYYCARTG
WLGPFDYWQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI
CNVNHKPSNT KVDKRVEPKS CDKTHTCPPC PAPELLGGPS VFLFPPKPKD
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY
TLPPSRDELT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTTPVLD
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPGK

轻链 (SEQ ID NO:84)

EIVLTQSPGT LSLSPGERAT LSCRASQSVG SSYLAWYQQK PGQAPRLLIY
GAFSRATGIP DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ QYGSSPWTFG
QGTKVEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK
VDNALQSGNS QESVTEQDSK DSTYLSSTL TLSKADYEKH KUYACEVTHQ
GLSSPVTKSF NRGEC

图10

Electronic Patent Application Fee Transmittal				
Application Number:		16306290		
Filing Date:		30-Nov-2018		
Title of Invention:		METHODS OF TREATING COLORECTAL CANCER		
First Named Inventor/Applicant Name:		Michael AXELSON		
Filer:		Brian Mason Dudley/Malinda Crowley		
Attorney Docket Number:		3338.0550001/ELE/C-K/BMD		
Filed as Large Entity				
Filing Fees for U.S. National Stage under 35 USC 371				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
RCE- 2ND AND SUBSEQUENT REQUEST	1820	1	2000	2000
Total in USD (\$)				2000

Electronic Acknowledgement Receipt	
EFS ID:	44567181
Application Number:	16306290
International Application Number:	
Confirmation Number:	7097
Title of Invention:	METHODS OF TREATING COLORECTAL CANCER
First Named Inventor/Applicant Name:	Michael AXELSON
Customer Number:	115018
Filer:	Brian Mason Dudley/Malinda Crowley
Filer Authorized By:	Brian Mason Dudley
Attorney Docket Number:	3338.0550001/ELE/C-K/BMD
Receipt Date:	20-DEC-2021
Filing Date:	30-NOV-2018
Time Stamp:	18:18:52
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$2000
RAM confirmation Number	E2021BJI20370438
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	2021-12-20-IDS-Pleading-3338-0550001.PDF	107817	no	3
			d88bf4f95ce724e964cff44e7f5d559f054ffb69		
Warnings:					
Information:					
2	Request for Continued Examination (RCE)	2021-12-20-RCE-3338-0550001.PDF	1349989	no	3
			fd2a873f8936635482c4cfc8492d7abecc685f04		
Warnings:					
Information:					
3	Information Disclosure Statement (IDS) Form (SB08)	2021-12-20-Third-Supplemental-IDS-3338-0550001.PDF	119690	no	1
			0812ea794a65ed87cd3bcb471e6fd8e7cdfaa2c2		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
4	Transmittal Letter	2021-12-20-Transmittal-3338-0550001.PDF	204682	no	1
			7566df9cf1a04a31664430b61b51b28b2b89a395		
Warnings:					
Information:					
5	Non Patent Literature	NPL47_GATALICA_.PDF	2978683	no	8
			df6f5f9331efd82d64fbac1fa7708513b2899c8		
Warnings:					
Information:					
6	Non Patent Literature	NPL48_Patel.PDF	246773	no	7
			baafb85d3f5adc37a6ca4af4d86826cbddb59e7d4		
Warnings:					

Information:					
7	Non Patent Literature	NPL49_NCT02060188_V49.PDF	540770	no	22
			27ee71fdfe5f7992869500b9a819526a55283540		
Warnings:					
Information:					
8	Foreign Reference	FP19_CN110505882A.pdf	3265745	no	150
			ff706b420f0912e3ab2dff3338025e25647a5a53d		
Warnings:					
Information:					
9	Fee Worksheet (SB06)	fee-info.pdf	38088	no	2
			1b6e898abfc656a2474c08cf8760048ed93f88ec		
Warnings:					
Information:					
Total Files Size (in bytes):			8852237		
This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503. <u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application. <u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course. <u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor: Michael AXELSON	Confirmation No.: 7097
Applicant: Bristol-Myers Squibb Company	Art Unit: 1647
Application No.: 16/306,290	Examiner: LOCKARD; Jon McClelland
International Filing Date: June 2, 2017	Atty. Docket: 3338.0550001/ELE/C-K/BMD
Title: METHODS OF TREATING COLORECTAL CANCER	

Third Supplemental Information Disclosure Statement

Mail Stop RCE

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Commissioner:

Listed on accompanying IDS Forms PTO/SB/08a/b equivalents are documents for consideration in view of 37 C.F.R. §§ 1.56, 1.97, and 1.98. The numbering on this Third Supplemental Information Disclosure Statement is a continuation of the numbering in Applicant's Second Supplemental Information Disclosure Statement filed on **September 7, 2021** in connection with the above-captioned application.

Applicant has listed publication dates on the attached IDS Form based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicant reserves the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

This is a filing under 37 C.F.R. § 1.97(b). This Information Disclosure Statement is being filed before the mailing of a first Office Action after the filing of a request for continued examination under 37 C.F.R. § 1.114. No statement or fee is required.

A concise explanation of the relevance of the non-English language document appears below in accordance with 37 C.F.R. § 1.98(a)(3).

Document **FP19**, CN-110505882-A, is in a foreign language. An English language abstract is appended to the face page of document **FP19**.

Copies of documents **FP19** and **NPL47-NPL49** are submitted.

It is respectfully requested that the Examiner initial and return a copy of the enclosed IDS Forms, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

/Brian M. Dudley/

Brian M. Dudley
Attorney for Applicant
Registration No. 77,546

Date: December 20, 2021

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

17576094_1.DOCX



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

115018 7590 01/20/2022
Sterne, Kessler, Goldstein & Fox P.L.L.C.
1100 New York Avenue NW
Washington, DC 20005

EXAMINER

LOCKARD, JON MCCLELLAND

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 01/20/2022

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/306,290	11/30/2018	Michael AXELSON	3338.0550001/ ELE/C-K/BMD	7097

TITLE OF INVENTION: METHODS OF TREATING COLORECTAL CANCER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$1200.00	\$0	04/20/2022

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

115018 7590 01/20/2022
Sterne, Kessler, Goldstein & Fox P.L.L.C.
1100 New York Avenue NW
Washington, DC 20005

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/306,290	11/30/2018	Michael AXELSON	3338.0550001/ ELE/C-K/BMD	7097

TITLE OF INVENTION: METHODS OF TREATING COLORECTAL CANCER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$1200.00	\$0	04/20/2022

EXAMINER	ART UNIT	CLASS-SUBCLASS
LOCKARD, JON MCCLELLAND	1647	424-139100

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

1 _____

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☐ Issue Fee ☐ Publication Fee (if required) ☐ Advance Order - # of Copies _____

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☐ Electronic Payment via EFS-Web ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____



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www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/306,290	11/30/2018	Michael AXELSON	3338.0550001/ ELE/C K/BMD	7097
115018	7590	01/20/2022	EXAMINER	
Sterne, Kessler, Goldstein & Fox P.L.L.C. 1100 New York Avenue NW Washington, DC 20005			LOCKARD, JON MCCLELLAND	
			ART UNIT	PAPER NUMBER
			1647	
DATE MAILED: 01/20/2022				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.** Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 16/306,290	Applicant(s) AXELSON, Michael	
	Examiner JON M LOCKARD	Art Unit 1647	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the Request for Continued Examination filed 20 December 2021.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☒ The allowed claim(s) is/are 1,3-5,7-8,10-13 and 16-23 (renumbered as claims 1-18, respectively). As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a) ☐ All b) ☐ Some* c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892) 2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____. 3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____. 4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____	5. ☐ Examiner's Amendment/Comment 6. ☒ Examiner's Statement of Reasons for Allowance 7. ☐ Other _____
--	---

/J.L/ Examiner, Art Unit 1647	/CHRISTINE J SAOUD/ Primary Examiner, Art Unit 1647
----------------------------------	--

Notice of Pre-AIA or AIA Status

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 20 December 2021 has been entered.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on 20 December 2021 has been considered by the examiner.

REASONS FOR ALLOWANCE

5. The following is an examiner's statement of reasons for allowance: The information disclosure statement (IDS) filed 20 December 2021 has been considered by the Examiner. After careful consideration, the Examiner has determined that none of the information contained therein raises new issues of patentability.
6. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue

fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Summary

7. Claims 1, 3-5, 7-8, 10-13 and 16-23 are allowed.

Advisory Information

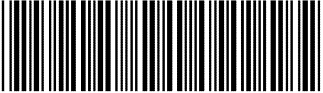
Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joanne Hama**, can be reached on **(571) 272-2911**. The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. M. L./
Examiner, Art Unit 1647
January 6, 2022

/Christine J Saoud/
Primary Examiner, Art Unit 1647

<i>Search Notes</i> 	Application/Control No. 16/306,290	Applicant(s)/Patent Under Reexamination AXELSON, Michael
	Examiner JON M LOCKARD	Art Unit 1647

CPC - Searched*		
Symbol	Date	Examiner

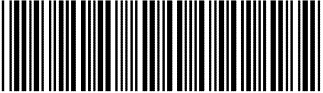
CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner
NONE		12/19/2020	JML

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

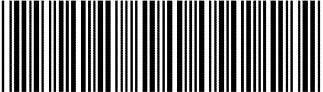
Search Notes		
Search Notes	Date	Examiner
EAST (USPAT, US-PGPUB, EPO, DERWENT): See attached search history.	12/19/2020	JML
STN (MEDLINE, SCISEARCH, EMBASE, BIOSIS): See attached search history.	12/19/2020	JML
PALM: Inventor search.	12/19/2020	JML

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<i>Search Notes</i> 	Application/Control No. 16/306,290	Applicant(s)/Patent Under Reexamination AXELSON, Michael
	Examiner JON M LOCKARD	Art Unit 1647

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
	EAST (USPAT): See attached search history.	04/23/2021	JML
	PALM: Inventor search.	04/23/2021	JML
	EAST (USPAT): See attached search history.	09/10/2021	JML
	PALM: Inventor search.	09/10/2021	JML
	EAST (USPAT): See attached search history.	01/06/2022	JML
	PALM: Inventor search.	01/06/2022	JML

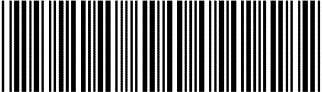
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Issue Classification 	Application/Control No. 16/306,290	Applicant(s)/Patent Under Reexamination AXELSON, Michael
	Examiner JON M LOCKARD	Art Unit 1647

CPC						
Symbol					Type	Version
C07K	/	16	/	2818	F	2013-01-01
A61P	/	35	/	00	I	2018-01-01
C07K	/	16	/	2878	I	2013-01-01
C07K	/	16	/	2827	I	2013-01-01
A61K	/	2039	/	507	A	2013-01-01

CPC Combination Sets					
Symbol				Type	Version
/	/	/	/		

/JON M LOCKARD/ Examiner, Art Unit 1647 (Assistant Examiner)	06 January 2022 (Date)	Total Claims Allowed: 18	
/CHRISTINE J SAOUD/ Primary Examiner, Art Unit 1647 (Primary Examiner)	07 January 2022 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure NONE

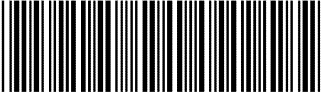
Issue Classification 	Application/Control No. 16/306,290	Applicant(s)/Patent Under Reexamination AXELSON, Michael
	Examiner JON M LOCKARD	Art Unit 1647

INTERNATIONAL CLASSIFICATION			
CLAIMED			
A61K		39	395
C07K		16	28
NON-CLAIMED			

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS

CROSS REFERENCES(S)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					

/JON M LOCKARD/ Examiner, Art Unit 1647 (Assistant Examiner)	06 January 2022 (Date)	Total Claims Allowed: 18	
/CHRISTINE J SAOUD/ Primary Examiner, Art Unit 1647 (Primary Examiner)	07 January 2022 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure NONE

Issue Classification 	Application/Control No. 16/306,290	Applicant(s)/Patent Under Reexamination AXELSON, Michael
	Examiner JON M LOCKARD	Art Unit 1647

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47															
CLAIMS															
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original

/JON M LOCKARD/ Examiner, Art Unit 1647 (Assistant Examiner)	06 January 2022 (Date)	Total Claims Allowed: 18	
/CHRISTINE J SAOUD/ Primary Examiner, Art Unit 1647 (Primary Examiner)	07 January 2022 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure NONE

Receipt date: 12/20/2021

Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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Substitute for form 1449/PTO THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	16/306,290
				Int'l Filing Date	June 2, 2017
				First Named Inventor	AXELSON; Michael
				Art Unit	1647
				Examiner Name	LOCKARD, JON MCCLELLAND
Sheet	1	of	1	Attorney Docket Number	3338.0550001/ELE/C-K/BMD

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ² Number ⁴ Kind Code ⁵ (if known)				
/J.L./	FP19	CN-110505882-A	11-26-2019	MERCK SHARP AND DOHME CORP		☐

NON-PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author(in CAPITAL LETTERS), title of the article(when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
/J.L./	NPL47	GATALICA, Z., et al., "High microsatellite instability (MSI-H) colorectal carcinoma: a brief review of predictive biomarkers in the era of personalized medicine," Fam Cancer 15(3):405-412, Springerlink, United States (February 2016).	☐
/J.L./	NPL48	PATEL, S.P., et al., "Modulation of Immune System Inhibitory Checkpoints in Colorectal Cancer," Curr Colorectal Cancer Rep 9:391-397, Springerlink, United States (2013).	☐
/J.L./	NPL49	Anonymous: "A Study of Nivolumab and Nivolumab Plus Ipilimumab in Recurrent and Metastatic Colon Cancer (CheckMate 142)". Retrieved from the Internet: URL: https://clinicaltrials.gov/ct2/history/NCT02060188?V_49=View#StudyPageTop [retrieved on August 6, 2021], 22 pages.	

17255030_1

Examiner Signature	/JON M LOCKARD/	Date Considered	01/03/2022
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

/J.L./

EAST Search History

EAST Search History (Interference)

/J.L./

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	14,242	PDCD1 CD279 PD-1 PD1 SLEB2 hPD-1 hPD-I hSLE1 "Programmed cell death 1"	USPAT	OR	ON	2022/01/06 21:02
L2	2,568	I1 near5 (antibody or antibodies)	USPAT	OR	ON	2022/01/06 21:03
L3	11,598	CTLA4 ALPS5 CD152 CELIAC3 CTLA-4 GRD4 IDDM12 "cytotoxic T-lymphocyte associated protein 4"	USPAT	OR	ON	2022/01/06 21:03
L4	4,023	I3 near5 (antibody or antibodies)	USPAT	OR	ON	2022/01/06 21:03
L5	426	(colorectal adj cancer) same ((microsatellite adj instability) or msi-h)	USPAT	OR	ON	2022/01/06 21:04
L6	799	I2 with I4	USPAT	OR	ON	2022/01/06 21:04
L7	0	I5 same I6	USPAT	OR	ON	2022/01/06 21:04
L8	10	I5 and I6	USPAT	OR	ON	2022/01/06 21:04
L9	5	axelson-m\$.in.	USPAT	OR	ON	2022/01/06 21:05
L10	0	I8 and I9	USPAT	OR	ON	2022/01/06 21:05
L11	0	(I1 or I3) and I9	USPAT	OR	ON	2022/01/06 21:05

1/6/2022 9:06:00 PM

C:\Users\jlockard\Documents\EAST\Workspaces\16306290.wsp

Inventor Information for 16/306290

/J.L./

Inventor Name	City	State/Country
AXELSON, MICHAEL	PRINCETON	NEW JERSEY

Applo Info	Comments	Petition Info	Atty/Agent Info	Community Data	Foreign Data	Inventors	Applicants	Address	Fees	Post Info	Pre Gr
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PCT / / [Search](#) or PG PUBS # [Search](#)
Attorney Docket # [Search](#)
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To: ckim@sternekessler.com,e-office@sternekessler.com,pcalvo@sternekessler.com
From: PAIR_eOfficeAction@uspto.gov
Cc: PAIR_eOfficeAction@uspto.gov
Subject: Private PAIR Correspondence Notification for Customer Number 115018

Jan 20, 2022 04:18:09 AM

Dear PAIR Customer:

Sterne, Kessler, Goldstein & Fox P.L.L.C.
1100 New York Avenue NW
Washington, DC 20005
UNITED STATES

The following USPTO patent application(s) associated with your Customer Number, 115018 , have new outgoing correspondence. This correspondence is now available for viewing in Private PAIR.

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Application	Document	Mailroom Date	Attorney Docket No.
16306290	NOA	01/20/2022	3338.0550001/ELE/C-K/BMD
	1449	01/20/2022	3338.0550001/ELE/C-K/BMD

To view your correspondence online or update your email addresses, please visit us anytime at <https://sportal.uspto.gov/secure/myportal/privatepair>.

If you have any questions, please email the Electronic Business Center (EBC) at EBC@uspto.gov with 'e-Office Action' on the subject line or call 1-866-217-9197 during the following hours:

Monday - Friday 6:00 a.m. to 12:00 a.m.

Thank you for prompt attention to this notice,

UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT APPLICATION INFORMATION RETRIEVAL SYSTEM

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

115018 7590 01/20/2022
Sterne, Kessler, Goldstein & Fox P.L.L.C.
1100 New York Avenue NW
Washington, DC 20005

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/306,290	11/30/2018	Michael AXELSON	3338.0550001/ ELE/C-K/BMD	7097

TITLE OF INVENTION: METHODS OF TREATING COLORECTAL CANCER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$1200.00	\$0	04/20/2022

EXAMINER	ART UNIT	CLASS-SUBCLASS
LOCKARD, JON MCCLELLAND	1647	424-139100

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

Sterne, Kessler, Goldstein

1. & Fox P.L.L.C.

2. _____

3. _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

Bristol-Myers Squibb Company

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Princeton, New Jersey

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☒ Issue Fee ☐ Publication Fee (if required) ☐ Advance Order - # of Copies _____

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☒ Electronic Payment via EFS-Web ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. 19-0036

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Brian M. Dudley/Date April 19, 2022Typed or printed name Brian M. DudleyRegistration No. 77,546

Electronic Acknowledgement Receipt	
EFS ID:	45504144
Application Number:	16306290
International Application Number:	
Confirmation Number:	7097
Title of Invention:	METHODS OF TREATING COLORECTAL CANCER
First Named Inventor/Applicant Name:	Michael AXELSON
Customer Number:	115018
Filer:	Brian Mason Dudley/Kim Perry
Filer Authorized By:	Brian Mason Dudley
Attorney Docket Number:	3338.0550001/ELE/C-K/BMD
Receipt Date:	19-APR-2022
Filing Date:	30-NOV-2018
Time Stamp:	19:59:26
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment		no			
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Issue Fee Payment (PTO-85B)	2022-04-19-Issue-Fee-3338-0550001.PDF	107718	no	1
			3da97232cfce387fedbd6a47fc8c3f965b9e185d		
Warnings:					

Information:	
Total Files Size (in bytes):	107718
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115018 7590 01/20/2022
Sterne, Kessler, Goldstein & Fox P.L.L.C.
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/306,290	11/30/2018	Michael AXELSON	3338.0550001/ ELE/C-K/BMD	7097

TITLE OF INVENTION: METHODS OF TREATING COLORECTAL CANCER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$1200.00	\$0	04/20/2022

EXAMINER	ART UNIT	CLASS-SUBCLASS
LOCKARD, JON MCCLELLAND	1647	424-139100

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Sterne, Kessler, Goldstein
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(A) NAME OF ASSIGNEE

Bristol-Myers Squibb Company

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Princeton, New Jersey

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☒ Corporation or other private group entity ☐ Government

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Authorized Signature /Brian M. Dudley/

Date April 19, 2022

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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/306,290	05/17/2022	11332529	3338.0550001/ELE/C-K/BMD	7097

115018 7590 04/27/2022
Sterne, Kessler, Goldstein & Fox P.L.L.C.
1100 New York Avenue NW
Washington, DC 20005

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment is 59 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

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INVENTOR(s) (Please see PAIR WEB site <http://pair.uspto.gov> for additional inventors):

Michael AXELSON, Princeton, NJ;

APPLICANT(s) (Please see PAIR WEB site <http://pair.uspto.gov> for additional applicants):

Bristol-Myers Squibb Company, Princeton, NJ;

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Application	Document	Mailroom Date	Attorney Docket No.
16306290	ISSUE.NTF	04/27/2022	3338.0550001/ELE/C-K/BMD

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