

SEQUENCE LISTING

<110> SANOFI

<120> Generation of a high producing recombinant Chinese hamster ovary cell line for therapeutic protein production

<130> BEX 21P1358

<150> EP20306068.6

<151> 2020-09-21

<160> 36

<170> PatentIn version 3.5

<210> 1

<211> 1188

<212> DNA

<213> Cricetulus griseus

<400> 1

atggcttggc ggcagatgcg gaagagagcc ctggacgccg ctatcatcct gggaggcgga	60
ggcctgctgt tcaccttta cctgacagcc accggcgacg accacttcta cgccgagtac	120
ctgatgcctg ccctgcagag actgctggac cctgagtctg cccaccggct ggccatcaga	180
ttcacctccc tgggcctgct gcccagagcc accttcagg actccgacat gctggaagt	240
cgggtgctgg gccacaagtt cagaaacccc gtgggaatcg ccgctggctt cgacaagcac	300
ggcgaggctg tggacggcct gtacaagctg ggcttcggct tcgtggaagt gggctccgtg	360
acaccccagc cccaggaagg caacccaga cctagagtgt tccggctgcc tgaggaccag	420
gccgtgatca acagatacgg cttcaactcc cacggcctgt ccgtggtgga acaccggctg	480
agagccagac agcagaagca gaacaagctg accgccgacg gcctgcccct gggcatcaat	540
ctgggcaaga acaagacctc cgaggacgct gccgccgact acgtggaagg cgtgagagt	600
ctgggacctc tggccgatta cctggctctg aacgtgtcct cccccaacac cgctggcctg	660
agaagcctgc agggaaaggc cgagctgaga aggctgctgg ccaaggtgct gcaggaacgg	720
gacgctctga agggcgccca gaaacctgcc gtgctcgtga agatcgcccc tgacctgacc	780
gcccaggaca aagaggatat cgcctccgtg gccagagagc tgggcatcga cggactgatc	840
gtgaccaaca ccaccgtgtc tcggcctacc ggactgcagg gcgctctgag atctgagatg	900
ggcggcctgt ctggcaagcc tctgagggac ctgtccaccc agaccatcag agagatgtac	960

accctgaccc agggccggat ccccatcatt ggagtgggcg gagtgtcctc tggccaggac 1020
gccctggaaa agatccaggc tggcgcctct ctggtgcagc tgtataccgc cctgaccttt 1080
ctggggccctc ccgtgggtggt gcgagtgaag agagaactgg aagccctgct gaaagagcgg 1140
ggcttcaaca ccgtgaccga ggccatcggc gctgaccaca gaagatga 1188

<210> 2
<211> 395
<212> PRT
<213> *Cricetulus griseus*

<400> 2

Met Ala Trp Arg Gln Met Arg Lys Arg Ala Leu Asp Ala Ala Ile Ile
1 5 10 15

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

Asp Asp His Phe Tyr Ala Glu Tyr Leu Met Pro Ala Leu Gln Arg Leu
35 40 45

Leu Asp Pro Glu Ser Ala His Arg Leu Ala Ile Arg Phe Thr Ser Leu
50 55 60

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

Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly Ile Ala Ala Gly
85 90 95

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

Gly Phe Val Glu Val Gly Ser Val Thr Pro Gln Pro Gln Glu Gly Asn
115 120 125

Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln Ala Val Ile Asn
130 135 140

Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val Glu His Arg Leu
145 150 155 160

Arg Ala Arg Gln Gln Lys Gln Asn Lys Leu Thr Ala Asp Gly Leu Pro
165 170 175

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

Asp Tyr Val Glu Gly Val Arg Val Leu Gly Pro Leu Ala Asp Tyr Leu
195 200 205

Val Val Asn Val Ser Ser Pro Asn Thr Ala Gly Leu Arg Ser Leu Gln
210 215 220

Gly Lys Ala Glu Leu Arg Arg Leu Leu Ala Lys Val Leu Gln Glu Arg
225 230 235 240

Asp Ala Leu Lys Gly Ala Gln Lys Pro Ala Val Leu Val Lys Ile Ala
245 250 255

Pro Asp Leu Thr Ala Gln Asp Lys Glu Asp Ile Ala Ser Val Ala Arg
260 265 270

Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr Thr Val Ser Arg
275 280 285

Pro Thr Gly Leu Gln Gly Ala Leu Arg Ser Glu Met Gly Gly Leu Ser
290 295 300

Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile Arg Glu Met Tyr
305 310 315 320

Thr Leu Thr Gln Gly Arg Ile Pro Ile Ile Gly Val Gly Gly Val Ser
325 330 335

Ser Gly Gln Asp Ala Leu Glu Lys Ile Gln Ala Gly Ala Ser Leu Val
340 345 350

Gln Leu Tyr Thr Ala Leu Thr Phe Leu Gly Pro Pro Val Val Val Arg
355 360 365

Val Lys Arg Glu Leu Glu Ala Leu Leu Lys Glu Arg Gly Phe Asn Thr
 370 375 380

Val Thr Glu Ala Ile Gly Ala Asp His Arg Arg
 385 390 395

<210> 3
 <211> 1188
 <212> DNA
 <213> Homo sapiens

<400> 3
 atggccttggc ggcacctgaa gaagagggcc caggacgccg tgatcatcct gggaggcggga 60
 ggcctgctgt tcgcctctta cctgatggct accggcgacg agcggttcta cgccgagcat 120
 ctgatgcca cactgcaggg cctgctggac cctgagtctg cccatagact ggccgtgcgg 180
 ttcacctccc tgggactgct gcctagagcc cggttccagg actccgacat gctggaagtg 240
 cgggtgctgg gccacaagtt cagaaacccc gtgggaatcg ccgctggctt cgacaagcac 300
 ggcgaggctg tggacggcct gtacaagatg ggcttcggct tcgtggaaat cggctccgtg 360
 accccaagc cccaggaagg caaccccaga cctcgggtgt tcagactgcc tgaggaccag 420
 gctgtgatca acagatacgg cttcaactcc cacggcctgt ccgtggtgga acaccggctg 480
 agagccagac agcagaagca ggccaagctg accgaggatg gcctgcctct gggagtgaac 540
 ctgggcaaga acaagacctc cgtggacgcc gccgaggatt acgctgaagg cgtgcgagtg 600
 ctgggacccc tggctgatta cctggctctg aacgtgtcct cccccaacac cgctggcctg 660
 agatctctgc agggcaaggc cgagctgcgg agactgctga caaaggtgct gcaggaacgc 720
 gacggcctgc ggagagtga tagacctgcc gtgctcgtga agatcgcccc cgacctgacc 780
 agccaggaca aagaggatat cgcctccgtc gtgaaagagc tgggcatcga cggactgata 840
 gtgaccaaca ccaccgtgtc taggcctgcc ggactgcagg gggctctgag atctgaaacc 900
 ggcggactgt ccggcaagcc tctgagggat ctgtccaccc agaccatcag agagatgtac 960
 gccctgaccc agggccgggt gccaatcatt ggagtgggcg gactgtcctc cggccaggat 1020
 gccctggaaa agatcagagc cggcgcttcc ctgggtgcagc tgtacaccgc tctgaccttt 1080
 tggggccctc ccgtcgtggg caaagtgaag agagagctgg aagccctgct gaaagagcag 1140
 ggatttggcg gcgtgaccga tgccatcggc gctgaccaca gaagatga 1188

<210> 4
<211> 395
<212> PRT
<213> Homo sapiens

<400> 4

Met Ala Trp Arg His Leu Lys Lys Arg Ala Gln Asp Ala Val Ile Ile
1 5 10 15

Leu Gly Gly Gly Gly Leu Leu Phe Ala Ser Tyr Leu Met Ala Thr Gly
20 25 30

Asp Glu Arg Phe Tyr Ala Glu His Leu Met Pro Thr Leu Gln Gly Leu
35 40 45

Leu Asp Pro Glu Ser Ala His Arg Leu Ala Val Arg Phe Thr Ser Leu
50 55 60

Gly Leu Leu Pro Arg Ala Arg Phe Gln Asp Ser Asp Met Leu Glu Val
65 70 75 80

Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly Ile Ala Ala Gly
85 90 95

Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr Lys Met Gly Phe
100 105 110

Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro Gln Glu Gly Asn
115 120 125

Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln Ala Val Ile Asn
130 135 140

Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val Glu His Arg Leu
145 150 155 160

Arg Ala Arg Gln Gln Lys Gln Ala Lys Leu Thr Glu Asp Gly Leu Pro
165 170 175

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

Asp Tyr Ala Glu Gly Val Arg Val Leu Gly Pro Leu Ala Asp Tyr Leu
195 200 205

Val Val Asn Val Ser Ser Pro Asn Thr Ala Gly Leu Arg Ser Leu Gln
210 215 220

Gly Lys Ala Glu Leu Arg Arg Leu Leu Thr Lys Val Leu Gln Glu Arg
225 230 235 240

Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu Val Lys Ile Ala
245 250 255

Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile Ala Ser Val Val Lys
260 265 270

Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr Thr Val Ser Arg
275 280 285

Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr Gly Gly Leu Ser
290 295 300

Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile Arg Glu Met Tyr
305 310 315 320

Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val Gly Gly Val Ser
325 330 335

Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly Ala Ser Leu Val
340 345 350

Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro Val Val Gly Lys
355 360 365

Val Lys Arg Glu Leu Glu Ala Leu Leu Lys Glu Gln Gly Phe Gly Gly
370 375 380

Val Thr Asp Ala Ile Gly Ala Asp His Arg Arg
385 390 395

<210> 5
 <211> 1122
 <212> DNA
 <213> Homo sapiens

<400> 5
 atgaccacct ccgcctccag ccacctgaac aagggcatca aacaggtgta catgagcctg 60
 cccagggcg agaaggtgca ggccatgtac atctggatcg acggcaccgg cgagggactg 120
 cggtgcaaga ccagaaccct ggactccgag cctaagtgcg tggaagaact gcccagagtgg 180
 aacttcgacg gtcctccac cctgcagtcc gagggctcca actccgacat gtacctggtg 240
 cctgccgcca tgttccggga ccctttccgg aaggaccca acaagctggt gctgtgcgag 300
 gtgttcaagt acaacagacg gcctgccgag acaaacctgc ggcatacctg caagcggatc 360
 atggacatgg tgtccaacca gcacccttgg tttggcatgg aacaggagta caccctgatg 420
 ggacccgacg gccacccctt cggctggcct tctaacggct tccctggccc ccagggcccc 480
 tactatttg gcgtgggagc cgaccgggccc tacggcagag atatcgtgga agcccactac 540
 cgggcctgcc tgtacgccgg agtgaagatc gccggcacca acgccgaagt gatgcccgcc 600
 cagtgggagt tccagatcgg cccttgcgag ggcatctcca tgggcgatca cctgtgggtg 660
 gcccggttca tcctgcacag agtgtgcgag gacttcggcg tgatgccac cttcgacccc 720
 aagcccatcc ccggcaactg gaacggcgct ggctgccaca ccaacttctc caccaaggcc 780
 atgcgggaag agaacggcct gaagtacatc gaggaagcca tcgagaagct gtccaagcgg 840
 caccagtacc acatcagagc ctacgaccct aagggcggcc tggacaacgc cagaaggctg 900
 accggctttc acgagacatc caacatcaac gacttctctg ccggcgtggc caacagatcc 960
 gcctccatcc ggatccctag aaccgtgggc caggaaaaga agggctactt cgaggacaga 1020
 cggccctccg ccaactgcga cccctttagc gtgaccgagg ccctgatccg gacctgcctg 1080
 ctgaacgaga caggcgacga gcccttccag tacaagaact ga 1122

<210> 6
 <211> 373
 <212> PRT
 <213> Homo sapiens

<400> 6

Met Thr Thr Ser Ala Ser Ser His Leu Asn Lys Gly Ile Lys Gln Val
 1 5 10 15

Tyr Met Ser Leu Pro Gln Gly Glu Lys Val Gln Ala Met Tyr Ile Trp
20 25 30

Ile Asp Gly Thr Gly Glu Gly Leu Arg Cys Lys Thr Arg Thr Leu Asp
35 40 45

Ser Glu Pro Lys Cys Val Glu Glu Leu Pro Glu Trp Asn Phe Asp Gly
50 55 60

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

Pro Ala Ala Met Phe Arg Asp Pro Phe Arg Lys Asp Pro Asn Lys Leu
85 90 95

Val Leu Cys Glu Val Phe Lys Tyr Asn Arg Arg Pro Ala Glu Thr Asn
100 105 110

Leu Arg His Thr Cys Lys Arg Ile Met Asp Met Val Ser Asn Gln His
115 120 125

Pro Trp Phe Gly Met Glu Gln Glu Tyr Thr Leu Met Gly Thr Asp Gly
130 135 140

His Pro Phe Gly Trp Pro Ser Asn Gly Phe Pro Gly Pro Gln Gly Pro
145 150 155 160

Tyr Tyr Cys Gly Val Gly Ala Asp Arg Ala Tyr Gly Arg Asp Ile Val
165 170 175

Glu Ala His Tyr Arg Ala Cys Leu Tyr Ala Gly Val Lys Ile Ala Gly
180 185 190

Thr Asn Ala Glu Val Met Pro Ala Gln Trp Glu Phe Gln Ile Gly Pro
195 200 205

Cys Glu Gly Ile Ser Met Gly Asp His Leu Trp Val Ala Arg Phe Ile
210 215 220

Leu His Arg Val Cys Glu Asp Phe Gly Val Ile Ala Thr Phe Asp Pro
 225 230 235 240

Lys Pro Ile Pro Gly Asn Trp Asn Gly Ala Gly Cys His Thr Asn Phe
 245 250 255

Ser Thr Lys Ala Met Arg Glu Glu Asn Gly Leu Lys Tyr Ile Glu Glu
 260 265 270

Ala Ile Glu Lys Leu Ser Lys Arg His Gln Tyr His Ile Arg Ala Tyr
 275 280 285

Asp Pro Lys Gly Gly Leu Asp Asn Ala Arg Arg Leu Thr Gly Phe His
 290 295 300

Glu Thr Ser Asn Ile Asn Asp Phe Ser Ala Gly Val Ala Asn Arg Ser
 305 310 315 320

Ala Ser Ile Arg Ile Pro Arg Thr Val Gly Gln Glu Lys Lys Gly Tyr
 325 330 335

Phe Glu Asp Arg Arg Pro Ser Ala Asn Cys Asp Pro Phe Ser Val Thr
 340 345 350

Glu Ala Leu Ile Arg Thr Cys Leu Leu Asn Glu Thr Gly Asp Glu Pro
 355 360 365

Phe Gln Tyr Lys Asn
 370

<210> 7
 <211> 1122
 <212> DNA
 <213> Canis lupus

<400> 7
 atggccacct ccgctccag ccacctgaac aagggcacatca aacaggtgta catgagcctg 60
 cccagggcg agaaggtgca ggccatgtac atctggatcg acggcaccgg cgagggactg 120
 cgggtgcaaga ccagaaccct ggactccgag cccaagggcg tggaagaact gcccgagtgg 180
 aacttcgacg gctcctccac cttccagtcc gagggctcca actccgacat gtacctggtg 240

cctgccgcca tgttccggga ccctttccgg aaggacccca acaagctggt gttctgcgag 300
gtgttcaagt acaaccggaa gcccgccgag acaaacctgc ggcatacctg caagcggatc 360
atggacatgg tgtccaacca gcacccttgg tttggcatgg aacaggagta caccctgatg 420
ggcaccgacg gccacccctt cggctggcct tctaacggct tccctggccc ccagggcccc 480
tactattgtg gcgtgggcgc cgacaaggcc tacggcagag acatcgtgga agcccactac 540
cgggcctgcc tgtacgccgg catcaagatc gctggcacca acgccgaagt gatgcccgcc 600
cagtgggagt tccagatcgg cccttgcgag ggcatcgaca tgggcgatca cctgtgggtg 660
gcccggttca tcctgcacag agtgtgcgag gacttcggcg tgatcgccac cttcgacccc 720
aagcccatcc ccggcaactg gaacggcgct ggctgccaca ccaacttctc caccaaggcc 780
atgcgggaag agaacggcct gaagtacatc gaggaatcca tcgagaagct gtccaagcgg 840
caccagtacc acatccgggc ctacgacccc aagggcggcc tggataacgc cagacggctg 900
accggcttcc acgagacatc caacatcaac gacttctctg ccggcgtggc caacagaggc 960
gcctccatcc ggatcccccg gaccgtgggc caggaaaaga agggctactt cgaggacaga 1020
cggccctccg ccaactgcga cccctttagc gtgaccgagg ccctgatccg gacctgcctg 1080
ctgaacgaga caggcgacga gcccttcag tacaagaact ga 1122

<210> 8
<211> 373
<212> PRT
<213> Canis lupus

<400> 8

Met Ala Thr Ser Ala Ser Ser His Leu Asn Lys Gly Ile Lys Gln Val
1 5 10 15

Tyr Met Ser Leu Pro Gln Gly Glu Lys Val Gln Ala Met Tyr Ile Trp
20 25 30

Ile Asp Gly Thr Gly Glu Gly Leu Arg Cys Lys Thr Arg Thr Leu Asp
35 40 45

Ser Glu Pro Lys Gly Val Glu Glu Leu Pro Glu Trp Asn Phe Asp Gly
50 55 60

Ser Ser Thr Phe Gln Ser Glu Gly Ser Asn Ser Asp Met Tyr Leu Val
65 70 75 80

Pro Ala Ala Met Phe Arg Asp Pro Phe Arg Lys Asp Pro Asn Lys Leu
85 90 95

Val Phe Cys Glu Val Phe Lys Tyr Asn Arg Lys Pro Ala Glu Thr Asn
100 105 110

Leu Arg His Thr Cys Lys Arg Ile Met Asp Met Val Ser Asn Gln His
115 120 125

Pro Trp Phe Gly Met Glu Gln Glu Tyr Thr Leu Met Gly Thr Asp Gly
130 135 140

His Pro Phe Gly Trp Pro Ser Asn Gly Phe Pro Gly Pro Gln Gly Pro
145 150 155 160

Tyr Tyr Cys Gly Val Gly Ala Asp Lys Ala Tyr Gly Arg Asp Ile Val
165 170 175

Glu Ala His Tyr Arg Ala Cys Leu Tyr Ala Gly Ile Lys Ile Ala Gly
180 185 190

Thr Asn Ala Glu Val Met Pro Ala Gln Trp Glu Phe Gln Ile Gly Pro
195 200 205

Cys Glu Gly Ile Asp Met Gly Asp His Leu Trp Val Ala Arg Phe Ile
210 215 220

Leu His Arg Val Cys Glu Asp Phe Gly Val Ile Ala Thr Phe Asp Pro
225 230 235 240

Lys Pro Ile Pro Gly Asn Trp Asn Gly Ala Gly Cys His Thr Asn Phe
245 250 255

Ser Thr Lys Ala Met Arg Glu Glu Asn Gly Leu Lys Tyr Ile Glu Glu
260 265 270

Ser Ile Glu Lys Leu Ser Lys Arg His Gln Tyr His Ile Arg Ala Tyr
275 280 285

Asp Pro Lys Gly Gly Leu Asp Asn Ala Arg Arg Leu Thr Gly Phe His
290 295 300

Glu Thr Ser Asn Ile Asn Asp Phe Ser Ala Gly Val Ala Asn Arg Gly
305 310 315 320

Ala Ser Ile Arg Ile Pro Arg Thr Val Gly Gln Glu Lys Lys Gly Tyr
325 330 335

Phe Glu Asp Arg Arg Pro Ser Ala Asn Cys Asp Pro Phe Ser Val Thr
340 345 350

Glu Ala Leu Ile Arg Thr Cys Leu Leu Asn Glu Thr Gly Asp Glu Pro
355 360 365

Phe Gln Tyr Lys Asn
370

<210> 9

<211> 373

<212> PRT

<213> Cricetulus griseus

<400> 9

Met Ala Thr Ser Ala Ser Ser His Leu Asn Lys Gly Ile Lys Gln Met
1 5 10 15

Tyr Met Ser Leu Pro Gln Gly Glu Lys Val Gln Ala Met Tyr Ile Trp
20 25 30

Val Asp Gly Thr Gly Glu Gly Leu Arg Cys Lys Thr Arg Thr Leu Asp
35 40 45

Cys Glu Pro Lys Cys Val Glu Glu Leu Pro Glu Trp Asn Phe Asp Gly
50 55 60

Ser Ser Thr Phe Gln Ser Glu Ser Ser Asn Ser Asp Met Tyr Leu Ser
65 70 75 80

Pro Val Ala Met Phe Arg Asp Pro Phe Arg Lys Glu Pro Asn Lys Leu

85

90

95

Val Phe Cys Glu Val Phe Lys Tyr Asn Gln Lys Pro Ala Glu Thr Asn
 100 105 110

Leu Arg His Thr Cys Lys Arg Ile Met Asp Met Val Ser Asn Gln His
 115 120 125

Pro Trp Phe Gly Met Glu Gln Glu Tyr Thr Leu Leu Gly Thr Asp Gly
 130 135 140

His Pro Phe Gly Trp Pro Ser Asp Gly Phe Pro Gly Pro Gln Gly Leu
 145 150 155 160

Tyr Tyr Cys Gly Val Gly Ala Asp Lys Ala Tyr Arg Arg Asp Ile Met
 165 170 175

Glu Ala His Tyr Arg Ala Cys Leu Tyr Ala Gly Val Lys Ile Thr Gly
 180 185 190

Thr Tyr Ala Glu Val Lys His Ala Gln Trp Glu Phe Gln Ile Gly Pro
 195 200 205

Cys Glu Gly Ile Arg Met Gly Asp His Leu Trp Val Ala Arg Phe Ile
 210 215 220

Leu His Arg Val Cys Lys Asp Phe Gly Val Ile Ala Thr Phe Asp Ser
 225 230 235 240

Lys Pro Ile Pro Gly Asn Trp Asn Gly Ala Gly Cys His Thr Asn Phe
 245 250 255

Ser Thr Lys Thr Met Arg Glu Glu Asn Gly Leu Lys His Ile Lys Glu
 260 265 270

Ala Ile Glu Lys Leu Ser Lys Arg His Arg Tyr His Ile Arg Ala Tyr
 275 280 285

Asp Pro Lys Gly Gly Leu Asp Asn Ala Arg Arg Leu Thr Gly Phe His
 290 295 300

Lys Thr Ser Asn Ile Asn Asp Phe Ser Ala Gly Val Ala Asp Arg Ser
305 310 315 320

Ala Ser Ile Arg Ile Pro Arg Thr Val Gly Gln Glu Lys Lys Gly Tyr
325 330 335

Phe Glu Ala Arg Cys Pro Ser Ala Asn Cys Asp Pro Phe Ala Val Thr
340 345 350

Glu Ala Ile Val Arg Thr Cys Leu Leu Asn Glu Thr Gly Asp Gln Pro
355 360 365

Phe Gln Tyr Lys Asn
370

<210> 10
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> corresponding piece of DNA for generating DHODH gRNA

<400> 10
ggatgcagcc atcatccttg 20

<210> 11
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide used for obtaining DHODH gRNA (Sequence1')

<400> 11
ggatgcagcc atcatccttg gtttt 25

<210> 12
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide used for obtaining DHODH gRNA (Sequence1')

<400> 12

caaggatgat ggctgcatcc cggtg 25

<210> 13
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide used for obtaining DHODH gRNA (Sequence2')

<400> 13
gatgcagcca tcatccttgg gtttt 25

<210> 14
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide used for obtaining DHODH gRNA (Sequence2')

<400> 14
ccaaggatga tggctgcatc cggtg 25

<210> 15
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide used for obtaining DHODH gRNA (Sequence3')

<400> 15
gcagccatca tccttggggg gtttt 25

<210> 16
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide used for obtaining DHODH gRNA (Sequence3')

<400> 16
cccccaagga tgatggctgc cggtg 25

<210> 17
<211> 25
<212> DNA

<213> Artificial Sequence
 <220>
 <223> oligonucleotide used for obtaining DHODH gRNA (Sequence4')
 <400> 17
 gccatcatcc ttgggggagg gtttt 25

<210> 18
 <211> 25
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> oligonucleotide used for obtaining DHODH gRNA (Sequence4')
 <400> 18
 cctcccccaa ggatgatggc cggtg 25

<210> 19
 <211> 25
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> oligonucleotide used for obtaining DHODH gRNA (Sequence5')
 <400> 19
 gctattcgct tcacgtccct gtttt 25

<210> 20
 <211> 25
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> oligonucleotide used for obtaining DHODH gRNA (Sequence5')
 <400> 20
 agggacgtga agcgaatagc cggtg 25

<210> 21
 <211> 25
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> oligonucleotide used for obtaining DHODH gRNA (Sequence6')
 <400> 21

gcctctacaa actgggcttt gtttt 25

<210> 22
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide used for obtaining DHODH gRNA (Sequence6')

<400> 22
aaagcccagt ttgtagaggc cggtg 25

<210> 23
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide used for obtaining DHODH gRNA (Sequence7')

<400> 23
ggctttgggt ttgtcgaggt gtttt 25

<210> 24
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide used for obtaining DHODH gRNA (Sequence7')

<400> 24
acctcgacaa acccaaagcc cggtg 25

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

<220>
<223> oligonucleotide used for obtaining DHODH gRNA (Sequence8')

<400> 25
gctggtctga ggagcctaca gtttt 25

<210> 26
<211> 25
<212> DNA

<213> Artificial Sequence

<220>

<223> oligonucleotide used for obtaining DHODH gRNA (Sequence8')

<400> 26

tgtaggctcc tcagaccagc cgggtg

25

<210> 27

<211> 14437

<212> DNA

<213> Cricetulus griseus

<220>

<221> misc_feature

<222> (1992)..(2015)

<223> target of plasmids pBH6840 KO DHODH SEQ1 and pBH6841 KO DHODH SEQ4

<220>

<221> misc_feature

<222> (2129)..(2147)

<223> target of plasmids pBH6842 KO DHODH SEQ5

<220>

<221> misc_feature

<222> (4015)..(4047)

<223> target of plasmids pBH6843 KO DHODH SEQ7

<400> 27

ccgagccac attctccaat ggagtggagg cagaggcggg cccagtggca gaaggagcat 60

ggcgtggaga cagatgagag tgagtctgtt gcgggtgctt acgcttggtc ggaaaacagg 120

ttgggagtgg acgaggctgg gagattgaaa ggctggggcc cttgcagtgt gggctgcatg 180

tgtgctcagc taggggcatg caaaaagcaa gcgtgctggg cagaggctga gttgattgtg 240

agagatcgcg ggcttttttt tttttttttt tcttaaactg agctagtatc gggcccctgt 300

gagcacatgg tggctagcat tatggaaagg atccagggcg gaatgaaata agacacgcag 360

ccacccttcc agataaagtg tggttagaat gggagtcccg tgcgaagagt ccgtagattg 420

tgtccctggc ttgggaaaga gtgcgcagat attgtttctt gacacgtgag aatttctccc 480

tccagaggag ggagaatgaa tacttggttt gctgtacagg caaatctgat cacatcctct 540

acttccttat ttagtggaca aatccatta aaaatataat cactgattgt ggtgaggggt 600

tgtgctgtga catgggagct ggaaccgaac tctgcactta accactgaac catctccagc 660

ccccaaatct gtattttggc tgacaccccc acattttctcc taccttactt taagaaatgc	720
tttcctttta gttccaaaca gacctgtctt cctctacccc attctctggc ctttctcatt	780
ggcttcagcc acctagagat tcctttctcca gctgcttcct cctcttttagc ttttgtgtct	840
ccttggaag tcaaccttag cctggaagga gcctcaagat ccttccatta cttatctctt	900
cgtgtcagtt ttcttgggtt tgtgtttaca tggccattaa tttctctctt cattagatag	960
attacacact tctgaaggac agggacctgg tgtggtttgc ttgcctttgg tgaaggattg	1020
aatgaatgca ttagccactt ggcatctggc agtgataatt atcaaaaagc attgtgagcc	1080
tcctttgaac tagggtagt attctctacc cagagtgtga agctatgttt gtattacaac	1140
cacttttata ttatacacat aggacatttc aggccagtaa cttttctagg tataatttta	1200
aaatatagac accatgtcct aactacagta taaaggagaa atgaaaacat gtatttcagt	1260
atgtagaagt cagaacacag ttcacctaca tagatggcca ggtgtttaag cctctattta	1320
gaagggtg gc gttggtatac aaacagcact gtataccctt tctggtgggg ttttaggaac	1380
agtgaccaag tcttagtaat gttttgtgca aactgtacaa ttgtccttaa attacaaggt	1440
atctttatct ctgtaaaagt caccctgtac atgtaaacca tgtggttgtg tggatgaacta	1500
tagcttgctt cttgcctctc ctattatcct cagataatag gaagttttcc tcacataaat	1560
agcaatagca agttcaaaca tcatacagta catagggaaa ctagtgtgtt agctttaatt	1620
aaagaagaat attgacagga ctgatttctc cacaccaaatt gtattagcat cattccctca	1680
ttaactagta aaaattttcc catgtgacct ctagggggca gtactgcctg tcttgaaaat	1740
tccctgcctg gtccttagga aaatattcag ggctagaacc catgtaagca gtgtaggtac	1800
tgcacttacc tttgtagatg tgtaagtggg caggatatga agggggacag tgtgagcagg	1860
gaaggactgt cactttgtgt agttgttatg tcctctgggc aggtgtgaag ggtcaggaag	1920
ggtactgcag gctggtctga tgggggtccc catggggcct tttctctccc ccactagaag	1980
cgggccctgg atgcagccat catccttggg ggaggaggac ttctcttcac ctcttacctg	2040
acagccacgg gcgatgacca tttctatgct gaatatctga tgccggccct gcagaggctg	2100
ctagaccag aatcagccca ccggctagct attcgcttca cgtccctggg gtccttcct	2160
cgagctacat ttcaggactc tgacatgctg gtaggtcccc cggtcacct gtgttacatt	2220
tgtgtttgta ggggaggtca catccttcag cacttcggta ttcctctgct gccactgggc	2280

ttttgaaaac cagagctgca ggttcacaag cagctgggac ctggagccca gcccaggaa	2340
gggacttttc ttctgtgtta caccctgtac ttacagaaca gcactcagca tatagccggt	2400
gcttacagct ttaatcctca cagataccct ttgagggagg tcctatctca tctccatcta	2460
caaatcagga aactgaggta cagactaagt aagtgacttg cccaaggta cacagctggg	2520
aggtggcagg accaggattc aaacctatag agtttgactc cagtgtccaa ctttggtcac	2580
tggcctgcct tgctgagatc cctctgctga acaggaacat cttctggagt cattaagcag	2640
ctactggatg caggggacag ggtcagcagg gaagggtgt cacttgtaga tactgtgtcc	2700
tctgtctgga taggtgtgaa gtctcagagt gggtgctgca gcctggcctg atgggtccgt	2760
cctttcccc catcagaagc agaccctggc tgtagtcac accctgaggg gtggaggact	2820
taagtcctag gcaacctcct gcccagcca cattcagcca caactcactc ctgtggccca	2880
cctggcacca ttataacag agccagtgtg gcccttctac tgtctctctg aatgctcccc	2940
ttttgagatg ggcctagggt gtccagggtg gtctcaaact tggggtccca aatgatttca	3000
gaatctcagc ttctgagta agtgggatca cacagtatgc accactgtgc gcagtgggtcc	3060
ctgttccccg atagccaggc cggttgatac tcttagcccc attcaccttt ctcggttttc	3120
taagtcttca gttttctatc atgacgagac tctcctgggg gagggggatg gctgggtgct	3180
tctggaatgc ttggctgacc cggtctcctg attgaccggt ttaccataa tctcaaagaa	3240
gcctgacatc aacaccccag gctctgtcac acagccaggg atgagaactg gcttgagggt	3300
agcctcaagg aaggcctgtt ctagctgaac ttctgcctc atggttatga agtgctgcgt	3360
gcacattttt accttccttg tgctcattct cgtctcctgt ggattttgag agcatgtagc	3420
tttccccttg gggactggcc tctaagagct cactggcagc accattgcct gccagtgtcc	3480
accttcagc tctccatggt gcccatgggc tggcttcttg acagttatgg aggaagggcc	3540
agctagggct tgtatgctag gctggctaca ggctacctca aggctggtga caccaaggac	3600
tccttctcct gccaggttg agtagatagg aagatacaca gtaattgtgc aagacagcac	3660
ctgtctcctc ttcacttggt gtgggacact atctttctct cccactgcc ttgagacccc	3720
ctggtgacag actccagcag acatcagaag cacctgcaga atgctgatgc agatagatac	3780
cccaggggtg ctttcctccc aaagatccct attttctggg ccagtgatg cttagcaagc	3840
tccaggggaa ttcttataca gtatgctggg atccctgctg tgagaaccac ttggtatagc	3900

tgcttatacc tctgacctgt ctccttccca ggaagtgaga gtcctgggcc ataaattccg	3960
aaatccggta gggattgctg cgggatttga caagcacggg gaagctgtag atggcctcta	4020
caaactgggc tttgggtttg tcgaggtagg aagtgtgact cccagcctc aggaaggaaa	4080
ccccagaccc agagtgttcc gcctcccga ggaccaagct gtcattaaca ggtaggtggt	4140
ggctcaatgt catagggaca tctcctcccc tgctgggatc tctgagatgg aacctgtttt	4200
gtgcttttct catatgatca gtggacagtc tgtcctttgg gatagtcagg agcacctttg	4260
aacacctgtt gtgtactagg cagctctcgc cccaacctg ggaaacagct gttaggattt	4320
taccaggtat tcccactgag gctctgagag ctggtgctgg ttgcaaagaa cagcttgga	4380
aggcttgggc tgttgggctt cagtgtgagc ttttttacat tgttgctcta ttgcctttgt	4440
ccaatgttgg ctaacaggaa tataatgatc tcacatgtaa ttgaaatat tctaataatg	4500
cattaaaaac tagtgaactt gataatacat ttataattat tatattttta attattatga	4560
tttaattata aacagtgtgt tctaaagtca ttttaacctg cagtcaatgt aaaaatcatt	4620
ggttaactat cgtcctcttt ttattggttt ccgggtcccc aatgccttta cttctggttc	4680
ctctcacttg gccagggctg gtggccacaa gcttcagcag cgttgggtact gtacaggtga	4740
cccttgcttt caatgaacag ggacatggta ttcaaagtga cagctgctct taggaggaga	4800
atccttcgac tgtatgaagc cttgcggttt gttgttctgt atagttagta taactgcaaa	4860
gggaagacct tcgtactttt tgctaggaga tttttggaga acctccttgt ggggattttg	4920
gcaggcctgt ggagtgctt cctactgctt gtttcaggaa actgatttac aagtcataga	4980
tctttctgtt acattacagg cagggactga tgtctttagg actggccaga caaaatactt	5040
gtgtttctga tttggctgtt acaagtgact tcgggtctta ggatgatggt acttgggaca	5100
gggagtggtg agggacaggc acctgtgctc ttgggcatgt gcgaacttag ctttcttgct	5160
catatacaca gtgtgtgttc agtataggca tgctaacgga tgggtattta cacctgcaga	5220
cccacatgcc acaatccatg cagtgttgct ctggctgcaa gcaacaaagt gatgtaacca	5280
gatctcattt gttatcattc ttgtcactag cacaaaataa ctgacagcag gcagcttaag	5340
gaatggggtc aggtattttg gctcacagtt tgaggggaca cgccctcccg gtggcaggag	5400
cctgaggcag agggtcactc tgtacctaca gtgaggaagc agcaaggga ggatgctggt	5460
gcttgggtct ctttctccgt cttgctcagc tggggtgtga atccatggtg ctgcccatgt	5520

ttgcggtggg	tcttcctgc	tccattcaac	cttcccagaa	acagtcttcc	agacacacaa	5580
caggtgtgtt	tccatggtga	ctctaagtca	catctagttg	acaatgaagc	ataaccagtg	5640
gtgagagcat	ggaaatggtc	tcaggtacgt	tttccaaact	gccacctttt	aattccaccc	5700
cttacctgtg	ggtttatgtg	ctccaggtac	ggattcaaca	gccacgggct	ctcagtgggtg	5760
gaacacaggc	tacgggccag	acagcagaag	cagaacaagc	tcactgcagg	taaactcagg	5820
tgttgtggga	gggacttact	aactctatta	caaagaaaca	tggggagggc	atgggattca	5880
gcaataagaa	acaaatgagc	aaacaattaa	aacccacag	aacaactcag	gggattgtcc	5940
agcttctacc	acagcctcaa	aggtctcaac	cagatggcat	aattcagcaa	aaccttgctg	6000
gtctctggca	tccatggaac	ctgaattgtg	tcttaactta	ggggcttgaa	gatcagcaga	6060
gagcatgtgt	ggagctaaga	tgcgccccga	gttcatcttc	ccacatcccg	ccctgctgct	6120
gtccttctgt	tcactgtgta	aatagtgtgt	attagttctg	gaagagctac	agaagagaat	6180
agagttgtca	cactcctgtc	cttccactca	ggggaccagc	tgtcctcaaa	tctcacttcg	6240
gaaacaacct	ttgcttttgg	tggattctca	tggagacgct	ccagtttgtc	ctctgtggtc	6300
tgcatggctc	tctgaagtgc	atthttgggg	caaagccctg	ggtggtggcc	cccctcccca	6360
tgtctccctg	tgtggcttct	gcagtcctatg	gagatttttc	tcctttgcct	ctggaatgtc	6420
tttcaggagg	tcttagtctc	atthgatgtc	cccatagtgt	gacaattaag	ccaaggactt	6480
ctgcatttat	ttgaggagct	aaggaagaga	gggctgaagc	atthgacgag	tttagagggt	6540
gggaacagga	aatgacaatg	tttaaaaaaa	cccctggttt	tgacggaacc	gggtctgcca	6600
gccctgtaga	accttgaaca	caatgtttgt	ggtttgtggc	gttctcctgc	ctcctgcctt	6660
ccgtttcttc	gttttaaatgc	cttctgtggg	ctaggtttat	tgccattgtc	ctgtgtccac	6720
ccttcaccc	cattctgtgc	cctcacagtc	actggagtga	ggccaagtcc	tgtgtctttg	6780
ccctgcctac	atgtgtctgc	tgacagctag	cagcctcata	gaaacttttc	atcagcacca	6840
tgccataggaa	ccctagtggg	tagaagagac	tgtgctttgt	gtaaagtgtg	gttcagcctt	6900
cctgactcca	gaactgtgac	tgtgggcagg	tgaccactaa	tgaaaggctc	agttgcctct	6960
tgggaagccat	actctcaatc	cagtttactt	gtgctaaagc	ttacagtgat	cctggcttgc	7020
tgggtgctag	acttgaagct	ttgagacctt	gttctgtata	tagtctaata	cctggctcca	7080
cccagcccac	ttaggaaatt	agttacacaa	atcttacttt	taagttgatg	accagaaga	7140

tgacgggttg tgagagatgg actgtgagaa gggggctagc aatacagtgg gggatgttgc	7200
ccgtgtcctc cctggcctgg tatgggtgag ctgacttggt gttctaggtc tggctggatt	7260
ggcagatgga cagcagcctg ggccactgac atactaggag ttgtaagaaa gttgagttgt	7320
aataaagatg aatccaggaa actcctttct gccaaagaga acatgagtct gaaagagcat	7380
ttttctagag gcttggcctt ttgagagtga cagggggcag gtgtgagtaa ttacaccag	7440
gccccaggag tgtcttgagg ctacagagat gtatcatcac cctaattata agttcttttc	7500
tcagagaaca agaaagattt attacacact tccatctact ttttaggcat gatagttgaa	7560
aacatttcct agtgttttcc tgtgtagctc aggctggcct cagacttaca gcaatcctcc	7620
tgcagactaa atttccatgt gtggcctcca gtgttttata cttttgtttt taatcatttc	7680
acatacagtc cttgaccaa ggctcatgag attcaggttg ttcttgctga catgcccac	7740
aatacctgcc tactctctct tttgttatct ctcaaaccac tgatctgtga atatagcaag	7800
tgtcattggg agtcatttta ttgctacata cttcaagaag agcagtagta tttgtttttt	7860
tccccatgtc cctgatttgt ctggactcag atccttggcc acccatgcag tcagtgttgg	7920
ggatgggttc catctcatgg attgggcctt aaatacaatc agattctggt tggttactcc	7980
cgcagctttg tgctactgtt tcactagtgc atccagggca ggtcatcatt gtagatcaaa	8040
agatgtgtag cggggtttgt gtttaccttt ctcttttgtt aacatgcaga atacctccca	8100
gtaccatgga caccaccaga gggatgaagg ctgtaggtag gcaccagctc gacttctccc	8160
tatttaataa cttgtgtagg tgttgtcttt agcaatagag cttgtcagt tttcagagag	8220
caaccaatat cttgacaat agcctgggtt gtttgggtat tctcatgggg cccctttggc	8280
caacaacttc tttgaaagtc tgggtcaaatt cttcactaaa accatctggc actgggcatt	8340
ttttggttgg gaggctttta tgactgcttc tattttacta ggggttataa gtttgtttac	8400
attgcttatc cgatcttgat ttaactttag tagatggtat gtatcaagaa aattattcat	8460
ttattttcaa ttttccattt aggtagagta taggttttta aaacacatcc ctatgattct	8520
ttggatttcc ttggtgtctg ttgttatgtc actcttttca tctctaattt tgtaaatttg	8580
gatctttcct ctttgccttt taattaattt ggctaagggt ttgtcaatct tactggtttt	8640
ctcaaagaac caactcttcg tttcattgat tctttgcatt atttttgtct gtttctattt	8700
cattgatttc agccctgagt ttgattattt cctgccatct actcctcctg ggtgtgactt	8760

cttgttggtc tagagctttc aggtgtgcta gtatgaaatc tctctaattt atgtaggcac	8820
ttagtgctac ataaagtttt gggtttttgt tttgttttga cctatttttc attcagtagt	8880
gagttgttca gtttcagttg ttcagtttcc atgagtttgt aagctttctg ttgtttttgt	8940
aggtgttgat attcagcttt aatctgtggt ggtatgatag ggtattattt cagttttctt	9000
gtatcttttg agacttgctt tatggcctag tatatggcca gttttggaga aagttccatg	9060
aggtgctgag aagaaacgtt ttgtgtttgg gtgaaatgtt ctataaatta ggtccatttg	9120
gtttaacaca tcatttagct ccatcatttc tttgttcagt ttttgtctgg atgacctgtc	9180
tattgtcgag agttggggag tatcaaagta tcccactatg tgtgtgtgtg tgcggagggg	9240
tcaatatgtg atttaagcta tagtagagtt tcttttatga acttggatgc ctttgtgctt	9300
ggtgcataga tgtttagaat ttcaatatcc tcttggtggg tttttccttt gatgagtatg	9360
tagtttcctt ccctatctat ctcttgatta gatttgattt gaaatctatt ctgtcatata	9420
ttaaaatggc ttcacccatt tgctttcttg tccatttgct tggaatatct ttttccatcc	9480
ttttactctg aggtgatatc tatccttgat gttaaagtat gtttcttgga ttcagttaaa	9540
gaatgaatcc tatttttgaa cccaattttt tagtctgtgt cttatttatt gggaaattga	9600
ggccactgat atcagtgttt gttgattcct gttatattat tgttatggcg taggcccctt	9660
cccttttgat ttgctggctt gagattattt attcaggctg aagttttcct tgtagtacct	9720
tctatcaagc tggatttgta gacagaaacc acttaagttt ctttttattg tagattgtca	9780
ttctttcttc atctctgtga ttaaagtgtt tgctggctat agtagtctgg gctggcatct	9840
gtggtagaat gtctgcccag gaccttgac ttttagagtc tcgattgaag tcaggggtta	9900
ttctaatagg tttgtctgcc gttatatgtt atctggtcct tctctattgt ggcttttggg	9960
attctttctt tgttctgtac attctgtttt ttgattatta tgtgttgtgg ggaatttatt	10020
tttggcccag tccgtttggg gttctatttg tttcttatac catgataggc acttccttct	10080
ttaggttagg taacttttca tctgtgattt tgttgaaaat attttctgtg ctttgacct	10140
gggtttcttc tccttttgct atccctgtta cttatagatt tttggtgttt tcatagtatc	10200
ctagatttcc tggatgtttt gtgcctggat tttgttttct ttcttttttt gtagatttaa	10260
cattttcttt gactgcagta tccttgcttc ctatcttgct ctcatgtctt gagactctgt	10320
cttccatttc ttgtatgatt ttggtgaggc ttgcttctaa gatttctgtt ctagttccta	10380

aatTTTTcat	ttccagcttt	acctcaattt	gggttttctt	tagcaattcc	atttcctctt	10440
tcatgtgttg	aacaattttc	ttcatttcat	tgcactgttt	gtgttttcat	taatgggttt	10500
attcataatct	tcttttaggga	ccttgaacat	attcataata	gctattctga	gagccttgct	10560
ttatgcttcc	ctgtattgca	tttctcggag	cctgctgtgg	tagggttgct	gggctctagt	10620
ggagacatgt	cgttctggct	gttactgggt	ttttacactg	gtgtctaggc	gactgggttt	10680
gagaagattg	taattctagg	tgctgatatc	tggtcttggt	tttgttgggg	tgatgttcag	10740
ttccttggtt	tctgttgccc	ccccccctca	gggggggtgt	ggtaactgga	ttggttgccct	10800
ggtagggaat	gcttctgaga	tcctgccaga	accctgccac	tggcagtctt	gggtagaaag	10860
tgtttctagg	tgttgggagc	tgacactaat	gattgaggat	gggttagaag	cagtgggtggc	10920
gggagagtcc	acaggaggag	gagagctggg	tgtgccacca	gggtctgcac	agaggcctgg	10980
gaatgagaac	agagatgaag	gtgaggcctc	agcaggtagt	ctgctacaag	gttgggataa	11040
ggctgggaga	ttggaacttg	gggacaggag	ggagagtga	gatcgagac	ccatcccctg	11100
gccaggtggg	ggaagcctgg	aggagaagat	ctgtgtgatc	tgctggaaat	gggtccctta	11160
gtaacttctt	gaagtttctt	tgattttgag	gctgctgttg	ggggtcccct	gtatgccaaag	11220
catgtggtat	atcactgaga	tagaatctcc	atagccctgc	ttcttttttg	agactgggtc	11280
tcatatcggc	caggttggcc	ttgaactagc	tatgttgacc	ttgaactttt	ccttacctat	11340
acctgagaac	tgggattaca	agtgcccatc	acaccagct	tcctattgtt	tttgcttttt	11400
tcctagtatt	taagcttctg	gcttcccat	taaaatttaa	aagatgaaag	gcttagtaca	11460
cgggaagcat	ccttgaaggt	gcacacactt	gccatataga	gaggatgaag	tggttctaag	11520
tcatcaggca	gcagccccag	gatcagacag	ttcacattct	ccatcatctg	gttcagggga	11580
gccccacctg	tactctgaat	gttgccctggg	aaactgtggg	gacacactct	tgatatttac	11640
agatgggctg	cctctgggaa	taaacctggg	gaagaataag	acttcggagg	atgctgctgc	11700
agactatgta	gagggtgttc	gtgtcctggg	ccccttggt	gactacctgg	tggtgaatgt	11760
gtccagtccc	aacactgctg	gtctgaggag	cctacaggga	aaggctgagc	tgcgccgcct	11820
gctggccaag	gtgtgtcatt	acaccatcac	atgcctgttg	tccttactcc	ttttcattct	11880
tcaggtgaag	attcaggaca	actgaggaga	aactgttctt	cacagctggc	ctaggagccc	11940
tcatcacaca	ttttccaagt	accctctcat	gtctcacagc	cccggtcata	cacaatagac	12000

agttcactgc tttaaaacca caggcaagca gagcagagca ggcggggctc ccatgtatca	12060
ctctgtcccc agaactgtga atgctcagca cttgtgacac acctccttgt ttgttttcag	12120
gaacaaaatc aaaacccttg agcagttatc tcggcggggg gtgcgggggt gggggaattg	12180
ctggtgcttt agttgacctt aggtgaaaat gctggcctgc actgcggggc tatgggctgg	12240
gtcccatct ctggcttgct aacctaggtg ctgcaggaga gggacgcttt gaaggagcg	12300
cagaagccag cagtgcctgt gaagatcgcc cccgacctca cggcccagga caaggaggac	12360
attgccagtg tggcgagaga ggtttgagtt ggggtggtcc agggcagggt ggggtagcc	12420
ttcatcgtcc actgctgctg ggataacaca gaaggcatg attggtgact tcctctgtgt	12480
gaagtggaca gctggttgat tgtctgtcat tgtatagttc atctggtagc aaacagttag	12540
tttgaaaatg tgtttggtga gtctttttct tgcttctgat ctgtcttcat ccagaaagtc	12600
tgaggcctgt gctagtctct gccagtctca cctgggactt agaatggtgt ctgtcccttt	12660
ccagcttgctg taaacaccag gcttctctgg ctaaaaaggt agtaggaaca cagtctgctg	12720
ttctggactt cagtcttggt ctactgtgta ctccctgaga tactcacaga cagcttgttc	12780
taagggtcaa actctgtgta ggcactgtga tgggttcagc aggagatgct gctgtgtctt	12840
cagcattgag aggctaattc tgatggcttc tccaatcaag atgtaggtga ggcctgtgag	12900
ggtcttgctc tgcagagctg gcccctggcc tgggtggctgc ttcaatcctc aaaagacagt	12960
ttccttgagt acttcagatc catggcttaa ggctcttttt ctgtcttgctg ctgcagctgg	13020
gcattgatgg attaattgtc aaaaacacca cagtgagtcg cccgactggc ctccaagggtg	13080
ctctgcgttc tgagatggga ggactgagcg ggaagccact ccgagatctg tcgaccaga	13140
ccatccggga gatgtacacc ctactcaag gtaaggcttt tttgtttgtt tgtttgaggc	13200
aggatttctc tgtttaacac ctctggctgt cctggaactc acttggtaga ccaggctggc	13260
ctggaactca cagcttcctt agtgctggga ttaaaggcat gtgccaccat tgcctggcta	13320
aggcaagact tctttggaca aatgtgaggt cctggatctt ccctcattca ctgtgtttgc	13380
tgagaactct ggttctgccc tcacggctg tgtttgctgg gactgaggcc tgatggagcc	13440
ctgggtcttt agccctccct tcccggcctt gctatgtgct tctctccagg caggattccc	13500
attatcgggg ttggtggtgt gagcagtggg caagatgcgc tggagaagat ccaggcaggg	13560
gcctccctgg tgcagctgta cacggccctc accttcctgg ggccaccgt cgtggtcagg	13620

gtcaagcgtg agctggaggc acttctaaag tgagtagggt tcgatgcagc tgagacgtag 13680
 aaagtgacac ttgtcatcag tctattgtgt actcccagag ggccggaggg aacactgagg 13740
 gcatgggtggg acgatttctc tgctgcagct ttggccaagg acaaacagtg ccagaggaat 13800
 tcagaatgct tctgaggcag ggctcattac aaggcaggac ttgccacttg cccaggggct 13860
 gggcatggag gatgaagtag taattttacat tgactcagtg tctggaagct gcaggttata 13920
 aagtcacttc ctttcctgca cagaaggcct ggctgtacat atgtgcaggg gcctgggtga 13980
 gggcagagta gcagtgggtg taagggtgtgt tgggtgggac ggtgtggtaa gcggtgtgct 14040
 catggtgagt gtgggcttcc ttaggacagg ctattttgtt tctgtccaga gagcggggtt 14100
 ttaacacagt cacagaagcc attggagcag atcatcggag gtgacggttc ctgccagatg 14160
 ccccatccag aacgtgcccc ccaactcaag caagccttgt ggctgcatca taagaggaag 14220
 atctgtctca agctatgtcc cttgactgtg tgacctggct ggactgcata agccagtcac 14280
 gggtatcact agacagtaaa ggcttttctt aatgagacca tgaactctac agtcactttc 14340
 tggatctaag tcctgggatc cctcagtatt ataaggacat tggctctttg ggaggaaaaa 14400
 tcatggagaa aataaagcca tttcaatctg ttttcaa 14437

<210> 28
 <211> 395
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> amino acid sequence of human DHODH G202A

<400> 28

Met Ala Trp Arg His Leu Lys Lys Arg Ala Gln Asp Ala Val Ile Ile
 1 5 10 15

Leu Gly Gly Gly Gly Leu Leu Phe Ala Ser Tyr Leu Met Ala Thr Gly
 20 25 30

Asp Glu Arg Phe Tyr Ala Glu His Leu Met Pro Thr Leu Gln Gly Leu
 35 40 45

Leu Asp Pro Glu Ser Ala His Arg Leu Ala Val Arg Phe Thr Ser Leu
 50 55 60

Gly Leu Leu Pro Arg Ala Arg Phe Gln Asp Ser Asp Met Leu Glu Val
65 70 75 80

Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly Ile Ala Ala Gly
85 90 95

Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr Lys Met Gly Phe
100 105 110

Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro Gln Glu Gly Asn
115 120 125

Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln Ala Val Ile Asn
130 135 140

Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val Glu His Arg Leu
145 150 155 160

Arg Ala Arg Gln Gln Lys Gln Ala Lys Leu Thr Glu Asp Gly Leu Pro
165 170 175

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

Asp Tyr Ala Glu Gly Val Arg Val Leu Ala Pro Leu Ala Asp Tyr Leu
195 200 205

Val Val Asn Val Ser Ser Pro Asn Thr Ala Gly Leu Arg Ser Leu Gln
210 215 220

Gly Lys Ala Glu Leu Arg Arg Leu Leu Thr Lys Val Leu Gln Glu Arg
225 230 235 240

Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu Val Lys Ile Ala
245 250 255

Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile Ala Ser Val Val Lys
260 265 270

Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr Thr Val Ser Arg

275

280

285

Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr Gly Gly Leu Ser
 290 295 300

Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile Arg Glu Met Tyr
 305 310 315 320

Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val Gly Gly Val Ser
 325 330 335

Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly Ala Ser Leu Val
 340 345 350

Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro Val Val Gly Lys
 355 360 365

Val Lys Arg Glu Leu Glu Ala Leu Leu Lys Glu Gln Gly Phe Gly Gly
 370 375 380

Val Thr Asp Ala Ile Gly Ala Asp His Arg Arg
 385 390 395

<210> 29
 <211> 18
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> corresponding piece of DNA for generating GS gRNA

<400> 29
 gagtatgtga agactttg

18

<210> 30
 <211> 20
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> corresponding piece of DNA for generating GS gRNA

<400> 30
 ccatctttat tctcatgggg

20

<210> 31
<211> 5562
<212> DNA
<213> *Cricetulus griseus*

<220>
<221> misc_feature
<222> (4467)..(4484)
<223> target of GS-1 gRNA

<220>
<221> misc_feature
<222> (4611)..(4630)
<223> target of GS-2 gRNA

<400> 31
accttccacc atggccacct cagcaagttc ccacttgaac aaaaacatca agcaaagtga 60
cttgtgcctg cccaggggtg agaaagtcca agccatgtat atctgggttg atggtactgg 120
agaaggactg cgctgcaaaa cccgcaccct ggactgtgag cccaagtgtg tagaaggatga 180
gcatgggcag gagcaggaca tgtgcctgga agtgggcaag cagcctgaga ttgaccttc 240
cttctgtttt gtttgcaaag tctttcaaaa gcaggtctct tcaggcctca gtcagtcacc 300
cgtaagctgc cgagtagtct ggaggcatag aaaacaatgg aggcctttat ttagatggaa 360
tcttgtgtgt gctggtacac tgaagaaaaa tattgggtca tttttagtag ggggtgggagg 420
ttggagtatt gctaacctag ccaaccccag gaacctagtt tgaaagacct gtaactagaa 480
tatgctatca agtttataga gcagtgggtc tcaacctttc aaatgcttta cacttgaata 540
caactcctca tgttctgggtg attaccccca tccaacat tgctaacttc ttaactgaaa 600
tttactact gctacgaatc ataatgtatc tgtgtttttg gatggtctta ggtgaccct 660
gtgaaagggt tgtgagacca tcctcaaagg ggttgtgacc tacaggttga gacccttttg 720
agtgtgtgtt ttattagtat ttatacagtg gaattctggg tgcaaagcac atgctccaaa 780
gtagtttctc tgggactggc ctttgtttt cagatgggga tacttttaaa aacttgcaaa 840
ggaacaaaaa aaaaaaaaaa tgcagaaaaa aggagggggg ggagggcacg cttttaatcc 900
cagtacttgg gaggcagagg caggcggatc tctgtgagtt gaagcccagc ctggtctaca 960
agagctagtt ccaggacagc ctcaaagcc acagagaaac cctgtctcaa aacaaacaaa 1020
cacacaaaaa aattaaaaaa aaaaaaaaaa tttcaaagga gacctgtttt attttagttg 1080

tggcctttgt tttggtagga agggcagcta gtttaggatg agttttttatt attctaagat	1140
gttgccgttt gagtgaatga atgaccagat gacagcatat aacatgtact tgttacttgg	1200
cagaagtagg taggtcgttc tgtttctgcc ttcagctcat aggtaactgg ggagacaaac	1260
tggcccaaaa acaaggaaaa ggaacaagtg gtaggagagc aactgtttcc tcatctacaa	1320
gagcacagcc tgagctacaa cagtcaggcc cggagaggga tgagagaagg gaggggatga	1380
ggtggcctag tgaggagtc agttttgctc tgtgccatga gtgtctcact cactggaagt	1440
ggtgtcagaa tgactgggtgc acagtagact tacagagagg actcatctgt ttgttgcttg	1500
ggtggttctt gtgatgcagt gctcttgga acctcagaag gaggaacata gggataggtg	1560
ggcatagaca tcaggttgtc cctaattaat gatgatacat ttacatacat gccactcaga	1620
agacacagta gattttcagt gatggaaata tgatgagagg ctagctgtct tgttgtata	1680
ttttaataa atttttaata aatttcattgt gtgtgagtca gtgcgtgtgt gcgtttgctc	1740
gcccagtgct gtgccagcag aggtctgagg aggggtgtgag aatcccagga actgaagtta	1800
acagttgtgg ttaagagtac ttatcactcg ttaccagcac ctacatggtg gtcacaacc	1860
atctgtaact ccaatttcag gggctccaac cccctcttct gcaggcatac acttgcacag	1920
atatacatgc aagtaaaaca cccctacaca cataaaaata aatacgtctt cttaaaagtt	1980
aattttccat ctttatttgg cccagagtta cctgagtgga attttgatgg ctctagtacc	2040
tttcagtctg agggctcaa cagtgacatg tatctcagcc ctgttgccat gtttcgggac	2100
cccttccgca gagatcccaa caagctggtg ttctgtgaag ttttcaagta caaccggaag	2160
cctgcaggtg tgtatggggg gggcgtgaat gtcttaagaa tctagggatg gatgatcaga	2220
tgtccatcct tctaccctga acttgcctgc tgaaaaacag tgtgggtccgc ccctccatgg	2280
tcccttttat tggttgtata aacagtgttg aatcttccat ctgtttgctg ataggggtcc	2340
ccagtacag tcttgatctg cttctacatt taaaaagctg taattcgtac ttaagcgttt	2400
tggggtttaa ctactagatc tgccatttat tgccagtac cttggcatac tttgccccat	2460
gcttctattt tgctgaatta tgtgtagaga gagacgagac agagcatgct tgaactgagg	2520
gcgtactgtg ctctgtgtgg aagtcaaccg acaacctgtg gaatcagttc tctcctgctg	2580
tatttgtaga ttctggaggt ggaactcagg ttgccatgag cattatgatt cctggctaag	2640
ctgtttgccc atgaagcctt ctgtacctgc tcatagaatt ttgtttatgc cgtgctatcc	2700

atactcagtt ttcagatagc ttcttaaacc cagggaactc taatttacat aaactctctt	2760
ccagtactgc cagtaaggct tgggtggcct ataccttcag tacctctgtt ttgaaaagga	2820
agtattgttg gtcaagggtg tgtacctcag catggcagcc atggggttcc tggctgtgcc	2880
gcttgcccta taacctgggc acgtcaccaa acaccctctc tcagggcttc attttctcat	2940
ttgtgaaagt gaagattgct aacactcatc tcaaactcag ttaaatagata aattgctttt	3000
ctagcttggg aattgttttc agttacactc acctctccct cgctttctct ctcttttttg	3060
taccagccaa tactgtgtaa tttagcactc agactcacct ggaatgtaaa cctaattggac	3120
aaattattct cagtaaaatg acagctctgg ccttaagtgc ctacgaaact aggggaatacg	3180
tttgacaagc aggagcagct gtcttgtgaa tagagggtgg aagtgtctgg catgtggtac	3240
ttggaaagtg gccagcgtgc agataggatg aacacttggt ttgctctcac tccattccca	3300
tgagatttca tagctgactt taattataaa aagtctctca gccttttcct gcaaatgtac	3360
tatcattgct tcttcacagt ggttgggcct gagtaggtcc agcctatgat gacttcagct	3420
gtgtaagagt tgaggacact actccttaca gcatgttgat gctttattcc tagagaccaa	3480
tttaaggcac tcgtgtaaac ggataatgga catggtgagc aaccagcacc cctggtttgg	3540
aatggaacag gagtatactc tgatgggaac agatgggcac ccttttggtt ggccttccaa	3600
tggctttcct gggccccaag gtaagttccc cagggtgaaat aaaagcttcc tccccataag	3660
ttcttactgt ccagagacag gagcagctcc caaatcagca aacagactgg cagctgaaaa	3720
taacagactg tccttgcata cctcaaatac agatgtgctt tgaatttaaa gtgacaggat	3780
ggtgatgaga tggctcagtg ggtaaagggt cttgccacca ggcttgacag cccgagttta	3840
tccctgagac ccatataagt tattctctga ccatctgcac atgcatgcat atacaaaaag	3900
tgaaaagcta ttcagagtgg gcagtagttc taccaaggct acagcaaaga ggaaagacct	3960
agcctcctac ctgcaggtga agacaggatg tgcgaaagca agtcttagga cttgtcatt	4020
ttctggcttt ggggggttat ggactctgat tcttcactga ttgctcttga ttctccttca	4080
ggtccgtatt actgtggtgt gggcgagac aaagcctatg gcagggatat cgtggaggct	4140
cactaccgag cctgcttgta tgctgggggtc aagattacag gaacaaatgc tgaggtcagt	4200
cctgcccagg taaatggcac tattctgttc cttttcctcc cctctgaaga cttggcacat	4260
ggggactttg gttaacaagg gtgatgactt aaaagtgggt cagggtagag gtaagtagaa	4320

caagctagga gcttgagttg gcctgaacag ttagttggcc ttattctaaa ggtcaacatg	4380
ttctttctag tgggaattcc aaataggacc ctgtgaagga atccgcatgg gagatcatct	4440
ctgggtggcc cgtttcatct tgcatacagc atgtgaagac tttggggtaa tagcaacctt	4500
tgacccaag cccattcctg ggaactggaa tggcgcaggc tgccatacca acttttagcac	4560
caaggccatg cgggaggaga atggtctgaa gtaagtagct tcctctggag ccatctttat	4620
tctcatgggg tggaagggtt ttgtgttagg gttgggaaag ttggacttct cacaaactac	4680
atgcatgct cttcgtgttt gtcataagcc tatcgttttg taccggttg agaagtgaca	4740
gtactctagg aatagaatta cagctgtgat atgggaaagt tgtcacgtag gttcaagcat	4800
ttaaaggctt ttagtaagaa ctaaatacac atacaagcaa gtgggtgact taattcttac	4860
tgatgggaag aggccagtga tgggggtctt cccatccaaa agataattgg tattacatgt	4920
tgaggactgg tctgaagcac ttgagacata ggtcacaagg cagacacagc ctgcatcaag	4980
tatttattgg tttcttatgg aactcatgcc tgctcctgcc cttgaaggac aggtttctag	5040
tgacaaggct agaccctcac ctttactgct tccaccaggc acatcgagga ggccatcgag	5100
aaactaagca agcggcaccg gtaccacatt cgagcctacg atcccaaggg gggcctggac	5160
aatgcccgtc gtctgactgg gttccacgaa acgtccaaca tcaacgactt ttctgctggt	5220
gtcgccaatc gcagtgccag catccgcatt ccccgactg tcggccagga gaagaaaggt	5280
tactttgaag accgccgcc ctctgccaat tgtgaccctt ttgcagtgc agaagccatc	5340
gtccgcacat gccttctcaa tgagactggc gacgagccct tccaatacaa aaactaatta	5400
gactttgagt gatcttgagc ctttcctagt tcatcccacc ccgcccagc tgtctcattg	5460
taactcaaag gatggaatat caaggtcttt ttattcctcg tgcccagtta atcttgcttt	5520
tattggtcag aatagaggag tcaagttctt aatccctata ca	5562

<210> 32
 <211> 56
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> GS1_F primer

<400> 32	
acactctttc cctacacgac gctcttccga tcttggcctt attctaaagg tcaaca	56

<210> 33
<211> 52
<212> DNA
<213> Artificial Sequence

<220>
<223> GS1_R primer

<400> 33
gtgactggag ttcagacgtg tgctcttccg atctcattct cctcccgcac gg 52

<210> 34
<211> 1417
<212> DNA
<213> *Cricetulus griseus*

<400> 34
ccgagccgag aatgggagta gagccgactg cttgattccc acaccaatct cctcgccgct 60
ctcacttcgc ctcgttctcg tggctcgtgg ccctgtccac cccgtccatc atcccgccgg 120
ccaccgctca gagcaccttc caccatggcc acctcagcaa gttcccactt gaacaaaaac 180
atcaagcaaa tgtacttgtg cctgccccag ggtgagaaaag tccaagccat gtatatctgg 240
gttgatggta ctggagaagg actgcgctgc aaaacccgca ccctggactg tgagcccaag 300
tgtgtagaag agttacctga gtggaatfff gatggctcta gtacctttca gtctgagggc 360
tccaacagtg acatgtatct cagccctgtt gccatgtttc gggaccctt cgcagagat 420
cccaacaagc tgggtgttctg tgaagttttc aagtacaacc ggaagcctgc agagaccaat 480
ttaaggcact cgtgtaaacg gataatggac atggtagaca accagcacc cttggtttgga 540
atggaacagg agtatactct gatgggaaca gatgggcacc cttttggttg gcctttcaat 600
ggctttcctg ggccccaagg tccgtattac tgtggtgtgg gcgcagacaa agcctatggc 660
agggatatcg mggaggctca ctaccgcgcc tgcttgatat ctgggggtcaa gattacagga 720
acaaatgctg aggtcatgcc tgcccagtgg gaattccaaa taggaccctg tgaaggaatc 780
cgcaggagat catctctggg tggcccgttt catcttgcat cgagtatgtg aagacttttg 840
ggtaatagca acctttgacc ccaagcccat tcctgggaac tggaatggtg caggctgcca 900
taccaacttt agcaccaagg ccatgcggga ggagaatggt ctgaagcaca tcgaggaggc 960
catcgagaaa ctaagcaagc ggcaccggtg ccacattcga gcctacgatc ccaagggggg 1020
cctggacaat gcccgtggtc tgactgggtt ccacgaaacg tccaacatca acgacttttc 1080

tgctggtgtc gccaatcgca gtgccagcat ccgcattccc cggactgtcg gccaggagaa	1140
gaaagggttac tttgaagacc gccgcccctc tgccaattgt gaccctttg cagtgcaga	1200
agccatcgtc cgcacatgcc ttctcaatga gactggcgac gagcccttcc aatacaaaaa	1260
ctaattagac tttgagtgat cttgagcctt tcctagttca tcccaccccg cccagctgt	1320
ctcattgtaa ctcaaaggat ggaatatcaa ggtcttttta ttcctcgtgc ccagttaatc	1380
ttgcttttat tggtcagaat agaggagtca agttctt	1417

<210> 35
 <211> 16
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> GS F primer

<400> 35	
acctttgacc ccaagc	16

<210> 36
 <211> 17
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> GS R primer

<400> 36	
cgtcgccagt ctcattg	17