

SEQUENCE LISTING

<110> JCR Pharmaceuticals Co., Ltd.

<120> Method of Production of Antibody-Lysosomal Enzyme Fusion Protein

<130> 1228JP

<150> JP 2021-037528

<151> 2021-03-09

<160> 42

<170> PatentIn version 3.5

<210> 1

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of an exemplified linker 1

<400> 1

Gly Gly Gly Gly Ser
1 5

<210> 2

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of an exemplified linker 2

<400> 2

Gly Gly Gly Gly Gly Ser
1 5

<210> 3

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of an exemplified linker 3

<400> 3

Ser Gly Gly Gly Gly
1 5

<210> 4
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of an exemplified linker 4

<400> 4

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

<210> 5
<211> 760
<212> PRT
<213> Homo sapiens

<400> 5

Met Met Asp Gln Ala Arg Ser Ala Phe Ser Asn Leu Phe Gly Gly Glu
1 5 10 15

Pro Leu Ser Tyr Thr Arg Phe Ser Leu Ala Arg Gln Val Asp Gly Asp
20 25 30

Asn Ser His Val Glu Met Lys Leu Ala Val Asp Glu Glu Glu Asn Ala
35 40 45

Asp Asn Asn Thr Lys Ala Asn Val Thr Lys Pro Lys Arg Cys Ser Gly
50 55 60

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

Phe Met Ile Gly Tyr Leu Gly Tyr Cys Lys Gly Val Glu Pro Lys Thr
85 90 95

Glu Cys Glu Arg Leu Ala Gly Thr Glu Ser Pro Val Arg Glu Glu Pro
100 105 110

Gly Glu Asp Phe Pro Ala Ala Arg Arg Leu Tyr Trp Asp Asp Leu Lys
115 120 125

Arg Lys Leu Ser Glu Lys Leu Asp Ser Thr Asp Phe Thr Gly Thr Ile
130 135 140

Lys Leu Leu Asn Glu Asn Ser Tyr Val Pro Arg Glu Ala Gly Ser Gln
145 150 155 160

Lys Asp Glu Asn Leu Ala Leu Tyr Val Glu Asn Gln Phe Arg Glu Phe
165 170 175

Lys Leu Ser Lys Val Trp Arg Asp Gln His Phe Val Lys Ile Gln Val
180 185 190

Lys Asp Ser Ala Gln Asn Ser Val Ile Ile Val Asp Lys Asn Gly Arg
195 200 205

Leu Val Tyr Leu Val Glu Asn Pro Gly Gly Tyr Val Ala Tyr Ser Lys
210 215 220

Ala Ala Thr Val Thr Gly Lys Leu Val His Ala Asn Phe Gly Thr Lys
225 230 235 240

Lys Asp Phe Glu Asp Leu Tyr Thr Pro Val Asn Gly Ser Ile Val Ile
245 250 255

Val Arg Ala Gly Lys Ile Thr Phe Ala Glu Lys Val Ala Asn Ala Glu
260 265 270

Ser Leu Asn Ala Ile Gly Val Leu Ile Tyr Met Asp Gln Thr Lys Phe
275 280 285

Pro Ile Val Asn Ala Glu Leu Ser Phe Phe Gly His Ala His Leu Gly
290 295 300

Thr Gly Asp Pro Tyr Thr Pro Gly Phe Pro Ser Phe Asn His Thr Gln
305 310 315 320

Phe Pro Pro Ser Arg Ser Ser Gly Leu Pro Asn Ile Pro Val Gln Thr

325

330

335

Ile Ser Arg Ala Ala Ala Glu Lys Leu Phe Gly Asn Met Glu Gly Asp
 340 345 350

Cys Pro Ser Asp Trp Lys Thr Asp Ser Thr Cys Arg Met Val Thr Ser
 355 360 365

Glu Ser Lys Asn Val Lys Leu Thr Val Ser Asn Val Leu Lys Glu Ile
 370 375 380

Lys Ile Leu Asn Ile Phe Gly Val Ile Lys Gly Phe Val Glu Pro Asp
 385 390 395 400

His Tyr Val Val Val Gly Ala Gln Arg Asp Ala Trp Gly Pro Gly Ala
 405 410 415

Ala Lys Ser Gly Val Gly Thr Ala Leu Leu Lys Leu Ala Gln Met
 420 425 430

Phe Ser Asp Met Val Leu Lys Asp Gly Phe Gln Pro Ser Arg Ser Ile
 435 440 445

Ile Phe Ala Ser Trp Ser Ala Gly Asp Phe Gly Ser Val Gly Ala Thr
 450 455 460

Glu Trp Leu Glu Gly Tyr Leu Ser Ser Leu His Leu Lys Ala Phe Thr
 465 470 475 480

Tyr Ile Asn Leu Asp Lys Ala Val Leu Gly Thr Ser Asn Phe Lys Val
 485 490 495

Ser Ala Ser Pro Leu Leu Tyr Thr Leu Ile Glu Lys Thr Met Gln Asn
 500 505 510

Val Lys His Pro Val Thr Gly Gln Phe Leu Tyr Gln Asp Ser Asn Trp
 515 520 525

Ala Ser Lys Val Glu Lys Leu Thr Leu Asp Asn Ala Ala Phe Pro Phe
 530 535 540

Leu Ala Tyr Ser Gly Ile Pro Ala Val Ser Phe Cys Phe Cys Glu Asp
545 550 555 560

Thr Asp Tyr Pro Tyr Leu Gly Thr Thr Met Asp Thr Tyr Lys Glu Leu
565 570 575

Ile Glu Arg Ile Pro Glu Leu Asn Lys Val Ala Arg Ala Ala Glu
580 585 590

Val Ala Gly Gln Phe Val Ile Lys Leu Thr His Asp Val Glu Leu Asn
595 600 605

Leu Asp Tyr Glu Arg Tyr Asn Ser Gln Leu Leu Ser Phe Val Arg Asp
610 615 620

Leu Asn Gln Tyr Arg Ala Asp Ile Lys Glu Met Gly Leu Ser Leu Gln
625 630 635 640

Trp Leu Tyr Ser Ala Arg Gly Asp Phe Phe Arg Ala Thr Ser Arg Leu
645 650 655

Thr Thr Asp Phe Gly Asn Ala Glu Lys Thr Asp Arg Phe Val Met Lys
660 665 670

Lys Leu Asn Asp Arg Val Met Arg Val Glu Tyr His Phe Leu Ser Pro
675 680 685

Tyr Val Ser Pro Lys Glu Ser Pro Phe Arg His Val Phe Trp Gly Ser
690 695 700

Gly Ser His Thr Leu Pro Ala Leu Leu Glu Asn Leu Lys Leu Arg Lys
705 710 715 720

Gln Asn Asn Gly Ala Phe Asn Glu Thr Leu Phe Arg Asn Gln Leu Ala
725 730 735

Leu Ala Thr Trp Thr Ile Gln Gly Ala Ala Asn Ala Leu Ser Gly Asp
740 745 750

Val Trp Asp Ile Asp Asn Glu Phe
755 760

<210> 6
<211> 628
<212> PRT
<213> Homo sapiens

<400> 6

Ala Glu Ala Pro His Leu Val His Val Asp Ala Ala Arg Ala Leu Trp
1 5 10 15

Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe Cys Pro Pro Leu Pro
20 25 30

His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln Leu Asn
35 40 45

Leu Ala Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val Arg
50 55 60

Thr His Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg
65 70 75 80

Gly Leu Ser Tyr Asn Phe Thr His Leu Asp Gly Tyr Leu Asp Leu Leu
85 90 95

Arg Glu Asn Gln Leu Leu Pro Gly Phe Glu Leu Met Gly Ser Ala Ser
100 105 110

Gly His Phe Thr Asp Phe Glu Asp Lys Gln Gln Val Phe Glu Trp Lys
115 120 125

Asp Leu Val Ser Ser Leu Ala Arg Arg Tyr Ile Gly Arg Tyr Gly Leu
130 135 140

Ala His Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp His
145 150 155 160

His Asp Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn Tyr

165

170

175

Tyr Asp Ala Cys Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu Arg
 180 185 190

Leu Gly Gly Pro Gly Asp Ser Phe His Thr Pro Pro Arg Ser Pro Leu
 195 200 205

Ser Trp Gly Leu Leu Arg His Cys His Asp Gly Thr Asn Phe Phe Thr
 210 215 220

Gly Glu Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu His Arg Lys Gly
 225 230 235 240

Ala Arg Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala Gln
 245 250 255

Gln Ile Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr Asn
 260 265 270

Asp Glu Ala Asp Pro Leu Val Gly Trp Ser Leu Pro Gln Pro Trp Arg
 275 280 285

Ala Asp Val Thr Tyr Ala Ala Met Val Val Lys Val Ile Ala Gln His
 290 295 300

Gln Asn Leu Leu Leu Ala Asn Thr Thr Ser Ala Phe Pro Tyr Ala Leu
 305 310 315 320

Leu Ser Asn Asp Asn Ala Phe Leu Ser Tyr His Pro His Pro Phe Ala
 325 330 335

Gln Arg Thr Leu Thr Ala Arg Phe Gln Val Asn Asn Thr Arg Pro Pro
 340 345 350

His Val Gln Leu Leu Arg Lys Pro Val Leu Thr Ala Met Gly Leu Leu
 355 360 365

Ala Leu Leu Asp Glu Glu Gln Leu Trp Ala Glu Val Ser Gln Ala Gly
 370 375 380

Thr Val Leu Asp Ser Asn His Thr Val Gly Val Leu Ala Ser Ala His
 385 390 395 400

Arg Pro Gln Gly Pro Ala Asp Ala Trp Arg Ala Ala Val Leu Ile Tyr
 405 410 415

Ala Ser Asp Asp Thr Arg Ala His Pro Asn Arg Ser Val Ala Val Thr
 420 425 430

Leu Arg Leu Arg Gly Val Pro Pro Gly Pro Gly Leu Val Tyr Val Thr
 435 440 445

Arg Tyr Leu Asp Asn Gly Leu Cys Ser Pro Asp Gly Glu Trp Arg Arg
 450 455 460

Leu Gly Arg Pro Val Phe Pro Thr Ala Glu Gln Phe Arg Arg Met Arg
 465 470 475 480

Ala Ala Glu Asp Pro Val Ala Ala Ala Pro Arg Pro Leu Pro Ala Gly
 485 490 495

Gly Arg Leu Thr Leu Arg Pro Ala Leu Arg Leu Pro Ser Leu Leu Leu
 500 505 510

Val His Val Cys Ala Arg Pro Glu Lys Pro Pro Gly Gln Val Thr Arg
 515 520 525

Leu Arg Ala Leu Pro Leu Thr Gln Gly Gln Leu Val Leu Val Trp Ser
 530 535 540

Asp Glu His Val Gly Ser Lys Cys Leu Trp Thr Tyr Glu Ile Gln Phe
 545 550 555 560

Ser Gln Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro Ser Thr
 565 570 575

Phe Asn Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly Ser
 580 585 590

Tyr Arg Val Arg Ala Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe Ser
595 600 605

Asp Pro Val Pro Tyr Leu Glu Val Pro Val Pro Arg Gly Pro Pro Ser
610 615 620

Pro Gly Asn Pro
625

<210> 7
<211> 626
<212> PRT
<213> Homo sapiens

<400> 7

Ala Pro His Leu Val His Val Asp Ala Ala Arg Ala Leu Trp Pro Leu
1 5 10 15

Arg Arg Phe Trp Arg Ser Thr Gly Phe Cys Pro Pro Leu Pro His Ser
20 25 30

Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln Leu Asn Leu Ala
35 40 45

Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val Arg Thr His
50 55 60

Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu
65 70 75 80

Ser Tyr Asn Phe Thr His Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu
85 90 95

Asn Gln Leu Leu Pro Gly Phe Glu Leu Met Gly Ser Ala Ser Gly His
100 105 110

Phe Thr Asp Phe Glu Asp Lys Gln Gln Val Phe Glu Trp Lys Asp Leu
115 120 125

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

130

135

140

Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp His His Asp
 145 150 155 160

Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp
 165 170 175

Ala Cys Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly
 180 185 190

Gly Pro Gly Asp Ser Phe His Thr Pro Pro Arg Ser Pro Leu Ser Trp
 195 200 205

Gly Leu Leu Arg His Cys His Asp Gly Thr Asn Phe Phe Thr Gly Glu
 210 215 220

Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu His Arg Lys Gly Ala Arg
 225 230 235 240

Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala Gln Gln Ile
 245 250 255

Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu
 260 265 270

Ala Asp Pro Leu Val Gly Trp Ser Leu Pro Gln Pro Trp Arg Ala Asp
 275 280 285

Val Thr Tyr Ala Ala Met Val Val Lys Val Ile Ala Gln His Gln Asn
 290 295 300

Leu Leu Leu Ala Asn Thr Thr Ser Ala Phe Pro Tyr Ala Leu Leu Ser
 305 310 315 320

Asn Asp Asn Ala Phe Leu Ser Tyr His Pro His Pro Phe Ala Gln Arg
 325 330 335

Thr Leu Thr Ala Arg Phe Gln Val Asn Asn Thr Arg Pro Pro His Val
 340 345 350

Gln Leu Leu Arg Lys Pro Val Leu Thr Ala Met Gly Leu Leu Ala Leu
355 360 365

Leu Asp Glu Glu Gln Leu Trp Ala Glu Val Ser Gln Ala Gly Thr Val
370 375 380

Leu Asp Ser Asn His Thr Val Gly Val Leu Ala Ser Ala His Arg Pro
385 390 395 400

Gln Gly Pro Ala Asp Ala Trp Arg Ala Ala Val Leu Ile Tyr Ala Ser
405 410 415

Asp Asp Thr Arg Ala His Pro Asn Arg Ser Val Ala Val Thr Leu Arg
420 425 430

Leu Arg Gly Val Pro Pro Gly Pro Gly Leu Val Tyr Val Thr Arg Tyr
435 440 445

Leu Asp Asn Gly Leu Cys Ser Pro Asp Gly Glu Trp Arg Arg Leu Gly
450 455 460

Arg Pro Val Phe Pro Thr Ala Glu Gln Phe Arg Arg Met Arg Ala Ala
465 470 475 480

Glu Asp Pro Val Ala Ala Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg
485 490 495

Leu Thr Leu Arg Pro Ala Leu Arg Leu Pro Ser Leu Leu Leu Val His
500 505 510

Val Cys Ala Arg Pro Glu Lys Pro Pro Gly Gln Val Thr Arg Leu Arg
515 520 525

Ala Leu Pro Leu Thr Gln Gly Gln Leu Val Leu Val Trp Ser Asp Glu
530 535 540

His Val Gly Ser Lys Cys Leu Trp Thr Tyr Glu Ile Gln Phe Ser Gln
545 550 555 560

Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro Ser Thr Phe Asn
565 570 575

Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg
580 585 590

Val Arg Ala Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro
595 600 605

Val Pro Tyr Leu Glu Val Pro Val Pro Arg Gly Pro Pro Ser Pro Gly
610 615 620

Asn Pro
625

<210> 8
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 1 of CDR 1 in the light chain of anti-hTfR
antibody

<400> 8

Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr
1 5 10

<210> 9
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 2 of CDR 1 in the light chain of anti-hTfR
antibody

<400> 9

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

<210> 10
<211> 6

<212> PRT
<213> Artificial Sequence

<220>

<223> Amino acid sequence 1 of CDR 2 in the light chain of anti-hTfR antibody

<400> 10

Lys Val Ser Asn Arg Phe
1 5

<210> 11

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence 2 of CDR 2 in the light chain of anti-hTfR antibody

<400> 11

Lys Val Ser Asn Arg Phe Ser
1 5

<210> 12

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of CDR 3 in the light chain of anti-hTfR antibody

<400> 12

Ser Gln Ser Thr His Val Pro Trp Thr
1 5

<210> 13

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence 1 of CDR1 in the heavy chain of anti-h,s,t,q antibody

<400> 13

Gly Tyr Ser Phe Met Asn Tyr Trp
1 5

<210> 14
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 2 of CDR1 in the heavy chain of anti-h,s,t,q
antibody

<400> 14

Gly Tyr Ser Phe Met Asn Tyr Trp Leu Gly
1 5 10

<210> 15
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 1 of CDR 2 in the heavy chain of anti-hTfR
antibody

<400> 15

Ile Tyr Pro Gly Gly Asp Tyr Pro
1 5

<210> 16
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 2 of CDR 2 in the heavy chain of anti-hTfR
antibody

<400> 16

Asp Ile Tyr Pro Gly Gly Asp Tyr Pro Thr Tyr Ser Glu Lys Phe Lys
1 5 10 15

Val

<210> 17
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 1 of CDR 3 in the heavy chain of anti-hTfR antibody

<400> 17

Ser Gly Asn Tyr Asp Glu Val Ala Tyr
1 5

<210> 18
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 2 of CDR 3 in the heavy chain of anti-hTfR antibody

<400> 18

Ala Arg Ser Gly Asn Tyr Asp Glu Val Ala Tyr
1 5 10

<210> 19
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of framework region 3 in the heavy chain of anti-h,s,t,q antibody

<400> 19

Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr Leu Gln
1 5 10 15

Leu Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
20 25 30

<210> 20
<211> 112
<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of the variable region of the light chain of anti-hTfR antibody

<400> 20

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

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

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

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

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

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

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

<210> 21

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of the variable region of the heavy chain of anti-h,s,t,q antibody

<400> 21

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

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

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

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

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

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

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

Leu Val Thr Val Ser Ser
115

<210> 22

<211> 219

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of the light chain of anti-hTfR antibody

<400> 22

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

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

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

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

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

65		70		75		80									
Ser	Arg	Val	Glu	Ala	Glu	Asp	Val	Gly	Val	Tyr	Tyr	Cys	Ser	Gln	Ser
			85					90						95	
Thr	His	Val	Pro	Trp	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	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> 23
 <211> 226
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Amino acid sequence of Fab heavy chain of anti-h,s,t,q antibody

<400> 23

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

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

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

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

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

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

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

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

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

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

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

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

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

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

His Thr

225

<210> 24
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer Hyg-Sfi5', synthetic sequence

<400> 24
gaggccgcct cggcctctga 20

<210> 25
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer Hyg-BstX3', synthetic sequence

<400> 25
aaccatcgtg atgggtgcta ttcctttgc 29

<210> 26
<211> 740
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide sequence encoding the amino acid sequence of the light chain of anti-hTfR antibody, synthetic sequence

<400> 26
acgcgtgccg ccaccatggg ctggagctgg attctgctgt tcctcctgag cgtgacagca 60
ggagtgcaca gcgacatcgt gatgaccag actcccctga gcctgagcgt gacacctggc 120
cagcctgcca gcatcagctg cagaagctct cagagcctgg tgcacagcaa cggcaacacc 180
tacctgcact ggtatctgca gaagcccggc cagagccctc agctgctgat ctacaaggtg 240
tccaacagat tcagcggcgt gcccagaca ttctccggca gcggctctgg caccgacttc 300
accctgaaga tttccagagt ggaagccgag gacgtgggcg tgtactactg cagccagagc 360
accacgtgc cctggacatt cggccagggc accaaggtgg aaatcaagag aaccgtggcc 420
gctcccagcg tgttcatctt cccacctagc gacgagcagc tgaagtccgg cacagcctct 480

gtcgtgtgcc tgctgaacaa cttctacccc cgcgaggcca aggtgcagtg gaaggtggac 540
aacgccctgc agagcggcaa cagccaggaa agcgtgaccg agcaggactc caaggacagc 600
acctacagcc tgagcagcac cctgaccctg agcaaggccg actacgagaa gcacaaggtg 660
tacgcctgcg aagtgacca ccagggcctg tctagccccg tgaccaagag cttcaacaga 720
ggcgagtgct aagcggccgc 740

<210> 27
<211> 869
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of fusion protein of the Fab heavy chain of anti-hTfR antibody and hIDUA

<400> 27

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

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

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

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

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

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

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

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

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

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

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

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

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

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

His Thr Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
225 230 235 240

Ser Ala Glu Ala Pro His Leu Val His Val Asp Ala Ala Arg Ala Leu
245 250 255

Trp Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe Cys Pro Pro Leu
260 265 270

Pro His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln Leu
275 280 285

Asn Leu Ala Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val
290 295 300

Arg Thr His Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly
305 310 315 320

Arg Gly Leu Ser Tyr Asn Phe Thr His Leu Asp Gly Tyr Leu Asp Leu
325 330 335

Leu Arg Glu Asn Gln Leu Leu Pro Gly Phe Glu Leu Met Gly Ser Ala
340 345 350

Ser Gly His Phe Thr Asp Phe Glu Asp Lys Gln Gln Val Phe Glu Trp
355 360 365

Lys Asp Leu Val Ser Ser Leu Ala Arg Arg Tyr Ile Gly Arg Tyr Gly
370 375 380

Leu Ala His Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp
385 390 395 400

His His Asp Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn
405 410 415

Tyr Tyr Asp Ala Cys Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu
420 425 430

Arg Leu Gly Gly Pro Gly Asp Ser Phe His Thr Pro Pro Arg Ser Pro
435 440 445

Leu Ser Trp Gly Leu Leu Arg His Cys His Asp Gly Thr Asn Phe Phe
450 455 460

Thr Gly Glu Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu His Arg Lys
465 470 475 480

Gly Ala Arg Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala
485 490 495

Gln Gln Ile Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr
500 505 510

Asn Asp Glu Ala Asp Pro Leu Val Gly Trp Ser Leu Pro Gln Pro Trp
515 520 525

Arg Ala Asp Val Thr Tyr Ala Ala Met Val Val Lys Val Ile Ala Gln
530 535 540

His Gln Asn Leu Leu Leu Ala Asn Thr Thr Ser Ala Phe Pro Tyr Ala

545		550		555		560									
Leu	Leu	Ser	Asn	Asp	Asn	Ala	Phe	Leu	Ser	Tyr	His	Pro	His	Pro	Phe
				565					570					575	
Ala	Gln	Arg	Thr	Leu	Thr	Ala	Arg	Phe	Gln	Val	Asn	Asn	Thr	Arg	Pro
			580					585					590		
Pro	His	Val	Gln	Leu	Leu	Arg	Lys	Pro	Val	Leu	Thr	Ala	Met	Gly	Leu
		595					600					605			
Leu	Ala	Leu	Leu	Asp	Glu	Glu	Gln	Leu	Trp	Ala	Glu	Val	Ser	Gln	Ala
	610					615					620				
Gly	Thr	Val	Leu	Asp	Ser	Asn	His	Thr	Val	Gly	Val	Leu	Ala	Ser	Ala
625					630					635					640
His	Arg	Pro	Gln	Gly	Pro	Ala	Asp	Ala	Trp	Arg	Ala	Ala	Val	Leu	Ile
				645					650					655	
Tyr	Ala	Ser	Asp	Asp	Thr	Arg	Ala	His	Pro	Asn	Arg	Ser	Val	Ala	Val
			660					665					670		
Thr	Leu	Arg	Leu	Arg	Gly	Val	Pro	Pro	Gly	Pro	Gly	Leu	Val	Tyr	Val
		675					680					685			
Thr	Arg	Tyr	Leu	Asp	Asn	Gly	Leu	Cys	Ser	Pro	Asp	Gly	Glu	Trp	Arg
		690				695					700				
Arg	Leu	Gly	Arg	Pro	Val	Phe	Pro	Thr	Ala	Glu	Gln	Phe	Arg	Arg	Met
705					710					715					720
Arg	Ala	Ala	Glu	Asp	Pro	Val	Ala	Ala	Ala	Pro	Arg	Pro	Leu	Pro	Ala
			725						730				735		
Gly	Gly	Arg	Leu	Thr	Leu	Arg	Pro	Ala	Leu	Arg	Leu	Pro	Ser	Leu	Leu
			740					745					750		
Leu	Val	His	Val	Cys	Ala	Arg	Pro	Glu	Lys	Pro	Pro	Gly	Gln	Val	Thr
		755					760					765			

Arg Leu Arg Ala Leu Pro Leu Thr Gln Gly Gln Leu Val Leu Val Trp
 770 775 780

Ser Asp Glu His Val Gly Ser Lys Cys Leu Trp Thr Tyr Glu Ile Gln
 785 790 795 800

Phe Ser Gln Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro Ser
 805 810 815

Thr Phe Asn Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly
 820 825 830

Ser Tyr Arg Val Arg Ala Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe
 835 840 845

Ser Asp Pro Val Pro Tyr Leu Glu Val Pro Val Pro Arg Gly Pro Pro
 850 855 860

Ser Pro Gly Asn Pro
 865

<210> 28
 <211> 2688
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Nucleotide seuquence encoding the amino acid sequence of fusion
 protein of the Fab heavy chain of anti-hTfR antibody and hIDUA,
 synthetic sequence

<400> 28
 acgcgtcgcc accatggggtt ggagcctcat cttgctcttc cttgtcgctg ttgctacgcg 60
 agtcggcagc gaggtgcaac tagtgcagtc tggagcagag gtgaaaaagc ccggggagtc 120
 tctgaagatt tcctgtaagg gttctggata cagctttatg aactactggc tgggatgggt 180
 gcgccagatg cccgggaaag gcctggagtg gatgggggac atctaccccg gcggagacta 240
 ccctacatac agcgagaagt tcaaggtcca ggtcaccatc tcagccgaca agtccatcag 300
 caccgcctac ctgcagttga gcagcctgaa ggcctcggac accgccatgt attactgtgc 360

gagatcaggc aattacgacg aagtggccta ctggggccaa ggaaccctgg tcaccgtctc	420
ctcagctagc accaagggcc catcgggtctt ccccctggca ccctcctcca agagcacctc	480
tgggggcaca gcggccctgg gctgcctggg caaggactac ttccccgaac cggtgacggt	540
gtcgtggaac tcaggcgccc tgaccagcgg cgtgcacacc ttcccggctg tcctacagtc	600
ctcaggactc tactccctca gcagcgtggg gaccgtgccc tccagcagct tgggcaccca	660
gacctacatc tgcaacgtga atcacaagcc cagcaacacc aaggtggaca agaaagttga	720
gccgaagagc tgtgataaga cgcatacggg tggcggaggg tctggagggtg gcggatcagg	780
cggagggtgga tctgccgagg ccccgcacct ggtgcacgtg gacgcggccc gcgcgctgtg	840
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tgaccagtac gtcctcagct gggaccagca gctcaacctc gcctatgtgg gcgccgtccc	960
tcaccgcggc atcaagcagg tccggacca ctggctgctg gagcttgtca ccaccagggg	1020
gtccactgga cggggcctga gctacaactt caccacctg gacgggtact tggaccttct	1080
cagggagaac cagctcctcc cagggtttga gctgatgggc agcgctcgg gccacttcac	1140
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gagatacatc ggtaggtacg gactggcgca tgtttccaag tggaacttcg agacgtggaa	1260
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ctacgatgcc tgctcggagg gtctgcgcgc gccagcccc gccctgcggc tgggaggccc	1380
cggcgactcc ttccacaccc caccgcgatc cccgtgagc tggggcctcc tgcgccactg	1440
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ctgggccgaa gtgtcgcagg ccgggaccgt cctggacagc aaccacacgg tgggcgtcct	1980

ggccagcgcc caccgcccc agggcccggc cgacgcctgg cgcgccgcgg tgctgatcta	2040
cgcgagcgac gacacccgcg cccaccccaa ccgcagcgtc gcggtgacct tgcggctgcg	2100
cggggtgccc cccggcccg gcctgggtcta cgtcacgcgc tacctggaca acgggctctg	2160
cagccccgac ggcgagtggc ggcgcctggg ccggcccgtc ttccccacgg cagagcagtt	2220
ccggcgcatg cgcgcggctg aggacccggt ggccgcggcg ccccgcccct taccgcccgg	2280
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cgagatccag ttctctcagg acggttaaggc gtacaccccg gtcagcagga agccatcgac	2520
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<210> 29
 <211> 53
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer IRES5', synthetic sequence

<400> 29	
caactcgagc ggccgcccc cccccctctc cttccccccc ccctaacgtt act	53

<210> 30
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer IRES3', synthetic sequence

<400> 30	
caagaagctt ccagaggaac tg	22

<210> 31
 <211> 30
 <212> DNA

<213> Artificial Sequence

<220>

<223> Primer mPGKP5', synthetic sequence

<400> 31
gcgagatcctt accgggtagg ggaggcgctt 30

<210> 32
<211> 30
<212> DNA
<213> Artificial Sequence

<220>

<223> Primer mPGKP3', synthetic sequence

<400> 32
gaggaattcg atgatcggtc gaaaggcccc 30

<210> 33
<211> 36
<212> DNA
<213> Artificial Sequence

<220>

<223> Primer GS5', synthetic sequence

<400> 33
aatatggcca caaccatggc gacctcagca agttcc 36

<210> 34
<211> 38
<212> DNA
<213> Artificial Sequence

<220>

<223> Primer GS3', synthetic sequence

<400> 34
ggaggatccc tcgagttagt tttgtattg gaagggt 38

<210> 35
<211> 28
<212> DNA
<213> Artificial Sequence

<220>

<223> Primer puro5', synthetic sequence

<400> 35
gcttaagatg accgagtaca agcccacg 28

<210> 36
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer puro3', synthetic sequence

<400> 36
cccatcgtga tggtcaggca ccgggcttgc 30

<210> 37
<211> 44
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer SV40polyA5', synthetic sequence

<400> 37
caacaagcgg ccgccctcga gttcccttta gtgagggtta atgc 44

<210> 38
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer SV40polyA3', synthetic sequence

<400> 38
cccctgaacc tgaaacataa aatg 24

<210> 39
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer mIRES-GS5', synthetic sequence

<400> 39
acacgatgat aagcttgcca caacc 25

<210> 40

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

<220>
 <223> Primer mIRES-GS3', synthetic sequence

<400> 40
 ctccacgata tccctgcat a 21

<210> 41
 <211> 2076
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> CMVE-EF-1 alpha p-IFN beta MAR, synthetic sequence

<400> 41
 aagcttaaat tatctctaag gcatgtgaac tggctgtctt ggttttcatc tgtacttcat 60
 ctgctacctc tgtgacctga aacatattta taattccatt aagctgtgca tatgatagat 120
 ttatcatatg tattttcctt aaaggatttt tgtaagaact aattgaattg atacctgtaa 180
 agtctttatc aactaccca ataaataata aatctctttg ttcagctctc tgtttctata 240
 aatatgtacc agttttattg tttttagtgg tagtgatttt attctctttc tatatatata 300
 cacacacatg tgtgcattca taaatatata caatttttat gaataaaaaa ttattagcaa 360
 tcaatattga aaaccactga tttttgttta tgtgagcaaa cagcagatta aaagaaattc 420
 ctgcaggagt caatgggaaa aaccatttgg agccaagtac actgactcaa tagggacttt 480
 ccattgggtt ttgcccagta cataaggta atagggggtg agtcaacagg aaagtcccat 540
 tggagccaag tacattgagt caataggac tttccaatgg gttttgcca gtacataagg 600
 tcaatgggag gtaagccaat gggtttttcc cattactgac atgtatactg agtcattagg 660
 gactttcaa tgggttttgc ccagtacata aggtcaatag gggatgaatca acaggaaagt 720
 cccattggag ccaagtacac tgagtcaata gggactttcc attgggtttt gccagttaca 780
 aaaggccaat aggggggtgag tcaatgggtt tttccatta ttggcacata cataaggta 840
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 agcacatggc ccacagtccc tgagaagttg gggggagggg tgggcaattg aactggtgcc 960
 tagagaaggt ggggcttggg taaactggga aagtgatgtg gtgtactggc tccacctttt 1020

tccccagggt gggggagaac catatataag tgcagtagtc tctgtgaaca ttcaaggttc	1080
tgccttctcc ctctgtgag tttggtaagt cactgactgt ctatgcctgg gaaagggtgg	1140
gcaggagggtg gggcagtgca ggaaaagtgg cactgtgaac cctgcagccc tagacaattg	1200
tactaacctt cttctctttc ctctcctgac aggttggtgt acagtagctt ccaacgcgta	1260
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tctaaaatgt atatagaagc ccaaaagaca ataacaaaaa tattcttgta gaacaaaatg	1380
ggaaagaatg ttccactaaa tatcaagatt tagagcaaag catgagatgt gtggggatag	1440
acagtgaggc tgataaaata gagtagagct cagaaacaga ccattgata tatgtaagtg	1500
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acacaaaaaa attccagtga attataagtc taaatggaga aggcaaaact ttaaactctt	1680
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tcaaagtcct aaccacaaag aaaagattgt taattagatt gcatgaatat taagacttat	1800
ttttaaaatt aaaaaacat taagaaaagt caggccatag aatgacagaa aatatttgca	1860
acaccccagt aaagagaatt gtaatatgca gattataaaa agaagtctta caaatcagta	1920
aaaaataaaa ctagacaaaa atttgaacag atgaaagaga aactctaaat aatcattaca	1980
catgagaaac tcaatctcag aaatcagaga actatcattg catatacact aaattagaga	2040
aatattaaaa ggctaagtaa catctgtggc gaattc	2076

<210> 42
 <211> 2130
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> IRES-HygroR-mPGKpA, synthetic sequence

<400> 42	
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attttccacc atattgccgt cttttggcaa tgtgagggcc cggaacctg gccctgtctt	180

cttgacgagc attcctaggg gtctttcccc tctcgccaaa ggaatgcaag gtctgttgaa	240
tgtcgtgaag gaagcagttc ctctggaagc ttcttgaaga caaacaacgt ctgtagcgac	300
cctttgcagg cagcgggaacc ccccacctgg cgacaggtgc ctctgcggcc aaaagccacg	360
tgtataagat acacctgcaa aggcgggcaca accccagtg c acgttgtga gttggatagt	420
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gaaggtagcc cattgtatgg gatctgatct ggggcctcgg tgcacatgct ttacatgtgt	540
ttagtcgagg ttaaaaaaac gtctaggccc cccgaaccac ggggacgtgg ttttcctttg	600
aaaaacacga tgataatatg gccacaacca tgaaaaagcc tgaactcacc gcgacgtctg	660
tcgagaagtt tctgatcgaa aagttcgaca gcgtctccga cctgatgcag ctctcggagg	720
gcgaagaatc tcgtgctttc agcttcgatg taggagggcg tggatatgtc ctgcgggtaa	780
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cgctcccgat tccggaagtg cttgacattg gggaattcag cgagagcctg acctattgca	900
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acatcttctt ctggaggccg tggttggctt gtatggagca gcagacgcgc tacttcgagc	1380
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gtcgatgcga cgcaatcgtc cgatccggag ccgggactgt cgggcgtaca caaatcgccc	1560
gcagaagcgc ggccgtctgg accgatggct gtgtagaagt actcgccgat agtggaacc	1620
gacgccccag cactcgtccg agggcaaagg aatagtcgag aaattgatga tctattaagc	1680
aataaagacg tccactaaaa tggaagtttt tcctgtcata ctttgtttaag aagggtgaga	1740
acagagtacc tacattttga atggaaggat tggagctacg ggggtggggg tggggtggga	1800

ttagataaat gcctgctctt tactgaaggc tctttactat tgctttatga taatgtttca	1860
tagttggata tcataattta aacaagcaaa accaaattaa gggccagctc attcctccac	1920
tcacgatcta tagatccact agcttggcgt aatcatggtc atagctgttt cctgtgtgaa	1980
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agtcgggaaa cctgtcgtgc cagcggatcc	2130