
A
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Variant 1321 38 MHVAQPAVVLASSRGIASFVCEYAMPGKATEVRVTVLRQADSQVTEVCAATYMIGNEGTFLDDSICTGTASGNQVNLTIKGLRAMDTGLYICQVELMYPPPYYLGIGNGTQIYVIDPEPCPDSD
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Sequence numbering (top), and numbering according to Swiss-Prot entry P16410 (bottom)
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SEQ ID
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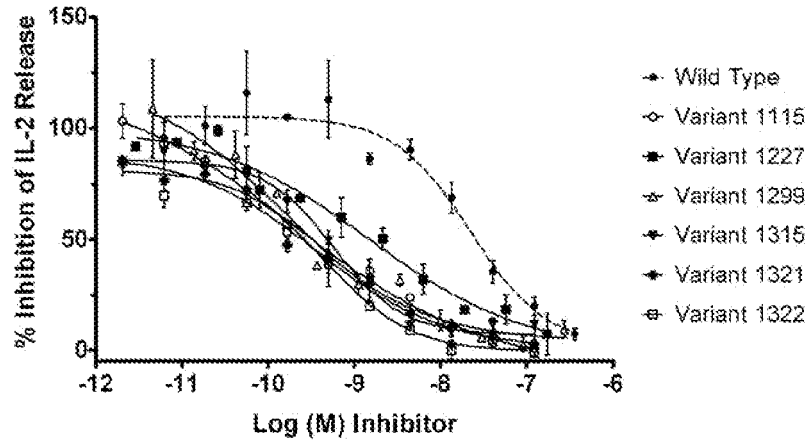
Figure 1

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
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21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
C	E	Y	R_{24}	N	P	R_{27}	K	A	T	E	V	R	V	T	V	L	R	Q	A
41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
D	S	Q	V	T	E	V	C	A	A	T	Y	M	R_{54}	G	R_{56}	E	R_{58}	R_{59}	R_{60}
61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
R_{61}	D	R_{63}	R_{64}	R_{65}	C	T	G	T	R_{70}	S	G	N	Q	V	N	L	T	I	R_{80}
81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
G	L	R	A	R_{85}	D	T	G	L	Y	I	C	R_{93}	V	E	L	M	Y	P	P
101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120
P	Y	Y	L	G	I	G	N	G	T	Q	I	Y	V	I	D	P	E	P	C
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P	D	S	D																

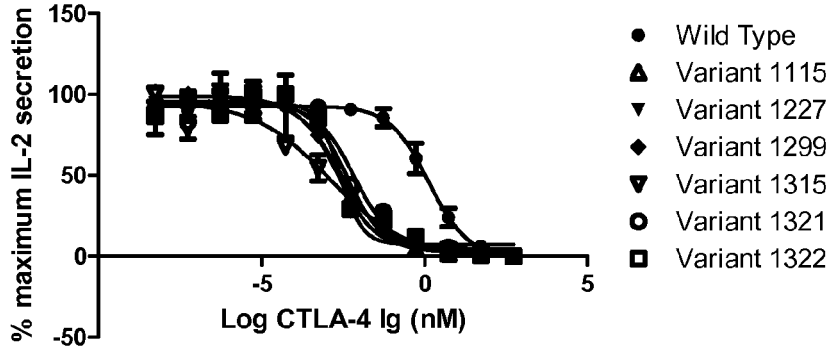
R_{16} = R, I, S or V
R_{24} = T or A
R_{27} = S or G
R_{54} = M or K
R_{56} = N or S
R_{58} = A, L or G
R_{59} = T or S
R_{60} = F or T
R_{61} = L or Q
R_{63} = D or Y
R_{64} = S or P
R_{65} = I, N or D
R_{70} = A or S
R_{80} = Q or R
R_{85} = Q, M or S
R_{93} = Q or H

Figure 2

A


% Inhibition of IL-2 Release
150
100
50
0
-12
-11
-10
-9
-8
-7
-6
Log (M) Inhibitor
Wild Type
Variant 1115
Variant 1227
Variant 1299
Variant 1315
Variant 1321
Variant 1322

B


% maximum IL-2 secretion
150
100
50
0
-50
-5
0
5
Log CTLA-4 Ig (nM)
Wild Type
Variant 1115
Variant 1227
Variant 1299
Variant 1315
Variant 1321
Variant 1322

C

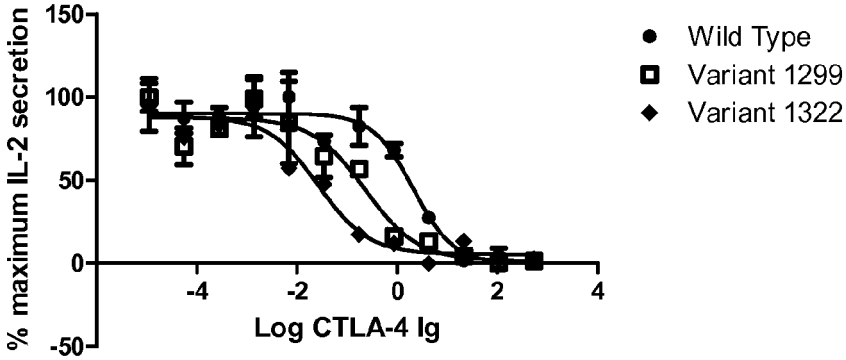
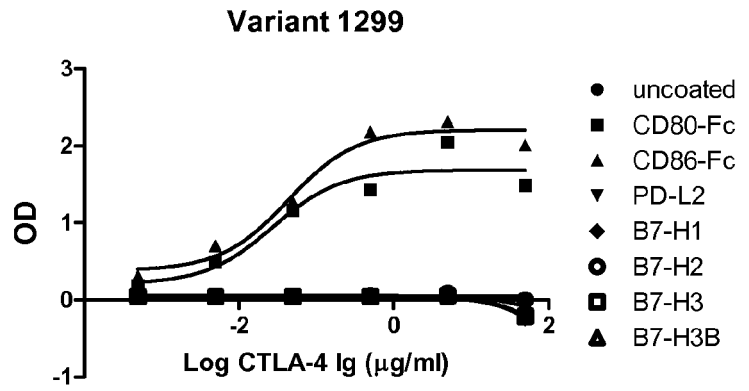

% maximum IL-2 secretion
150
100
50
0
-50
-4
-2
0
2
4
Log CTLA-4 Ig
Wild Type
Variant 1299
Variant 1322

Figure 3

A


Variant 1299
OD
3
2
1
0
-1
-2
0
2
Log CTLA-4 Ig (μg/ml)
uncoated
CD80-Fc
CD86-Fc
PD-L2
B7-H1
B7-H2
B7-H3
B7-H3B

B

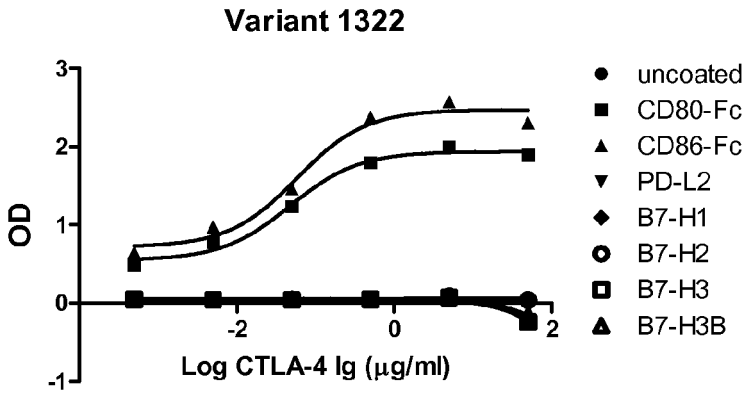
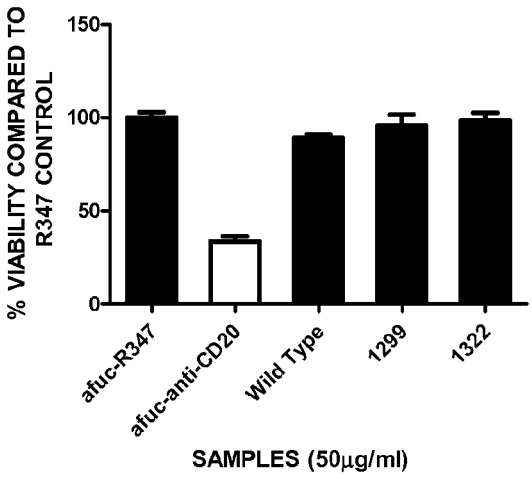

Variant 1322
OD
3
2
1
0
-1
-2
0
2
Log CTLA-4 Ig (μg/ml)
uncoated
CD80-Fc
CD86-Fc
PD-L2
B7-H1
B7-H2
B7-H3
B7-H3B

Figure 4

A


% VIABILITY COMPARED TO R347 CONTROL
150
100
50
0
afuc-R347
afuc-anti-CD20
Wild Type
1299
1322
SAMPLES (50µg/ml)

B

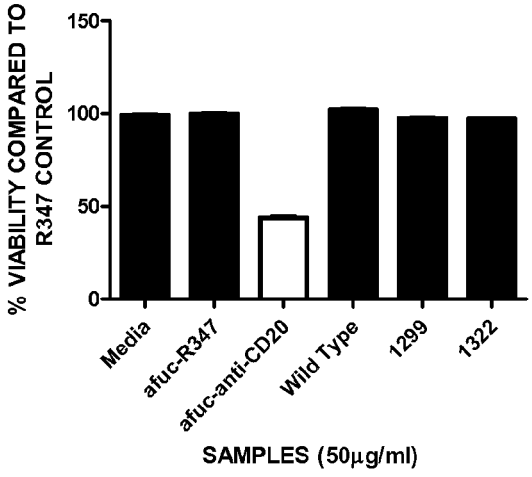

% VIABILITY COMPARED TO R347 CONTROL
150
100
50
0
Media
afuc-R347
afuc-anti-CD20
Wild Type
1299
1322
SAMPLES (50µg/ml)

Figure 5

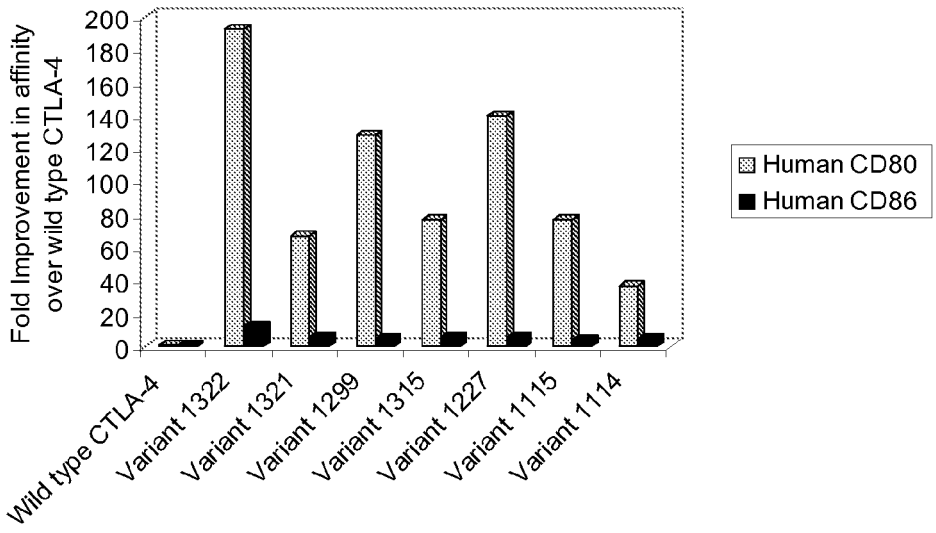
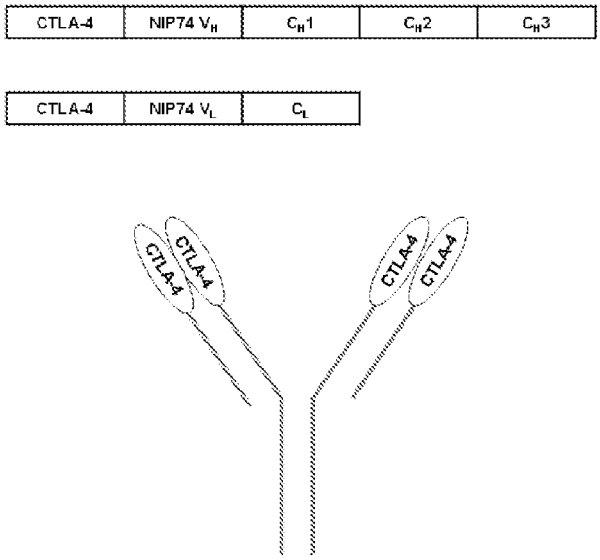

Fold Improvement in affinity over wild type CTLA-4
200
180
160
140
120
100
80
60
40
20
0
Wild type CTLA-4
Variant 1322
Variant 1321
Variant 1299
Variant 1315
Variant 1227
Variant 1115
Variant 1114
Human CD80
Human CD86

Figure 6

A


CTLA-4
NIP74 V_H
C_H1
C_H2
C_H3
CTLA-4
NIP74 V_L
C_L
CTLA-4
CTLA-4
CTLA-4
CTLA-4

B

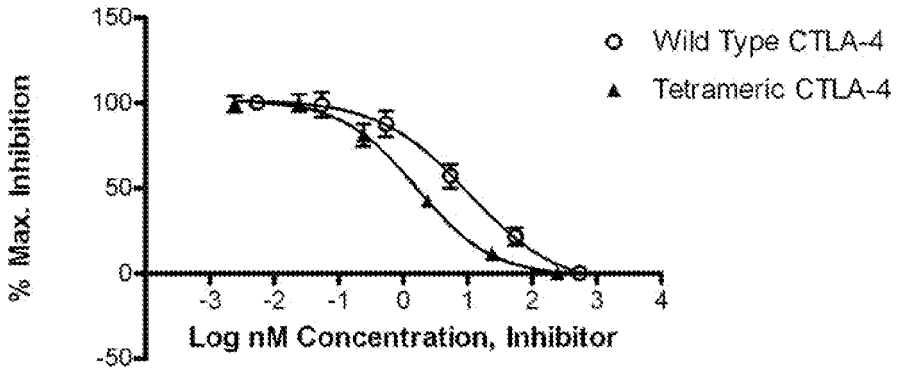

% Max. Inhibition
150
100
50
0
-50
-3
-2
-1
0
1
2
3
4
Log nM Concentration, Inhibitor
Wild Type CTLA-4
Tetrameric CTLA-4

Figure 7

SEQUENCE LISTING

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1               5                  10                  15

Leu Asn Phe Phe Gln Leu Leu Val Leu Ala Gly Leu Ser His Phe Cys
            20                  25                  30

Ser Gly Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu
        35                  40                  45

Ser Cys Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile
    50                  55                  60

Tyr Trp Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp
65                  70                  75                  80

Met Asn Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr
                85                  90                  95

Asn Asn Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly
            100                 105                 110

Thr Tyr Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg
        115                 120                 125

Glu His Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr
    130                 135                 140

Pro Ser Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile
145                 150                 155                 160

Ile Cys Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu
                165                 170                 175

Glu Asn Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp
            180                 185                 190
```

```
Pro Glu Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met
        195                 200                 205

Thr Thr Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg
    210                 215                 220

Val Asn Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro
225                 230                 235                 240

Asp Asn Asp Pro Ala Phe Leu Tyr Lys Val Val Gly Ala Ala Asp Tyr
                245                 250                 255

Lys Asp Asp Asp Asp Lys Ala Ala His His His His His His His His
            260                 265                 270

His His
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1               5                   10                  15

Pro Cys Pro Arg Leu Ile Leu Leu Phe Val Leu Leu Ile Arg Leu Ser
            20                  25                  30

Gln Val Ser Ser Asp Val Asp Glu Gln Leu Ser Lys Ser Val Lys Asp
        35                  40                  45

Lys Val Leu Leu Pro Cys Arg Tyr Asn Ser Pro His Glu Asp Glu Ser
    50                  55                  60

Glu Asp Arg Ile Tyr Trp Gln Lys His Asp Lys Val Val Leu Ser Val
65                  70                  75                  80

Ile Ala Gly Lys Leu Lys Val Trp Pro Glu Tyr Lys Asn Arg Thr Leu
                85                  90                  95

Tyr Asp Asn Thr Thr Tyr Ser Leu Ile Ile Leu Gly Leu Val Leu Ser
            100                 105                 110

Asp Arg Gly Thr Tyr Ser Cys Val Val Gln Lys Lys Glu Arg Gly Thr
        115                 120                 125
```

Tyr Glu Val Lys His Leu Ala Leu Val Lys Leu Ser Ile Lys Ala Asp
130 135 140

Phe Ser Thr Pro Asn Ile Thr Glu Ser Gly Asn Pro Ser Ala Asp Thr
145 150 155 160

Lys Arg Ile Thr Cys Phe Ala Ser Gly Gly Phe Pro Lys Pro Arg Phe
165 170 175

Ser Trp Leu Glu Asn Gly Arg Glu Leu Pro Gly Ile Asn Thr Thr Ile
180 185 190

Ser Gln Asp Pro Glu Ser Glu Leu Tyr Thr Ile Ser Ser Gln Leu Asp
195 200 205

Phe Asn Thr Thr Arg Asn His Thr Ile Lys Cys Leu Ile Lys Tyr Gly
210 215 220

Asp Ala His Val Ser Glu Asp Phe Thr Trp Glu Lys Pro Pro Glu Asp
225 230 235 240

Pro Pro Asp Ser Lys Tyr Pro Ala Phe Leu Tyr Lys Val Val Gly Ala
245 250 255

Ala Asp Tyr Lys Asp Asp Asp Asp Lys Ala Ala His His His His His
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His His His His His
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Met Gly His Thr Trp Arg Gln Gly Ile Ser Pro Ser Lys Cys Pro Tyr
1 5 10 15

Leu Lys Phe Phe Gln Leu Leu Val Leu Ala Cys Leu Ser His Phe Cys
20 25 30

Ser Gly Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu
35 40 45

Ser Cys Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile
50 55 60

Tyr Trp Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp
65 70 75 80

```
Met Asn Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr
                85                  90                  95

Asn Asn Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly
            100                 105                 110

Thr Tyr Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg
        115                 120                 125

Glu His Leu Ala Glu Val Met Leu Ser Val Lys Ala Asp Phe Pro Thr
    130                 135                 140

Pro Ser Ile Thr Asp Phe Glu Ile Pro Pro Ser Asn Ile Arg Arg Ile
145                 150                 155                 160

Ile Cys Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu
                165                 170                 175

Glu Asn Gly Glu Glu Leu Asn Ala Ile Ser Thr Thr Val Ser Gln Asp
            180                 185                 190

Pro Glu Thr Glu Leu Tyr Thr Val Ser Ser Lys Leu Asp Phe Asn Met
        195                 200                 205

Thr Thr Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg
    210                 215                 220

Val Asn Gln Thr Phe Asn Trp Asn Thr Pro Lys Gln Glu His Phe Pro
225                 230                 235                 240

Asp Asn Asp Pro Ala Phe Leu Tyr Lys Val Val Gly Ala Ala Asp Tyr
                245                 250                 255

Lys Asp Asp Asp Asp Lys Ala Ala His His His His His His His His
            260                 265                 270

His His
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1               5                   10                  15
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Ala Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu
            20                  25                  30

Pro Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val
        35                  40                  45

Val Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu
    50                  55                  60

Gly Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Gly Arg Thr
65                  70                  75                  80

Ser Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile
                85                  90                  95

Lys Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr
            100                 105                 110

Gly Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala
        115                 120                 125

Asn Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn
    130                 135                 140

Val Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro
145                 150                 155                 160

Lys Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr
                165                 170                 175

Asp Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp
            180                 185                 190

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

Thr Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser
    210                 215                 220

Pro Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Asp
225                 230                 235                 240

Pro Ala Phe Leu Tyr Lys Val Val Gly Ala Ala Asp Tyr Lys Asp Asp
                245                 250                 255

Asp Asp Lys Ala Ala His His His His His His His His His His
            260                 265                 270
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1               5                  10                  15

Val Leu Leu Ile Ser Asp Ala Val Ser Val Glu Thr Gln Ala Tyr Phe
            20                  25                  30

Asn Gly Thr Ala Tyr Leu Pro Cys Pro Phe Thr Lys Ala Gln Asn Ile
        35                  40                  45

Ser Leu Ser Glu Leu Val Val Phe Trp Gln Asp Gln Gln Lys Leu Val
    50                  55                  60

Leu Tyr Glu His Tyr Leu Gly Thr Glu Lys Leu Asp Ser Val Asn Ala
65                  70                  75                  80

Lys Tyr Leu Gly Arg Thr Ser Phe Asp Arg Asn Asn Trp Thr Leu Arg
                85                  90                  95

Leu His Asn Val Gln Ile Lys Asp Met Gly Ser Tyr Asp Cys Phe Ile
            100                 105                 110

Gln Lys Lys Pro Pro Thr Gly Ser Ile Ile Leu Gln Gln Thr Leu Thr
        115                 120                 125

Glu Leu Ser Val Ile Ala Asn Phe Ser Glu Pro Glu Ile Lys Leu Ala
    130                 135                 140

Gln Asn Val Thr Gly Asn Ser Gly Ile Asn Leu Thr Cys Thr Ser Lys
145                 150                 155                 160

Gln Gly His Pro Lys Pro Lys Lys Met Tyr Phe Leu Ile Thr Asn Ser
                165                 170                 175

Thr Asn Glu Tyr Gly Asp Asn Met Gln Ile Ser Gln Asp Asn Val Thr
            180                 185                 190

Glu Leu Phe Ser Ile Ser Asn Ser Leu Ser Leu Ser Phe Pro Asp Gly
        195                 200                 205

Val Trp His Met Thr Val Val Cys Val Leu Glu Thr Glu Ser Met Lys
    210                 215                 220

Ile Ser Ser Lys Pro Leu Asn Phe Thr Gln Glu Phe Pro Ser Pro Gln
225                 230                 235                 240

Thr Tyr Trp Lys Glu Tyr Pro Ala Phe Leu Tyr Lys Val Val Gly Ala
                245                 250                 255
```

```
Ala Asp Tyr Lys Asp Asp Asp Asp Lys Ala Ala His His His His His
            260                 265                 270

His His His His His
        275


<210>  6
<211>  271
<212>  PRT
<213>  Artificial sequence

<220>
<223>  Synthetic sequence: Cynomolgus CD86 flag his 10

<400>  6

Met Gly Leu Ser Asn Thr Leu Phe Val Met Ala Phe Leu Leu Ser Gly
1               5                   10                  15


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


Pro Cys Gln Phe Ala Asn Ser Gln Asn Arg Ser Leu Ser Glu Leu Val
        35                  40                  45


Val Phe Trp Gln Asn Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu
    50                  55                  60


Gly Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Gly Arg Thr
65                  70                  75                  80


Ser Phe Asp Pro Glu Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile
                85                  90                  95


Lys Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Arg Pro Thr
            100                 105                 110


Gly Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala
        115                 120                 125


Asn Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn
    130                 135                 140


Met Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro
145                 150                 155                 160


Glu Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr
                165                 170                 175


Asp Gly Val Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp
            180                 185                 190
```

```
Val Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met
        195                 200                 205


Thr Ile Phe Cys Val Leu Glu Thr Asp Lys Thr Gln Leu Leu Ser Ser
    210                 215                 220


Pro Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Asp
225                 230                 235                 240


Pro Ala Phe Leu Tyr Lys Val Val Gly Ala Ala Asp Tyr Lys Asp Asp
                245                 250                 255


Asp Asp Lys Ala Ala His His His His His His His His His His
            260                 265                 270


<210>  7
<211>  357
<212>  PRT
<213>  Artificial sequence

<220>
<223>  Synthetic sequence: CTLA4 Fc variant-1 [Wild type CTLA-4 IgG1 Fc
(modified hinge)]

<400>  7

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


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


Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35                  40                  45


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


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


Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu
                85                  90                  95


Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
            100                 105                 110


Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Gln Glu Pro Lys
        115                 120                 125


Ser Ser Asp Lys Thr His Thr Ser Pro Pro Ser Pro Ala Pro Glu Leu
    130                 135                 140


Leu Gly Gly Ser Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
```

145 150 155 160

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
165 170 175

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
180 185 190

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
195 200 205

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
210 215 220

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
225 230 235 240

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
245 250 255

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
260 265 270

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
275 280 285

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
290 295 300

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
305 310 315 320

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
325 330 335

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
340 345 350

Leu Ser Pro Gly Lys
355

<210> 8
<211> 357
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA4 Fc variant-2 [Wild type CTLA-4 IgG1 Fc (modified hinge) with YTE]

<400> 8

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

```
Ala Ser Phe Val Cys Glu Tyr Ala Ser Pro Gly Lys Ala Thr Glu Val
            20                  25                  30

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35                  40                  45

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

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

Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu
                85                  90                  95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
            100                 105                 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Gln Glu Pro Lys
        115                 120                 125

Ser Ser Asp Lys Thr His Thr Ser Pro Pro Ser Pro Ala Pro Glu Leu
    130                 135                 140

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

Leu Tyr Ile Thr Arg Glu Pro Glu Val Thr Cys Val Val Val Asp Val
                165                 170                 175

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
            180                 185                 190

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
        195                 200                 205

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
    210                 215                 220

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
225                 230                 235                 240

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
                245                 250                 255

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
            260                 265                 270

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
        275                 280                 285
```

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
290 295 300

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
305 310 315 320

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
325 330 335

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
340 345 350

Leu Ser Pro Gly Lys
355

<210> 9
<211> 357
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA4 Fc variant-3 [Wild type CTLA-4 IgG1 Fc with TM and YTE]

<400> 9

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

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

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

Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Val Glu Pro Lys
115 120 125

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe
130 135 140

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

Leu Tyr Ile Thr Arg Glu Pro Glu Val Thr Cys Val Val Val Asp Val
165 170 175

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
180 185 190

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
195 200 205

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
210 215 220

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
225 230 235 240

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
245 250 255

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
260 265 270

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
275 280 285

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
290 295 300

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
305 310 315 320

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
325 330 335

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
340 345 350

Leu Ser Pro Gly Lys
355

<210> 10
<211> 354
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA4 Fc variant-4 [Wild type CTLA-4 IgG4 Fc with YTE and hinge Proline]

<400> 10

```
Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Ile
1               5                  10                  15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35                  40                  45

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

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

Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu
                85                  90                  95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
            100                 105                 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Val Glu Ser Lys
        115                 120                 125

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
    130                 135                 140

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Tyr Ile
145                 150                 155                 160

Thr Arg Glu Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
                165                 170                 175

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
            180                 185                 190

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
        195                 200                 205

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
    210                 215                 220

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
225                 230                 235                 240

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
                245                 250                 255

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
            260                 265                 270
```

```
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
        275                 280                 285


Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
    290                 295                 300


Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
305                 310                 315                 320


Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
                325                 330                 335


Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
            340                 345                 350


Gly Lys
```

<210> 11
<211> 357
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1322 IgG1 Fc with TM and YTE (357aa)

<400> 11

```
Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Ile
1               5                   10                  15


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


Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35                  40                  45


Ala Ala Thr Tyr Met Lys Gly Ser Glu Leu Ser Thr Gln Asp Tyr Pro
    50                  55                  60


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


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


Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
            100                 105                 110


Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Val Glu Pro Lys
        115                 120                 125
```

```
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe
    130                 135                 140

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

Leu Tyr Ile Thr Arg Glu Pro Glu Val Thr Cys Val Val Val Asp Val
                165                 170                 175

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
            180                 185                 190

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
        195                 200                 205

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
    210                 215                 220

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
225                 230                 235                 240

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
                245                 250                 255

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
            260                 265                 270

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
        275                 280                 285

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
    290                 295                 300

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
305                 310                 315                 320

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
                325                 330                 335

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
            340                 345                 350

Leu Ser Pro Gly Lys
        355
```

<210> 12
<211> 357
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1321 IgG1 Fc with TM and YTE (357aa)

<400> 12

```
Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Ser
1               5                  10                  15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35                  40                  45

Ala Ala Thr Tyr Met Lys Gly Asn Glu Gly Thr Phe Leu Asp Asp Ser
    50                  55                  60

Ile Cys Thr Gly Thr Ala Ser Gly Asn Gln Val Asn Leu Thr Ile Arg
65                  70                  75                  80

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

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
            100                 105                 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Val Glu Pro Lys
        115                 120                 125

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe
    130                 135                 140

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

Leu Tyr Ile Thr Arg Glu Pro Glu Val Thr Cys Val Val Val Asp Val
                165                 170                 175

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
            180                 185                 190

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
        195                 200                 205

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
    210                 215                 220

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
225                 230                 235                 240

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
                245                 250                 255

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
```

260 265 270

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
275 280 285

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
290 295 300

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
305 310 315 320

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
325 330 335

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
340 345 350

Leu Ser Pro Gly Lys
355

<210> 13
<211> 357
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1299 IgG1 Fc with TM and YTE (357aa)

<400> 13

Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Arg
1 5 10 15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

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

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

Gly Leu Arg Ala Gln Asp Thr Gly Leu Tyr Ile Cys Gln Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Val Glu Pro Lys
115 120 125

```
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe
    130                 135                 140

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

Leu Tyr Ile Thr Arg Glu Pro Glu Val Thr Cys Val Val Val Asp Val
                165                 170                 175

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
            180                 185                 190

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
        195                 200                 205

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
    210                 215                 220

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
225                 230                 235                 240

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
                245                 250                 255

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
            260                 265                 270

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
        275                 280                 285

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
    290                 295                 300

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
305                 310                 315                 320

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
                325                 330                 335

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
            340                 345                 350

Leu Ser Pro Gly Lys
        355


<210>  14
<211>  357
<212>  PRT
<213>  Artificial sequence

<220>
```

<223> Synthetic sequence: CTLA-4 Variant 1315 IgG1 Fc with TM and YTE (357aa)

<400> 14

```
Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Ser
1               5                  10                  15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35                  40                  45

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

Ile Cys Thr Gly Thr Ala Ser Gly Asn Gln Val Asn Leu Thr Ile Arg
65                  70                  75                  80

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

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
            100                 105                 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Val Glu Pro Lys
        115                 120                 125

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe
    130                 135                 140

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

Leu Tyr Ile Thr Arg Glu Pro Glu Val Thr Cys Val Val Val Asp Val
                165                 170                 175

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
            180                 185                 190

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
        195                 200                 205

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
    210                 215                 220

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
225                 230                 235                 240

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
                245                 250                 255
```

```
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
            260                 265                 270

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
        275                 280                 285

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
    290                 295                 300

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
305                 310                 315                 320

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
                325                 330                 335

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
            340                 345                 350

Leu Ser Pro Gly Lys
        355
```

<210> 15
<211> 357
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1115 IgG1 Fc with TM and YTE (357aa)

<400> 15

```
Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Val
1               5                   10                  15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35                  40                  45

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

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

Gly Leu Arg Ala Gln Asp Thr Gly Leu Tyr Ile Cys Gln Val Glu Leu
                85                  90                  95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
            100                 105                 110
```

```
Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Val Glu Pro Lys
        115                 120                 125

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe
    130                 135                 140

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

Leu Tyr Ile Thr Arg Glu Pro Glu Val Thr Cys Val Val Val Asp Val
                165                 170                 175

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
            180                 185                 190

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
        195                 200                 205

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
    210                 215                 220

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
225                 230                 235                 240

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
                245                 250                 255

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
            260                 265                 270

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
        275                 280                 285

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
    290                 295                 300

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
305                 310                 315                 320

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
                325                 330                 335

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
            340                 345                 350

Leu Ser Pro Gly Lys
        355
```

<210> 16
<211> 357
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1227 IgG1 Fc with TM and YTE (357aa)

<400> 16

Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Ser
1 5 10 15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

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

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

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

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Val Glu Pro Lys
115 120 125

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe
130 135 140

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

Leu Tyr Ile Thr Arg Glu Pro Glu Val Thr Cys Val Val Val Asp Val
165 170 175

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
180 185 190

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
195 200 205

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
210 215 220

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
225 230 235 240

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro

245 250 255

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
260 265 270

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
275 280 285

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
290 295 300

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
305 310 315 320

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
325 330 335

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
340 345 350

Leu Ser Pro Gly Lys
355

<210> 17
<211> 456
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: NIP 74 heavy chain (for tetramer)

<400> 17

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

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

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

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

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

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

Ala Arg Arg Gly Tyr Asp Tyr Gly Ser Gly Ser Tyr Tyr Tyr Tyr Tyr
100 105 110

```
Gly Met Asp Val Trp Gly Lys Gly Thr Met Val Thr Val Thr Ala Ser
        115                 120                 125

Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr
    130                 135                 140

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

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

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180                 185                 190

Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile
        195                 200                 205

Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val
    210                 215                 220

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
225                 230                 235                 240

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
                245                 250                 255

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
            260                 265                 270

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
        275                 280                 285

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
    290                 295                 300

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
305                 310                 315                 320

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
                325                 330                 335

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
            340                 345                 350

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
        355                 360                 365

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
    370                 375                 380
```

```
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
385                 390                 395                 400


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


Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
            420                 425                 430


Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
        435                 440                 445


Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455


<210>  18
<211>  217
<212>  PRT
<213>  Artificial sequence

<220>
<223>  Synthetic sequence: NIP 74 light chain (for tetramer)

<400>  18

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


Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
            20                  25                  30


Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
        35                  40                  45


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


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


Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
                85                  90                  95


Leu Ser Asp Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110


Gln Pro Lys Ala Asn Pro Thr Val Thr Leu Phe Pro Pro Ser Ser Glu
        115                 120                 125


Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe
    130                 135                 140


Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Gly Ser Pro Val
```

145 150 155 160

Lys Ala Gly Val Glu Thr Thr Lys Pro Ser Lys Gln Ser Asn Asn Lys
165 170 175

Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser
180 185 190

His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu
195 200 205

Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 19
<211> 608
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 tetramer heavy chain

<400> 19

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

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

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

Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Gly Gly Ser Gly
115 120 125

Ser Ala Thr Gly Gly Ser Gly Ser Thr Ala Ser Ser Gly Ser Gly Ser
130 135 140

Ala Thr Gly Gly Gly Gly Gly Gly Gln Val Gln Leu Val Gln Ser Gly
145 150 155 160

```
Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
                165                 170                 175

Ser Gly Tyr Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala
            180                 185                 190

Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly
        195                 200                 205

Gly Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg
    210                 215                 220

Asp Thr Ser Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser
225                 230                 235                 240

Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Arg Gly Tyr Asp Tyr Gly
                245                 250                 255

Ser Gly Ser Tyr Tyr Tyr Tyr Tyr Gly Met Asp Val Trp Gly Lys Gly
            260                 265                 270

Thr Met Val Thr Val Thr Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        275                 280                 285

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
    290                 295                 300

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
305                 310                 315                 320

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                325                 330                 335

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            340                 345                 350

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

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
    370                 375                 380

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
385                 390                 395                 400

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                405                 410                 415

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            420                 425                 430
```

```
Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        435                 440                 445

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    450                 455                 460

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
465                 470                 475                 480

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                485                 490                 495

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            500                 505                 510

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        515                 520                 525

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    530                 535                 540

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
545                 550                 555                 560

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                565                 570                 575

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            580                 585                 590

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        595                 600                 605


<210>  20
<211>  369
<212>  PRT
<213>  Artificial sequence

<220>
<223>  Synthetic sequence: CTLA-4 tetramer light chain

<400>  20

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35                  40                  45

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

50 55 60

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

Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Gly Gly Ser Gly
115 120 125

Ser Thr Ala Gly Gly Ser Gly Ser Ala Thr Ser Ser Gly Ser Gly Ser
130 135 140

Ala Thr Gly Gly Gly Gly Gly Gly Gln Ser Val Val Thr Gln Pro Pro
145 150 155 160

Ser Val Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys Thr Gly
165 170 175

Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His Trp Tyr Gln Gln
180 185 190

Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Gly Asn Ser Asn Arg
195 200 205

Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser
210 215 220

Ala Ser Leu Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr
225 230 235 240

Tyr Cys Gln Ser Tyr Asp Ser Ser Leu Ser Asp Val Val Phe Gly Gly
245 250 255

Gly Thr Lys Leu Thr Val Leu Gly Gln Pro Lys Ala Asn Pro Thr Val
260 265 270

Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr
275 280 285

Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala
290 295 300

Trp Lys Ala Asp Gly Ser Pro Val Lys Ala Gly Val Glu Thr Thr Lys
305 310 315 320

Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser

325 330 335

Leu Thr Pro Glu Gln Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val
340 345 350

Thr His Glu Gly Ser Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys
355 360 365

Ser

<210> 21
<211> 22
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: 5prime oligonucleotide for amplification of CTLA4 for fusion to NIP74 VH

<400> 21
gcttgcgcgc actccgcaat gc 22

<210> 22
<211> 22
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: 3prime oligonucleotide for amplification of CTLA4 for fusion to NIP74 VH

<400> 22
ccagaaccag aagaagcggt ag 22

<210> 23
<211> 23
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: 5prime oligonucleotide for amplification of CTLA4 for fusion to NIP74 VL

<400> 23
gcttgtgcac tccgcaatgc acg 23

<210> 24
<211> 23
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: 3prime oligonucleotide for amplification of CTLA4 for fusion to NIP74 VL

<400> 24
gagccagaag aggtagcaga acc 23

<210> 25

<211> 70
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence:5prime oligonucleotide for amplification of NIP74 VH for CTLA4 fusion

<400> 25
ctaccgcttc ttctggttct ggttctgcta ccggtggtgg tggtggtggc caggtgcagc 60

tggtgcagtc 70

<210> 26
<211> 18
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence:3prime oligonucleotide for amplification of NIP74 VH for CTLA4 fusion

<400> 26
ccaggggaa gaccgatg 18

<210> 27
<211> 74
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: 5prime oligonucleotide for amplification of NIP74 VL for CTLA4 fusion

<400> 27
ggttctgcta cctcttctgg ctctggttct gcgaccggtg gtggcggtgg tggccagtct 60

gtcgtgacgc agcc 74

<210> 28
<211> 53
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: 3prime oligonucleotide for amplification of NIP74 VL for CTLA4 fusion

<400> 28
gcacttaatt aagttagatc tattctgact cacctaggac ggtcagcttg gtc 53

<210> 29
<211> 22
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: 5prime oligonucleotide for assembly of CTLA4 - NIP74 VH fusion

<400> 29
gcttgcgcgc actccgcaat gc 22

<210> 30
<211> 18
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: 3prime oligonucleotide for assembly of CTLA4 - NIP74 VH fusion

<400> 30
ccaggggaa gaccgatg 18

<210> 31
<211> 23
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: 5prime oligonucleotide for assembly of CTLA4 - NIP74 VL fusion

<400> 31
gcttgtgcac tccgcaatgc acg 23

<210> 32
<211> 53
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: 3prime oligonucleotide for assembly of CTLA4 - NIP74 VL fusion

<400> 32
gcacttaatt aagttagatc tattctgact cacctaggac ggtcagcttg gtc 53

<210> 33
<211> 64
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: Randomisation oligonucleotide for construction of targeted "loop 4" ribosome display library

<220>
<221> misc_feature
<222> (22)..(23)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (25)..(26)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (28)..(29)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (31)..(32)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (34)..(35)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (37)..(38)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (40)..(41)
<223> n is a, c, g, or t

<400> 33
ccactggagg tgcccgtgca snnsnnsnns nnsnnsnnsn ncaactcatt ccccatcatg 60

tagg 64

<210> 34
<211> 25
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: Overlap oligonucleotide for construction of targeted "loop 4" ribosome display library

<400> 34
tgcacgggca cctccagtgg aaatc 25

<210> 35
<211> 124
<212> PRT
<213> Homo sapiens

<400> 35

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

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

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

Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 36
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1315

<400> 36

Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Ser
1 5 10 15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

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

Ile Cys Thr Gly Thr Ala Ser Gly Asn Gln Val Asn Leu Thr Ile Arg
65 70 75 80

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

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 37
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1322

<400> 37

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

Ala Ala Thr Tyr Met Lys Gly Ser Glu Leu Ser Thr Gln Asp Tyr Pro
50 55 60

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

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

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 38
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1321

<400> 38

Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Ser
1 5 10 15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

Ala Ala Thr Tyr Met Lys Gly Asn Glu Gly Thr Phe Leu Asp Asp Ser
50 55 60

Ile Cys Thr Gly Thr Ala Ser Gly Asn Gln Val Asn Leu Thr Ile Arg
65 70 75 80

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

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 39
<211> 124
<212> PRT

<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 0943

<400> 39

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

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

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

Gly Leu Arg Ala Leu Asp Thr Gly Leu Tyr Ile Cys Gln Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 40
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 0898

<400> 40

Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Val
1 5 10 15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

Ala Ala Thr Tyr Met Met Gly Asn Glu Leu Thr Phe Pro Asp Asp Ser
50 55 60

Ile Cys Thr Gly Thr Ser Ser Gly Asn Gln Val Asn Leu Thr Ile Gln

65 70 75 80

Gly Leu Arg Ala Leu Asp Thr Gly Leu Tyr Ile Cys Gln Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 41
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1319

<400> 41

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

Ala Ala Thr Tyr Met Met Gly Ser Glu Leu Ser Thr Gln Asp Tyr Pro
50 55 60

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

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

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 42
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1115

<400> 42

```
Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Val
1               5                   10                  15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35                  40                  45

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

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

Gly Leu Arg Ala Gln Asp Thr Gly Leu Tyr Ile Cys Gln Val Glu Leu
                85                  90                  95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
            100                 105                 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
        115                 120
```

<210> 43
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1299

<400> 43

```
Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Arg
1               5                   10                  15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35                  40                  45

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

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

Gly Leu Arg Ala Gln Asp Thr Gly Leu Tyr Ile Cys Gln Val Glu Leu
                85                  90                  95
```

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 44
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1249

<400> 44

Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Arg
1 5 10 15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

Ala Ala Thr Tyr Met Met Gly Asn Glu Pro Thr Phe Leu Asp Asp Ser
50 55 60

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

Gly Leu Arg Ala Val Asp Thr Gly Leu Tyr Ile Cys Thr Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asp Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 45
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1303

<400> 45

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

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

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

Gly Leu Arg Ala Arg Asp Thr Gly Leu Tyr Ile Cys Gln Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 46
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1114

<400> 46

Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Arg
1 5 10 15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

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

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

Gly Leu Arg Ala Lys Asp Thr Gly Leu Tyr Ile Cys Gln Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 47

<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 1227

<400> 47

Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Ser
1 5 10 15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

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

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

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

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 48
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 0722

<400> 48

Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Val
1 5 10 15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Gly Gln Val Thr Glu Val Cys
35 40 45

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

Ile Cys Thr Gly Thr Ser Ser Gly Asn Gln Val Asn Leu Thr Ile Gln

65 70 75 80

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

Met Tyr Pro Pro Pro Tyr Tyr Arg Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 49
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 0645

<400> 49

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

Ala Ala Thr Tyr Met Met Gly Asn Glu Leu Ala Phe Pro Asp Asp Ser
50 55 60

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

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

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 50
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 0636

<400> 50

Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Ile

1 5 10 15

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

Arg Val Thr Val Leu Arg Gln Ala Gly Ser Gln Val Thr Glu Val Cys
35 40 45

Ala Ala Thr Tyr Met Lys Gly Asn Glu Ser Thr Phe Leu Asp Asp Ser
50 55 60

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

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

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Val Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 51
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 0745

<400> 51

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

Ala Ala Thr Tyr Met Met Gly Gly Glu Ser Thr Phe Leu Asp Asp Ser
50 55 60

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

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

Met Tyr Pro Pro Pro Tyr Tyr Arg Gly Val Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
        115   120

<210> 52
<211> 123
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 0673

<400> 52

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35   40   45

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

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

Leu Arg Ala Met Asp Ser Gly Leu Tyr Ile Cys Lys Val Glu Leu Met
                85   90   95

Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile Tyr
            100   105   110

Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
        115   120

<210> 53
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 0788

<400> 53

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
        35   40   45

```
Ala Ala Thr Tyr Met Met Gly Asn Glu Ser Thr Phe Leu Asp Asp Ser
    50                  55                  60

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

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

Met Tyr Pro Pro Pro Tyr Tyr Gln Gly Ile Gly Ser Gly Thr Gln Ile
            100                 105                 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
        115                 120
```

<210> 54
<211> 123
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 0701

<400> 54

```
Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Ile
1               5                   10                  15

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Glu Thr Glu Val Cys
        35                  40                  45

Ala Ala Tyr Met Val Gly Asn Glu Leu Thr Phe Leu Gly Asp Ser Ile
    50                  55                  60

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

Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu Met
                85                  90                  95

Tyr Pro Pro Pro Tyr Tyr Glu Gly Ile Gly Asn Gly Thr Gln Ile Tyr
            100                 105                 110

Val Phe Asp Pro Glu Pro Cys Pro Asp Ser Asp
        115                 120
```

<210> 55
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 Variant 0439

<400> 55

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

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

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

Ala Ala Thr Tyr Met Met Gly Ser Glu Leu Ser Thr Gln Asp Tyr Pro
50 55 60

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

Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 56
<211> 233
<212> PRT
<213> Homo sapiens

<400> 56

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
1 5 10 15

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
20 25 30

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
35 40 45

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
50 55 60

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
65 70 75 80

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
85 90 95

```
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            100                 105                 110

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        115                 120                 125

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
    130                 135                 140

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
145                 150                 155                 160

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                165                 170                 175

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            180                 185                 190

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
        195                 200                 205

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
    210                 215                 220

Lys Ser Leu Ser Leu Ser Pro Gly Lys
225                 230
```

<210> 57
<211> 233
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: Fc Variant-1

<400> 57

```
Gln Glu Pro Lys Ser Ser Asp Lys Thr His Thr Ser Pro Pro Ser Pro
1               5                   10                  15

Ala Pro Glu Leu Leu Gly Gly Ser Ser Val Phe Leu Phe Pro Pro Lys
            20                  25                  30

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
        35                  40                  45

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
    50                  55                  60

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
65                  70                  75                  80

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                85                  90                  95
```

```
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            100                 105                 110

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        115                 120                 125

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
    130                 135                 140

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
145                 150                 155                 160

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                165                 170                 175

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            180                 185                 190

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
        195                 200                 205

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
    210                 215                 220

Lys Ser Leu Ser Leu Ser Pro Gly Lys
225                 230
```

<210> 58
<211> 233
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: Fc Variant-2

<400> 58

```
Gln Glu Pro Lys Ser Ser Asp Lys Thr His Thr Ser Pro Pro Ser Pro
1               5                   10                  15

Ala Pro Glu Leu Leu Gly Gly Ser Ser Val Phe Leu Phe Pro Pro Lys
            20                  25                  30

Pro Lys Asp Thr Leu Tyr Ile Thr Arg Glu Pro Glu Val Thr Cys Val
        35                  40                  45

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
    50                  55                  60

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
65                  70                  75                  80
```

```
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                85                  90                  95

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            100                 105                 110

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        115                 120                 125

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
    130                 135                 140

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
145                 150                 155                 160

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                165                 170                 175

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            180                 185                 190

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
        195                 200                 205

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
    210                 215                 220

Lys Ser Leu Ser Leu Ser Pro Gly Lys
225                 230
```

<210> 59
<211> 233
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: Fc Variant-3

<400> 59

```
Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
1               5                   10                  15

Ala Pro Glu Phe Glu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
            20                  25                  30

Pro Lys Asp Thr Leu Tyr Ile Thr Arg Glu Pro Glu Val Thr Cys Val
        35                  40                  45

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
    50                  55                  60

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
65                  70                  75                  80
```

```
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                85                  90                  95

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            100                 105                 110

Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        115                 120                 125

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
    130                 135                 140

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
145                 150                 155                 160

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                165                 170                 175

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            180                 185                 190

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
        195                 200                 205

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
    210                 215                 220

Lys Ser Leu Ser Leu Ser Pro Gly Lys
225                 230


<210>  60
<211>  230
<212>  PRT
<213>  Artificial sequence

<220>
<223>  Synthetic sequence: Fc Variant-4

<400>  60

Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu
1               5                   10                  15

Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
            20                  25                  30

Thr Leu Tyr Ile Thr Arg Glu Pro Glu Val Thr Cys Val Val Val Asp
        35                  40                  45

Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly
    50                  55                  60
```

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn
65 70 75 80

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
85 90 95

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
100 105 110

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
115 120 125

Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn
130 135 140

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

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
165 170 175

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg
180 185 190

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
195 200 205

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
210 215 220

Ser Leu Ser Leu Gly Lys
225 230

<210> 61
<211> 61
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence: Overlap oligonucleotide for construction of hotspot mutagenesis ribosome display library

<400> 61
gagatatatc catggccgca atgcacgtgg cccagcctgc tgtggtactg gccagcagcc 60

g 61

<210> 62
<211> 80
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence:Overlap oligonucleotide for construction of hotspot mutagenesis ribosome display library

<220>
<221> misc_feature
<222> (25)..(26)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (52)..(53)
<223> n is a, c, g, or t

<400> 62
cggacctcag tggctttgcc tggsnntgca tactcacaca caaagctggc snngcctcgg 60

ctgctggcca gtaccacagc 80

<210> 63
<211> 70
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence:Overlap oligonucleotide for construction of hotspot mutagenesis ribosome display library

<400> 63
ggcaaagcca ctgaggtccg ggtgacagtg cttcggcagg ctgacagcca ggtgactgaa 60

gtctgtgcgg 70

<210> 64
<211> 70
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence:Overlap oligonucleotide for construction of hotspot mutagenesis ribosome display library

<220>
<221> misc_feature
<222> (26)..(27)
<223> n is a, c, g, or t

<400> 64
gcagatggaa tcatctagga aggtsnnctc attccccatc atgtaggttg ccgcacagac 60

ttcagtcacc 70

<210> 65
<211> 72
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence:Overlap oligonucleotide for construction of hotspot mutagenesis ribosome display library

<220>
<221> misc_feature
<222> (29)..(30)
<223> n is a, c, g, or t

<400> 65
cctagatgat tccatctgca cgggcaccnn sagtggaaat caagtgaacc tcactatcca 60

aggactgagg gc 72

<210> 66
<211> 59
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence:Overlap oligonucleotide for construction of hotspot mutagenesis ribosome display library

<220>
<221> misc_feature
<222> (18)..(19)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (42)..(43)
<223> n is a, c, g, or t

<400> 66
ggtacatgag ctccacsnng cagatgtaga gtcccgtgtc snntgccctc agtccttgg 59

<210> 67
<211> 31
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic sequence:Overlap oligonucleotide for construction of hotspot mutagenesis ribosome display library

<400> 67
gtggagctca tgtacccacc gccatactac c 31

<210> 68
<211> 124
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 polypeptide

<220>
<221> VARIANT
<222> (16)..(16)
<223> Xaa is Arg, Ile, Ser or Val

<220>
<221> VARIANT
<222> (24)..(24)
<223> Xaa is Thr or Ala

<220>
<221> VARIANT
<222> (27)..(27)
<223> Xaa is Ser or Gly

<220>
<221> VARIANT
<222> (54)..(54)
<223> Xaa is Met or Lys

<220>

<221> VARIANT
<222> (56)..(56)
<223> Xaa is Asn or Ser

<220>
<221> VARIANT
<222> (58)..(58)
<223> Xaa is Ala, Leu or Gly

<220>
<221> VARIANT
<222> (59)..(59)
<223> Xaa is Thr or Ser

<220>
<221> VARIANT
<222> (60)..(60)
<223> Xaa is Phe or Thr

<220>
<221> VARIANT
<222> (61)..(61)
<223> Xaa is Leu or Gln

<220>
<221> VARIANT
<222> (63)..(63)
<223> Xaa is Asp or Tyr

<220>
<221> VARIANT
<222> (64)..(64)
<223> Xaa is Ser or Pro

<220>
<221> VARIANT
<222> (65)..(65)
<223> Xaa is Ile, Asn or Asp

<220>
<221> VARIANT
<222> (70)..(70)
<223> Xaa is Ala or Ser

<220>
<221> VARIANT
<222> (80)..(80)
<223> Xaa is Gln or Arg

<220>
<221> VARIANT
<222> (85)..(85)
<223> Xaa is Gln, Met or Ser

<220>
<221> VARIANT
<222> (93)..(93)
<223> Xaa is Gln or His

<400> 68

```
Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly Xaa
1               5                  10                  15


Ala Ser Phe Val Cys Glu Tyr Xaa Asn Pro Xaa Lys Ala Thr Glu Val
            20                  25                  30
```

Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys
35 40 45

Ala Ala Thr Tyr Met Xaa Gly Xaa Glu Xaa Xaa Xaa Xaa Asp Xaa Xaa
50 55 60

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

Gly Leu Arg Ala Xaa Asp Thr Gly Leu Tyr Ile Cys Xaa Val Glu Leu
85 90 95

Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile
100 105 110

Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp
115 120

<210> 69
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: CTLA-4 loop 4 motif

<400> 69

Ser Thr Gln Asp Tyr Pro Asn
1 5

<210> 70
<211> 19
<212> PRT
<213> Homo sapiens

<400> 70

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
1 5 10 15

Ala Pro Glu

<210> 71
<211> 19
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: modified human IgG1 Fc region comprising hinge

<400> 71

Gln Glu Pro Lys Ser Ser Asp Lys Thr His Thr Ser Pro Pro Ser Pro
1 5 10 15

Ala Pro Glu

<210> 72
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence: FLAG 10xhis tag

<400> 72

Asp Tyr Lys Asp Asp Asp Asp Lys Ala Ala His His His His His His
1 5 10 15

His His His His
20