
SV40 Promoter
GPT
IRES
eGFP
SV40pA
Tn-resistance marker
COI

FIG. 1

```
   **** *:*   ***:**. ********:*******.*****:********  :*******
 1 MWAFSELP--MPLLINLIVSLLGFVATVTLIPAFRGHFIAARLCGQDLNKTSRQQIPESQ     58  GPT_HUMAN
 1 MWAFSELP--MPLLVNLIVSLLGFVATVTLIPAFRGHFIAARLCGQDLNKTSRQQIPESQ     58  GPT_MACMU
 1 MWAFSELP--MPLLINLIVSLLGFVATVTLIPAFRGHFIAARLCGQDLNKTSRQQIPESQ     58  GPT_PANTR
 1 MWAFPELP--MPLLVNLVGSLLGFVATVTLIPAFRGHFIAAHLCGQDLNKTGRQQIPESQ     58  GPT_CANFA
 1 MWAFSEVP--IPLLVNLIGSLLGFVATLTLIPAFRGHFIAARLCGQDLNKTNRQQIPESQ     58  GPT_CAVPO
 1 MWAFPELPLPLPLLVNLIGSLLGFVATVTLIPAFRSHFIAARLCGQDLNKLSRQQIPESQ     60  GPT_RAT
 1 MWAFPELPLPLPLLVNLIGSLLGFVATVTLIPAFRSHFIAARLCGQDLNKLSQQQIPESQ     60  GPT_MOUSE
 1 MWAFPELPL--PLLVNLFGSLLGFVATVTLIPAFRSHFIAARLCGQDLNKLSRQQIPESQ     58  GPT_CRIGR

   ***.*********************::**********************************
59 GVISGAVFLIILFCFIPFPFLNCFVKEQCKAFPHHEFVALIGALLAICCMIFLGFADDVL    118  GPT_HUMAN
59 GVISGAVFLIILFCFIPFPFLNCFVKEQCKAFPHHEFVALIGALLAICCMIFLGFADDVL    118  GPT_MACMU
59 GVISGAVFLIILFCFIPFPFLNCFVKEQCKAFPHHEFVALIGALLAICCMIFLGFADDVL    118  GPT_PANTR
59 GVISGAVFLIILFCFIPFPFLNCFMEEQCKAFPHHEFVALIGALLAICCMIFLGFADDVL    118  GPT_CANFA
59 GVISGAVFLIILFCFIPFPFLNCFVKEQCKAFPHHEFVALIGALLAICCMIFLGFADDVL    118  GPT_CAVPO
61 GVISGAVFLIILFCFIPFPFLNCFVEEQCKAFPHHEFVALIGALLAICCMIFLGFADDVL    120  GPT_RAT
61 GVISGAVFLIILFCFIPFPFLNCFVEEQCKAFPHHEFVALIGALLAICCMIFLGFADDVL    120  GPT_MOUSE
59 GVICGAVFLIILFCFIPFPFLNCFVEEQCKAFPHHEFVALIGALLAICCMIFLGFADDVL    118  GPT_CRIGR

   ************************************* :**********************
119 NLRWRHKLLLPTAASLPLLMVYFTNFGNTTIVVPKPFRPILGLHLDLGILYYVYMGLLAV    178  GPT_HUMAN
119 NLRWRHKLLLPTAASLPLLMVYFTNFGNTTIVVPKPFRPILGLHLDLGILYYVYMGLLAV    178  GPT_MACMU
119 NLRWRHKLLLPTAASLPLLMVYFTNFGNTTIVVPKPFRPILGLHLDLGILYYVYMGLLAV    178  GPT_PANTR
119 NLRWRHKLLLPTAASLPLLMVYFTNFGNTTIVVPKPFRPILGLHLDLGILYYVYMGLLAV    178  GPT_CANFA
119 NLRWRHKLLLPTAASLPLLMVYFTNFGNTTIVVPKPFRPVLGLHLDLGILYYVYMGLLAV    178  GPT_CAVPO
121 NLRWRHKLLLPTAASLPLLMVYFTNFGNTTIVVPKPFRWILGLHLDLGILYYVYMGLLAV    180  GPT_RAT
121 NLRWRHKLLLPTAASLPLLMVYFTNFGNTTIVVPKPFRWILGLHLDLGILYYVYMGLLAV    180  GPT_MOUSE
119 NLRWRHKLLLPTAASLPLLMVYFTNFGNTTIVVPKPFRWILGLHLDLGILYYVYMGLLAV    178  GPT_CRIGR
```

FIG. 2A

```
    ************************************:** ****:******:*********
179 FCTNAINILAGINGLEAGQSLVISASIIVFNLVELEGDCRDDHVFSLYFMIPFFFTTLGL  238 GPT_HUMAN
179 FCTNAINILAGINGLEAGQSLVISASIIVFNLVELEGDCRDDHVFSLYFMIPFFFTTLGL  238 GPT_MACMU
179 FCTNAINILAGINGLEAGQSLVISASIIVFNLVELEGDCRDDHVFSLYFMIPFFFTTLGL  238 GPT_PANTR
179 FCTNAINILAGINGLEAGQSLVISASIIVFNLVELEGDYRDDHVFSLYFMIPFFFTTLGL  238 GPT_CANFA
179 FCTNAINILAGINGLEAGQSLVISASIIVFNLVELQGDYRDDHVFSLYFMIPFFFTTLGL  238 GPT_CAVPO
181 FCTNAINILAGINGLEAGQSLVISASIIVFNLVELEGDYRDDHVFSLYFMMPFFFTTLGL  240 GPT_RAT
181 FCTNAINILAGINGLEAGQSLVISASIIVFNLVELEGDYRDDHIFSLYFMIPFFFTTLGL  240 GPT_MOUSE
179 FCTNAINILAGINGLEAGQSLVISASIIVFNLVELEGDYRDDHVFSLYFMIPFFFTTLGL  238 GPT_CRIGR

    ********:**********************************:*************:: **
239 LYHNWYPSRVFVGDTFCYFAGMTFAVVGILGHFSKTMLLFFMPQVFNFLYSLPQLLHIIP  298 GPT_HUMAN
239 LYHNWYPSRVFVGDTFCYFAGMTFAVVGILGHFSKTMLLFFMPQVFNFLYSLPQLLHIIP  298 GPT_MACMU
239 LYHNWYPSRVFVGDTFCYFAGMTFAVVGILGHFSKTMLLFFMPQVFNFLYSLPQLLHIIP  298 GPT_PANTR
239 LYHNWYPSQVFVGDTFCYFAGMTFAVVGILGHFSKTMLLFFMPQVFNFLYSLPQLLHIIP  298 GPT_CANFA
239 LYHNWYPSQVFVGDTFCYFAGMTFAVVGILGHFSKTMLLFFMPQVFNFLYSLPQLLHIIP  298 GPT_CAVPO
241 LYHNWYPSQVFVGDTFCYFAGMTFAVVGILGHFSKTMLLFFMPQVFNFLYSLPQLFQIIP  300 GPT_RAT
241 LYHNWYPSRVFVGDTFCYFAGMTFAVVGILGHFSKTMLLFFMPQVFNFLYSLPQLFHIIP  300 GPT_MOUSE
239 LYHNWYPSQVFVGDTFCYFAGMTFAVVGILGHFSKTMLLFFIPQVFNFLYSLPQLLHAIP  298 GPT_CRIGR

    *****:**** **************:.*****.******  *:***:*:.: *** ****
299 CPRHRIPRLNIKTGKLEMSYSKFKTKSLSFLGTFILKVAESLQLVTVHQSETEDGEFTEC  358 GPT_HUMAN
299 CPRHRIPRLNIKTGKLEMSYSKFKTKSLSFLGTFILKVAESLRLVTIHQSDTEDGEFTEC  358 GPT_MACMU
299 CPRHRIPRLNIKTGKLEMSYSKFKTKSLSFLGTFILKVAESLQLVTVHQSETEDGEFTEC  358 GPT_PANTR
299 CPRHRIPRLNTKTGKLEMSYSKFKTKSLSFLGNFILKVAASLQLVTVHQSENEDGAFTEC  358 GPT_CANFA
299 CPRHRIPRLNTKTGKLEMSYSKFKTNSLSFLGTFILKVAERLQLVTVHRSEGEDGAFTEC  358 GPT_CAVPO
301 CPRHRMPRLNTKTGKLEMSYSKFKTKSLSFLGTFILKVAESLRLVTVHRGESEDGAFTEC  360 GPT_RAT
301 CPRHRMPRLNAKTGKLEMSYSKFKTKNLSFLGTFILKVAENLRLVTVHQGESEDGAFTEC  360 GPT_MOUSE
299 CPRHRIPRLNPKTGKLEMSYSKFKTKNLSFLGTFILKVAERLQLVTVHRGESEDGAFTEC  358 GPT_CRIGR
```

FIG. 2B

```
    *****:*****::** *******:*****::.** ***************
359 NNMTLINLLLKVLGPIHERNLTLLLLLLQILGSAITFSIRYQLVRLFYDV  408 GPT_HUMAN
359 NNMTLINLLLKIFGPIHERNLTLLLLLLQILGSAFTFSIRYQLVRLFYDV  408 GPT_MACMU
359 NNMTLINLLLKILGPIHERNLTLLLLLLQILGSAITFSIRYQLVRLFYDV  408 GPT_PANTR
359 NNMTLLNLLLKVLGPMHERNLTLLLLLLQILGSAVTFSIRYQLVRLFYDV  408 GPT_CANFA
359 NNMTLINLLLKIFGPIHERNLTLLLLLLQIVGSAVTFSIRYQLVRLFYDV  408 GPT_CAVPO
361 NNMTLINLLLKVFGPTHERNLTLFLLLLQVLSSAVTFSIRYQLVRLFYDV  410 GPT_RAT
361 NNMTLINLLLKVFGPIHERNLTLLLLLLQVLSSAATFSIRYQLVRLFYDV  410 GPT_MOUSE
359 NNMTLINLLLKIFGPIHERNLTLLLLLLQILSSAVTFSIRYQLVRLFYDV  408 GPT_CRIGR
```

FIG. 2C

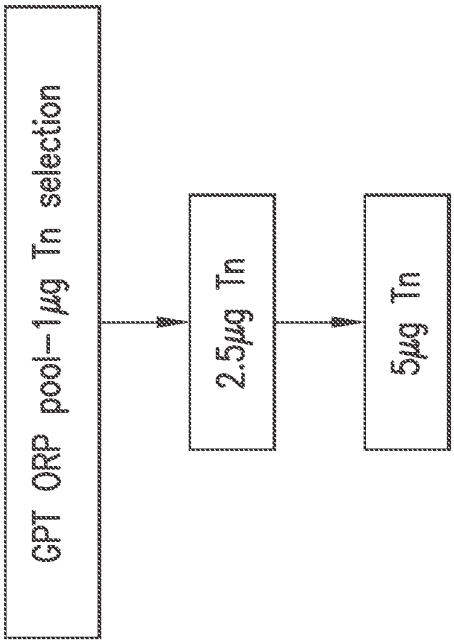

GPT ORP pool–1μg Tn selection
2.5μg Tn
5μg Tn

FIG.3B

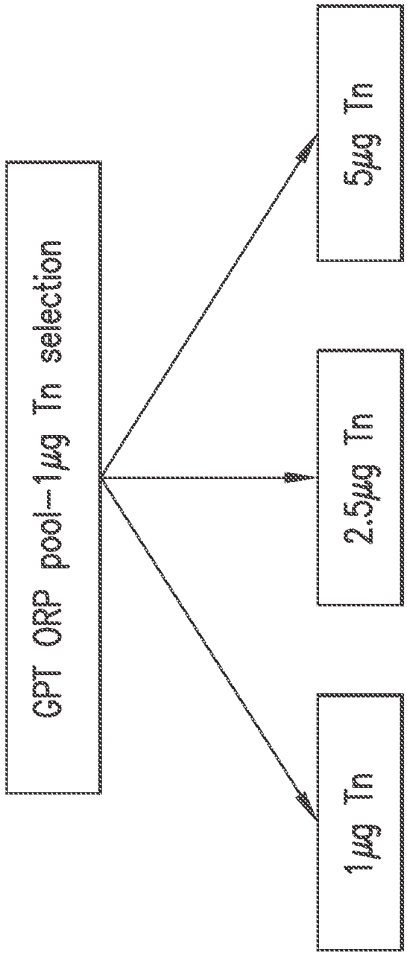
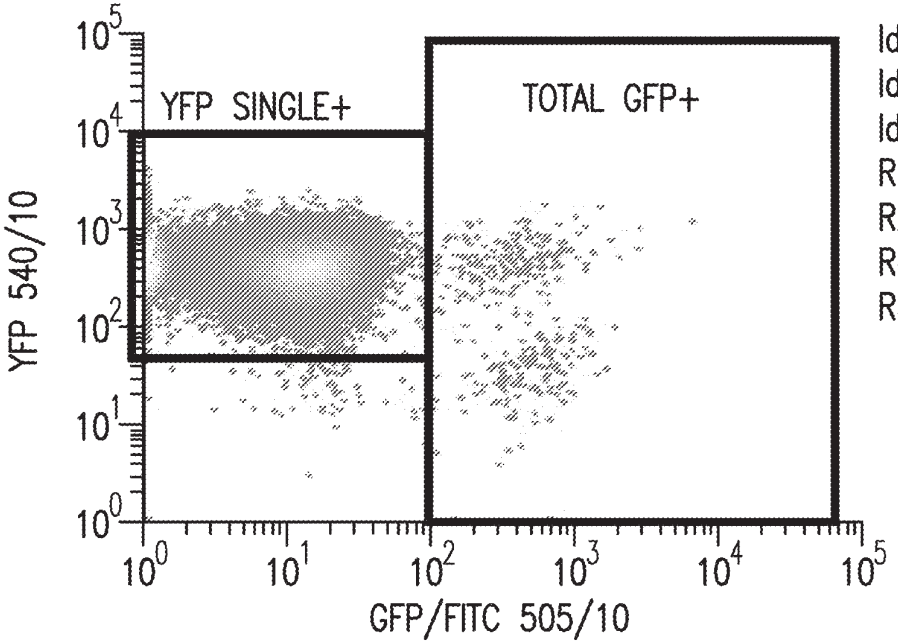

GPT ORP pool–1μg Tn selection
1μg Tn
2.5μg Tn
5μg Tn

FIG.3A

Selection efficiency with Hygromycin



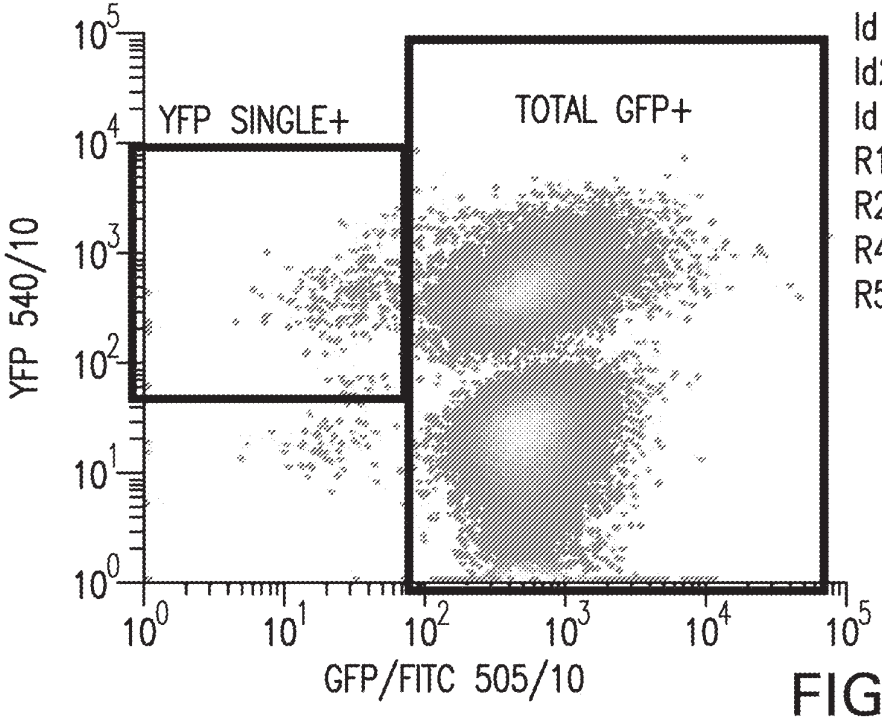
Id1: 005
Id2: 14 Jul2015

Id	Alias	Total	Gated	Region	Percent	%Gate
R1	R1	50000	50000	28315	56.63	56.63
R2	R2	50000	28315	26134	52.27	92.30
R4	YFP SINGLE+	50000	26134	25696	51.39	98.32
R5	TOTAL GFP+	50000	26134	354	0.71	1.35

No Hyg selection

FIG.4A

Selection efficiency with Hygromycin



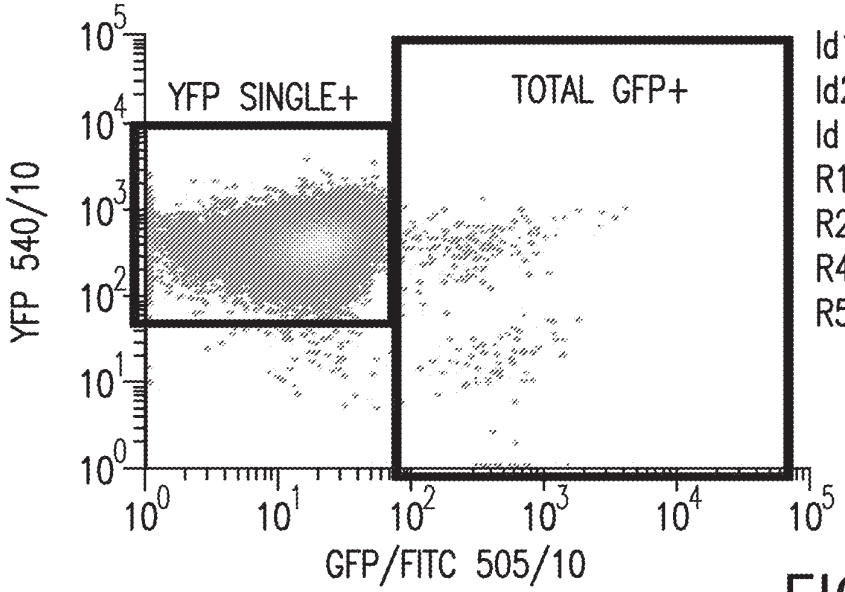
Id1: 006
Id2: 14 Jul2015

Id	Alias	Total	Gated	Region	Percent	%Gate
R1	R1	50000	50000	33318	66.64	66.64
R2	R2	50000	33318	29446	58.89	88.38
R4	YFP SINGLE+	50000	29446	263	0.53	0.89
R5	TOTAL GFP+	50000	29446	29100	58.20	98.82

400 μg/ml selection

FIG.4B

Selection efficiency with Tn and GPT
as a selectable marker



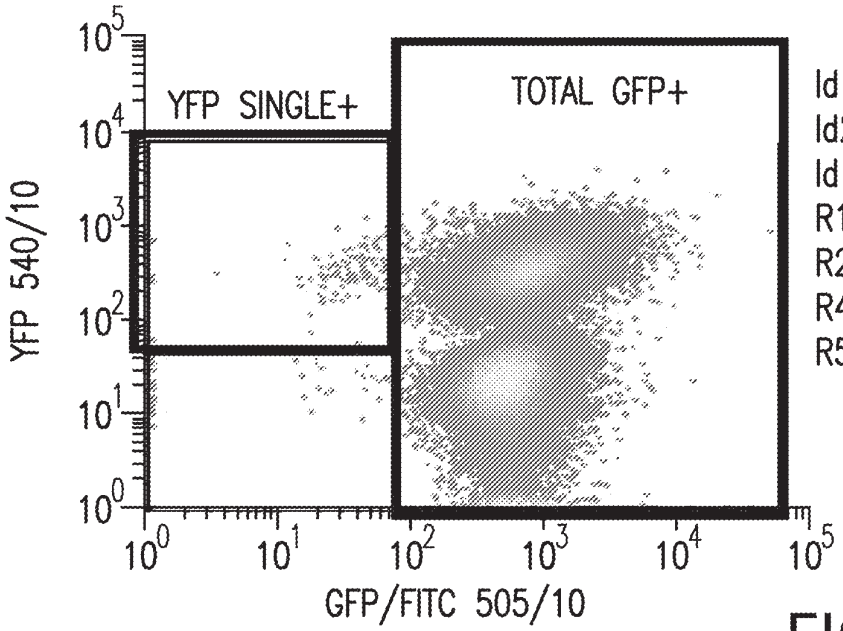
Id1: 008
Id2: 14 Jul2015

Id	Alias	Total	Gated	Region	Percent	%Gate
R1	R1	41183	41183	24495	59.48	59.48
R2	R2	41183	24495	24494	59.48	100.00
R4	YFP SINGLE+	41183	24494	24199	58.76	98.80
R5	TOTAL GFP+	41183	24494	217	0.53	0.89

No Tn selection;
CHO–GPT marker

FIG.5A

Selection efficiency with Tn and GPT
as a selectable marker



Id1: 009
Id2: 14 Jul2015

Id	Alias	Total	Gated	Region	Percent	%Gate
R1	R1	44227	44227	32032	72.43	72.43
R2	R2	44227	32032	32015	72.39	99.95
R4	YFP SINGLE+	44227	32015	114	0.26	0.36
R5	TOTAL GFP+	44227	32015	27823	62.91	86.91

1 μg/ml Tn selection;
CHO-GPT marker

FIG.5B

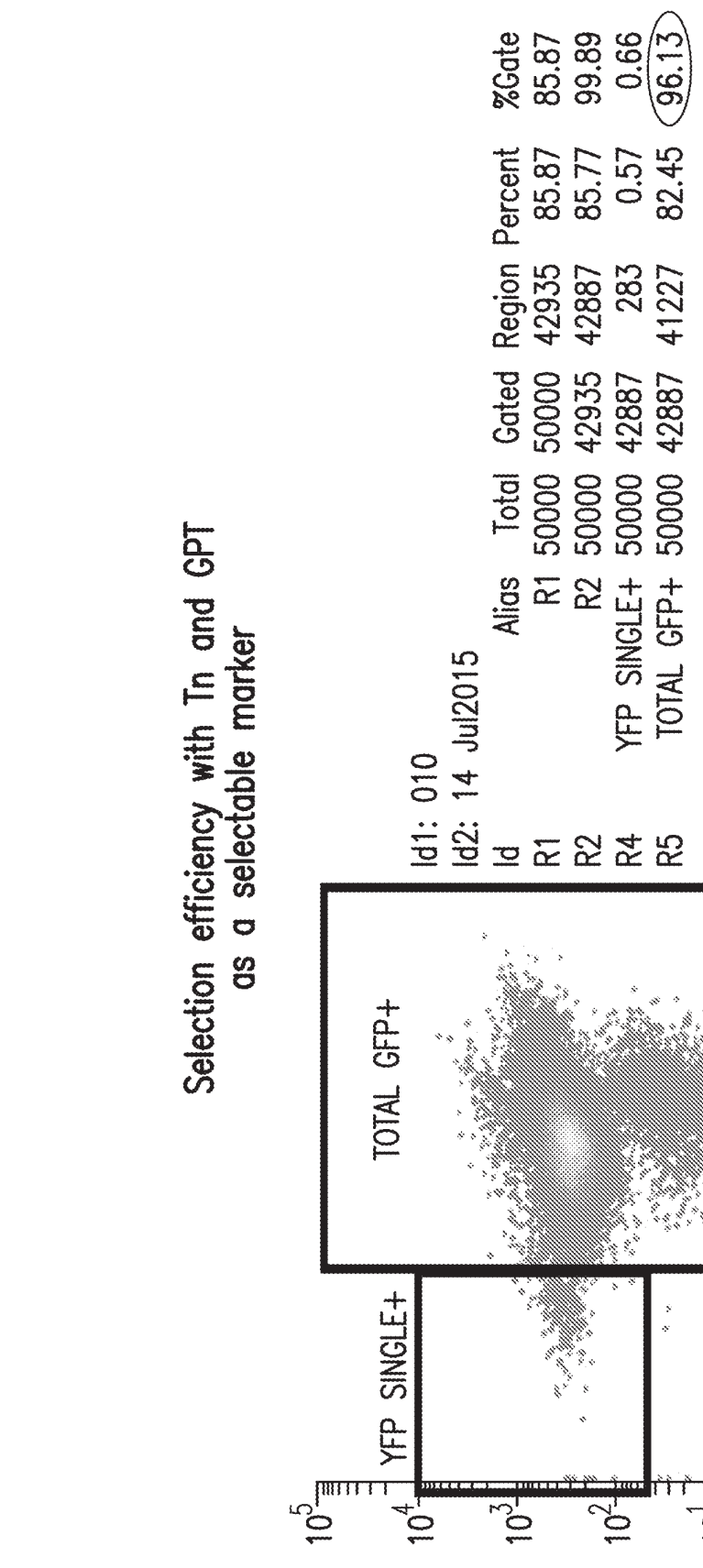
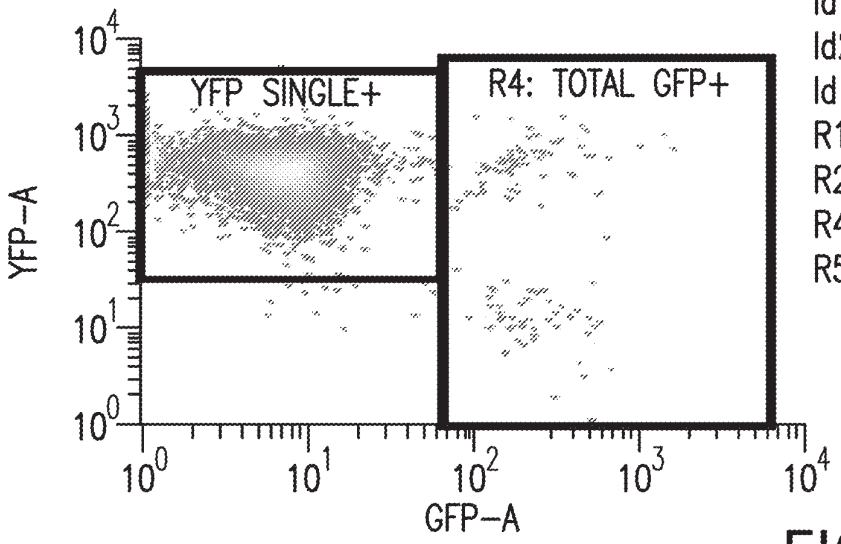

Selection efficiency with Tn and GPT
as a selectable marker
Id1: 010
Id2: 14 Jul2015
Id Alias Total Gated Region Percent %Gate
R1 R1 50000 50000 42935 85.87 85.87
R2 R2 50000 42935 42887 85.77 99.89
R4 YFP SINGLE+ 50000 42887 283 0.57 0.66
R5 TOTAL GFP+ 50000 42887 41227 82.45 96.13
2.5 μg/ml Tn selection;
CHO-GPT marker
TOTAL GFP+
YFP SINGLE+
YFP 540/10
GFP/FITC 505/10

FIG.5C

Selection efficiency with Tn and GPT
as a selectable marker



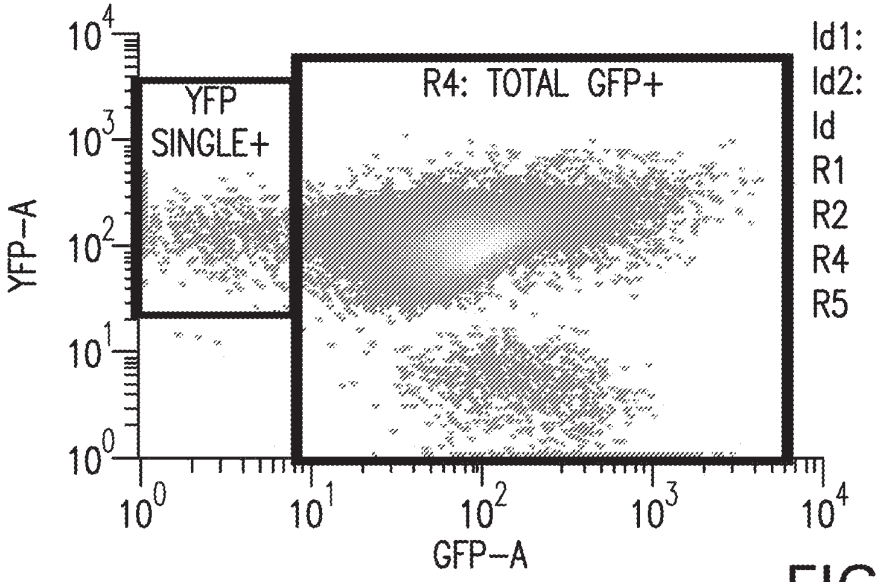
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Id2: 13 Jul2015

Id	Alias	Total	Gated	Region	Percent	%Gate
R1	10.63%	50000	50000	5315	10.63	10.63
R2	90.72%	50000	5315	4822	9.64	90.72
R4	TOTAL GFP+	50000	4822	126	0.25	2.61
R5	YFP SINGLE+	50000	4822	4680	9.36	97.06

No Tn selection;
Human-GPT marker

FIG.5D

Selection efficiency with Tn and GPT
as a selectable marker



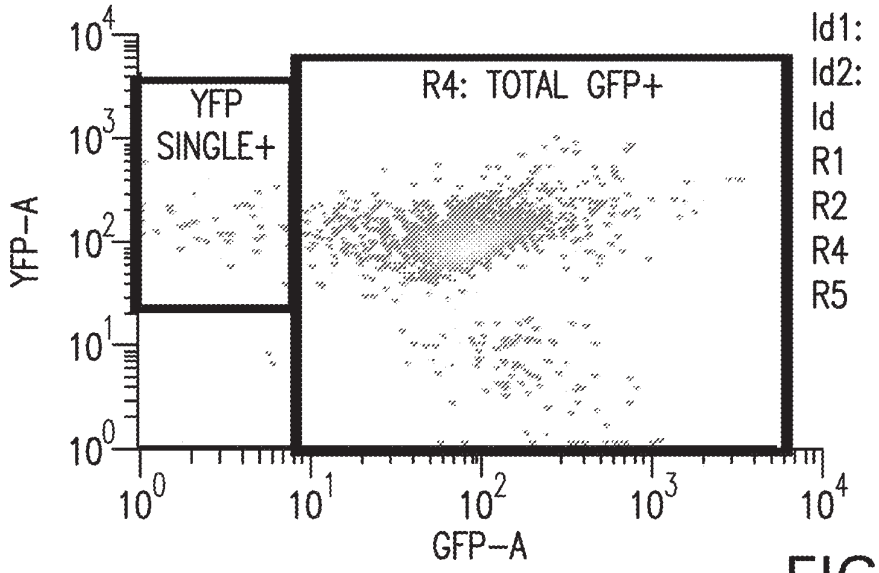
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Id2: 13Jul2015

Id	Alias	Total	Gated	Region	Percent	%Gate
R1	59.32%	31256	31256	18542	59.32	59.32
R2	97.62%	31256	18542	18101	57.91	97.62
R4	TOTAL GFP+	31256	18101	17558	56.17	97.00
R5	YFP SINGLE+	31256	18101	526	1.68	2.91

1 μg/ml Tn selection;
Human-GPT marker

FIG.5E

Selection efficiency with Tn and GPT
as a selectable marker



Id1: 007
Id2: 13Jul2015

Id	Alias	Total	Gated	Region	Percent	%Gate
R1	2.48%	50000	50000	1241	2.48	2.48
R2	98.87	50000	1241	1227	2.45	98.87
R4	TOTAL GFP+	50000	1227	1187	2.37	96.74
R5	YFP SINGLE+	50000	1227	35	0.07	2.85

2.5 μg/ml Tn selection;
Human-GPT marker

FIG.5F

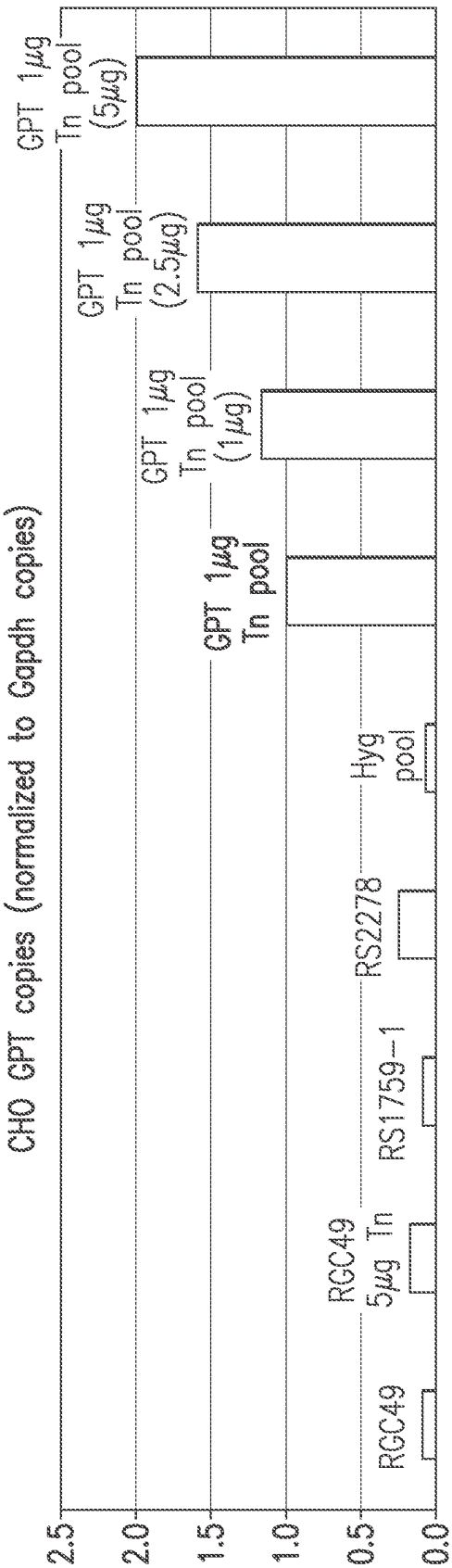

CHO GPT copies (normalized to Gapdh copies)
2.5
2.0
1.5
1.0
0.5
0.0
RGC49
RGC49
5μg Tn
RS1759−1
RS2278
Hyg pool
GPT 1μg Tn pool
GPT 1μg Tn pool (1μg)
GPT 1μg Tn pool (2.5μg)
GPT 1μg Tn pool (5μg)

FIG.6A

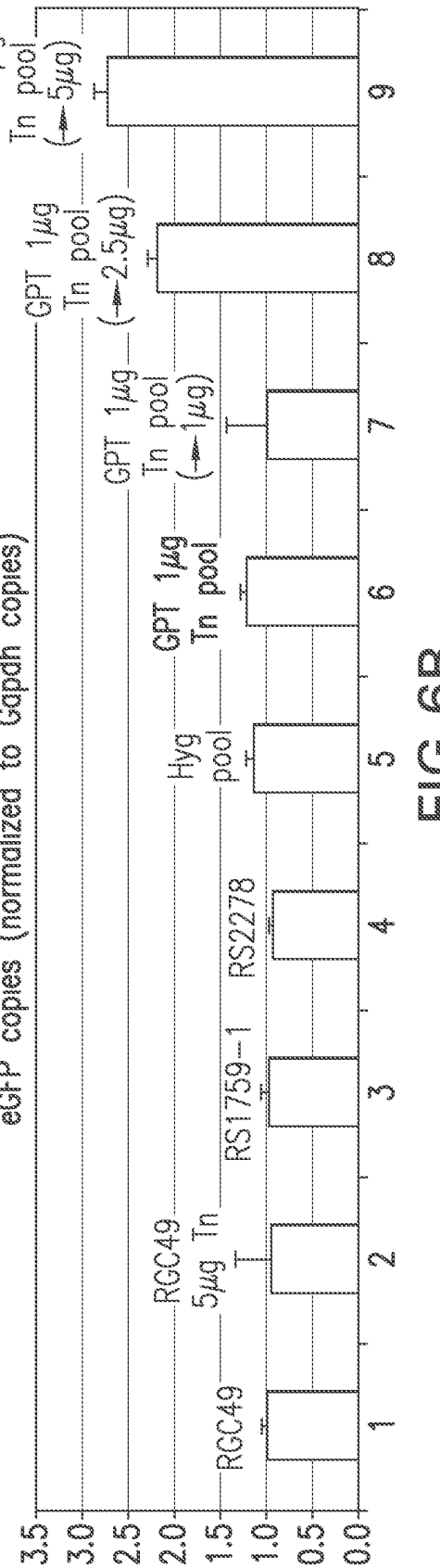

eGFP copies (normalized to Gapdh copies)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1
2
3
4
5
6
7
8
9
RGC49
RGC49
5μg Tn
RS1759−1
RS2278
Hyg pool
GPT 1μg Tn pool
GPT 1μg Tn pool (1μg)
GPT 1μg Tn pool (2.5μg)
GPT 1μg Tn pool (5μg)

FIG.6B

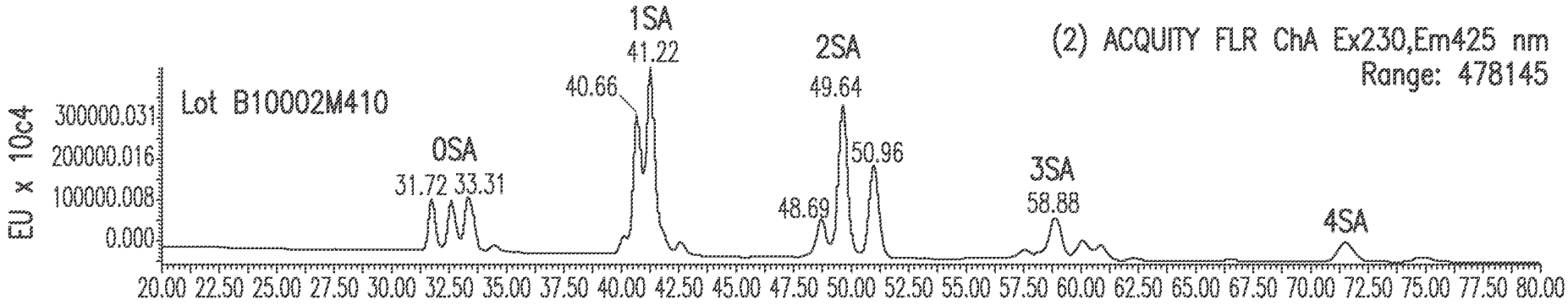

(2) ACQUITY FLR ChA Ex230,Em425 nm
Range: 478145
Lot B10002M410
EU x 10c4
300000.031
200000.016
100000.008
0.000
0SA
31.72 33.31
1SA
41.22
40.66
2SA
49.64
48.69
50.96
3SA
58.88
4SA
20.00 22.50 25.00 27.50 30.00 32.50 35.00 37.50 40.00 42.50 45.00 47.50 50.00 52.50 55.00 57.50 60.00 62.50 65.00 67.50 70.00 72.50 75.00 77.50 80.00

FIG.7A

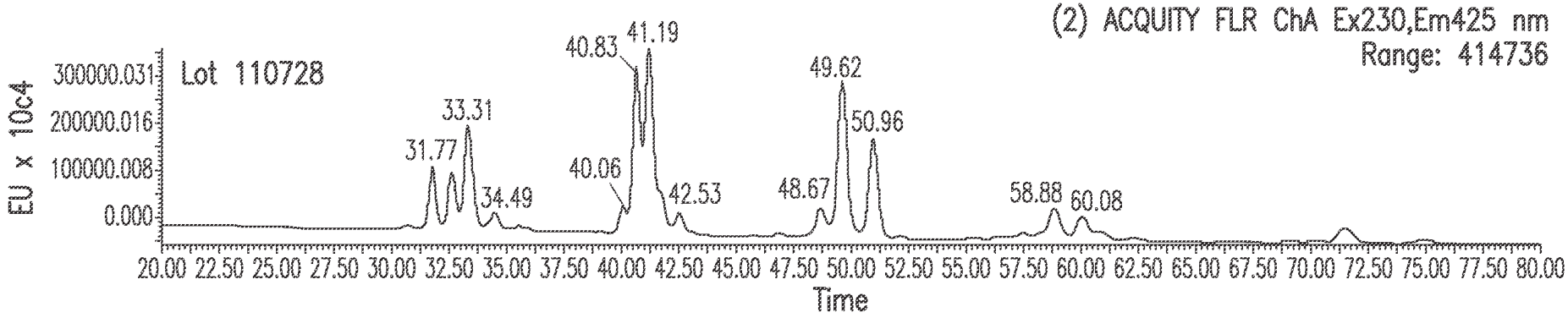

(2) ACQUITY FLR ChA Ex230,Em425 nm
Range: 414736
Lot 110728
EU x 10c4
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200000.016
100000.008
0.000
31.77
33.31
34.49
40.06
40.83
41.19
42.53
48.67
49.62
50.96
58.88
60.08
20.00 22.50 25.00 27.50 30.00 32.50 35.00 37.50 40.00 42.50 45.00 47.50 50.00 52.50 55.00 57.50 60.00 62.50 65.00 67.50 70.00 72.50 75.00 77.50 80.00
Time

FIG.7B

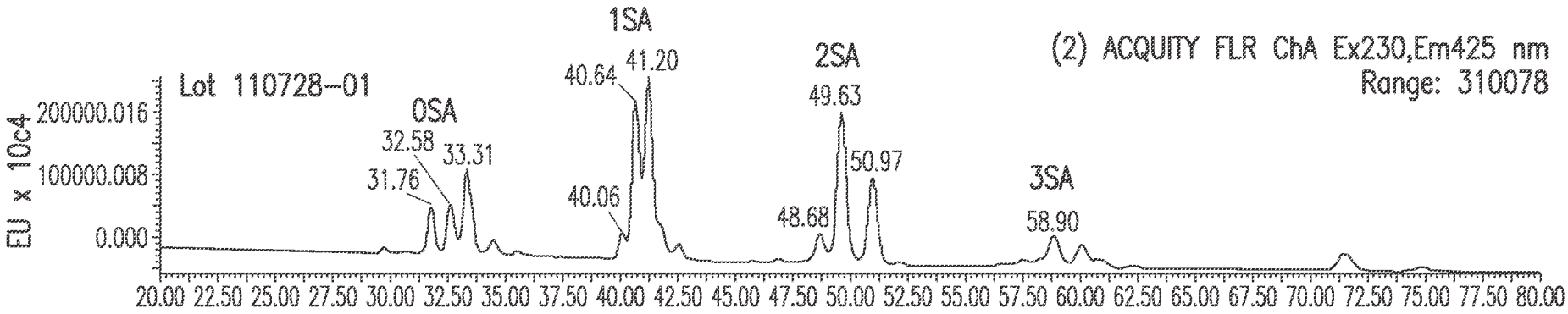

Lot 110728-01
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Range: 310078
EU x 10c4
200000.016
100000.008
0.000
0SA
1SA
2SA
3SA
31.76
32.58
33.31
40.06
40.64
41.20
48.68
49.63
50.97
58.90
20.00 22.50 25.00 27.50 30.00 32.50 35.00 37.50 40.00 42.50 45.00 47.50 50.00 52.50 55.00 57.50 60.00 62.50 65.00 67.50 70.00 72.50 75.00 77.50 80.00

FIG.7C

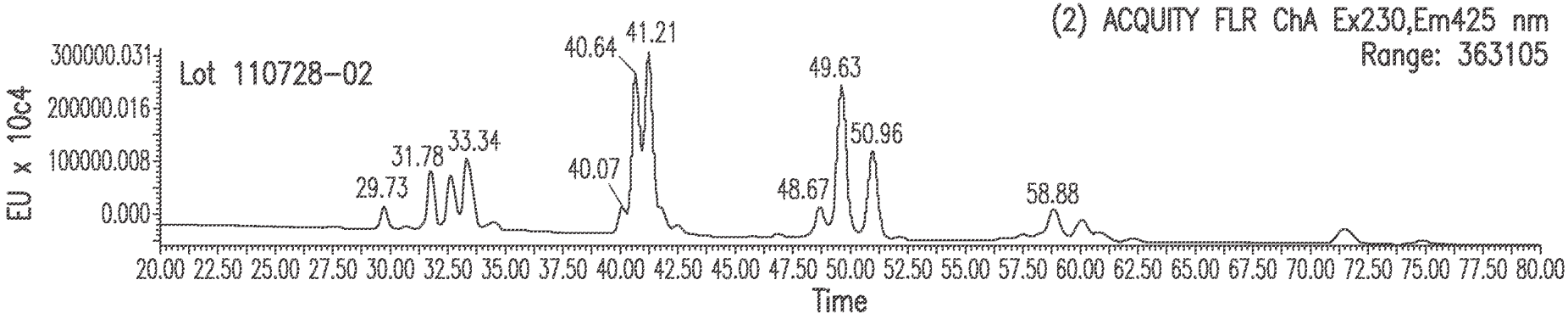

Lot 110728-02
(2) ACQUITY FLR ChA Ex230,Em425 nm
Range: 363105
EU x 10c4
300000.031
200000.016
100000.008
0.000
29.73
31.78
33.34
40.07
40.64
41.21
48.67
49.63
50.96
58.88
20.00 22.50 25.00 27.50 30.00 32.50 35.00 37.50 40.00 42.50 45.00 47.50 50.00 52.50 55.00 57.50 60.00 62.50 65.00 67.50 70.00 72.50 75.00 77.50 80.00
Time

FIG.7D

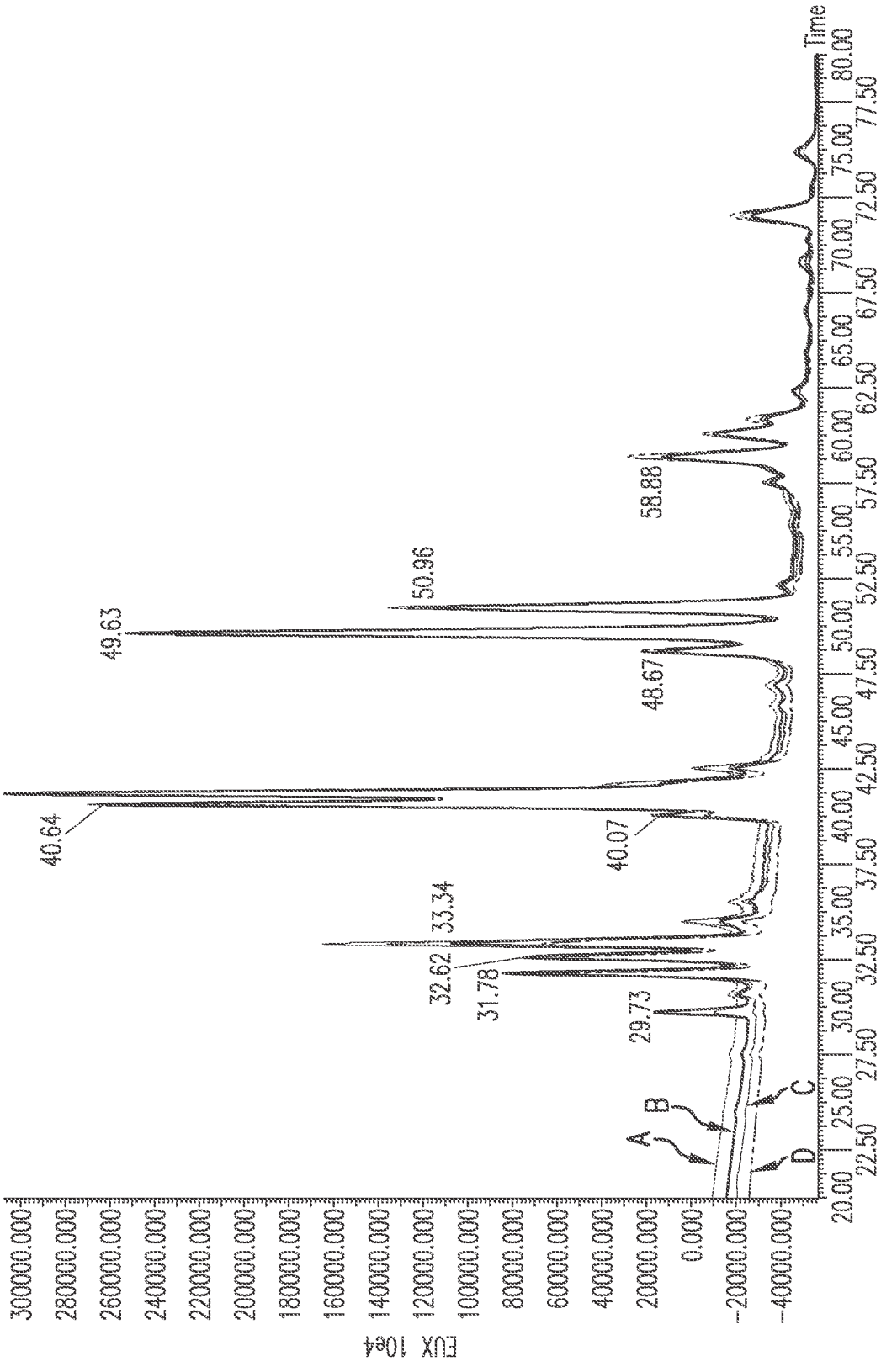

EUX 10e4
Time
41.21
40.64
49.63
50.96
58.88
48.67
40.07
33.34
32.62
31.78
29.73
A
B
C
D

FIG.8

SEQUENCE LISTING

<110> Regeneron Pharmaceuticals, Inc.
Deshpande, Dipali
Burakov, Darya
Chen, Gang
Fandl, James P.

<120> EFFICIENT SELECTIVITY OF RECOMBINANT PROTEINS

<130> 8700WO

<150> US 62/039,416
<151> 2014-08-19

<160> 17

<170> PatentIn version 3.5

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ctcccacacc tccccctgaa cctgaaacat aaaatgaatg caattgttgt tgttaacttg 180

tttattgcag cttataatgg ttacaaataa agcaatagca tcacaaattt cacaaataaa 240

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gtctaccggt ataacttcgt ataatgtata ctatacgaag ttagccggta gggcccctct 360

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aagcgtggcg ctttctcata gctcacgctg taggtatctc agttcggtgt aggtcgttcg 660

ctccaagctg ggctgtgtgc acgaaccccc cgttcagccc gaccgctgcg ccttatccgg 720

taactatcgt cttgagtcca acccggtaag acacgactta tcgccactgg cagcagccac 780

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<213> Cricetulus griseus

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<212> PRT
<213> Cricetulus griseus

<400> 3

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Gly Ser Leu Leu Gly Phe Val Ala Thr Val Thr Leu Ile Pro Ala Phe
20 25 30

Arg Ser His Phe Ile Ala Ala Arg Leu Cys Gly Gln Asp Leu Asn Lys
35 40 45

Leu Ser Arg Gln Gln Ile Pro Glu Ser Gln Gly Val Ile Cys Gly Ala
50 55 60

Val Phe Leu Ile Ile Leu Phe Cys Phe Ile Pro Phe Pro Phe Leu Asn
65 70 75 80

Cys Phe Val Glu Glu Gln Cys Lys Ala Phe Pro His His Glu Phe Val
85 90 95

Ala Leu Ile Gly Ala Leu Leu Ala Ile Cys Cys Met Ile Phe Leu Gly
100 105 110

Phe Ala Asp Asp Val Leu Asn Leu Arg Trp Arg His Lys Leu Leu Leu

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        115                 120                 125

Pro Thr Ala Ala Ser Leu Pro Leu Leu Met Val Tyr Phe Thr Asn Phe
    130                 135                 140

Gly Asn Thr Thr Ile Val Val Pro Lys Pro Phe Arg Trp Ile Leu Gly
145                 150                 155                 160

Leu His Leu Asp Leu Gly Ile Leu Tyr Tyr Val Tyr Met Gly Leu Leu
                165                 170                 175

Ala Val Phe Cys Thr Asn Ala Ile Asn Ile Leu Ala Gly Ile Asn Gly
            180                 185                 190

Leu Glu Ala Gly Gln Ser Leu Val Ile Ser Ala Ser Ile Ile Val Phe
        195                 200                 205

Asn Leu Val Glu Leu Glu Gly Asp Tyr Arg Asp Asp His Val Phe Ser
    210                 215                 220

Leu Tyr Phe Met Ile Pro Phe Phe Phe Thr Thr Leu Gly Leu Leu Tyr
225                 230                 235                 240

His Asn Trp Tyr Pro Ser Gln Val Phe Val Gly Asp Thr Phe Cys Tyr
                245                 250                 255

Phe Ala Gly Met Thr Phe Ala Val Val Gly Ile Leu Gly His Phe Ser
            260                 265                 270

Lys Thr Met Leu Leu Phe Phe Ile Pro Gln Val Phe Asn Phe Leu Tyr
        275                 280                 285

Ser Leu Pro Gln Leu Leu His Ala Ile Pro Cys Pro Arg His Arg Ile
    290                 295                 300

Pro Arg Leu Asn Pro Lys Thr Gly Lys Leu Glu Met Ser Tyr Ser Lys
305                 310                 315                 320

Phe Lys Thr Lys Asn Leu Ser Phe Leu Gly Thr Phe Ile Leu Lys Val
                325                 330                 335

Ala Glu Arg Leu Gln Leu Val Thr Val His Arg Gly Glu Ser Glu Asp
            340                 345                 350
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Gly Ala Phe Thr Glu Cys Asn Asn Met Thr Leu Ile Asn Leu Leu Leu
        355                 360                 365

Lys Ile Phe Gly Pro Ile His Glu Arg Asn Leu Thr Leu Leu Leu Leu
    370                 375                 380

Leu Leu Gln Ile Leu Ser Ser Ala Val Thr Phe Ser Ile Arg Tyr Gln
385                 390                 395                 400

Leu Val Arg Leu Phe Tyr Asp Val
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<210> 4
<211> 408
<212> PRT
<213> Homo sapiens

<400> 4

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Met Trp Ala Phe Ser Glu Leu Pro Met Pro Leu Leu Ile Asn Leu Ile
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Val Ser Leu Leu Gly Phe Val Ala Thr Val Thr Leu Ile Pro Ala Phe
            20                  25                  30

Arg Gly His Phe Ile Ala Ala Arg Leu Cys Gly Gln Asp Leu Asn Lys
        35                  40                  45

Thr Ser Arg Gln Gln Ile Pro Glu Ser Gln Gly Val Ile Ser Gly Ala
    50                  55                  60

Val Phe Leu Ile Ile Leu Phe Cys Phe Ile Pro Phe Pro Phe Leu Asn
65                  70                  75                  80

Cys Phe Val Lys Glu Gln Cys Lys Ala Phe Pro His His Glu Phe Val
                85                  90                  95

Ala Leu Ile Gly Ala Leu Leu Ala Ile Cys Cys Met Ile Phe Leu Gly
            100                 105                 110

Phe Ala Asp Asp Val Leu Asn Leu Arg Trp Arg His Lys Leu Leu Leu
        115                 120                 125

Pro Thr Ala Ala Ser Leu Pro Leu Leu Met Val Tyr Phe Thr Asn Phe
    130                 135                 140
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Gly Asn Thr Thr Ile Val Val Pro Lys Pro Phe Arg Pro Ile Leu Gly
145                 150                 155                 160

Leu His Leu Asp Leu Gly Ile Leu Tyr Tyr Val Tyr Met Gly Leu Leu
                165                 170                 175

Ala Val Phe Cys Thr Asn Ala Ile Asn Ile Leu Ala Gly Ile Asn Gly
            180                 185                 190

Leu Glu Ala Gly Gln Ser Leu Val Ile Ser Ala Ser Ile Ile Val Phe
        195                 200                 205

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

Leu Tyr Phe Met Ile Pro Phe Phe Phe Thr Thr Leu Gly Leu Leu Tyr
225                 230                 235                 240

His Asn Trp Tyr Pro Ser Arg Val Phe Val Gly Asp Thr Phe Cys Tyr
                245                 250                 255

Phe Ala Gly Met Thr Phe Ala Val Val Gly Ile Leu Gly His Phe Ser
            260                 265                 270

Lys Thr Met Leu Leu Phe Phe Met Pro Gln Val Phe Asn Phe Leu Tyr
        275                 280                 285

Ser Leu Pro Gln Leu Leu His Ile Ile Pro Cys Pro Arg His Arg Ile
    290                 295                 300

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

Phe Lys Thr Lys Ser Leu Ser Phe Leu Gly Thr Phe Ile Leu Lys Val
                325                 330                 335

Ala Glu Ser Leu Gln Leu Val Thr Val His Gln Ser Glu Thr Glu Asp
            340                 345                 350

Gly Glu Phe Thr Glu Cys Asn Asn Met Thr Leu Ile Asn Leu Leu Leu
        355                 360                 365
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Lys Val Leu Gly Pro Ile His Glu Arg Asn Leu Thr Leu Leu Leu Leu
    370                 375                 380

Leu Leu Gln Ile Leu Gly Ser Ala Ile Thr Phe Ser Ile Arg Tyr Gln
385                 390                 395                 400

Leu Val Arg Leu Phe Tyr Asp Val
                405
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<210> 5
<211> 408
<212> PRT
<213> Macaca mulatta

<400> 5

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Met Trp Ala Phe Ser Glu Leu Pro Met Pro Leu Leu Val Asn Leu Ile
1               5                   10                  15

Val Ser Leu Leu Gly Phe Val Ala Thr Val Thr Leu Ile Pro Ala Phe
            20                  25                  30

Arg Gly His Phe Ile Ala Ala Arg Leu Cys Gly Gln Asp Leu Asn Lys
        35                  40                  45

Thr Ser Arg Gln Gln Ile Pro Glu Ser Gln Gly Val Ile Ser Gly Ala
    50                  55                  60

Val Phe Leu Ile Ile Leu Phe Cys Phe Ile Pro Phe Pro Phe Leu Asn
65                  70                  75                  80

Cys Phe Val Lys Glu Gln Cys Lys Ala Phe Pro His His Glu Phe Val
                85                  90                  95

Ala Leu Ile Gly Ala Leu Leu Ala Ile Cys Cys Met Ile Phe Leu Gly
            100                 105                 110

Phe Ala Asp Asp Val Leu Asn Leu Arg Trp Arg His Lys Leu Leu Leu
        115                 120                 125

Pro Thr Ala Ala Ser Leu Pro Leu Leu Met Val Tyr Phe Thr Asn Phe
    130                 135                 140

Gly Asn Thr Thr Ile Val Val Pro Lys Pro Phe Arg Pro Ile Leu Gly
145                 150                 155                 160
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Leu His Leu Asp Leu Gly Ile Leu Tyr Tyr Val Tyr Met Gly Leu Leu
                165                 170                 175

Ala Val Phe Cys Thr Asn Ala Ile Asn Ile Leu Ala Gly Ile Asn Gly
            180                 185                 190

Leu Glu Ala Gly Gln Ser Leu Val Ile Ser Ala Ser Ile Ile Val Phe
        195                 200                 205

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

Leu Tyr Phe Met Ile Pro Phe Phe Phe Thr Thr Leu Gly Leu Leu Tyr
225                 230                 235                 240

His Asn Trp Tyr Pro Ser Arg Val Phe Val Gly Asp Thr Phe Cys Tyr
                245                 250                 255

Phe Ala Gly Met Thr Phe Ala Val Val Gly Ile Leu Gly His Phe Ser
            260                 265                 270

Lys Thr Met Leu Leu Phe Phe Met Pro Gln Val Phe Asn Phe Leu Tyr
        275                 280                 285

Ser Leu Pro Gln Leu Leu His Ile Ile Pro Cys Pro Arg His Arg Ile
    290                 295                 300

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

Phe Lys Thr Lys Ser Leu Ser Phe Leu Gly Thr Phe Ile Leu Lys Val
                325                 330                 335

Ala Glu Ser Leu Arg Leu Val Thr Ile His Gln Ser Asp Thr Glu Asp
            340                 345                 350

Gly Glu Phe Thr Glu Cys Asn Asn Met Thr Leu Ile Asn Leu Leu Leu
        355                 360                 365

Lys Ile Phe Gly Pro Ile His Glu Arg Asn Leu Thr Leu Leu Leu Leu
    370                 375                 380

Leu Leu Gln Ile Leu Gly Ser Ala Phe Thr Phe Ser Ile Arg Tyr Gln
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385 390 395 400

Leu Val Arg Leu Phe Tyr Asp Val
405

<210> 6
<211> 408
<212> PRT
<213> Pan troglodytes

<400> 6

Met Trp Ala Phe Ser Glu Leu Pro Met Pro Leu Leu Ile Asn Leu Ile
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Val Ser Leu Leu Gly Phe Val Ala Thr Val Thr Leu Ile Pro Ala Phe
20 25 30

Arg Gly His Phe Ile Ala Ala Arg Leu Cys Gly Gln Asp Leu Asn Lys
35 40 45

Thr Ser Arg Gln Gln Ile Pro Glu Ser Gln Gly Val Ile Ser Gly Ala
50 55 60

Val Phe Leu Ile Ile Leu Phe Cys Phe Ile Pro Phe Pro Phe Leu Asn
65 70 75 80

Cys Phe Val Lys Glu Gln Cys Lys Ala Phe Pro His His Glu Phe Val
85 90 95

Ala Leu Ile Gly Ala Leu Leu Ala Ile Cys Cys Met Ile Phe Leu Gly
100 105 110

Phe Ala Asp Asp Val Leu Asn Leu Arg Trp Arg His Lys Leu Leu Leu
115 120 125

Pro Thr Ala Ala Ser Leu Pro Leu Leu Met Val Tyr Phe Thr Asn Phe
130 135 140

Gly Asn Thr Thr Ile Val Val Pro Lys Pro Phe Arg Pro Ile Leu Gly
145 150 155 160

Leu His Leu Asp Leu Gly Ile Leu Tyr Tyr Val Tyr Met Gly Leu Leu
165 170 175

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Ala Val Phe Cys Thr Asn Ala Ile Asn Ile Leu Ala Gly Ile Asn Gly
            180                 185                 190

Leu Glu Ala Gly Gln Ser Leu Val Ile Ser Ala Ser Ile Ile Val Phe
        195                 200                 205

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

Leu Tyr Phe Met Ile Pro Phe Phe Phe Thr Thr Leu Gly Leu Leu Tyr
225                 230                 235                 240

His Asn Trp Tyr Pro Ser Arg Val Phe Val Gly Asp Thr Phe Cys Tyr
                245                 250                 255

Phe Ala Gly Met Thr Phe Ala Val Val Gly Ile Leu Gly His Phe Ser
            260                 265                 270

Lys Thr Met Leu Leu Phe Phe Met Pro Gln Val Phe Asn Phe Leu Tyr
        275                 280                 285

Ser Leu Pro Gln Leu Leu His Ile Ile Pro Cys Pro Arg His Arg Ile
    290                 295                 300

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

Phe Lys Thr Lys Ser Leu Ser Phe Leu Gly Thr Phe Ile Leu Lys Val
                325                 330                 335

Ala Glu Ser Leu Gln Leu Val Thr Val His Gln Ser Glu Thr Glu Asp
            340                 345                 350

Gly Glu Phe Thr Glu Cys Asn Asn Met Thr Leu Ile Asn Leu Leu Leu
        355                 360                 365

Lys Ile Leu Gly Pro Ile His Glu Arg Asn Leu Thr Leu Leu Leu Leu
    370                 375                 380

Leu Leu Gln Ile Leu Gly Ser Ala Ile Thr Phe Ser Ile Arg Tyr Gln
385                 390                 395                 400

Leu Val Arg Leu Phe Tyr Asp Val
                405
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<210> 7
<211> 408
<212> PRT
<213> Canis familiaris

<400> 7

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Met Trp Ala Phe Pro Glu Leu Pro Met Pro Leu Leu Val Asn Leu Val
1               5                  10                  15

Gly Ser Leu Leu Gly Phe Val Ala Thr Val Thr Leu Ile Pro Ala Phe
            20                  25                  30

Arg Gly His Phe Ile Ala Ala His Leu Cys Gly Gln Asp Leu Asn Lys
        35                  40                  45

Thr Gly Arg Gln Gln Ile Pro Glu Ser Gln Gly Val Ile Ser Gly Ala
    50                  55                  60

Val Phe Leu Ile Ile Leu Phe Cys Phe Ile Pro Phe Pro Phe Leu Asn
65                  70                  75                  80

Cys Phe Met Glu Glu Gln Cys Lys Ala Phe Pro His His Glu Phe Val
                85                  90                  95

Ala Leu Ile Gly Ala Leu Leu Ala Ile Cys Cys Met Ile Phe Leu Gly
            100                 105                 110

Phe Ala Asp Asp Val Leu Asn Leu Arg Trp Arg His Lys Leu Leu Leu
        115                 120                 125

Pro Thr Ala Ala Ser Leu Pro Leu Leu Met Val Tyr Phe Thr Asn Phe
    130                 135                 140

Gly Asn Thr Thr Ile Val Val Pro Lys Pro Phe Arg Pro Ile Leu Gly
145                 150                 155                 160

Leu His Leu Asp Leu Gly Ile Leu Tyr Tyr Val Tyr Met Gly Leu Leu
                165                 170                 175

Ala Val Phe Cys Thr Asn Ala Ile Asn Ile Leu Ala Gly Ile Asn Gly
            180                 185                 190

Leu Glu Ala Gly Gln Ser Leu Val Ile Ser Ala Ser Ile Ile Val Phe
```

```
        195                 200                 205

Asn Leu Val Glu Leu Glu Gly Asp Tyr Arg Asp Asp His Val Phe Ser
    210                 215                 220

Leu Tyr Phe Met Ile Pro Phe Phe Phe Thr Thr Leu Gly Leu Leu Tyr
225                 230                 235                 240

His Asn Trp Tyr Pro Ser Gln Val Phe Val Gly Asp Thr Phe Cys Tyr
                245                 250                 255

Phe Ala Gly Met Thr Phe Ala Val Val Gly Ile Leu Gly His Phe Ser
            260                 265                 270

Lys Thr Met Leu Leu Phe Phe Met Pro Gln Val Phe Asn Phe Leu Tyr
        275                 280                 285

Ser Leu Pro Gln Leu Leu His Ile Ile Pro Cys Pro Arg His Arg Ile
    290                 295                 300

Pro Arg Leu Asn Thr Lys Thr Gly Lys Leu Glu Met Ser Tyr Ser Lys
305                 310                 315                 320

Phe Lys Thr Lys Ser Leu Ser Phe Leu Gly Asn Phe Ile Leu Lys Val
                325                 330                 335

Ala Ala Ser Leu Gln Leu Val Thr Val His Gln Ser Glu Asn Glu Asp
            340                 345                 350

Gly Ala Phe Thr Glu Cys Asn Asn Met Thr Leu Leu Asn Leu Leu Leu
        355                 360                 365

Lys Val Leu Gly Pro Met His Glu Arg Asn Leu Thr Leu Leu Leu Leu
    370                 375                 380

Leu Leu Gln Ile Leu Gly Ser Ala Val Thr Phe Ser Ile Arg Tyr Gln
385                 390                 395                 400

Leu Val Arg Leu Phe Tyr Asp Val
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<210> 8
<211> 408
<212> PRT

<213> Cavia porcellus

<400> 8

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Gly Ser Leu Leu Gly Phe Val Ala Thr Leu Thr Leu Ile Pro Ala Phe
            20                  25                  30

Arg Gly His Phe Ile Ala Ala Arg Leu Cys Gly Gln Asp Leu Asn Lys
        35                  40                  45

Thr Asn Arg Gln Gln Ile Pro Glu Ser Gln Gly Val Ile Ser Gly Ala
    50                  55                  60

Val Phe Leu Ile Ile Leu Phe Cys Phe Ile Pro Phe Pro Phe Leu Asn
65                  70                  75                  80

Cys Phe Val Lys Glu Gln Cys Lys Ala Phe Pro His His Glu Phe Val
                85                  90                  95

Ala Leu Ile Gly Ala Leu Leu Ala Ile Cys Cys Met Ile Phe Leu Gly
            100                 105                 110

Phe Ala Asp Asp Val Leu Asn Leu Arg Trp Arg His Lys Leu Leu Leu
        115                 120                 125

Pro Thr Ala Ala Ser Leu Pro Leu Leu Met Val Tyr Phe Thr Asn Phe
    130                 135                 140

Gly Asn Thr Thr Ile Val Val Pro Lys Pro Phe Arg Pro Val Leu Gly
145                 150                 155                 160

Leu His Leu Asp Leu Gly Ile Leu Tyr Tyr Val Tyr Met Gly Leu Leu
                165                 170                 175

Ala Val Phe Cys Thr Asn Ala Ile Asn Ile Leu Ala Gly Ile Asn Gly
            180                 185                 190

Leu Glu Ala Gly Gln Ser Leu Val Ile Ser Ala Ser Ile Ile Val Phe
        195                 200                 205

Asn Leu Val Glu Leu Gln Gly Asp Tyr Arg Asp Asp His Val Phe Ser
    210                 215                 220
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```
Leu Tyr Phe Met Ile Pro Phe Phe Phe Thr Thr Leu Gly Leu Leu Tyr
225                 230                 235                 240

His Asn Trp Tyr Pro Ser Gln Val Phe Val Gly Asp Thr Phe Cys Tyr
                245                 250                 255

Phe Ala Gly Met Thr Phe Ala Val Val Gly Ile Leu Gly His Phe Ser
            260                 265                 270

Lys Thr Met Leu Leu Phe Phe Met Pro Gln Val Phe Asn Phe Leu Tyr
        275                 280                 285

Ser Leu Pro Gln Leu Leu His Ile Ile Pro Cys Pro Arg His Arg Ile
    290                 295                 300

Pro Arg Leu Asn Thr Lys Thr Gly Lys Leu Glu Met Ser Tyr Ser Lys
305                 310                 315                 320

Phe Lys Thr Asn Ser Leu Ser Phe Leu Gly Thr Phe Ile Leu Lys Val
                325                 330                 335

Ala Glu Arg Leu Gln Leu Val Thr Val His Arg Ser Glu Gly Glu Asp
            340                 345                 350

Gly Ala Phe Thr Glu Cys Asn Asn Met Thr Leu Ile Asn Leu Leu Leu
        355                 360                 365

Lys Ile Phe Gly Pro Ile His Glu Arg Asn Leu Thr Leu Leu Leu Leu
    370                 375                 380

Leu Leu Gln Ile Val Gly Ser Ala Val Thr Phe Ser Ile Arg Tyr Gln
385                 390                 395                 400

Leu Val Arg Leu Phe Tyr Asp Val
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<210> 9
<211> 410
<212> PRT
<213> Rattus norvegicus

<400> 9

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Met Trp Ala Phe Pro Glu Leu Pro Leu Pro Leu Pro Leu Leu Val Asn
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1               5                   10                  15

Leu Ile Gly Ser Leu Leu Gly Phe Val Ala Thr Val Thr Leu Ile Pro
            20                  25                  30

Ala Phe Arg Ser His Phe Ile Ala Ala Arg Leu Cys Gly Gln Asp Leu
        35                  40                  45

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

Gly Ala Val Phe Leu Ile Ile Leu Phe Cys Phe Ile Pro Phe Pro Phe
65                  70                  75                  80

Leu Asn Cys Phe Val Glu Glu Gln Cys Lys Ala Phe Pro His His Glu
                85                  90                  95

Phe Val Ala Leu Ile Gly Ala Leu Leu Ala Ile Cys Cys Met Ile Phe
            100                 105                 110

Leu Gly Phe Ala Asp Asp Val Leu Asn Leu Arg Trp Arg His Lys Leu
        115                 120                 125

Leu Leu Pro Thr Ala Ala Ser Leu Pro Leu Leu Met Val Tyr Phe Thr
    130                 135                 140

Asn Phe Gly Asn Thr Thr Ile Val Val Pro Lys Pro Phe Arg Trp Ile
145                 150                 155                 160

Leu Gly Leu His Leu Asp Leu Gly Ile Leu Tyr Tyr Val Tyr Met Gly
                165                 170                 175

Leu Leu Ala Val Phe Cys Thr Asn Ala Ile Asn Ile Leu Ala Gly Ile
            180                 185                 190

Asn Gly Leu Glu Ala Gly Gln Ser Leu Val Ile Ser Ala Ser Ile Ile
        195                 200                 205

Val Phe Asn Leu Val Glu Leu Glu Gly Asp Tyr Arg Asp Asp His Val
    210                 215                 220

Phe Ser Leu Tyr Phe Met Met Pro Phe Phe Phe Thr Thr Leu Gly Leu
225                 230                 235                 240
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Leu Tyr His Asn Trp Tyr Pro Ser Gln Val Phe Val Gly Asp Thr Phe
                245                 250                 255

Cys Tyr Phe Ala Gly Met Thr Phe Ala Val Val Gly Ile Leu Gly His
            260                 265                 270

Phe Ser Lys Thr Met Leu Leu Phe Phe Met Pro Gln Val Phe Asn Phe
        275                 280                 285

Leu Tyr Ser Leu Pro Gln Leu Phe Gln Ile Ile Pro Cys Pro Arg His
    290                 295                 300

Arg Met Pro Arg Leu Asn Thr Lys Thr Gly Lys Leu Glu Met Ser Tyr
305                 310                 315                 320

Ser Lys Phe Lys Thr Lys Ser Leu Ser Phe Leu Gly Thr Phe Ile Leu
                325                 330                 335

Lys Val Ala Glu Ser Leu Arg Leu Val Thr Val His Arg Gly Glu Ser
            340                 345                 350

Glu Asp Gly Ala Phe Thr Glu Cys Asn Asn Met Thr Leu Ile Asn Leu
        355                 360                 365

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

Leu Leu Leu Leu Gln Val Leu Ser Ser Ala Val Thr Phe Ser Ile Arg
385                 390                 395                 400

Tyr Gln Leu Val Arg Leu Phe Tyr Asp Val
                405                 410
```

<210> 10
<211> 410
<212> PRT
<213> Mus musculus

<400> 10

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Met Trp Ala Phe Pro Glu Leu Pro Leu Pro Leu Pro Leu Leu Val Asn
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Leu Ile Gly Ser Leu Leu Gly Phe Val Ala Thr Val Thr Leu Ile Pro
            20                  25                  30
```

```
Ala Phe Arg Ser His Phe Ile Ala Ala Arg Leu Cys Gly Gln Asp Leu
        35                  40                  45

Asn Lys Leu Ser Gln Gln Gln Ile Pro Glu Ser Gln Gly Val Ile Ser
    50                  55                  60

Gly Ala Val Phe Leu Ile Ile Leu Phe Cys Phe Ile Pro Phe Pro Phe
65                  70                  75                  80

Leu Asn Cys Phe Val Glu Glu Gln Cys Lys Ala Phe Pro His His Glu
                85                  90                  95

Phe Val Ala Leu Ile Gly Ala Leu Leu Ala Ile Cys Cys Met Ile Phe
            100                 105                 110

Leu Gly Phe Ala Asp Asp Val Leu Asn Leu Arg Trp Arg His Lys Leu
        115                 120                 125

Leu Leu Pro Thr Ala Ala Ser Leu Pro Leu Leu Met Val Tyr Phe Thr
    130                 135                 140

Asn Phe Gly Asn Thr Thr Ile Val Val Pro Lys Pro Phe Arg Trp Ile
145                 150                 155                 160

Leu Gly Leu His Leu Asp Leu Gly Ile Leu Tyr Tyr Val Tyr Met Gly
                165                 170                 175

Leu Leu Ala Val Phe Cys Thr Asn Ala Ile Asn Ile Leu Ala Gly Ile
            180                 185                 190

Asn Gly Leu Glu Ala Gly Gln Ser Leu Val Ile Ser Ala Ser Ile Ile
        195                 200                 205

Val Phe Asn Leu Val Glu Leu Glu Gly Asp Tyr Arg Asp Asp His Ile
    210                 215                 220

Phe Ser Leu Tyr Phe Met Ile Pro Phe Phe Phe Thr Thr Leu Gly Leu
225                 230                 235                 240

Leu Tyr His Asn Trp Tyr Pro Ser Arg Val Phe Val Gly Asp Thr Phe
                245                 250                 255
```

```
Cys Tyr Phe Ala Gly Met Thr Phe Ala Val Val Gly Ile Leu Gly His
            260                 265                 270

Phe Ser Lys Thr Met Leu Leu Phe Phe Met Pro Gln Val Phe Asn Phe
        275                 280                 285

Leu Tyr Ser Leu Pro Gln Leu Phe His Ile Ile Pro Cys Pro Arg His
    290                 295                 300

Arg Met Pro Arg Leu Asn Ala Lys Thr Gly Lys Leu Glu Met Ser Tyr
305                 310                 315                 320

Ser Lys Phe Lys Thr Lys Asn Leu Ser Phe Leu Gly Thr Phe Ile Leu
                325                 330                 335

Lys Val Ala Glu Asn Leu Arg Leu Val Thr Val His Gln Gly Glu Ser
            340                 345                 350

Glu Asp Gly Ala Phe Thr Glu Cys Asn Asn Met Thr Leu Ile Asn Leu
        355                 360                 365

Leu Leu Lys Val Phe Gly Pro Ile His Glu Arg Asn Leu Thr Leu Leu
    370                 375                 380

Leu Leu Leu Leu Gln Val Leu Ser Ser Ala Ala Thr Phe Ser Ile Arg
385                 390                 395                 400

Tyr Gln Leu Val Arg Leu Phe Tyr Asp Val
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<212> DNA
<213> Mus musculus

<400> 11

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