SEQUENCE LISTING

<110> UCB Biopharma SPRL
Oxford University Innovation Limited
The University of Adelaide

<120> GREMLIN-1 ANTAGONIST FOR THE PREVENTION AND TREATMENT OF CANCER

<130> N412703WO

<150> GB 1809946.5
<151> 2018-06-18

<150> GB 1815694.3
<151> 2018-09-26

<160> 43

<170> PatentIn version 3.5

<210> 1
<211> 184
<212> PRT
<213> Homo sapiens

<400> 1

Met Ser Arg Thr Ala Tyr Thr Val Gly Ala Leu Leu Leu Leu Leu Gly
1 5 10 15

Thr Leu Leu Pro Ala Ala Glu Gly Lys Lys Lys Gly Ser Gln Gly Ala
20 25 30

Ile Pro Pro Pro Asp Lys Ala Gln His Asn Asp Ser Glu Gln Thr Gln
35 40 45

Ser Pro Gln Gln Pro Gly Ser Arg Asn Arg Gly Arg Gly Gln Gly Arg
50 55 60

Gly Thr Ala Met Pro Gly Glu Glu Val Leu Glu Ser Ser Gln Glu Ala
65 70 75 80

Leu His Val Thr Glu Arg Lys Tyr Leu Lys Arg Asp Trp Cys Lys Thr
85 90 95

Gln Pro Leu Lys Gln Thr Ile His Glu Glu Gly Cys Asn Ser Arg Thr
100 105 110

Ile Ile Asn Arg Phe Cys Tyr Gly Gln Cys Asn Ser Phe Tyr Ile Pro
115 120 125

Arg His Ile Arg Lys Glu Glu Gly Ser Phe Gln Ser Cys Ser Phe Cys
130 135 140

Lys Pro Lys Lys Phe Thr Thr Met Met Val Thr Leu Asn Cys Pro Glu
145 150 155 160

Leu Gln Pro Pro Thr Lys Lys Lys Arg Val Thr Arg Val Lys Gln Cys
165 170 175

Arg Cys Ile Ser Ile Asp Leu Asp
180

<210> 2
<211> 139
<212> PRT
<213> Artificial Sequence

<220>
<223> Human truncated Gremlin-1 used in crystallography with N-terminal tag

<400> 2

Met Gly Ser Ser His His His His His His Ser Ser Gly Glu Asn Leu
1 5 10 15

Tyr Phe Gln Gly Ser Ala Met Pro Gly Glu Glu Val Leu Glu Ser Ser
20 25 30

Gln Glu Ala Leu His Val Thr Glu Arg Lys Tyr Leu Lys Arg Asp Trp
35 40 45

Cys Lys Thr Gln Pro Leu Lys Gln Thr Ile His Glu Glu Gly Cys Asn
50 55 60

Ser Arg Thr Ile Ile Asn Arg Phe Cys Tyr Gly Gln Cys Asn Ser Phe
65 70 75 80

Tyr Ile Pro Arg His Ile Arg Lys Glu Glu Gly Ser Phe Gln Ser Cys
85 90 95

Ser Phe Cys Lys Pro Lys Lys Phe Thr Thr Met Met Val Thr Leu Asn
100 105 110

Cys Pro Glu Leu Gln Pro Pro Thr Lys Lys Lys Arg Val Thr Arg Val
115 120 125

Lys Gln Cys Arg Cys Ile Ser Ile Asp Leu Asp
130 135

<210> 3
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Ab7326 HCDR1 combined Kabat & Chothia

<400> 3

Gly Tyr Thr Phe Thr Asp Tyr Tyr Met His
1 5 10

<210> 4
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Ab7326 HCDR1 Kabat

<400> 4

Asp Tyr Tyr Met His
1 5

<210> 5
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Ab7326 HCDR2 Kabat

<400> 5

Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe Gln
1 5 10 15

Gly

<210> 6
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Ab7326 HCDR3 Kabat

<400> 6

Asp Ala Arg Gly Ser Gly Ser Tyr Tyr Pro Asn His Phe Asp Tyr
1 5 10 15

<210> 7
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Ab7326 LCDR1 Kabat

<400> 7

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

Ala

<210> 8
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Ab7326 LCDR2 Kabat

<400> 8

Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 9
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<223> Ab7326 LCDR3 Kabat

<400> 9

Gln Gln Tyr Tyr Asp Thr Pro Thr
1 5

<210> 10
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Ab7326 Heavy chain variable region variant 1

<400> 10

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

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

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

Gly Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe
50 55 60

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

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

Ala Thr Asp Ala Arg Gly Ser Gly Ser Tyr Tyr Pro Asn His Phe Asp
100 105 110

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

<210> 11
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Ab7326 Light chain variable region variant 1

<400> 11

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

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

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

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

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

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

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

<210> 12
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Ab7326 Heavy chain variable region variant 2

<400> 12

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

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

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

Gly Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe
50 55 60

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

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

Ala Thr Asp Ala Arg Gly Ser Gly Ser Tyr Tyr Pro Asn His Phe Asp
100 105 110

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

<210> 13
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Ab7326 Light chain variable region variant 2

<400> 13

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

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

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

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

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

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

Tyr Tyr Asp Thr Pro Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys

100 105 110

<210> 14
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse full length IgG1 heavy chain variant 1

<400> 14

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

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

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

Gly Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe
50 55 60

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

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

Ala Thr Asp Ala Arg Gly Ser Gly Ser Tyr Tyr Pro Asn His Phe Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Lys Thr Thr
115 120 125

Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn
130 135 140

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

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

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

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
195 200 205

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
210 215 220

Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser
225 230 235 240

Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu
245 250 255

Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro
260 265 270

Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala
275 280 285

Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val
290 295 300

Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe
305 310 315 320

Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr
325 330 335

Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile
340 345 350

Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys
355 360 365

Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp
370 375 380

Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp

385 390 395 400

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

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

Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
435 440 445

<210> 15
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse full length IgG1 light chain variant 1

<400> 15

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

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

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

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

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

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

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

Arg Thr Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
115 120 125

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

Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
145 150 155 160

Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
165 170 175

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

Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
195 200 205

Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
210 215

<210> 16
<211> 454
<212> PRT
<213> Artificial Sequence

<220>
<223> Human full length IgG1 heavy chain variant 2

<400> 16

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

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

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

Gly Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe
50 55 60

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

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

Ala Thr Asp Ala Arg Gly Ser Gly Ser Tyr Tyr Pro Asn His Phe Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
355 360 365

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
370 375 380

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
385 390 395 400

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

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

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

Ser Leu Ser Pro Gly Lys
450

<210> 17
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Human full length IgG1 light chain variant 2

<400> 17

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

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

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

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

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

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

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

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

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

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

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

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

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

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

<210> 18
<211> 227

<212> PRT
<213> Artificial Sequence

<220>
<223> Fab heavy chain variant 1

<400> 18

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

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

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

Gly Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe
50 55 60

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

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

Ala Thr Asp Ala Arg Gly Ser Gly Ser Tyr Tyr Pro Asn His Phe Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125

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

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

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

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

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

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

Lys Ser Cys
225

<210> 19
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Fab light chain variant 1

<400> 19

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

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

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

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

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

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

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

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

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

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

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

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

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

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

<210> 20
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Human truncated Gremlin-1 used in crystallography without N-terminal tag

<400> 20

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

Val Thr Glu Arg Lys Tyr Leu Lys Arg Asp Trp Cys Lys Thr Gln Pro
20 25 30

Leu Lys Gln Thr Ile His Glu Glu Gly Cys Asn Ser Arg Thr Ile Ile
35 40 45

Asn Arg Phe Cys Tyr Gly Gln Cys Asn Ser Phe Tyr Ile Pro Arg His
50 55 60

Ile Arg Lys Glu Glu Gly Ser Phe Gln Ser Cys Ser Phe Cys Lys Pro
65 70 75 80

Lys Lys Phe Thr Thr Met Met Val Thr Leu Asn Cys Pro Glu Leu Gln
85 90 95

Pro Pro Thr Lys Lys Lys Arg Val Thr Arg Val Lys Gln Cys Arg Cys
100 105 110

Ile Ser Ile Asp Leu Asp
115

<210> 21
<211> 160
<212> PRT
<213> Artificial Sequence

<220>
<223> Mature Gremlin-1 sequence of SEQ ID NO: 1 lacking the signal peptide of amino acids 1-21

<400> 21

Lys Lys Lys Gly Ser Gln Gly Ala Ile Pro Pro Pro Asp Lys Ala Gln
1 5 10 15

His Asn Asp Ser Glu Gln Thr Gln Ser Pro Gln Gln Pro Gly Ser Arg
20 25 30

Asn Arg Gly Arg Gly Gln Gly Arg Gly Thr Ala Met Pro Gly Glu Glu
35 40 45

Val Leu Glu Ser Ser Gln Glu Ala Leu His Val Thr Glu Arg Lys Tyr
50 55 60

Leu Lys Arg Asp Trp Cys Lys Thr Gln Pro Leu Lys Gln Thr Ile His
65 70 75 80

Glu Glu Gly Cys Asn Ser Arg Thr Ile Ile Asn Arg Phe Cys Tyr Gly
85 90 95

Gln Cys Asn Ser Phe Tyr Ile Pro Arg His Ile Arg Lys Glu Glu Gly
100 105 110

Ser Phe Gln Ser Cys Ser Phe Cys Lys Pro Lys Lys Phe Thr Thr Met
115 120 125

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

Arg Val Thr Arg Val Lys Gln Cys Arg Cys Ile Ser Ile Asp Leu Asp
145 150 155 160

<210> 22
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IgG4P heavy chain variant 1

<400> 22

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

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

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

Gly Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe
50 55 60

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

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

Ala Thr Asp Ala Arg Gly Ser Gly Ser Tyr Tyr Pro Asn His Phe Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125

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

Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro

145 150 155 160

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

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

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn
195 200 205

Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser
210 215 220

Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln
260 265 270

Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile
325 330 335

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

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

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

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

Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

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

Leu Gly Lys
450

<210> 23
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IgG4P light chain variant 1

<400> 23

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

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

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

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

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

Ile Asn Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Phe Cys Gln Gln

85 90 95

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

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

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

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

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

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

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

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

<210> 24
<211> 1362
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IgG1 heavy chain DNA variant 1

<400> 24
caagtgcaac tggtggaatc cggggccgaa gtgaaaaagc ccggagccac tgtgaagatc 60

tcttgcaaag tgtccggcta caccttcacc gactattaca tgcactgggt ccagcaggca 120

cctgggaagg gccttgagtg gatgggtctg gtcgatcccg aggacggcga aactatctac 180

gccgagaagt tccagggtcg cgtcaccatc accgccgaca cttccaccga caccgcgtac 240

atggagctgt ccagcttgag gtccgaggac acagccgtgt actactgcgc cacggatgct 300

cggggaagcg gcagctacta cccgaaccac ttcgactact ggggacaggg cactctcgtg 360

actgtctcga gcgcttctac aaagggcccc tccgtgttcc cgctcgctcc atcatcgaag 420

tctaccagcg gaggcactgc ggctctcggt tgcctcgtga aggactactt cccggagccg 480

gtgaccgtgt cgtggaacag cggagccctg accagcgggg tgcacacctt tccggccgtc 540

ttgcagtcaa gcggccttta ctccctgtca tcagtggtga ctgtcccgtc cagctcattg 600

ggaacccaaa cctacatctg caatgtgaat cacaaaccta gcaacaccaa ggttgacaag 660

aaagtcgagc ccaaatcgtg tgacaagact cacacttgtc cgccgtgccc ggcacccgaa 720

ctgctgggag gtcccagcgt ctttctgttc cctccaaagc cgaaagacac gctgatgatc 780

tcccgcaccc cggaggtcac ttgcgtggtc gtggacgtgt cacatgagga cccagaggtg 840

aagttcaatt ggtacgtgga tggcgtcgaa gtccacaatg ccaaaactaa gcccagagaa 900

gaacagtaca attcgaccta ccgcgtcgtg tccgtgctca cggtgttgca tcaggattgg 960

ctgaacggga aggaatacaa gtgcaaagtg tccaacaagg cgctgccggc accgatcgag 1020

aaaactatct ccaaagcgaa gggacagcct agggaacctc aagtctacac gctgccacca 1080

tcacgggatg aactgactaa gaatcaagtc tcactgactt gtctggtgaa ggggttttac 1140

cctagcgaca ttgccgtgga gtgggaatcc aacggccagc cagagaacaa ctacaagact 1200

acccctccag tgctcgactc ggatggatcg ttcttccttt actcgaagct caccgtggat 1260

aagtcccggt ggcagcaggg aaacgtgttc tcctgctcgg tgatgcatga agccctccat 1320

aaccactata cccaaaagtc gctgtccctg tcgccgggaa ag 1362

<210> 25
<211> 657
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IgG1 light chain DNA variant 1

<400> 25
gacattgtga tgacccagtc ccccgattcg cttgcggtgt ccctgggaga acgggccacc 60

attaactgca agagctcaca gtccgtcctg tattcatcga acaacaagaa ttacctcgca 120

tggtatcagc agaagcctgg acagcctccc aagctgctca tctactgggc tagcacccgc 180

gaatccgggg tgccggatag attctccgga tcgggttcgg gcactgactt cactctgact 240

atcaactcac tgcaagccga ggatgtcgcg gtgtacttct gtcagcagta ctacgacacc 300

ccgacctttg gacaaggcac cagactggag attaagcgta cggtggccgc tccctccgtg 360

ttcatcttcc caccctccga cgagcagctg aagtccggca ccgcctccgt cgtgtgcctg 420

ctgaacaact tctacccccg cgaggccaag gtgcagtgga aggtggacaa cgccctgcag 480

tccggcaact cccaggaatc cgtcaccgag caggactcca aggacagcac ctactccctg 540

tcctccaccc tgaccctgtc caaggccgac tacgagaagc acaaggtgta cgcctgcgaa 600

gtgacccacc agggcctgtc agccccgtg accaagtcct tcaaccgggg cgagtgc 657

<210> 26
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IgG4P heavy chain DNA variant 1

<400> 26
caagtgcaac tggtggaatc cggggccgaa gtgaaaaagc ccggagccac tgtgaagatc 60

tcttgcaaag tgtccggcta caccttcacc gactattaca tgcactgggt ccagcaggca 120

cctgggaagg gccttgagtg gatgggtctg gtcgatcccg aggacggcga aactatctac 180

gccgagaagt tccagggtcg cgtcaccatc accgccgaca cttccaccga caccgcgtac 240

atggagctgt ccagcttgag gtccgaggac acagccgtgt actactgcgc cacggatgct 300

cggggaagcg gcagctacta cccgaaccac ttcgactact ggggacaggg cactctcgtg 360

actgtctcga gcgcttctac aaagggcccc tccgtgttcc ctctggcccc ttgctcccgg 420

tccacctccg agtctaccgc cgctctgggc tgcctggtca aggactactt ccccgagccc 480

gtgacagtgt cctggaactc tggcgccctg acctccggcg tgcacacctt ccctgccgtg 540

ctgcagtcct ccggcctgta ctccctgtcc tccgtcgtga ccgtgccctc ctccagcctg 600

ggcaccaaga cctacacctg taacgtggac cacaagccct ccaacaccaa ggtggacaag 660

cgggtggaat ctaagtacgg ccctccctgc ccccccctgcc ctgcccctga atttctgggc 720

ggaccttccg tgttcctgtt cccccccaaag cccaaggaca ccctgatgat ctcccggacc 780

cccgaagtga cctgcgtggt ggtggacgtg tcccaggaag atcccgaggt ccagttcaat 840

tggtacgtgg acggcgtgga agtgcacaat gccaagacca agcccagaga ggaacagttc 900

aactccacct accgggtggt gtccgtgctg accgtgctgc accaggactg gctgaacggc 960

aaagagtaca agtgcaaggt gtccaacaag ggcctgccct ccagcatcga aaagaccatc 1020

tccaaggcca agggccagcc ccgcgagccc caggtgtaca ccctgccccc tagccaggaa 1080

gagatgacca agaaccaggt gtccctgacc tgtctggtca agggcttcta cccctccgac 1140

attgccgtgg aatgggagtc caacggccag cccgagaaca actacaagac cacccccccct 1200

gtgctggaca gcgacggctc cttcttcctg tactctcggc tgaccgtgga caagtcccgg 1260

tggcaggaag gcaacgtctt ctcctgctcc gtgatgcacg aggccctgca caaccactac 1320

acccagaagt ccctgtccct gagcctgggc aag 1353

<210> 27
<211> 657
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IgG4P light chain DNA variant 1

<400> 27
gacattgtga tgacccagtc ccccgattcg cttgcggtgt ccctgggaga acgggccacc 60

attaactgca agagctcaca gtccgtcctg tattcatcga acaacaagaa ttacctcgca 120

tggtatcagc agaagcctgg acagcctccc aagctgctca tctactgggc tagcacccgc 180

gaatccgggg tgccggatag attctccgga tcgggttcgg gcactgactt cactctgact 240

atcaactcac tgcaagccga ggatgtcgcg gtgtacttct gtcagcagta ctacgacacc 300

ccgacctttg gacaaggcac cagactggag attaagcgta cggtggccgc tccctccgtg 360

ttcatcttcc caccctccga cgagcagctg aagtccggca ccgcctccgt cgtgtgcctg 420

ctgaacaact tctacccccg cgaggccaag gtgcagtgga aggtggacaa cgccctgcag 480

tccggcaact cccaggaatc cgtcaccgag caggactcca aggacagcac ctactccctg 540

tcctccaccc tgaccctgtc caaggccgac tacgagaagc acaaggtgta cgcctgcgaa 600

gtgacccacc agggcctgtc cagccccgtg accaagtcct tcaaccgggg cgagtgc 657

<210> 28
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse full length IgG1 heavy chain variant 2

<400> 28

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

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

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

Gly Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe
50 55 60

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

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

Ala Thr Asp Ala Arg Gly Ser Gly Ser Tyr Tyr Pro Asn His Phe Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Lys Thr Thr
115 120 125

Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn
130 135 140

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

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

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

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
195 200 205

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
210 215 220

Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser
225 230 235 240

Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu
245 250 255

Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro
260 265 270

Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala
275 280 285

Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val
290 295 300

Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe
305 310 315 320

Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr
325 330 335

Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile
340 345 350

Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys
355 360 365

Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp
370 375 380

Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp
385 390 395 400

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

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

Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys

435 440 445

<210> 29
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse full length IgG1 light chain variant 2

<400> 29

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

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

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

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

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

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

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

Arg Thr Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
115 120 125

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

Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
145 150 155 160

Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
165 170 175

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

Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
195 200 205

Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
210 215

<210> 30
<211> 454
<212> PRT
<213> Artificial Sequence

<220>
<223> Human full length IgG1 heavy chain variant 1

<400> 30

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

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

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

Gly Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe
50 55 60

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

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

Ala Thr Asp Ala Arg Gly Ser Gly Ser Tyr Tyr Pro Asn His Phe Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
355 360 365

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
370 375 380

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
385 390 395 400

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

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

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

Ser Leu Ser Pro Gly Lys
450

<210> 31
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Human full length IgG1 light chain variant 1

<400> 31

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

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

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

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

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

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

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

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

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

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

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

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

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

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

<210> 32
<211> 227
<212> PRT
<213> Artificial Sequence

<220>
<223> Fab heavy chain variant 2

<400> 32

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

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

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

Gly Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe
50 55 60

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

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

Ala Thr Asp Ala Arg Gly Ser Gly Ser Tyr Tyr Pro Asn His Phe Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125

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

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

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

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

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

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

Lys Ser Cys
225

<210> 33
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Fab light chain variant 2

<400> 33

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

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

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

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

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

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

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

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

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

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

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

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

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

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

<210> 34
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IgG4P heavy chain variant 2

<400> 34

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

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

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

Gly Leu Val Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Glu Lys Phe
50 55 60

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

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

Ala Thr Asp Ala Arg Gly Ser Gly Ser Tyr Tyr Pro Asn His Phe Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125

Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu

130 135 140

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

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

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

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn
195 200 205

Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser
210 215 220

Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln
260 265 270

Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile
325 330 335

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

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

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

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

Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

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

Leu Gly Lys
450

<210> 35
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IgG4P light chain variant 2

<400> 35

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

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

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

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

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr

65 70 75 80

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

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

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

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

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

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

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

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

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

<210> 36
<211> 16654
<212> DNA
<213> Homo sapiens

<400> 36
actcggtgcg ccttccgcgg accgggcgac ccagtgcacg gccgccgcgt cactctcggt 60

cccgctgacc ccgcgccgag ccccggcggc tctggccgcg gccgcactca gcgccacgcg 120

tcgaaagcgc aggccccgag gacccgccgc actgacaggt gagcgcggac gcacccggca 180

gggatgtgag tgggcggagg gaagagggcc gcaaaccaac ccaggacccg ctcagttcca 240

cgcgcggcag ccctccgtgc gcgcaggctc gggtgcgttg ttcgcggggg tgaattgtga 300

agaaccatcg cggggtcctt cctgctgagg ccgcggacac cgtgacctcg ctgctctggg 360

tctgcaggga aacgtaggaa aaaaagttgt caggagcggg caggatgacc cccacatccc 420

gtttccacct cccggaggcc cccgaacacg ctcctggtgc tggtggcagc agcgcctggc 480

agacgcgccc gcttagcgag ggcgcgaagt ccaggccgcc agagcgcagg agcatccgga 540

cctgctagtc ggccgctgac tgcgcggcga gttgccttga gagggtccca tgtgcttggg 600

gcgccgcgct gggtctgggg gcgtcttggg gcgcccattg gagtccgcgg gttggagcat 660

ccggagaatc catgatgtgt gcatttgccg atccccgagg tgagatggag actggcaagg 720

gcagagccgc tgtgttcagc cacagcggaa aaccgaacgg tgggtaatcc gacagctgcg 780

gtgcggggcg cggccctggc cgcggggtcc agcgaacccg cagtgctcac aaggcagaca 840

ccacacgcgc tcgcggaccg gccacgcact cgcgggcgct cgcttctcta ctccagcctc 900

ttccccgccc cgcgcacgcc cgagctgaat ggtagacgtt ctggcgccgg gcagcggcca 960

ccggctggtt cccacttccg cgcgcacccc ttaaactgtg ttctagaggc cccagcctcg 1020

ccttgcagcg cctcactagc tcctgaggac tagggactgg cggctgaggc gggttggcgg 1080

ctgcaacgag ctgggcgtct ttcgttctct ctcgctgcct ggctggctcc gctggcccct 1140

ccacagcttg cggagcaagg ccatagcagg ggagtgggag gtatattggg gctgtcacct 1200

ccttgctggc cggagttatt tgtagactac agactccgga agaacagacg cgccaccgct 1260

ctcgcttggc attgccttcg gatcgcagct cctccttggg ggtgccccag cttggcgttt 1320

atttgcctgc gccaggctct ggcgacggtc accgggccag gcggggaggg acggacggca 1380

ggtgaccagc ctctgctgtg aagaaattcc tgcgcgcccg gagctgtccc taatgcattc 1440

ccgggtcgaa tccgtctact gccttcccct cctcgaccga ctccgaatct cggctcttat 1500

agacagaaat acagcctcag cgttaggggt taaaatcccc ctcttaaacg gtccgagggc 1560

agagaggtga ccaccgatag gtaattggat ctcctgctgg aaagagcaaa tctgagcggt 1620

gtgcgcgtct gtttatgttc cccttcgaga tggtgccagg acacgaactg attaaaacaa 1680

tctattgtgt taagtgggtc actagggttt taagctgtcc cagggacccc agagtagtgg 1740

cttccttctg gctgtacaca caagttaaat aaatagcgta gaagaggtta agataacccc 1800

attctagggt gaggagtcct ctttcatccc tagggcttcc ccctcccctt ttctcttttt 1860

ttggaaggag ggggagcatg agagtcttga gggggggatg tacttttcaa agcaaggagg 1920

gaaagatctt aagaaaacta tatattctca ctgcccccca agccaagtct ataacagtag 1980

gtgatttgat tactatctct ggataaatgg cactgtcaaa ttgttaatat taactatttc 2040

agggatttt agcagggtag tggcagtatg tgtgcgtgtg tgtgtgtgtg tctgtgtgtg 2100

tgtgtttaac ctccaggtca ttgtaggaat tagagtcttt tgtaaacttt gtaatttcac 2160

aggtttccta ttttcttaaa agttcatttt tagtgaaatg ttttggtaac ccacgctctg 2220

taggaaatcc aggttggcta atgcggtctt tatgtgagta gttacacagg gaaggataaa 2280

aacctttat gtcctacatc tctgaatgag ggctgcctac cctgtctttg aaactaagcc 2340

gaagatgcct tcagtctgaa tggtcaagta ttaaaagtga taaaatgcaa agaaatttca 2400

tgccgcagac acctcccca agaactgctt gttgacagca aagctgtgga acatgttcca 2460

caacagagag taaaggacag ccaggaaata taaacctttt atgtaaagga aaggcaggtg 2520

ggggacagtg gttaggggag gtgactgcag cctctaacca aaaggcaacc atcaggcaag 2580

tgctaccagc ccgtgtcttc gatctgcaag gaattttctt tagttttaac atatgctctt 2640

agaaattcaa agtacaacag gaattcctgg gacaagagaa atctttttat tcacatgtga 2700

acatgaagat acaaaataga taattatttt atttatagca ctcttcaaat tgtattgcat 2760

tagaaaacat atccattgac ccactgttaa ggacagcact gggtgtcaat aggacagtgg 2820

ttaaggacct gtgtttgggg ctagatagaa ttgggtttaa actgctggct gggctgggca 2880

cagtggctca caccggtaat cccagcactt tgggaggcca aggaggacgg atcacctgag 2940

gtcgggagtt cgacaccagc ctgaccaaca tggaaaaatc ccgtctctac taaaaacaca 3000

aaattagcca ggcatggtgg tgcatgcctg caatcccagc tacttgggag gctgaggcag 3060

gagaattgct tgaaaccggg aggcggaggt tgtggtgagc ccagatagcg ccattgcatt 3120

ccagcctggg caacacgagt gaaaactccg tcaaaaaaac aaaacaaaac aaacaaacaa 3180

aaaaatgctg gctttcccac ttatgagctg tgtgaccttg gacaaatttc caacttttct 3240

gagtgtagat tccctgattg gtaaaaggaa gatgatatta tctacctcat attttgttat 3300

gaaaaataaa tgataaaatt gggtcagaaa tcagcataat gcctggcaca gtaagggctt 3360

caaaataaaa ggtagctctt attattagta atggtgttag gaaaagtagc aatgttatac 3420

agaaccagga tatatcacag ggcagttctg aaattaaatc ctgaatcctg gccgggtgag 3480

gtggctcacg cttgtaatcc taagcacttt cggagactga ggcaggcgga tcacgaggtc 3540

aggagtttga gaccagcctg gccaacacac tgaaatcccg tctctactaa aaatacaaaa 3600

attagctggg tgtggtggca ggcgcctata atctcagcta cttgggaggc tgaggcagga 3660

gaatcacttg agcccaggag gcggaggttg cagtgagctg atatcgtgcc agtgcactcc 3720

agcctgggtg acatctctta aaaaaaaaaa tcctgaatac cacactacgc agtgactaac 3780

acatctttca ctacagaaca gaacctgtaa cttggccgtc tctcagcagt gctgctcagt 3840

gaacatttaa taatttatta ctttctaact cgtttcttgt tgacctcaag aattgtacat 3900

agtcattaac tttcctaaga aaatctttga caaacataga gctcctgaga tatttcacaa 3960

ccaggtggtc tcctccctgt cctatgcaat gttgggcccc agcctgattt agccgacctg 4020

gtcttcagac ttgagaggct gtttagggtt cttacaacac aaaggggatg agactttatc 4080

ctctacctgt gtgccaacaa gggattcttc ttatctcctt ggtgcaactt gtctgaaaaa 4140

gaaagtcaac acaattatct tcttaaaagt taaagatcaa attaaaaata agctatagtt 4200

ttcccaaaga tttagacctg agaaaaagga atagatcttt ctaaaacctg gcctgcactt 4260

agagcatttg tagtcacttc cactatttct tatgctgaga gaataatttg atgtcatgcc 4320

tattgaatgt ctttctaaag cttgattcat caggaggaac tgaccagaag tccatgcaca 4380

gacatttggc tttcactgta attcctactc aaaactccct ttcactgatt atgagcaggt 4440

tgcttagcta aaatgagaaa tacagcaaga agagggatgg aaagagctgg cttaaacttt 4500

cccaaagaca tcatgaacac tgggaacagg tcatacatat accattttta tttctcagtc 4560

ctcagtatta gaatattgtg ttcctagagg ctttgtgaaa attggaatac attgccatga 4620

cctgcacagg atagaggtgg ttaatatggc ttaccttgct tgtagatgtt tactcttgat 4680

ccctaaggga aactggaagg aaagcatgct gtagagagga cctgctttga gagtatgtgt 4740

cctctgggac aagtggaatg aaagagagga tagaggcaaa gagaaaaaaa ggtggagatg 4800

gggtgagact tgctggtgga cagttgcaaa gaaaactcat gatgagaata acatcacatt 4860

tcttgaagaa gctgaactgc attgatggga agttgaggca gagtttgaaa agaagatata 4920

ctgtctgcaa aaaagaatca acggagatgt caggtatctt gatgcaccct gagtctatga 4980

gatgcagctt aatttaattt aatgatatga gtaggccatt tcataagtgg tggaaattac 5040

cataaagtgt ttgcagctaa tgacggcgca tgaatgatgt cataggaacc taagtctgga 5100

tgagctatgg attgaatttt tactatggga cacccttcta catgttgctg tggaaaagaa 5160

ttgtcctcaa gaaatgtaca tcttctgcat ttcctctaca tctctgatat ttacaaagtg 5220

cacattattt ggtgatacta caactgggat ttcaagtgca catcactact atttccttca 5280

ctgaagaatc aagagcagtc tgggggtggg gagagcttga gtgattgaca aggatgtggc 5340

agagccctgg ttccactatg aattatagtt cttaccctgc ttactgtcac tcatgtagag 5400

cagctagtgt gcctcagagc actgctgttc tctgagaagc tgaggtctcg attgacattc 5460

ttgaagttgg tgtttacttc tctctgaata aacaaaggtt ggcaactcag acatcttaca 5520

ataagtacta aagatttttg aagaataggt ttttaaaaaa tgaaaaaaca tttcactttc 5580

catagctaat aaatcttatt ttgaggaaaa tgtacttttc tttaaaaaaa aaaaaagcct 5640

gtctgtcact ctagaccctt tggcttagaa ggtaggcaca ctcacataga aacagaaagt 5700

ctgtccaaat taaaactgaa aaccacagtt gactaatttt gaatttatag ctctgctgtt 5760

ggcttctgcg atagtattaa tttcaatggc ttcaattaga aaatgaaacc catagcattc 5820

catatgagaa caggtaaaaa gtcagggaca tttggagttt tccaagaaaa agaaagacaa 5880

gtcttaggaa gctctctagg atggaaggaa tttgccacac tgagagttag acatccaaag 5940

gatagcaatt ggctcttctg ctcatgggca ctggtgaagg cattttaaaa tgcgaagaat 6000

ggtacctctg taaatcaatg aggttcataa taatcatgca tttaccaaat ttttataagc 6060

acctgccttg tgccaggcac tgagggtaag gtgatgaata agccctcatc aactgtcaga 6120

ctagatattt actcaataac agatgtgaaa atgccaagaa ggaaaagttg agtataaaga 6180

aagccttaag ttggttcaga gaaataaaat tgcatttttc ggatagatgt ttatggaatc 6240

ggccttatga ggtaaacttg tcctatgcag tgaacataca ttcccagtta gtctcagatt 6300

ggcctctgtg atgacaaact cagagggtcc tggtctagga ggggtgaatt tgtctggagg 6360

ccatttttcag gaggtatgga ggaagactgg ggcataggcc tggggccatc ccatgtactc 6420

ctcctctgaa atggggagca actgaattgt gttttatttt agatcttcgt ccaacttgaa 6480

taccagaaat tcgtgaaacc ttctcaaatt cacactatat tttgagacca ggagaaggct 6540

ccttgagaaa ttgccacact gtcttatcct agtctctgga aaaattcagt cctgtattat 6600

aactgggcgt ttctcataag tgctttttt ttttcttttt ctttttataa tactttaagt 6660

tctgggatac atgtgcagaa tgtgcaggtt tgttacatag gtatacacgt gccatggtgg 6720

tttgctgcac ccatcaaccc atcatctaca ttaggtattt ctcctaatgc tacccccttcc 6780

ctagcccccc acccctcgac aggccccagt gtttgatgtt cccctccctg tgtccatgtg 6840

ttctcattgt tcaactccca cttatgagtg agagcatgcg gtgtttggtt ttctgttcct 6900

gtgttagttt gctgagaatg atggtttttg gcttcatcca cgtccctgca aaggacatga 6960

actcatcctt tttatggctg catagtattc catggtgtat atgtgccaca tttgctttat 7020

ccagtctatc attgatgagc acttgggttg gctccaagtc tttgctatta tgactagtac 7080

tgcgataaac atgtgtatat gtgtctttat attagaatga tttataatcc tttaggtcta 7140

tacccagtaa taggattcct gggtcaaatg gtatttctgg ttctagatcc ttgaggaatt 7200

gccacactgt cttccacaac ggttgaacta atttacactc ccaccaacag tgtaaaagca 7260

ttcctatttc tccacatcct ctccaacatc tgttgtttcc tgactcttta atgacggcca 7320

ttctaactgg cgtgaaatgg tatctcattg tggttttgat ttgcatttct ctaatgacca 7380

ccgatgatga gctttttctc atatgtttgc tggccccata aatgtcttct tttgagaaat 7440

gtctgttcat atcctttgcc cacttttga tggggttgtt tgctttttc ttgtaaattt 7500

gtttgagttc ctggtagatt ctggatatta gccctttgtc agatggatag actgcaaaaa 7560

ttttctccca ttctgtaggt tgcctgttca ctctgatggt agtttctttt gccatgcaga 7620

agctgtttag tttaattaga tccaatttgt cagttttggc ttttgttgcc attgcttttg 7680

gtgttttagt catgaagtct ttgcccatgc ctatgtcctg aattgtattg ccctggtttt 7740

cttctaggat ttttatggtt ttaggtctta catttaagtc tttaatccat cttgaattaa 7800

tttttgtata aggtgtaagg aaagggtcca gtttcagttt tctgcgtatg gctagccagt 7860

tttcccaacg ttatttatta aatagggaat cctttcccca ttgcttgttt ttgtcaggtt 7920

tgtcaaagat cagacggttg tagatgtgtg gtgttatttc tgaggcctct gttctgttcc 7980

attggtctgt atatctgctt tgataccagt accgtgctgt tttggttact gtagccttgt 8040

agtacagttt gaagtcaggt agcgtgatgc tttgttcttt ttgcttagga ttgtcttggc 8100

tatatgggct ctttttggt tctatatgaa atttaaagta gtttttcat agacatctat 8160

agaactctcc accccaaatc aacagaatat acattcttct cagtatcgca tcacacttat 8220

tctaaaatga ccacataatt agaagtaaaa cactcctcag caaatgcaaa aaacagaaat 8280

cctaacagtc tgtcagaccc cagtgcaatc aaattagaac tcaggattaa gaaacttact 8340

gaaaaccaca caactgcatg gaaactgaac aacctgctcc tgaatgacta ctgggtaaat 8400

aacaaaatta aggcagaaat aaataggttc tttgaaagaa atgagaacaa agacacaata 8460

taccagaatc tctgggacac agctaaagca gtgtttagag ggaaattgat agcactaaat 8520

gcccacagga gaaagcggga cagatctaaa atcgacaccc taatatcaca attaaaagaa 8580

ctagagaaac aagagcaaac aaattcaaaa gctagcagaa gacaagaaat aactaagatc 8640

agagcagaac tgaaggagat agagacacaa aaaacccttc aaaaaatcaa tgaatccagg 8700

agctgttttt ttttttttga aaagattaat gaaatagact gctagccaaa ctaataaagg 8760

agaaaagaga gaagaatcaa atagacaata gacacaataa aaagtgataa aggggatatc 8820

accactgatc ccacagaaat acaaactacc atcagagaat actataaaca cctctacgca 8880

aataaactag aaaattggga agaaatggat acattcctga acgcatacac cctcccaaga 8940

ctaaaccagg aagaagttga atccctgaat agaccaatag caagttctga aattgaggca 9000

gtaattagta gcctaccaac caaaaaaagc ccaggaccag acagattcac agccgaagtc 9060

taccagaggt acaaagagga gctagtacca ttccttctga aactattcca aacaatagaa 9120

aaagaaggac tcctccctaa ctcattttat gaggccagca tcatcctgat accaaaacct 9180

ggcagagaca caacataaag gaaattcagg ccaatatccc tgatgaacat tgatgtgaaa 9240

atcctcaata aaatactggc agcacatcaa aaagcttacc tgccatgatc aagttggctt 9300

catccctggg atgcaaggct ggttcaacat acgcaaatca ataaacgtaa tcaatcacat 9360

acacagaacc aatgacaaaa accacatgat tatctcaata gatgcagaaa aggccttcga 9420

taaaattcaa caccccttca atgctaagaa ctctcaataa actaggtatt gatgaaacat 9480

atctcaaaat aataagagtt atttatgaca aacccacagc cagtatcata ctgaatgggc 9540

aaaagctgga agcattccct ttgaaaaccg ccacaaggat gacttctctc accactccta 9600

ttcaacatac tattggaagt tctggccagg gcaagcaggc aagacaaata aataaagggt 9660

attcaaatag gaagagagga agtcaaattg tctctgtttg cagatgacat gattgtatat 9720

ttagaaaacc ccatcatctc agcccaaaat ctccttaagc tgataagcaa cttcagcaaa 9780

gtctcaggat acaaaatcaa tgtgcaaaaa tcacaagcat tcctatacac caataataga 9840

caaacagcca aatcatgagt gaactcccat tcacaagtgc tacaaagaat aaaataccta 9900

ggaatccaac ttacaaggga tgtgaaggac ctcttcaagg agaactacag accactgctc 9960

aaggtaataa gagaggacac aaacaaatgg aaaaacattc catgctcatg gataggaaga 10020

atcaatatta tgaaaatggc catactgccc aaaacaattt atagattcaa tgccatcccc 10080

atcaagctac cactgacttc cttcacagaa ttagaaaaaa actactttaa atttcatatg 10140

gaactgaaaa aagagccggt atagccaaga cgatcctaag caaaaagaaa aaagctggaa 10200

gcatcatgct acctgacttc aaactatact acaaggctac agtaacaaaa acagcatggt 10260

atagtataag tgctttttt taaaagacaa agtaaagtaa ttttttgtt gttggggtaa 10320

aacaaaagct ctgcataaag agcagggatg ttgtaacata cactgaccaa aggtgggaaa 10380

cctacagttg gagcagaagc tgaatgtcac attatcagct ccgaacttat aatggtctaa 10440

aagtactagg ttaatgttgg aaagatggtg ccatttaaag atatcttaaa ttcaatattt 10500

aattatttta atttgacatt atcctagagt tgaatggtgt ttacttacca tgtgctgttc 10560

attagaaaat ctagatccta cactgccttt gcgcaaggta gttgctctaa taataccaac 10620

ctgtccagtt ttggtgggag aaataatgtt actgttaagt tgcacttagt ggttattatg 10680

tgtaatactg gtattccaaa gagagaagga aaatgtttgc tacacagctg tgttcttagg 10740

ttcagaaaac cacaggagtg ggacaggaga accttcagga ttcaggtccg attgttgtga 10800

tggccgcagg agggagactg tgaatttgaa actgcatcca ttgaaaagaa aatccctcca 10860

cactttaata attctctccg tgccccatgg cagcaagtgc ttataggcct tgctactcaa 10920

agcttaataa aaaggcagac ctgctgaatc ataatctgca tcttaacaat atccccagat 10980

attgtctgca ctttcttttt ttttttcttt ctttctttct tctttttttt gagacagagt 11040

ctcgctcagt cacccaggct ggagtgcagt ggcgcgatct cggctcactg caagctctga 11100

ctcccgggtt cacgccattc tcctgcctta gactcccgag tagctggcac tacaggcgcc 11160

cgccactacg cccggctaat ttttttgtat ttttagtaga gatggggttt caccgtgtta 11220

gccaggatgg tctcgatctc ctgacctcgt gatccgccgc ccatctgggc ctcccaaagt 11280

gctgggatta caggcgtgag ccactgcgcc cggccaattg tctgcacttt caagtctaag 11340

aagcactgtc ccaggaggaa aatcttttta gtctgaggct tctctcttgc actctccttt 11400

ttaaaaatat gctgctcctt ctccaccttt ccctcttctt ccgccttttc tgtctgcctt 11460

tactacctcc cctgaacatt caacttgtag aagagttccc ctttctctga attgcattct 11520

tcacttcatt cattcttttc tctctctgtc tatggtttcc tatttttgt cggttttccc 11580

tcacctcacc tccttgttat tttttgccat tgttcacata tcactgccct ttcagaccca 11640

tatctagctt ctgacccatc cactaatcca ttgccactaa tttattcagc atgcccatgc 11700

catttattaa tgtaaatatt tgcacatact tgttctatca tgcccatttt tctacctttt 11760

aaattgtata tacacagaca catgtgaatg acatatttca ctatttaaaa ggtagaaaaa 11820

tgtatatcgt ggtacaaagt gatacattga gtatctgtgc ccagtttcaa gatgagaata 11880

agtgagaggt gaagcctcat gagtcacgtc acctacacgc tactgtcttt cattccatct 11940

gcagtactgc cacacatttg gttagttctc caattgctgt cacattgaca tcgagttgga 12000

tctgaacagc gtacctgggg agacgaagta ttggtatctt tgcttaaatg gagtgattta 12060

ctgagagaca aagtgacatc tttaagatca gatagcaagt tactgcacca ggagcgcgac 12120

ctttcctgtt ttgttgtttt ccctctgtca aatgccttct ggtctccatg aatctctcct 12180

tccacatatg ataaaaatgc aaagtctcat aagcattcac agctcaggaa gcctcaggct 12240

agttggggag aaaagactgg gaggtttccg gaggaatgaa gtcctctgag cagagaggtt 12300

aattcatctt gctgtaaaac aaaatagaaa ataagttccc ctcaataagt gaacgtaata 12360

caaagacaaa tgtggttggt gccagaggcc aggaagaagt tcttgtgaga ataggtgcag 12420

agaagagcta ggccctggct gagtttaaac cttgacttag tcactgtggg actctgggtg 12480

agttactcca tggattgatg gctgggtcat ggagataata gtacctaatt catacaggta 12540

ctgtgagaag taaatggaat atttcacgtt aagtgtttaa cggtgcgttt aaatgctagg 12600

tgctattatt attaattttt aaattaactt tgccatgttt tgtgtcttcc cctctctgtg 12660

cttccтttct ttagtatgag ccgcacagcc tacacggtgg gagccctgct tctcctcttg 12720

gggaccctgc tgccggctgc tgaagggaaa aagaaagggt cccaaggtgc catccccccg 12780

ccagacaagg cccagcacaa tgactcagag cagactcagt cgccccagca gcctggctcc 12840

aggaaccggg ggcggggcca agggcggggc actgccatgc ccggggagga ggtgctggag 12900

tccagccaag aggccctgca tgtgacggag cgcaaatacc tgaagcgaga ctggtgcaaa 12960

acccagccgc ttaagcagac catccacgag gaaggctgca acagtcgcac catcatcaac 13020

cgcttctgtt acggccagtg caactctttc tacatcccca ggcacatccg gaaggaggaa 13080

ggttcctttc agtcctgctc cttctgcaag cccaagaaat tcactaccat gatggtcaca 13140

ctcaactgcc ctgaactaca gccacctacc aagaagaaga gagtcacacg tgtgaagcag 13200

tgtcgttgca tatccatcga tttggattaa gccaaatcca ggtgcaccca gcatgtccta 13260

ggaatgcagc cccaggaagt cccagaccta aaacaaccag attcttactt ggcttaaacc 13320

tagaggccag aagaaccccc agctgcctcc tggcaggagc ctgcttgtgc gtagttcgtg 13380

tgcatgagtg tggatgggtg cctgtgggtg tttttagaca ccagagaaaa cacagtctct 13440

gctagagagc actccctatt ttgtaaacat atctgcttta atggggatgt accagaaacc 13500

cacctcaccc cggctcacat ctaaaggggc ggggccgtgg tctggttctg actttgtgtt 13560

tttgtgccct cctggggacc agaatctcct ttcggaatga atgttcatgg aagaggctcc 13620

tctgagggca agagacctgt tttagtgctg cattcgacat ggaaaagtcc ttttaacctg 13680

tgcttgcatc ctccttttcct cctcctcctc acaatccatc tcttcttaag ttgatagtga 13740

ctatgtcagt ctaatctctt gtttgccaag gttcctaaat taattcactt aaccatgatg 13800

caaatgtttt tcattttgtg aagaccctcc agactctggg agaggctggt gtgggcaagg 13860

acaagcagga tagtggagtg agaaagggag ggtggagggt gaggccaaat caggtccagc 13920

aaaagtcagt agggacattg cagaagcttg aaaggccaat accagaacac aggctgatgc 13980

ttctgagaaa gtcttttcct agtatttaac agaacccaag tgaacagagg agaaatgaga 14040

ttgccagaaa gtgattaact ttggccgttg caatctgctc aaacctaaca ccaaactgaa 14100

aacataaata ctgaccactc ctatgttcgg acccaagcaa gttagctaaa ccaaaccaac 14160

tcctctgctt tgtccctcag gtggaaaaga gaggtagttt agaactctct gcataggggt 14220

gggaattaat caaaaaccgc agaggctgaa attcctaata cctttccttt atcgtggtta 14280

tagtcagctc atttccattc cactatttcc cataatgctt ctgagagcca ctaacttgat 14340

tgataaagat cctgcctctg ctgagtgtac ctgacagtag tctaagatga gagagtttag 14400

ggactactct gttttagcaa gagatatttt gggggtcttt ttgttttaac tattgtcagg 14460

agattgggct aaagagaaga cgacgagagt aaggaaataa agggaattgc ctctggctag 14520

agagtagtta ggtgttaata cctggtagag atgtaaggga tatgacctcc ctttctttat 14580

gtgctcactg aggatctgag gggaccctgt taggagagca tagcatcatg atgtattagc 14640

tgttcatctg ctactggttg gatggacata actattgtaa ctattcagta tttactggta 14700

ggcactgtcc tctgattaaa cttggcctac tggcaatggc tacttaggat tgatctaagg 14760

gccaaagtgc agggtgggtg aactttattg tactttggat ttggttaacc tgttttcttc 14820

aagcctgagg ttttatatac aaactccctg aatactcttt ttgccttgta tcttctcagc 14880

ctcctagcca agtcctatgt aatatggaaa acaaacactg cagacttgag attcagttgc 14940

cgatcaaggc tctggcattc agagaaccct tgcaactcga gaagctgttt ttatttcgtt 15000

tttgttttga tccagtgctc tcccatctaa caactaaaca ggagccattt caaggcggga 15060

gatattttaa acacccaaaa tgttgggtct gattttcaaa cttttaaact cactactgat 15120

gattctcacg ctaggcgaat ttgtccaaac acatagtgtg tgtgttttgt atacactgta 15180

tgaccccacc ccaaatcttt gtattgtcca cattctccaa caataaagca cagagtggat 15240

ttaattaagc acacaaatgc taaggcagaa ttttgagggt gggagagaag aaaagggaaa 15300

gaagctgaaa atgtaaaacc acaccaggga ggaaaaatga cattcagaac cagcaaacac 15360

tgaatttctc ttgttgtttt aactctgcca caagaatgca atttcgttaa cggagatgac 15420

ttaagttggc agcagtaatc ttcttttagg agcttgtacc acagtcttgc acataagtgc 15480

agatttggct caagtaaaga gaatttcctc aacactaact tcactgggat aatcagcagc 15540

gtaactaccc taaaagcata tcactagcca aagagggaaa tatctgttct tcttactgtg 15600

cctatattaa gactagtaca aatgtggtgt gtcttccaac tttcattgaa aatgccatat 15660

ctataccata ttttattcga gtcactgatg atgtaatgat atatttttc attattatag 15720

tagaatattt ttatggcaag atatttgtgg tcttgatcat acctattaaa ataatgccaa 15780

acaccaaata tgaattttat gatgtacact ttgtgcttgg cattaaaaga aaaaaacaca 15840

catcctggaa gtctgtaagt tgtttttgt tactgtaggt cttcaaagtt aagagtgtaa 15900

gtgaaaaatc tggaggagag gataatttcc actgtgtgga atgtgaatag ttaaatgaaa 15960

agttatggtt atttaatgta attattactt caaatccttt ggtcactgtg atttcaagca 16020

tgttttcttt ttctccttta tatgactttc tctgagttgg gcaaagaaga agctgacaca 16080

ccgtatgttg ttagagtctt ttatctggtc aggggaaaca aaatcttgac ccagctgaac 16140

atgtcttcct gagtcagtgc ctgaatcttt attttttaaa ttgaatgttc cttaaaggtt 16200

aacatttcta aagcaatatt aagaaagact ttaaatgtta ttttggaaga cttacgatgc 16260

atgtatacaa acgaatagca gataatgatg actagttcac acataaagtc cttttaagga 16320

gaaaatctaa aatgaaaagt ggataaacag aacatttata agtgatcagt taatgcctaa 16380

gagtgaaagt agttctattg acattcctca agatatttaa tatcaactgc attatgtatt 16440

atgtctgctt aaatcattta aaaacggcaa agaattatat agactatgag gtaccttgct 16500

gtgtaggagg atgaaagggg agttgatagt ctcataaaac taatttggct tcaagtttca 16560

tgaatctgta actagaattt aattttcacc ccaataatgt tctatatagc ctttgctaaa 16620

gagcaactaa taaattaaac ctattctttc tgtg 16654

<210> 37
<211> 555
<212> DNA

<213> Homo sapiens

<400> 37
atgagccgca cagcctacac ggtgggagcc ctgcttctcc tcttggggac cctgctgccg 60

gctgctgaag ggaaaaagaa agggtcccaa ggtgccatcc ccccgccaga caaggcccag 120

cacaatgact cagagcagac tcagtcgccc cagcagcctg gctccaggaa ccgggggcgg 180

ggccaagggc ggggcactgc catgcccggg gaggaggtgc tggagtccag ccaagaggcc 240

ctgcatgtga cggagcgcaa atacctgaag cgagactggt gcaaaaccca gccgcttaag 300

cagaccatcc acgaggaagg ctgcaacagt cgcaccatca tcaaccgctt ctgttacggc 360

cagtgcaact ctttctacat ccccaggcac atccggaagg aggaaggttc ctttcagtcc 420

tgctccttct gcaagcccaa gaaattcact accatgatgg tcacactcaa ctgccctgaa 480

ctacagccac ctaccaagaa gaagagagtc acacgtgtga agcagtgtcg ttgcatatcc 540

atcgatttgg attaa 555

<210> 38
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Mouse Grem1 forward primer

<400> 38
gcgcaagtat ctgaagcgag 20

<210> 39
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Mouse Grem1 reverse primer

<400> 39
cggttgatga tagtgcggct 20

<210> 40
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Human Grem1 forward primer

<400> 40
aggcccagca caatgactca g 21

<210> 41
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Human Grem1 reverse primer

<400> 41
gtctcgcttc aggtatttgc g 21

<210> 42
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Beta-actin forward primer

<400> 42
gatcattgct cctcctgagc 20

<210> 43
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Beta-actin reverse primer

<400> 43
gtcatagtcc gcctagaagc at 22