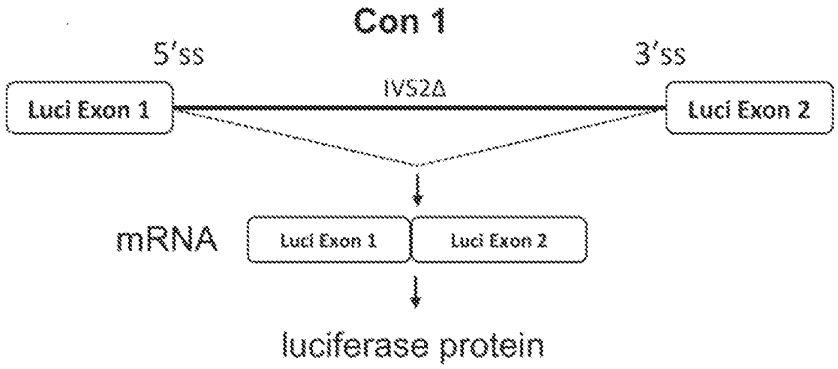

Con 1
5'ss
3'ss
IVS2Δ
Luci Exon 1
Luci Exon 2
mRNA
Luci Exon 1
Luci Exon 2
luciferase protein

Fig. 1a

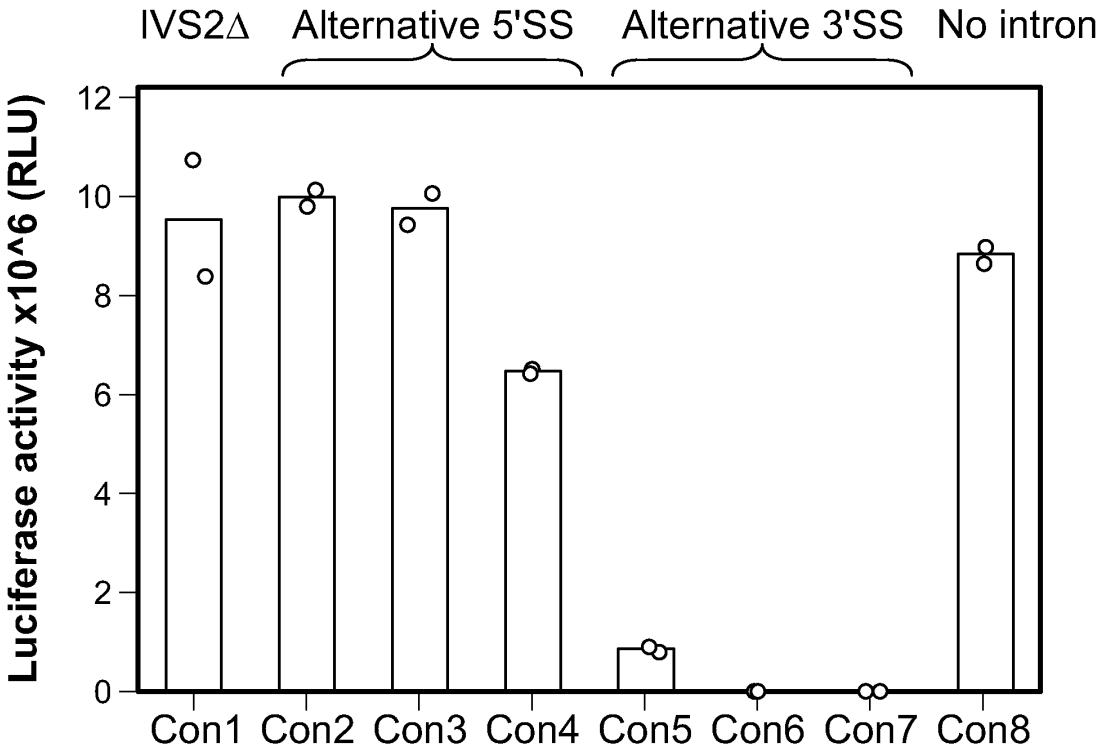

IVS2Δ
Alternative 5'SS
Alternative 3'SS
No intron
Luciferase activity x10^6 (RLU)
0
2
4
6
8
10
12
Con1
Con2
Con3
Con4
Con5
Con6
Con7
Con8

Fig. 1b

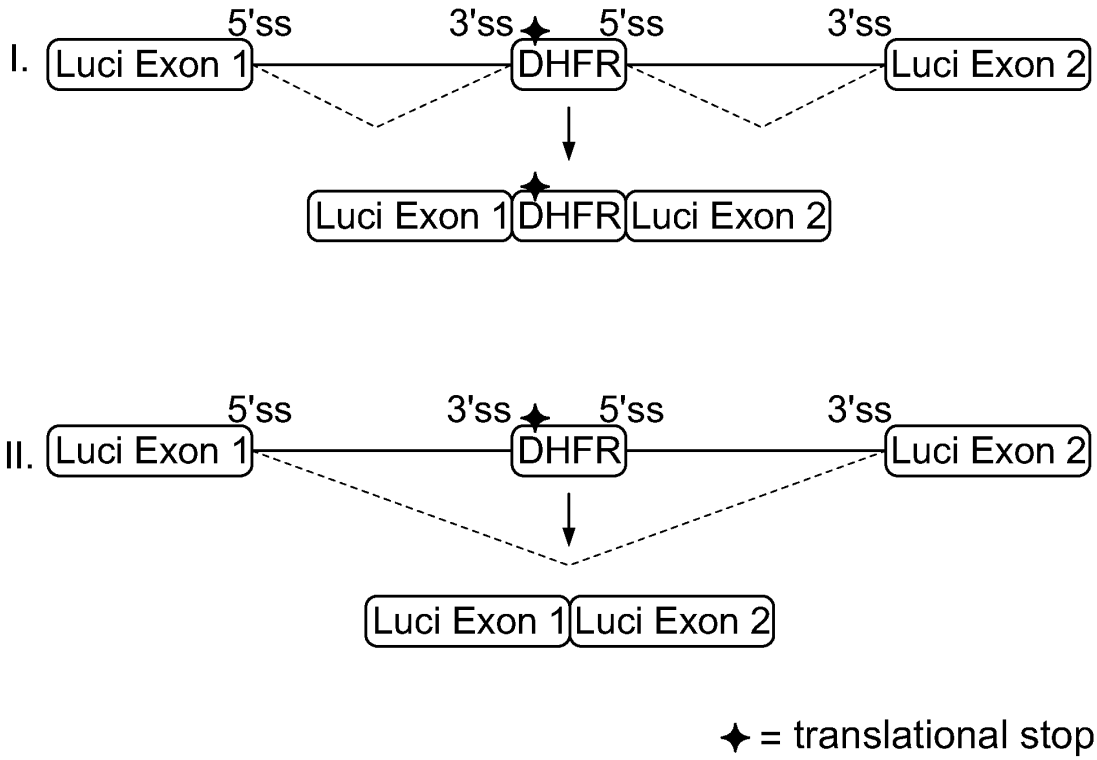

I.
5'ss
3'ss
5'ss
3'ss
Luci Exon 1
DHFR
Luci Exon 2
Luci Exon 1
DHFR
Luci Exon 2
II.
5'ss
3'ss
5'ss
3'ss
Luci Exon 1
DHFR
Luci Exon 2
Luci Exon 1
Luci Exon 2
= translational stop

**Fig. 2a**

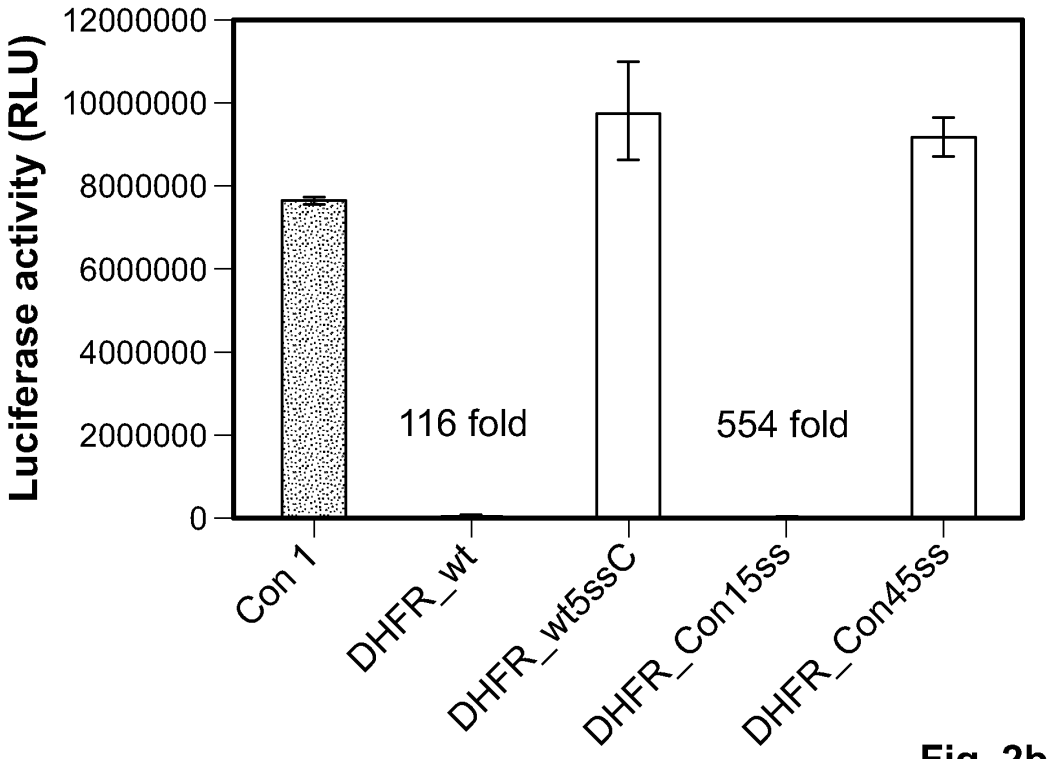

Luciferase activity (RLU)
12000000
10000000
8000000
6000000
4000000
2000000
0
116 fold
554 fold
Con 1
DHFR_wt
DHFR_wt5ssC
DHFR_Con15ss
DHFR_Con45ss

Fig. 2b

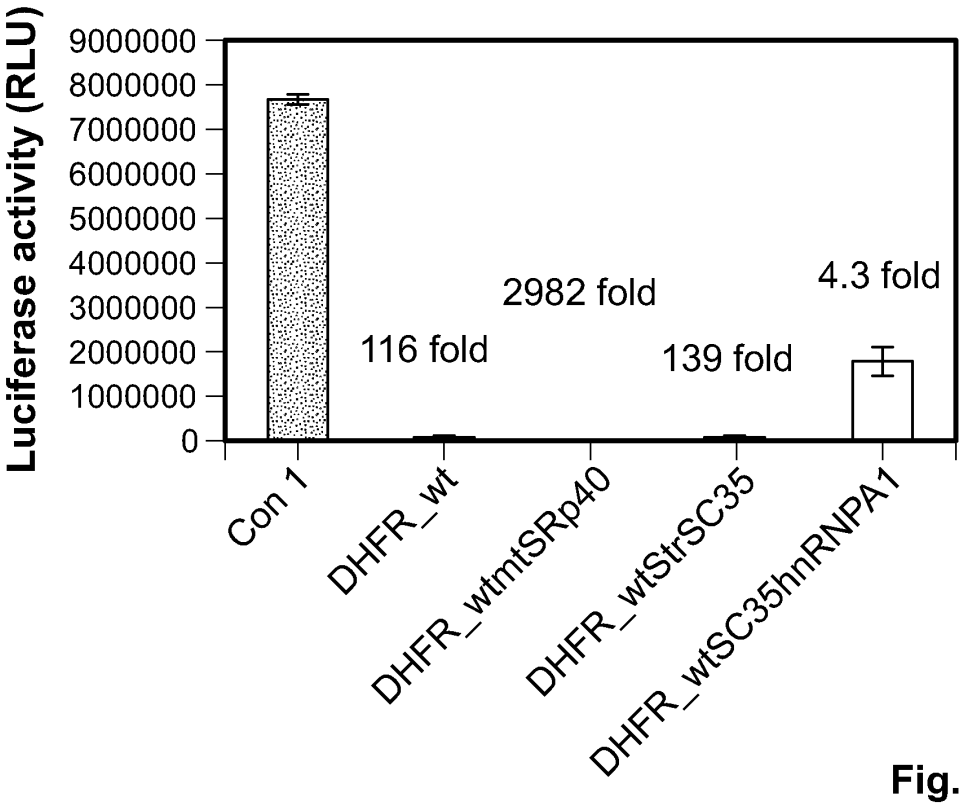

Luciferase activity (RLU)
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
116 fold
2982 fold
139 fold
4.3 fold
Con 1
DHFR_wt
DHFR_wtmtSRp40
DHFR_wtStrSC35
DHFR_wtSC35hnRNPA1

Fig. 2c

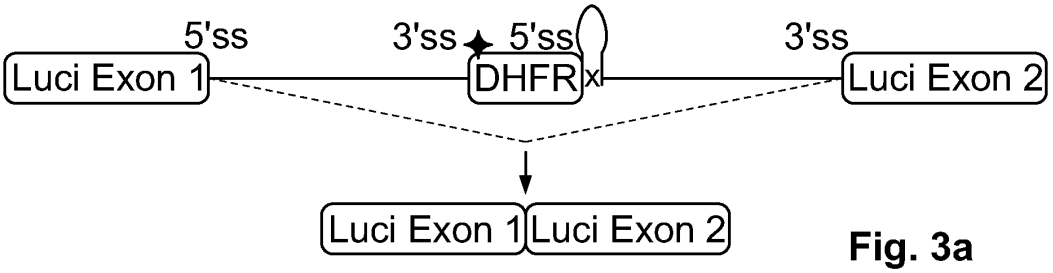



Fig. 3a

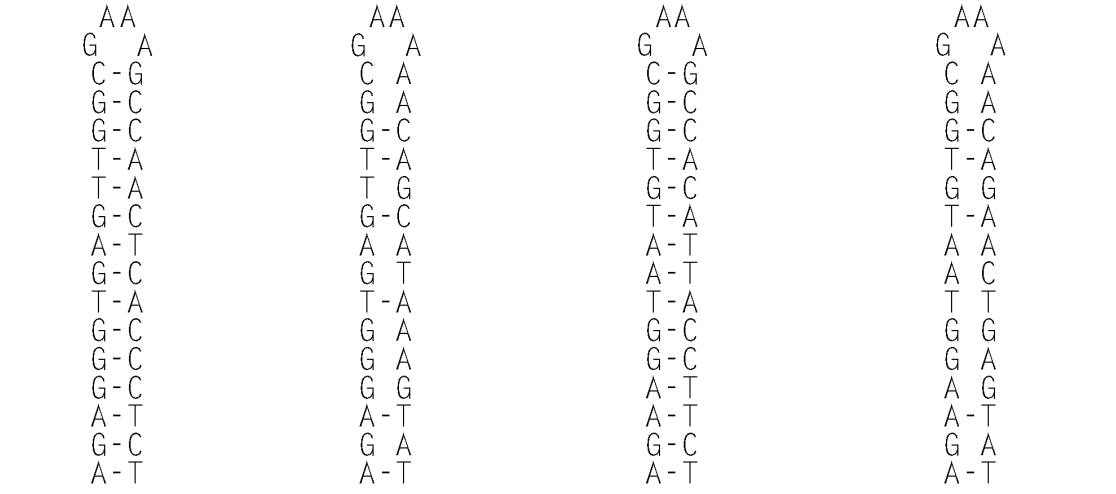



Fig. 3b

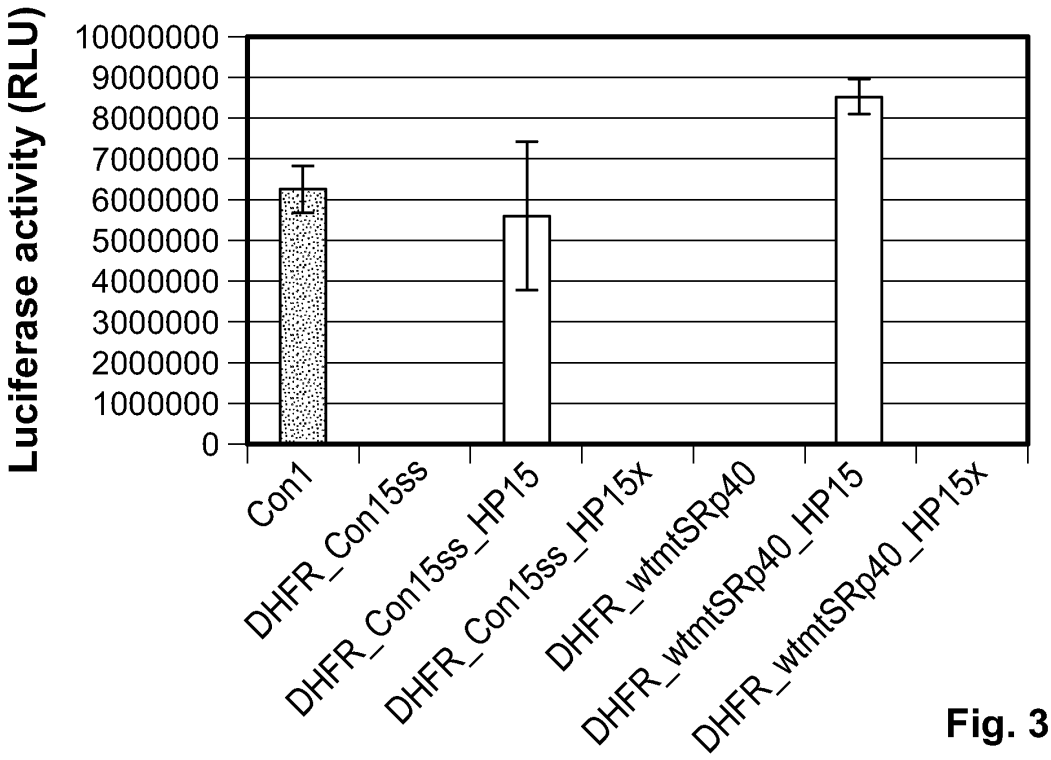



Fig. 3c

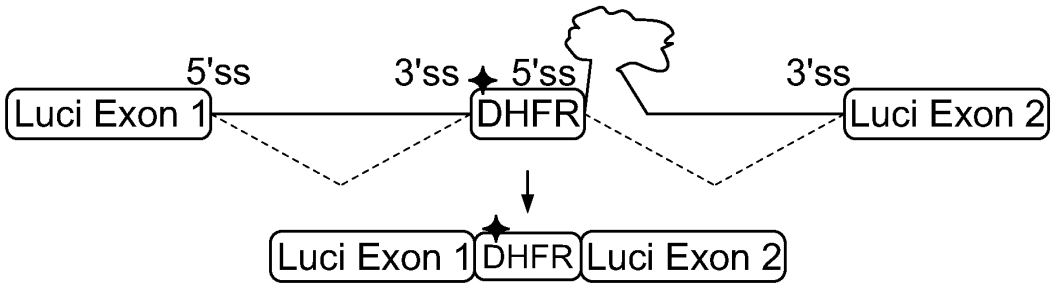

5'ss
3'ss
5'ss
3'ss
Luci Exon 1
DHFR
Luci Exon 2
Luci Exon 1
DHFR
Luci Exon 2

**Fig. 4a**

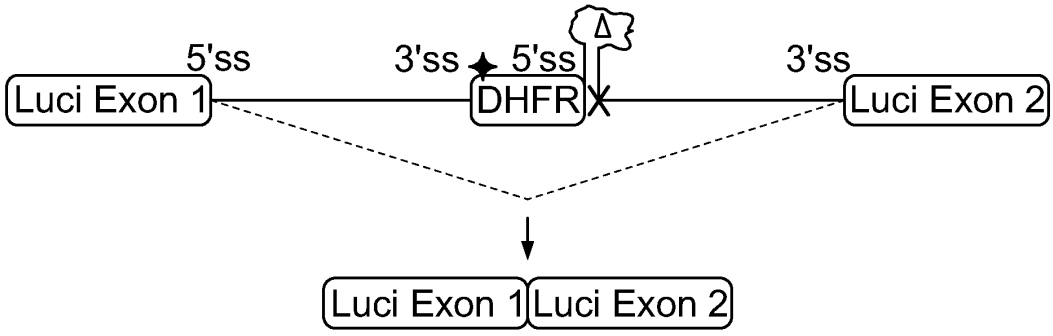

5'ss
3'ss
5'ss
3'ss
Luci Exon 1
DHFR
Luci Exon 2
Luci Exon 1
Luci Exon 2

**Fig. 4b**

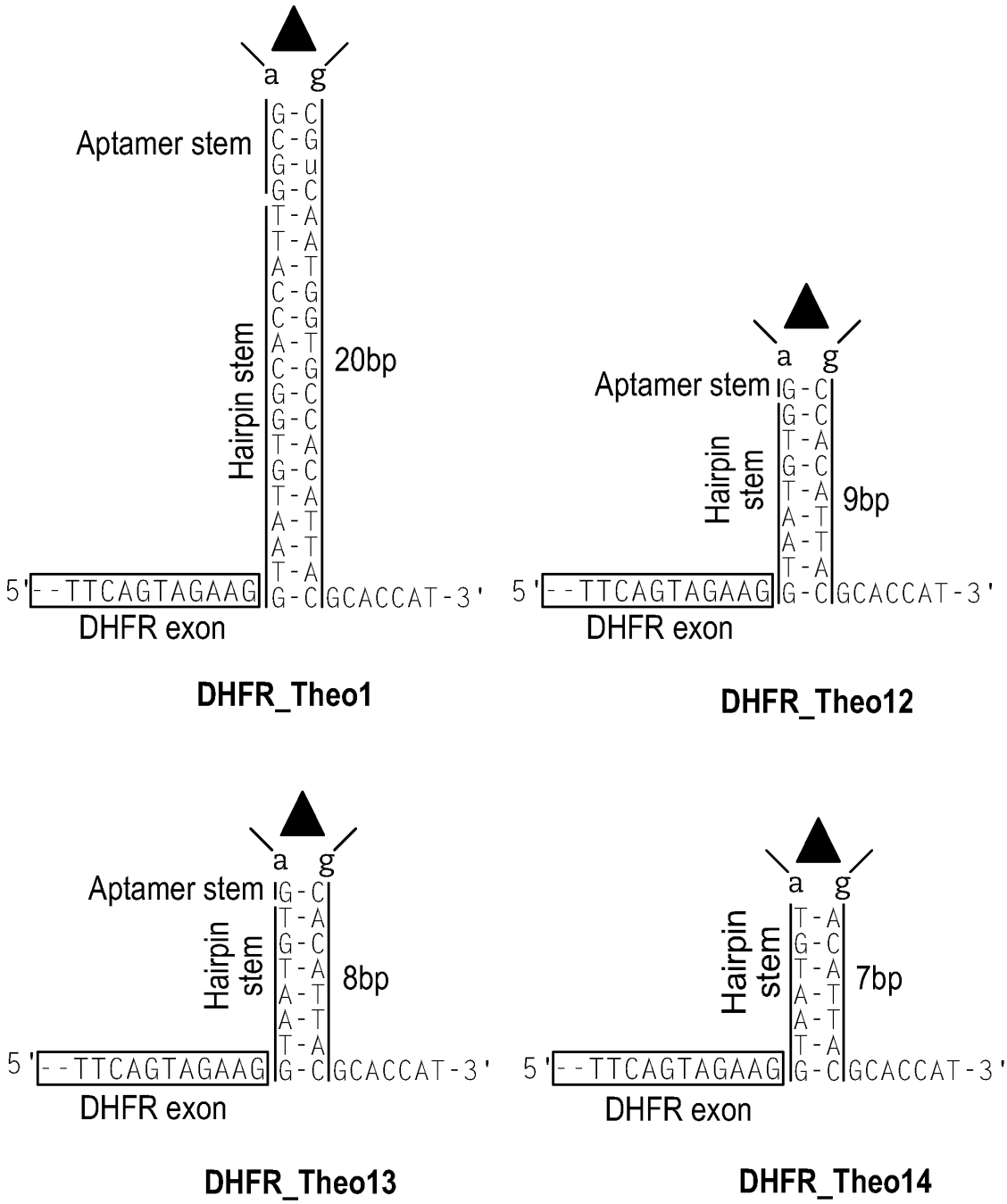

a g
Aptamer stem
G-C
C-G
G-u
G-C
Hairpin stem
T-A
T-A
A-T
C-G
C-G
A-T
C-G
G-C
G-C
T-A
G-C
T-A
A-T
A-T
T-A
20bp
5'--TTCAGTAGAAG
G-C
GCACCAT-3'
DHFR exon
DHFR_Theo1
a g
Aptamer stem
G-C
G-C
T-A
G-C
T-A
A-T
A-T
T-A
Hairpin stem
9bp
5'--TTCAGTAGAAG
G-C
GCACCAT-3'
DHFR exon
DHFR_Theo12
a g
Aptamer stem
G-C
T-A
G-C
T-A
A-T
A-T
T-A
Hairpin stem
8bp
5'--TTCAGTAGAAG
G-C
GCACCAT-3'
DHFR exon
DHFR_Theo13
a g
T-A
G-C
T-A
A-T
A-T
T-A
Hairpin stem
7bp
5'--TTCAGTAGAAG
G-C
GCACCAT-3'
DHFR exon
DHFR_Theo14

**Fig. 4c**

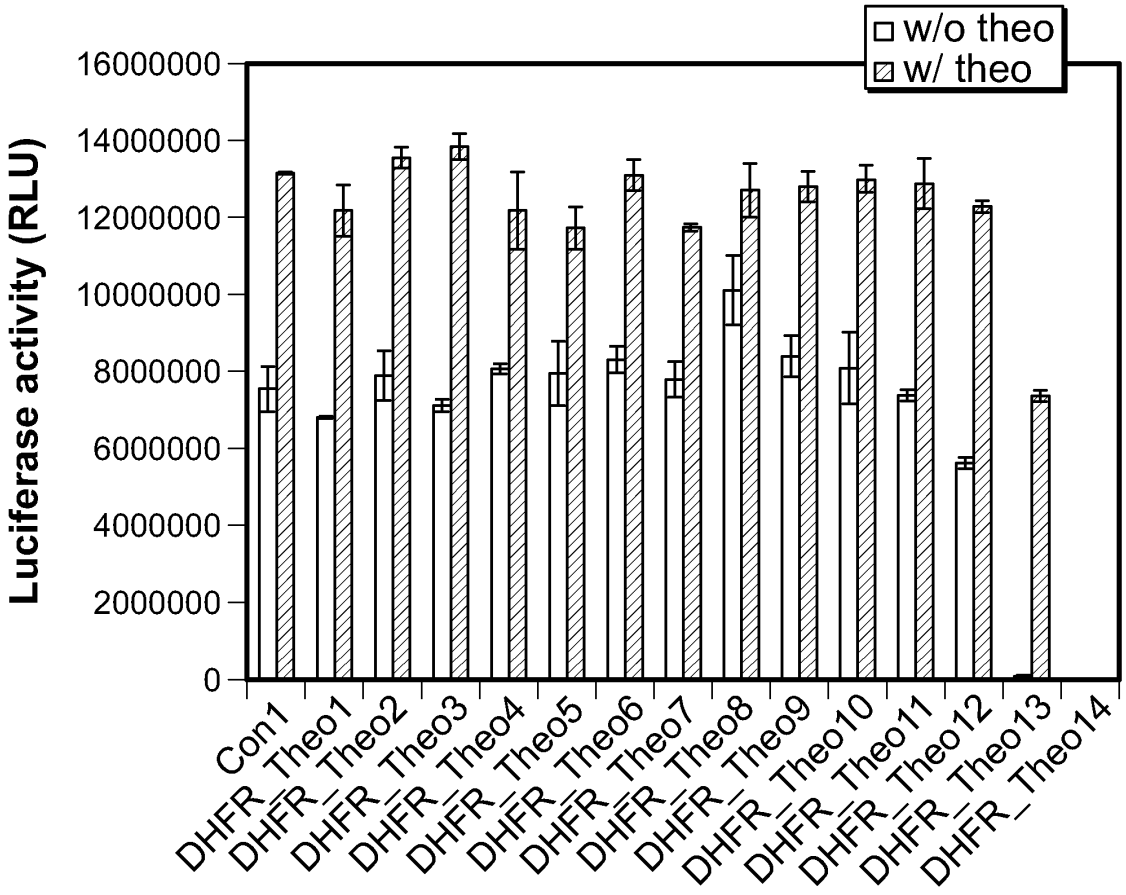
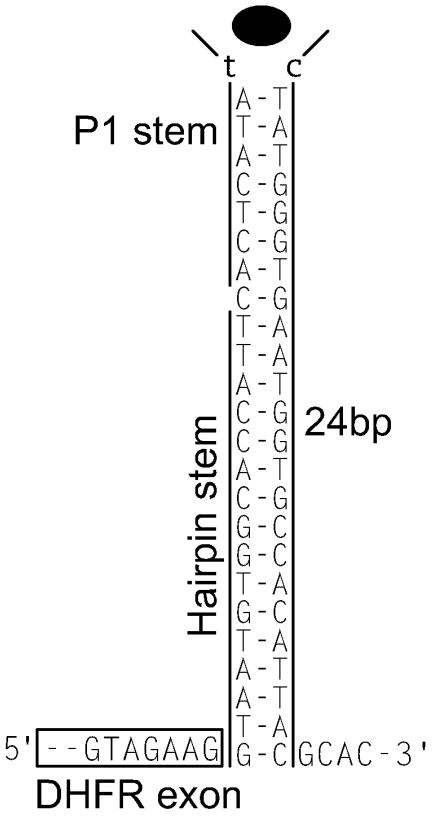
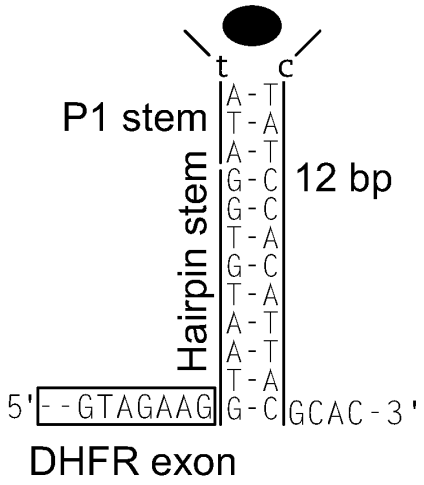

w/o theo
w/ theo
Luciferase activity (RLU)
16000000
14000000
12000000
10000000
8000000
6000000
4000000
2000000
0
Con1
DHFR_Theo1
DHFR_Theo2
DHFR_Theo3
DHFR_Theo4
DHFR_Theo5
DHFR_Theo6
DHFR_Theo7
DHFR_Theo8
DHFR_Theo9
DHFR_Theo10
DHFR_Theo11
DHFR_Theo12
DHFR_Theo13
DHFR_Theo14

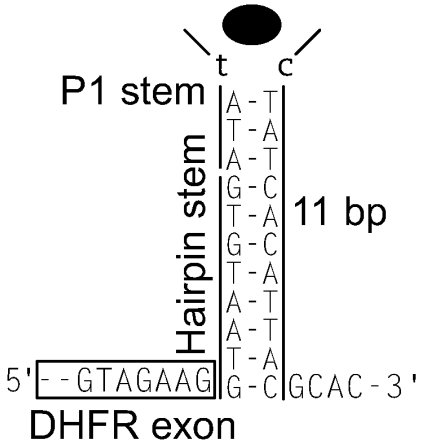
Fig. 4d




**DHFR _G1**

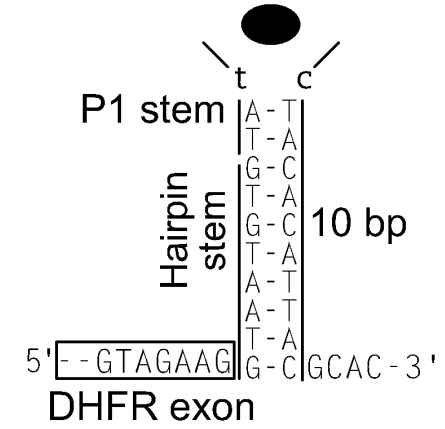



**DHFR _G13**

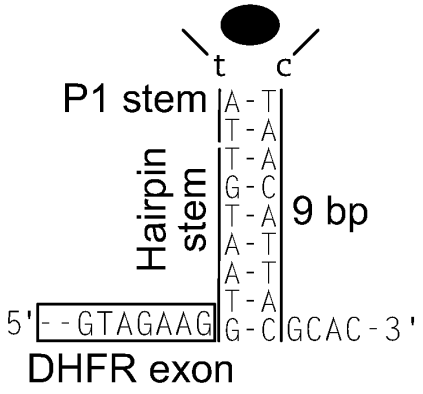



**DHFR _G14**

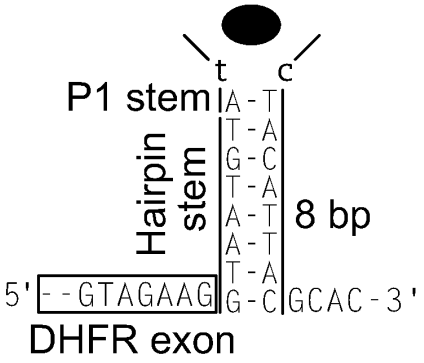
**Fig. 5a**



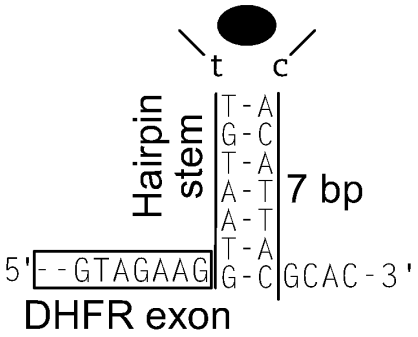

DHFR _G15




DHFR _G16




DHFR _G17




DHFR _G18

**Fig. 5a (Cont.)**

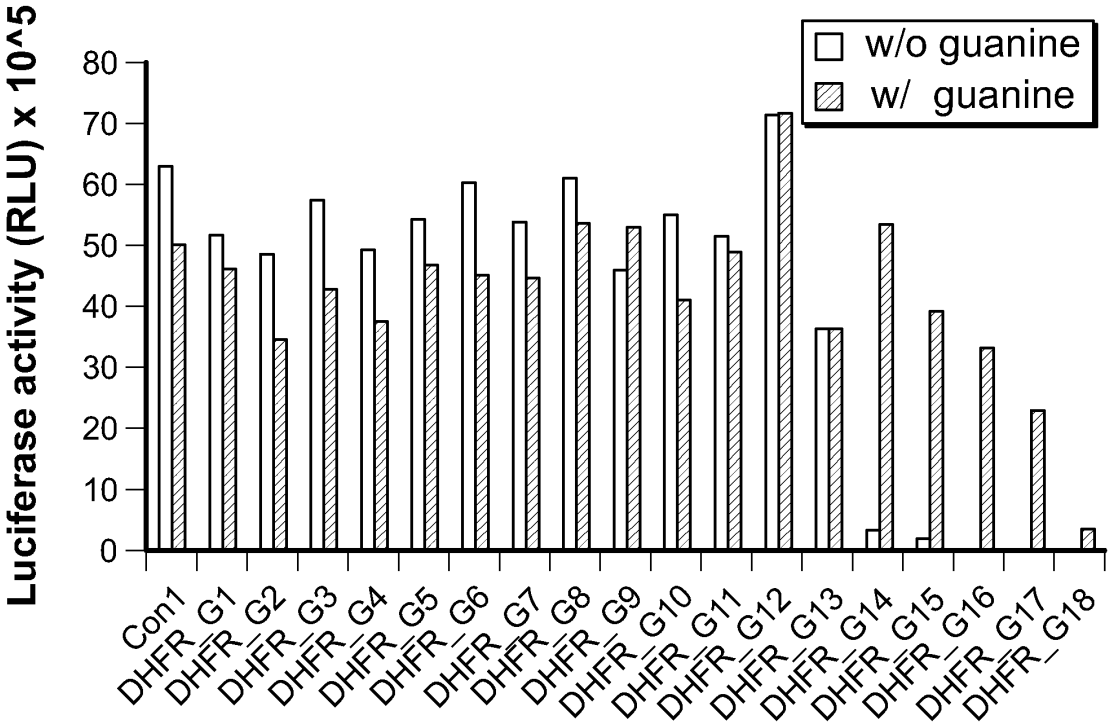

Luciferase activity (RLU) x 10^5
80
70
60
50
40
30
20
10
0
w/o guanine
w/ guanine
Con1
DHFR_G1
DHFR_G2
DHFR_G3
DHFR_G4
DHFR_G5
DHFR_G6
DHFR_G7
DHFR_G8
DHFR_G9
DHFR_G10
DHFR_G11
DHFR_G12
DHFR_G13
DHFR_G14
DHFR_G15
DHFR_G16
DHFR_G17
DHFR_G18

FIG. 5b

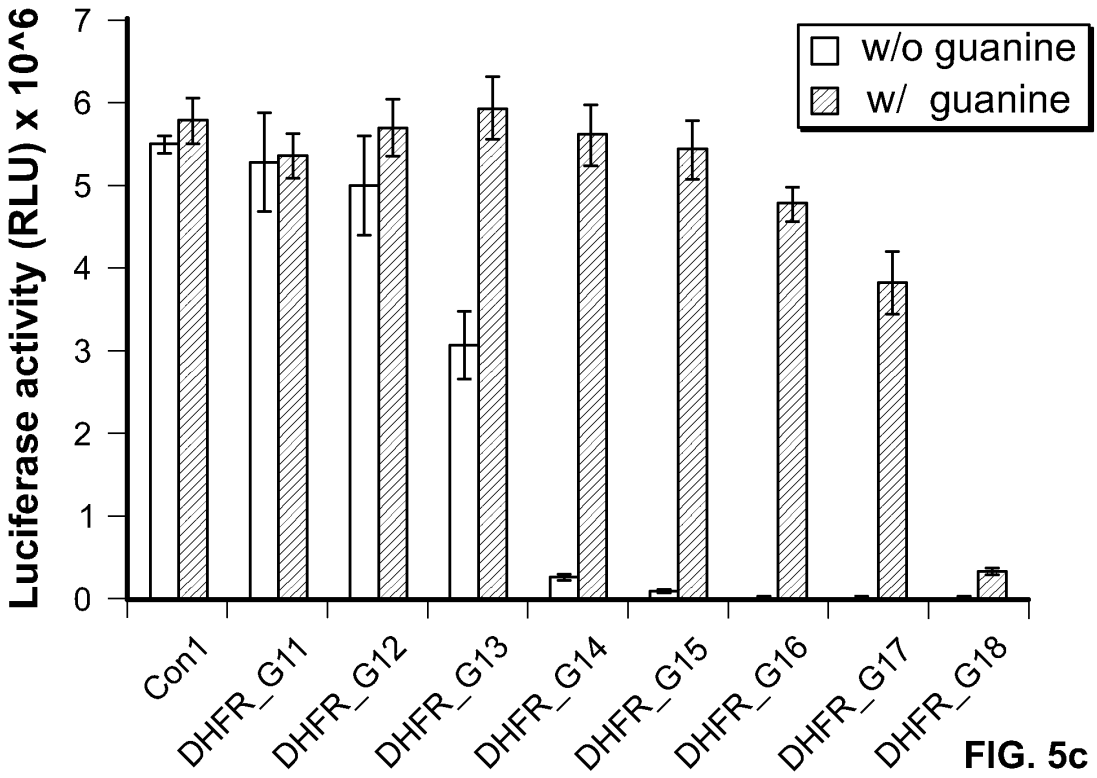

Luciferase activity (RLU) x 10^6
7
6
5
4
3
2
1
0
w/o guanine
w/ guanine
Con1
DHFR_G11
DHFR_G12
DHFR_G13
DHFR_G14
DHFR_G15
DHFR_G16
DHFR_G17
DHFR_G18

FIG. 5c

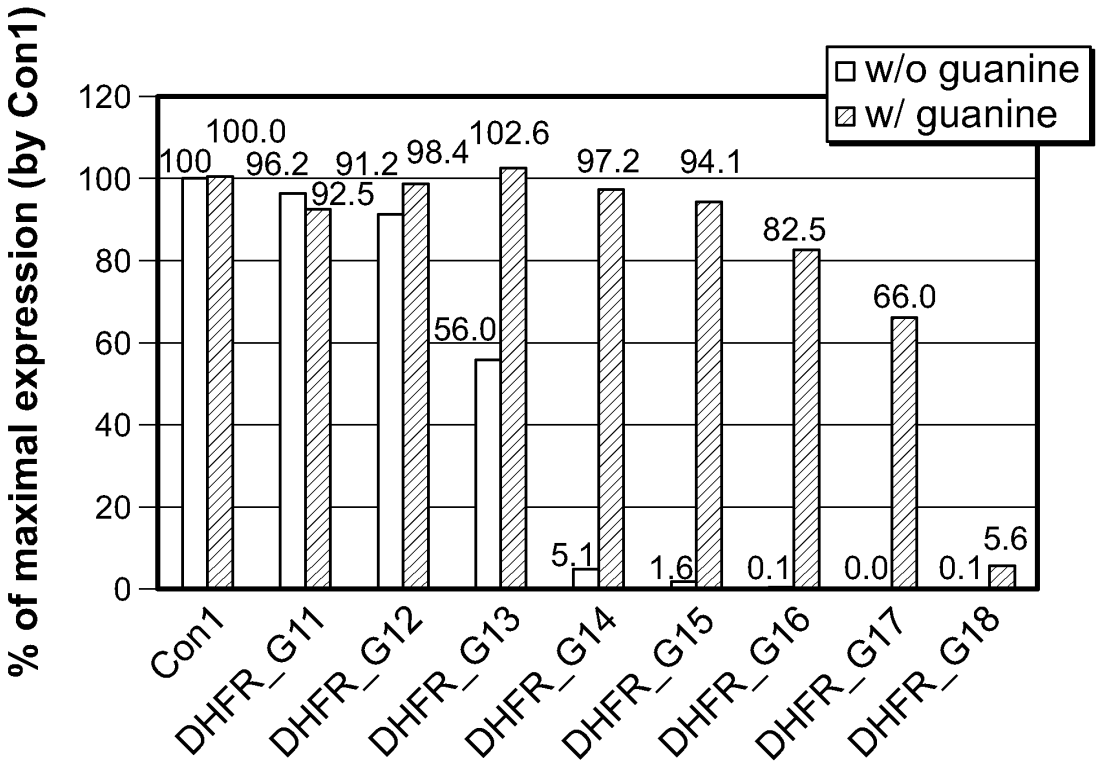



Fig. 5d

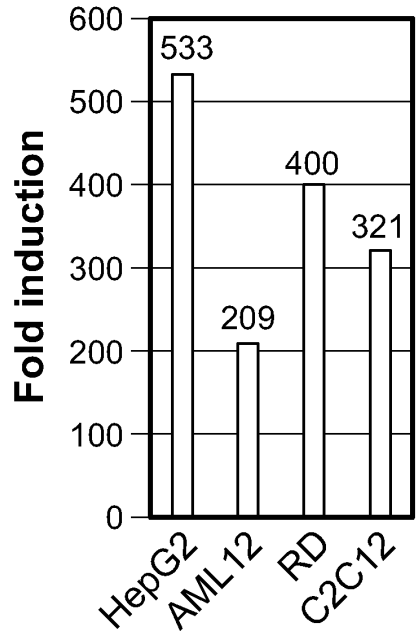



Fig. 5e

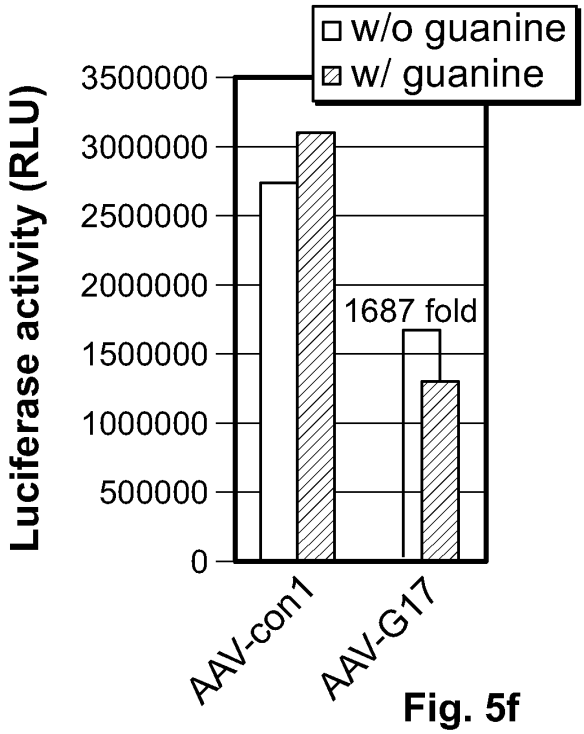



Fig. 5f

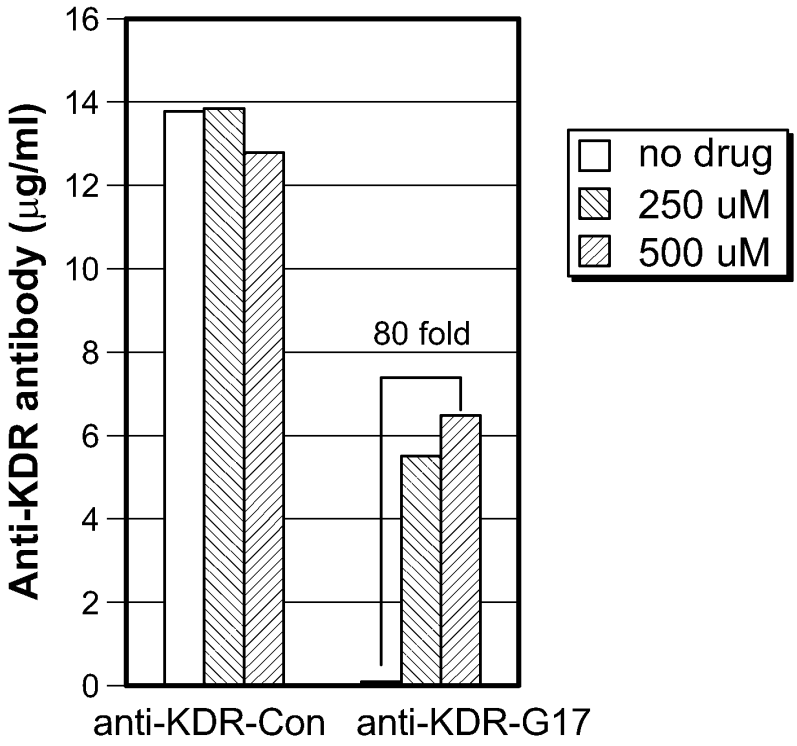

Anti-KDR antibody (μg/ml)
16
14
12
10
8
6
4
2
0
80 fold
no drug
250 uM
500 uM
anti-KDR-Con
anti-KDR-G17

Fig. 5g

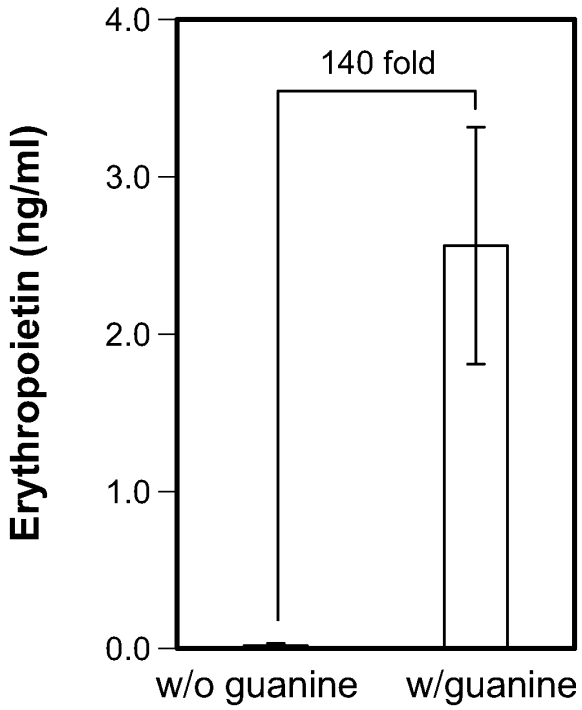

Erythropoietin (ng/ml)
4.0
3.0
2.0
1.0
0.0
140 fold
w/o guanine
w/guanine

Fig. 5h

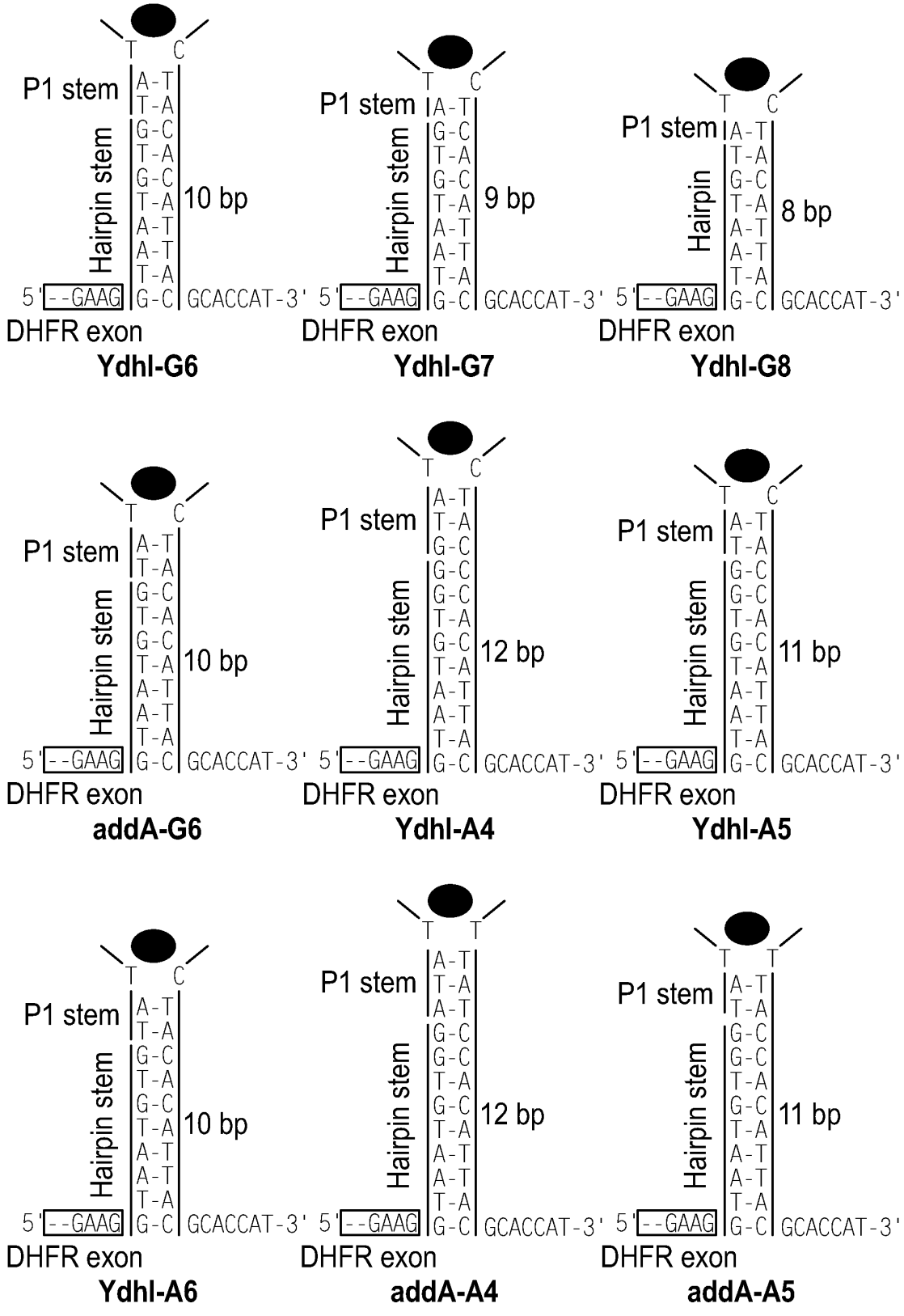

P1 stem
Hairpin stem
10 bp
5'--GAAG
GCACCAT-3'
DHFR exon
YdhI-G6
9 bp
YdhI-G7
Hairpin
8 bp
YdhI-G8
addA-G6
12 bp
YdhI-A4
11 bp
YdhI-A5
YdhI-A6
addA-A4
addA-A5

FIG. 6a

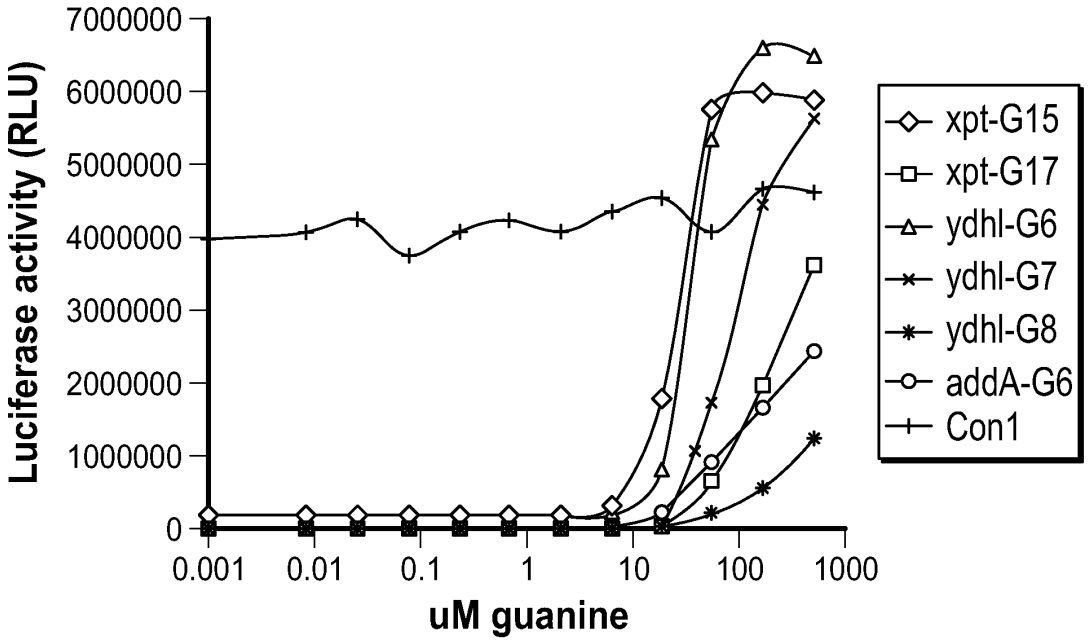

Luciferase activity (RLU)
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
0.001
0.01
0.1
1
10
100
1000
uM guanine
xpt-G15
xpt-G17
ydhl-G6
ydhl-G7
ydhl-G8
addA-G6
Con1

Fig. 6b

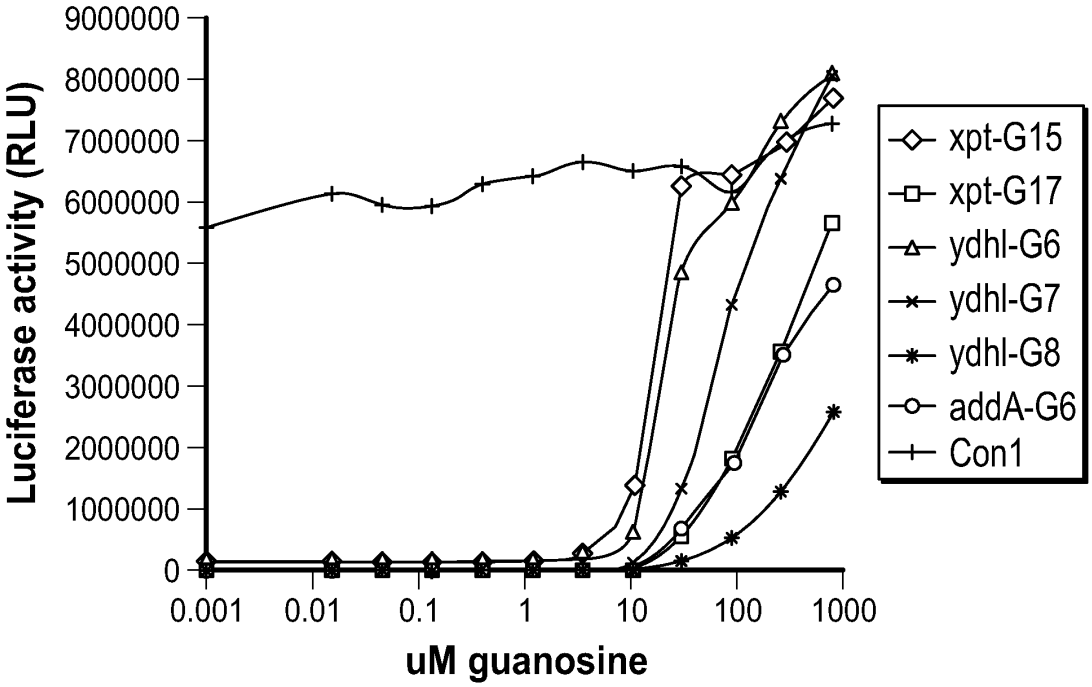

Luciferase activity (RLU)
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
0.001
0.01
0.1
1
10
100
1000
uM guanosine
xpt-G15
xpt-G17
ydhl-G6
ydhl-G7
ydhl-G8
addA-G6
Con1

Fig. 6c

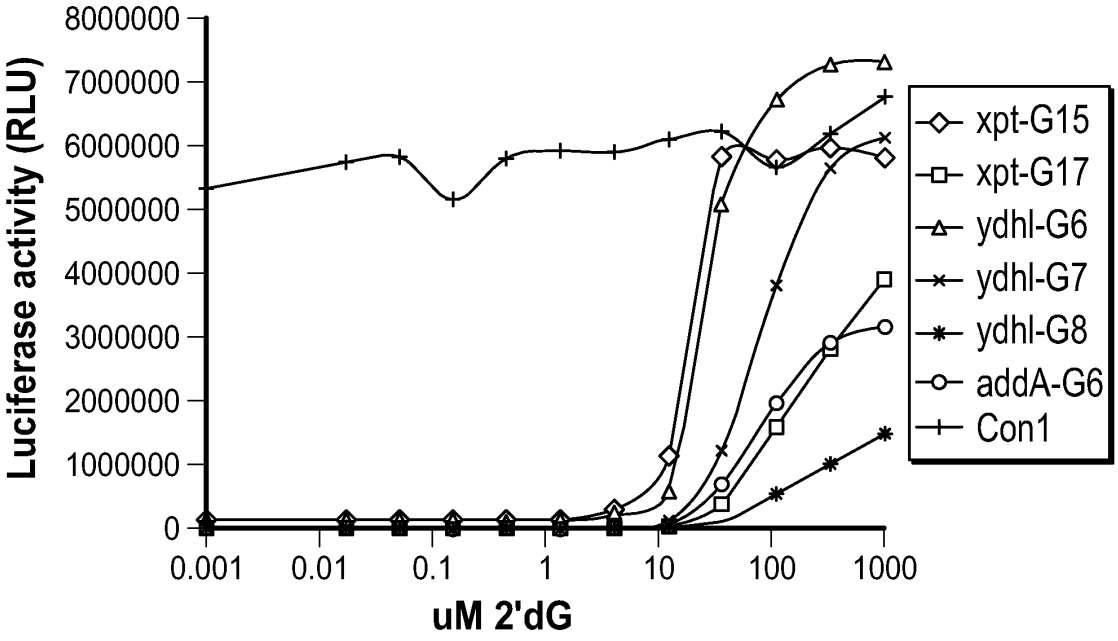

8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
Luciferase activity (RLU)
0.001
0.01
0.1
1
10
100
1000
uM 2'dG
xpt-G15
xpt-G17
ydhl-G6
ydhl-G7
ydhl-G8
addA-G6
Con1

Fig. 6d

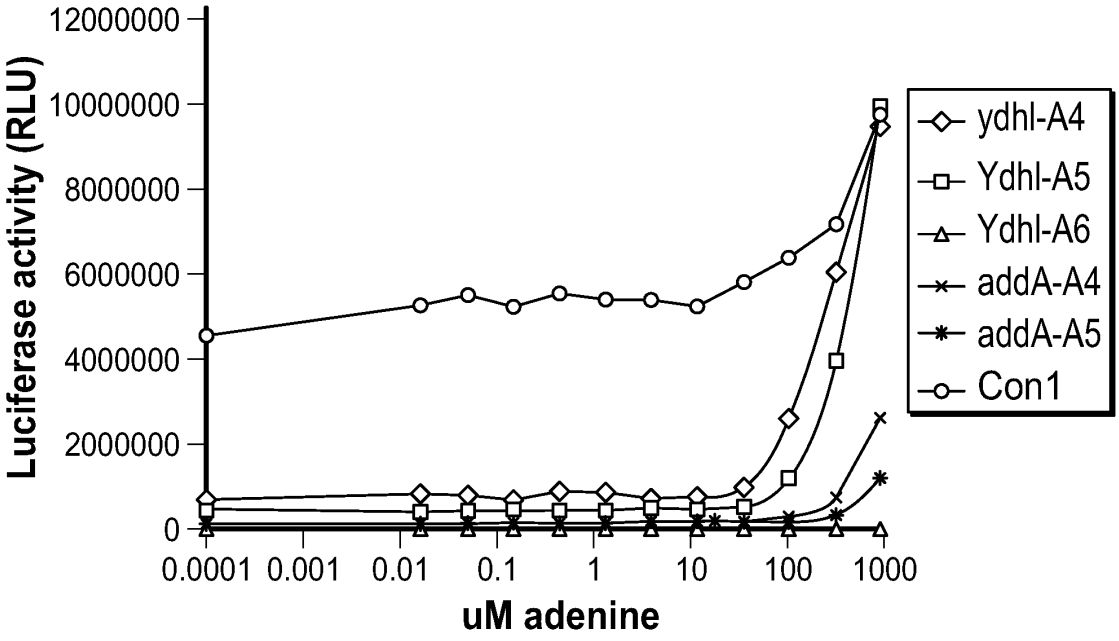

12000000
10000000
8000000
6000000
4000000
2000000
0
Luciferase activity (RLU)
0.0001
0.001
0.01
0.1
1
10
100
1000
uM adenine
ydhl-A4
Ydhl-A5
Ydhl-A6
addA-A4
addA-A5
Con1

Fig. 6e

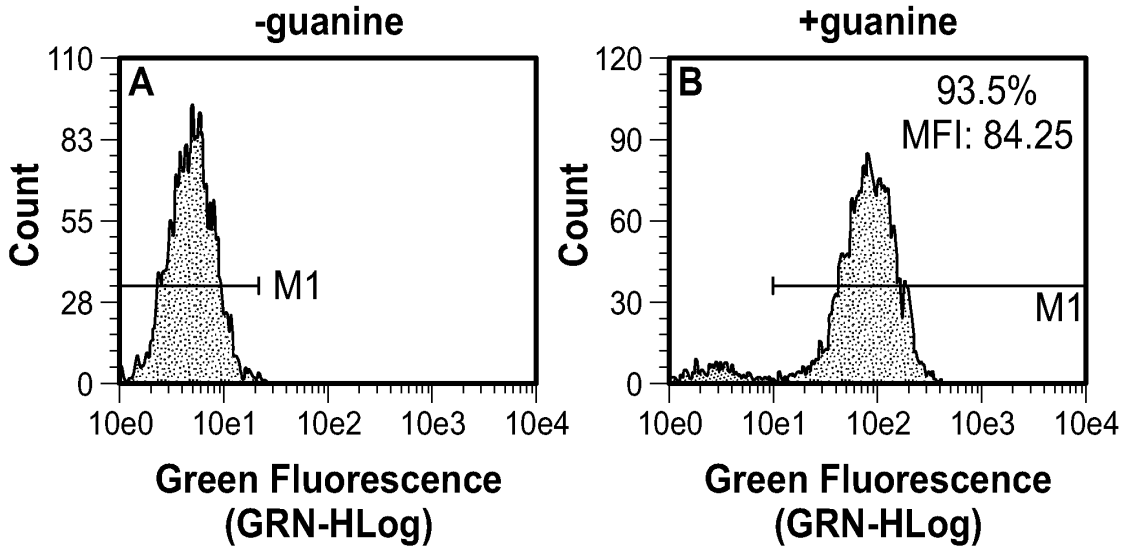

-guanine
+guanine
A
B
93.5%
MFI: 84.25
M1
M1
Count
Count
110
83
55
28
0
120
90
60
30
0
10e0
10e1
10e2
10e3
10e4
Green Fluorescence
(GRN-HLog)
Green Fluorescence
(GRN-HLog)

Fig. 7a

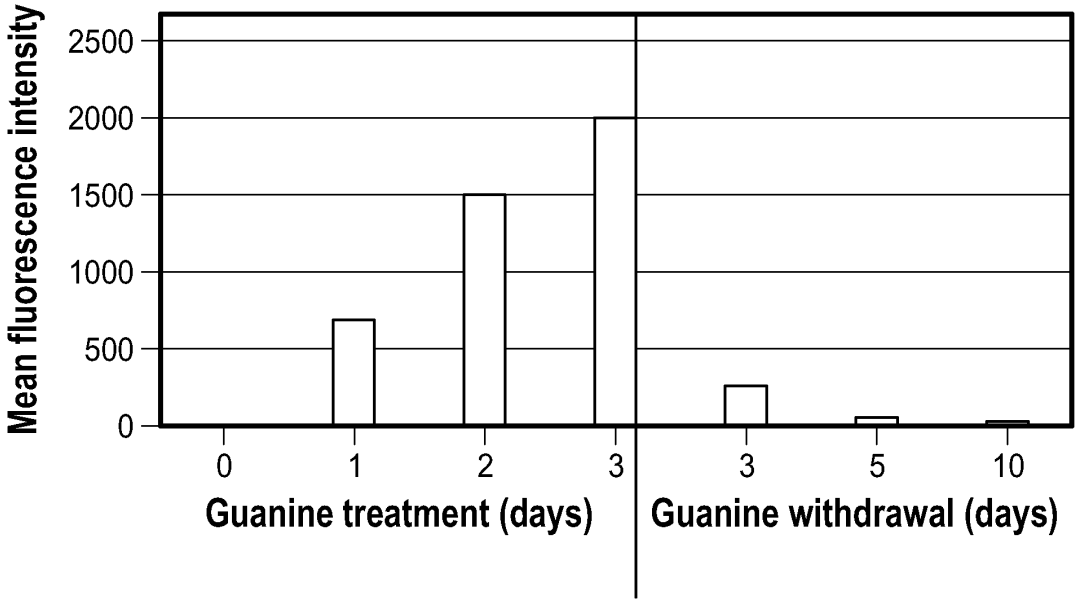

Mean fluorescence intensity
2500
2000
1500
1000
500
0
0
1
2
3
3
5
10
Guanine treatment (days)
Guanine withdrawal (days)

Fig. 7b

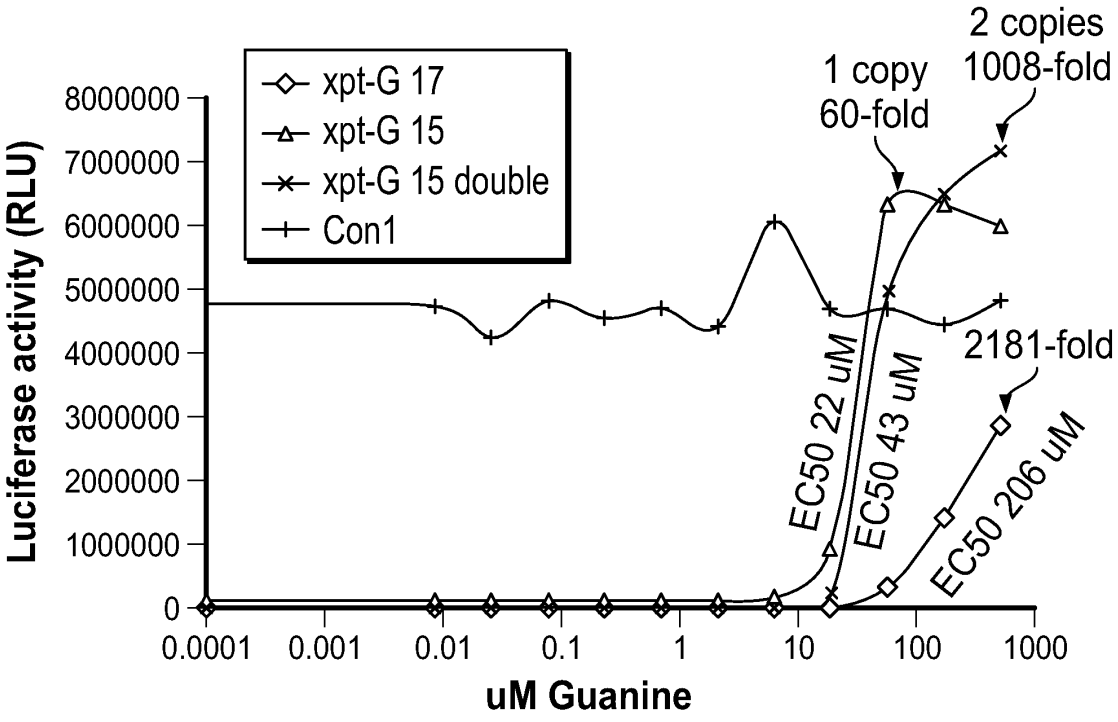

xpt-G 17
xpt-G 15
xpt-G 15 double
Con1
Luciferase activity (RLU)
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
0.0001
0.001
0.01
0.1
1
10
100
1000
uM Guanine
1 copy
60-fold
2 copies
1008-fold
2181-fold
EC50 22 uM
EC50 43 uM
EC50 206 uM

Fig. 8a

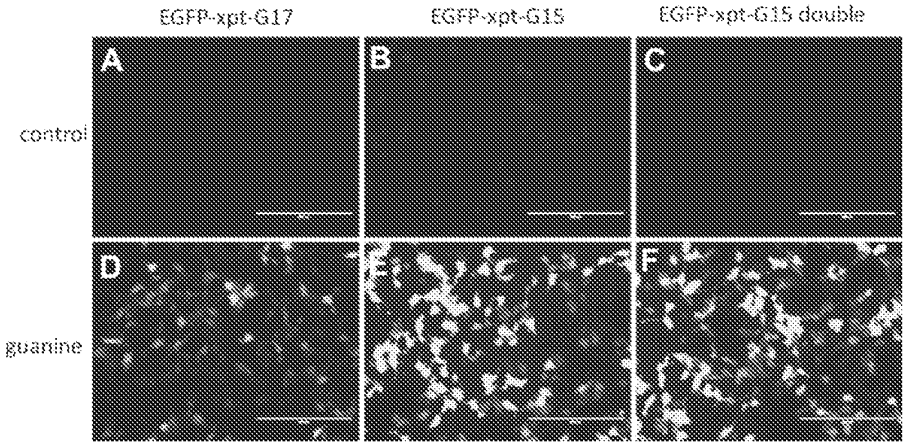

EGFP-xpt-G17
EGFP-xpt-G15
EGFP-xpt-G15 double
A
B
C
D
E
F
control
guanine

Fig. 8b

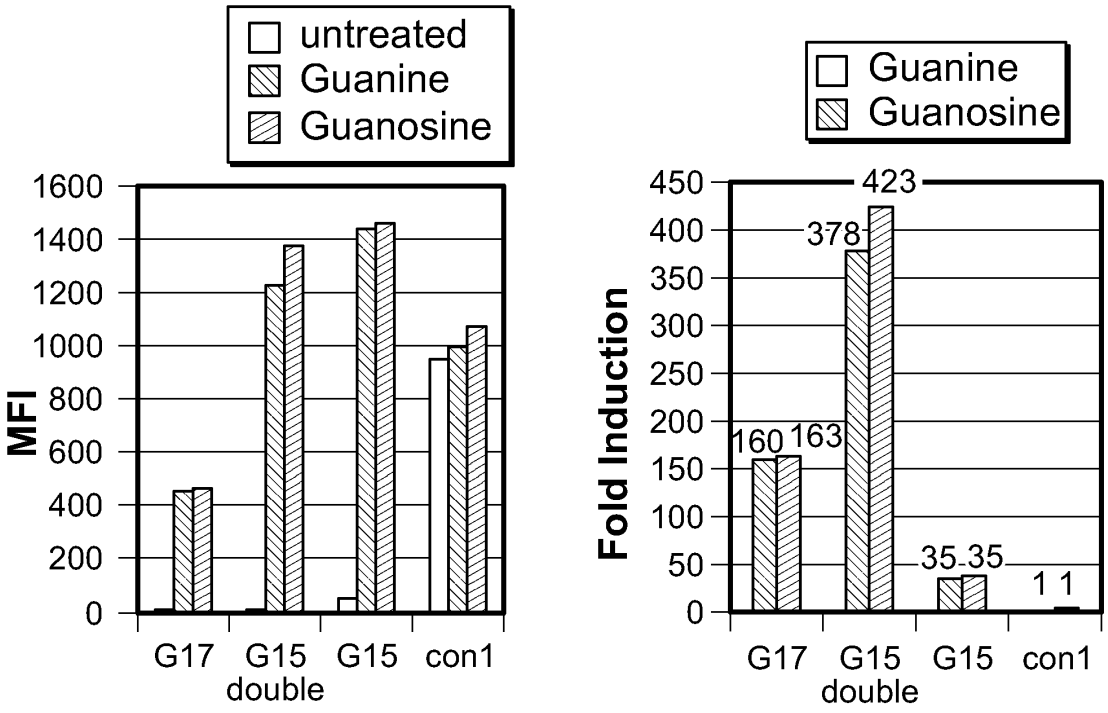

untreated
Guanine
Guanosine
MFI
1600
1400
1200
1000
800
600
400
200
0
G17
G15 double
G15
con1
Guanine
Guanosine
Fold Induction
450
400
350
300
250
200
150
100
50
0
423
378
160
163
35
35
1
1
G17
G15 double
G15
con1

Fig. 8c

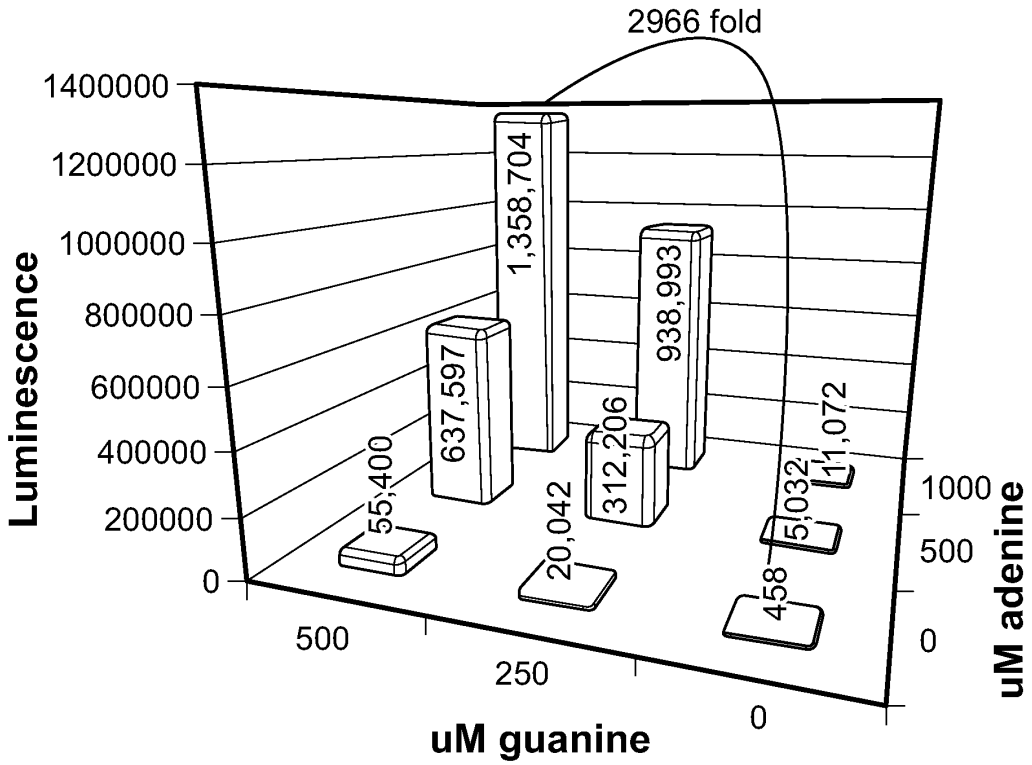

2966 fold
Luminescence
1400000
1200000
1000000
800000
600000
400000
200000
0
1,358,704
938,993
637,597
312,206
55,400
20,042
11,072
5,032
458
500
250
0
uM guanine
1000
500
0
uM adenine

Fig. 8d

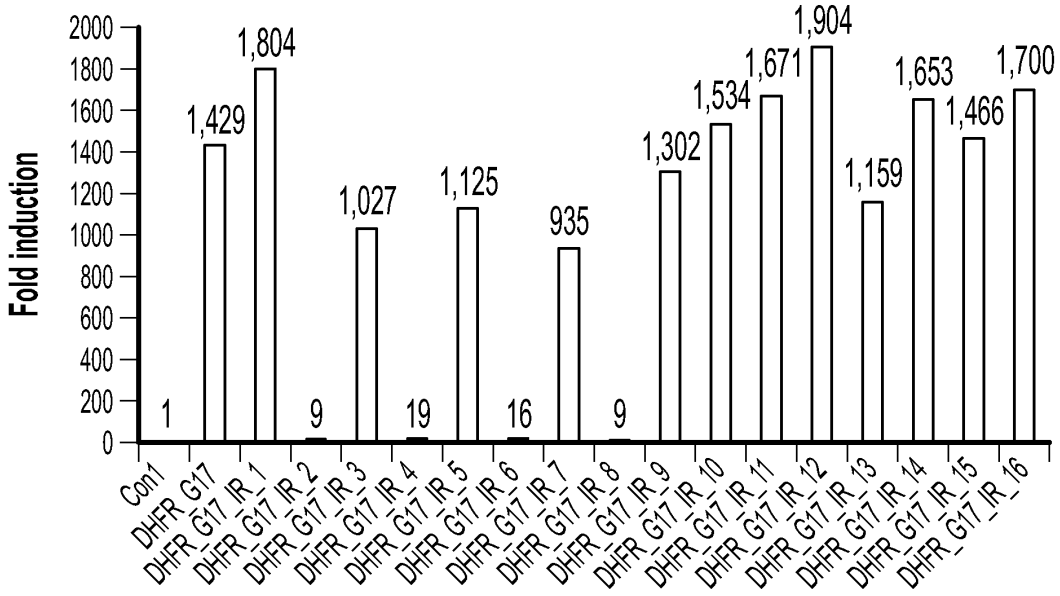

Fold induction
2000
1800
1600
1400
1200
1000
800
600
400
200
0
1
1,429
1,804
9
1,027
19
1,125
16
935
9
1,302
1,534
1,671
1,904
1,159
1,653
1,466
1,700
Con1
DHFR_G17
DHFR_G17_IR_1
DHFR_G17_IR_2
DHFR_G17_IR_3
DHFR_G17_IR_4
DHFR_G17_IR_5
DHFR_G17_IR_6
DHFR_G17_IR_7
DHFR_G17_IR_8
DHFR_G17_IR_9
DHFR_G17_IR_10
DHFR_G17_IR_11
DHFR_G17_IR_12
DHFR_G17_IR_13
DHFR_G17_IR_14
DHFR_G17_IR_15
DHFR_G17_IR_16

Fig. 9a

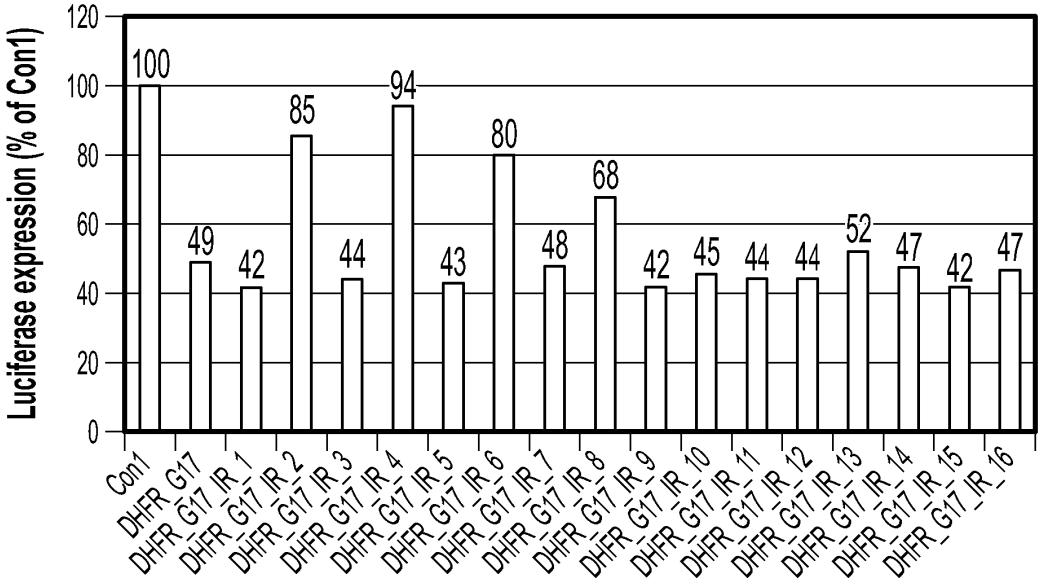

Luciferase expression (% of Con1)
120
100
80
60
40
20
0
100
49
42
85
44
94
43
80
48
68
42
45
44
44
52
47
42
47
Con1
DHFR_G17
DHFR_G17_IR_1
DHFR_G17_IR_2
DHFR_G17_IR_3
DHFR_G17_IR_4
DHFR_G17_IR_5
DHFR_G17_IR_6
DHFR_G17_IR_7
DHFR_G17_IR_8
DHFR_G17_IR_9
DHFR_G17_IR_10
DHFR_G17_IR_11
DHFR_G17_IR_12
DHFR_G17_IR_13
DHFR_G17_IR_14
DHFR_G17_IR_15
DHFR_G17_IR_16

Fig. 9b

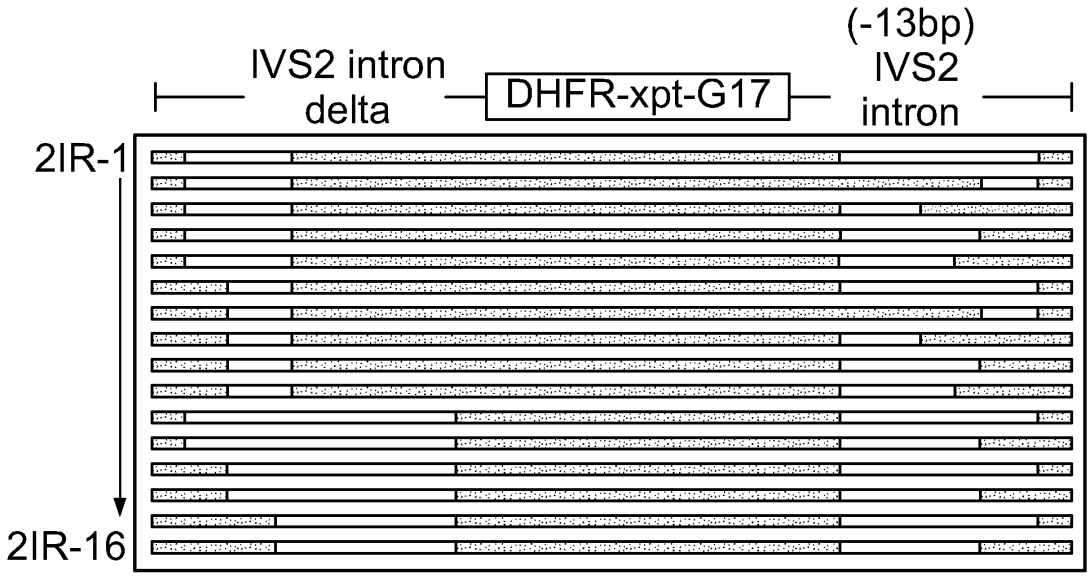

IVS2 intron delta
DHFR-xpt-G17
(-13bp) IVS2 intron
2IR-1
2IR-16

Fig. 9c

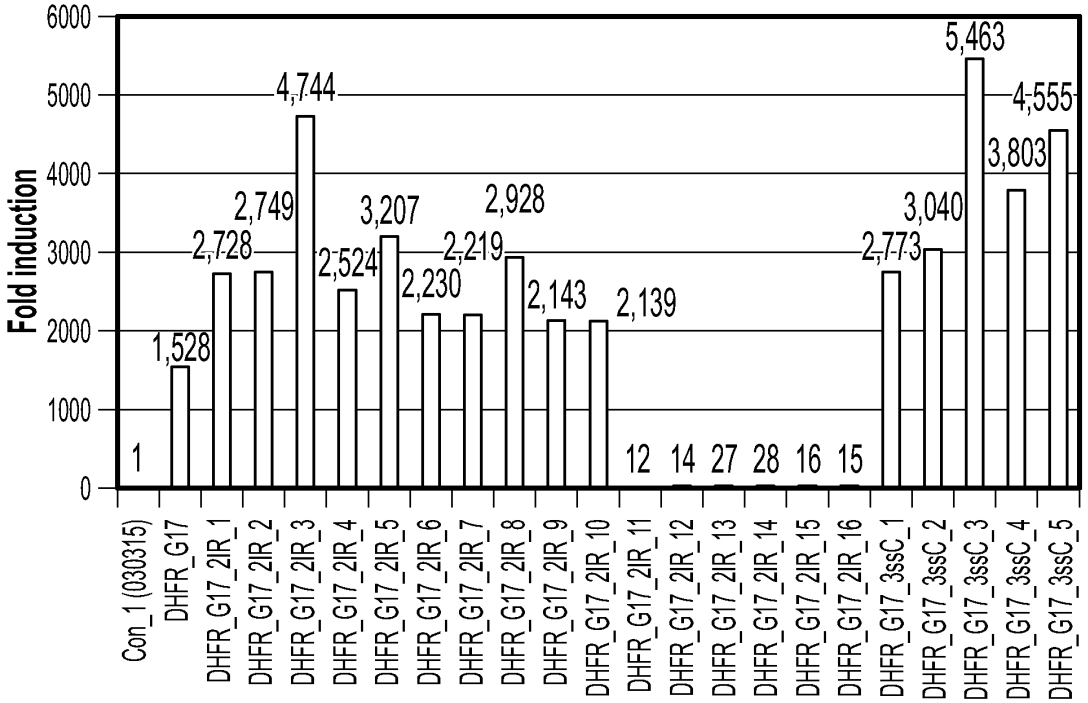

Fold induction
6000
5000
4000
3000
2000
1000
0
1
1,528
2,728
2,749
4,744
2,524
3,207
2,230
2,219
2,928
2,143
2,139
12
14
27
28
16
15
2,773
3,040
5,463
3,803
4,555
Con_1 (030315)
DHFR_G17
DHFR_G17_2IR_1
DHFR_G17_2IR_2
DHFR_G17_2IR_3
DHFR_G17_2IR_4
DHFR_G17_2IR_5
DHFR_G17_2IR_6
DHFR_G17_2IR_7
DHFR_G17_2IR_8
DHFR_G17_2IR_9
DHFR_G17_2IR_10
DHFR_G17_2IR_11
DHFR_G17_2IR_12
DHFR_G17_2IR_13
DHFR_G17_2IR_14
DHFR_G17_2IR_15
DHFR_G17_2IR_16
DHFR_G17_3ssC_1
DHFR_G17_3ssC_2
DHFR_G17_3ssC_3
DHFR_G17_3ssC_4
DHFR_G17_3ssC_5

Fig. 9d

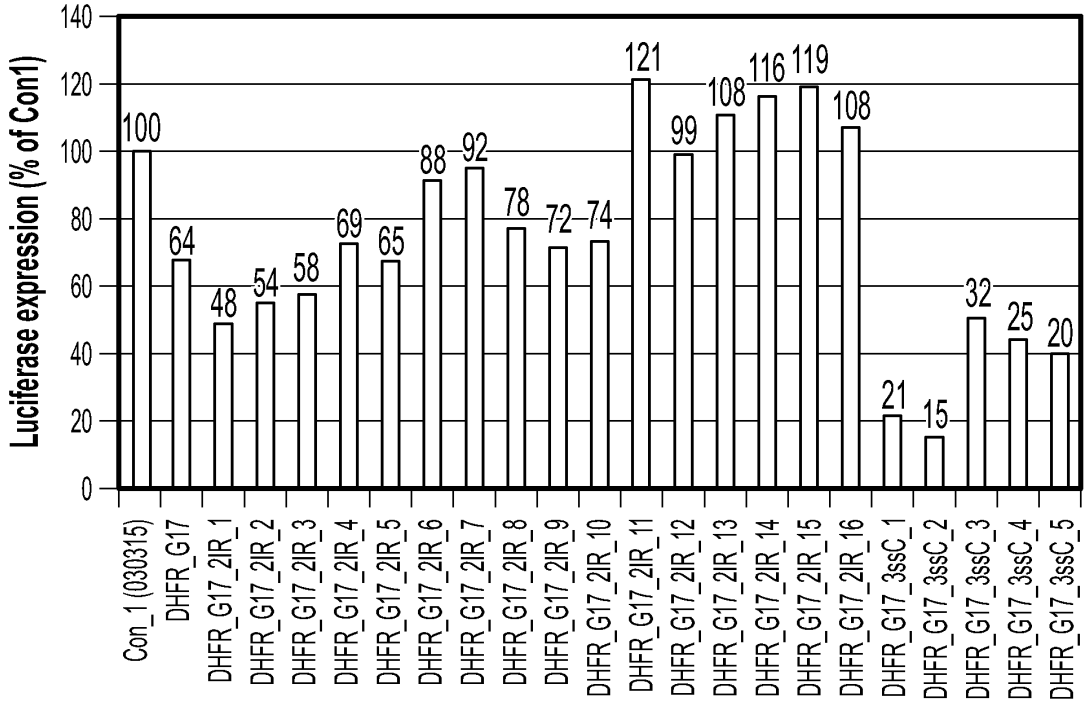

Luciferase expression (% of Con1)
140
120
100
80
60
40
20
0
100
64
48
54
58
69
65
88
92
78
72
74
121
99
108
116
119
108
21
15
32
25
20
Con_1 (030315)
DHFR_G17
DHFR_G17_2IR_1
DHFR_G17_2IR_2
DHFR_G17_2IR_3
DHFR_G17_2IR_4
DHFR_G17_2IR_5
DHFR_G17_2IR_6
DHFR_G17_2IR_7
DHFR_G17_2IR_8
DHFR_G17_2IR_9
DHFR_G17_2IR_10
DHFR_G17_2IR_11
DHFR_G17_2IR_12
DHFR_G17_2IR_13
DHFR_G17_2IR_14
DHFR_G17_2IR_15
DHFR_G17_2IR_16
DHFR_G17_3ssC_1
DHFR_G17_3ssC_2
DHFR_G17_3ssC_3
DHFR_G17_3ssC_4
DHFR_G17_3ssC_5

**Fig. 9e**

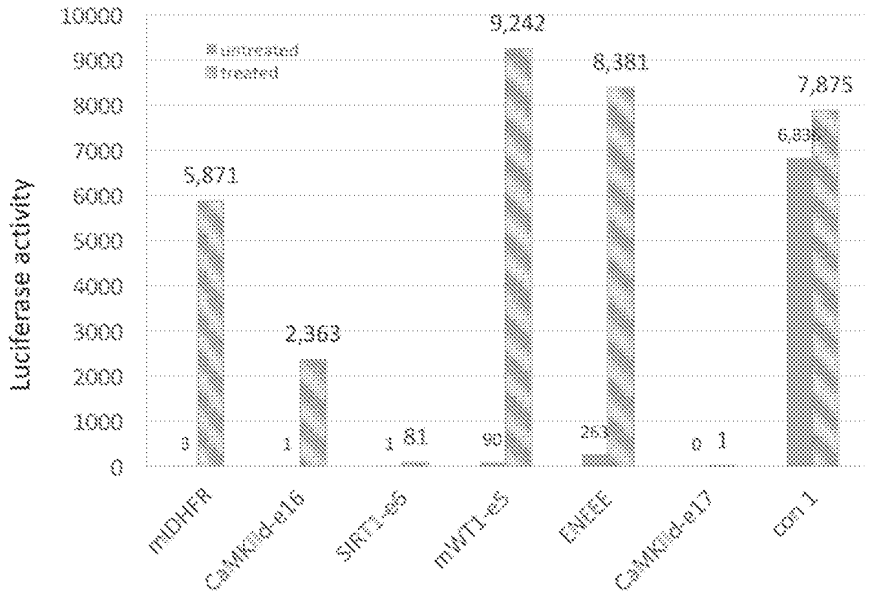



Fig. 10a

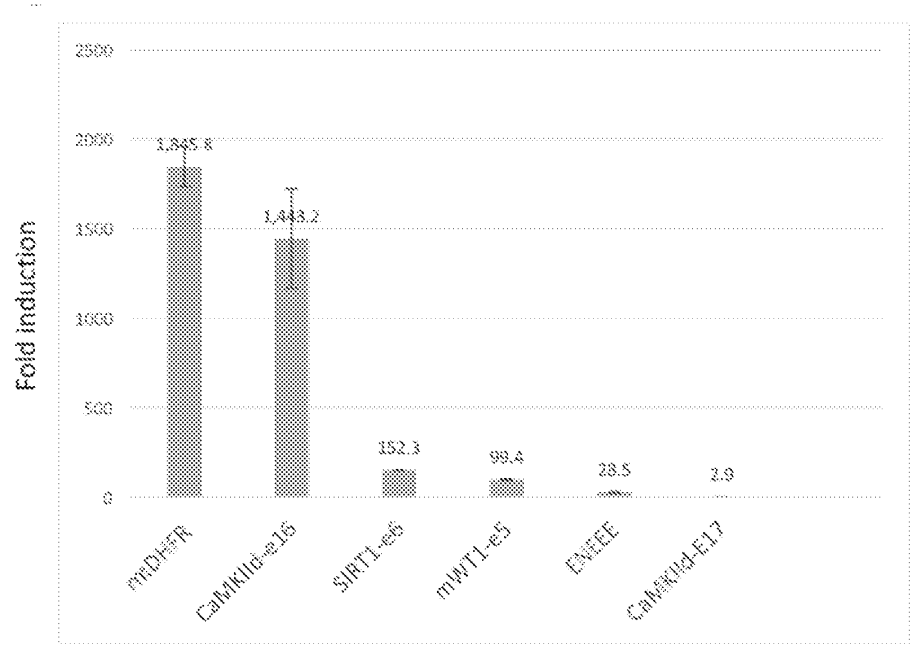



Fig. 10b

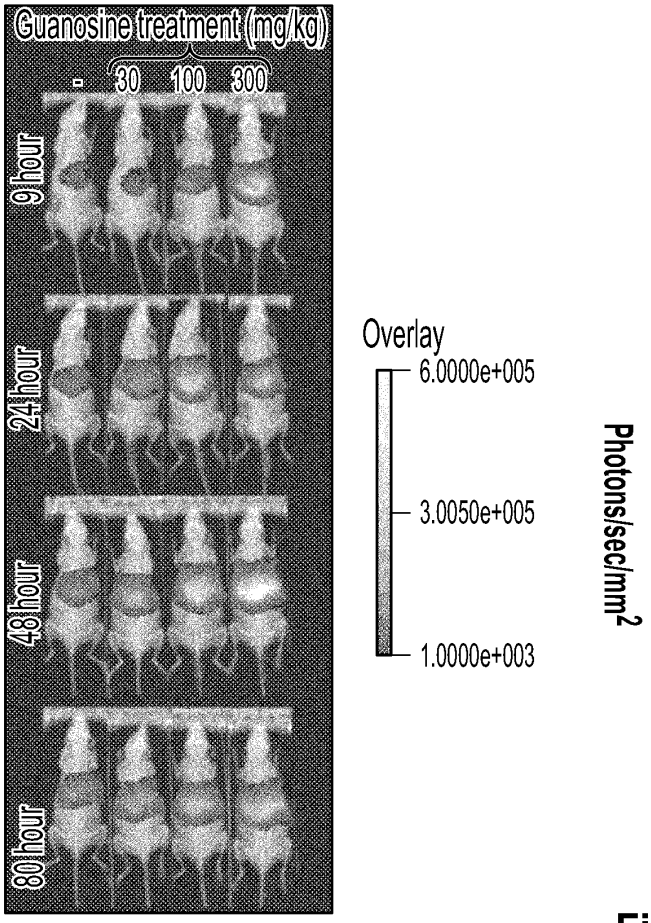



Fig. 11a

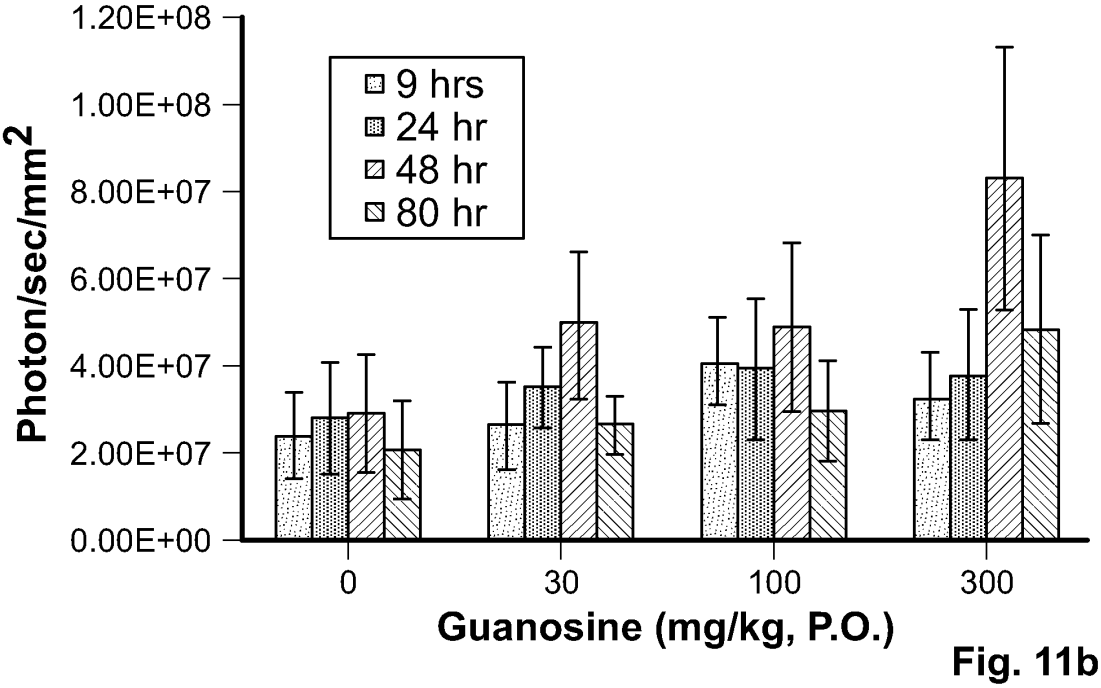



Fig. 11b

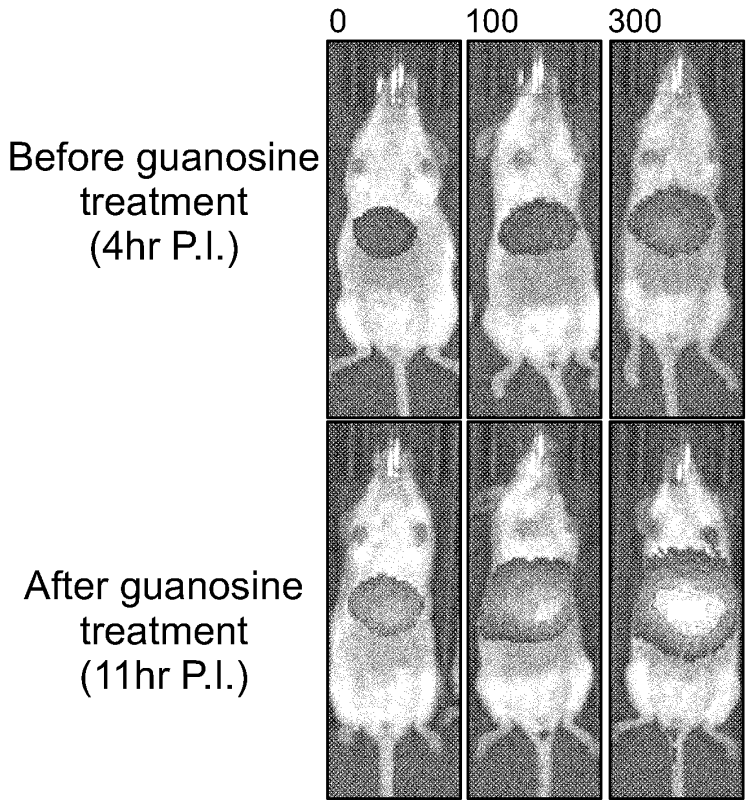



Fig. 11c

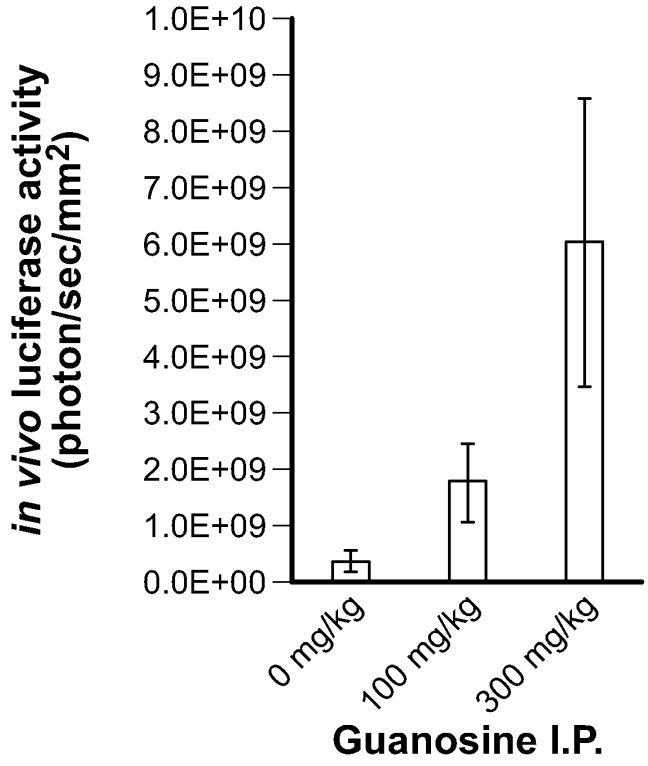



Fig. 11d

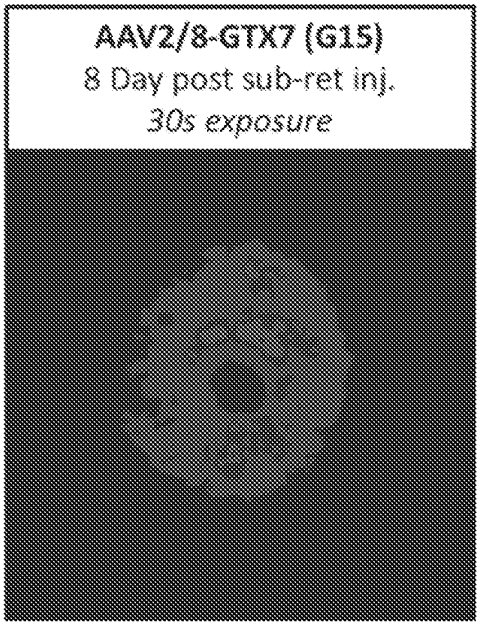



Fig. 12

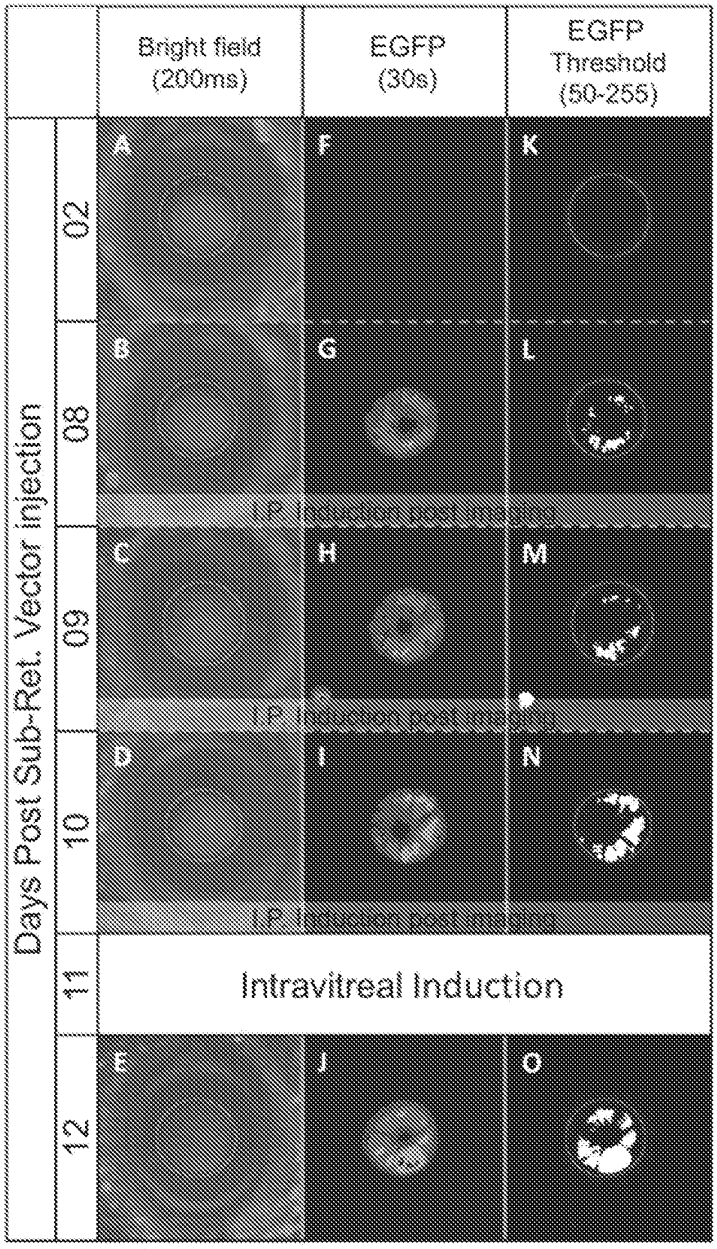

Bright field (200ms)
EGFP (30s)
EGFP Threshold (50-255)
Days Post Sub-Ret. Vector injection
02
08
09
10
11
12
A
B
C
D
E
F
G
H
I
J
K
L
M
N
O
I.P. Injection post-ret. vector
I.P. Injection post-ret. vector
I.P. Injection post-ret. vector
Intravitreal Induction

Fig. 13a

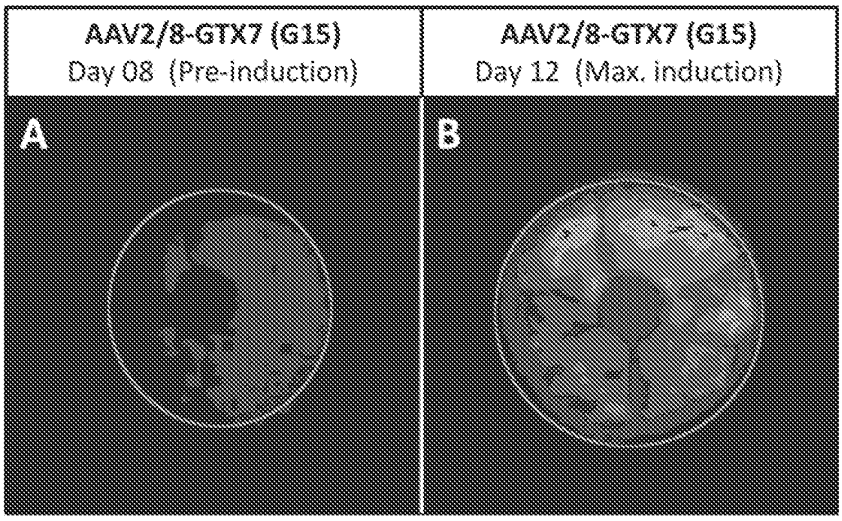

AAV2/8-GTX7 (G15)
Day 08 (Pre-induction)
AAV2/8-GTX7 (G15)
Day 12 (Max. induction)
A
B
30s exposure

Fig. 13b

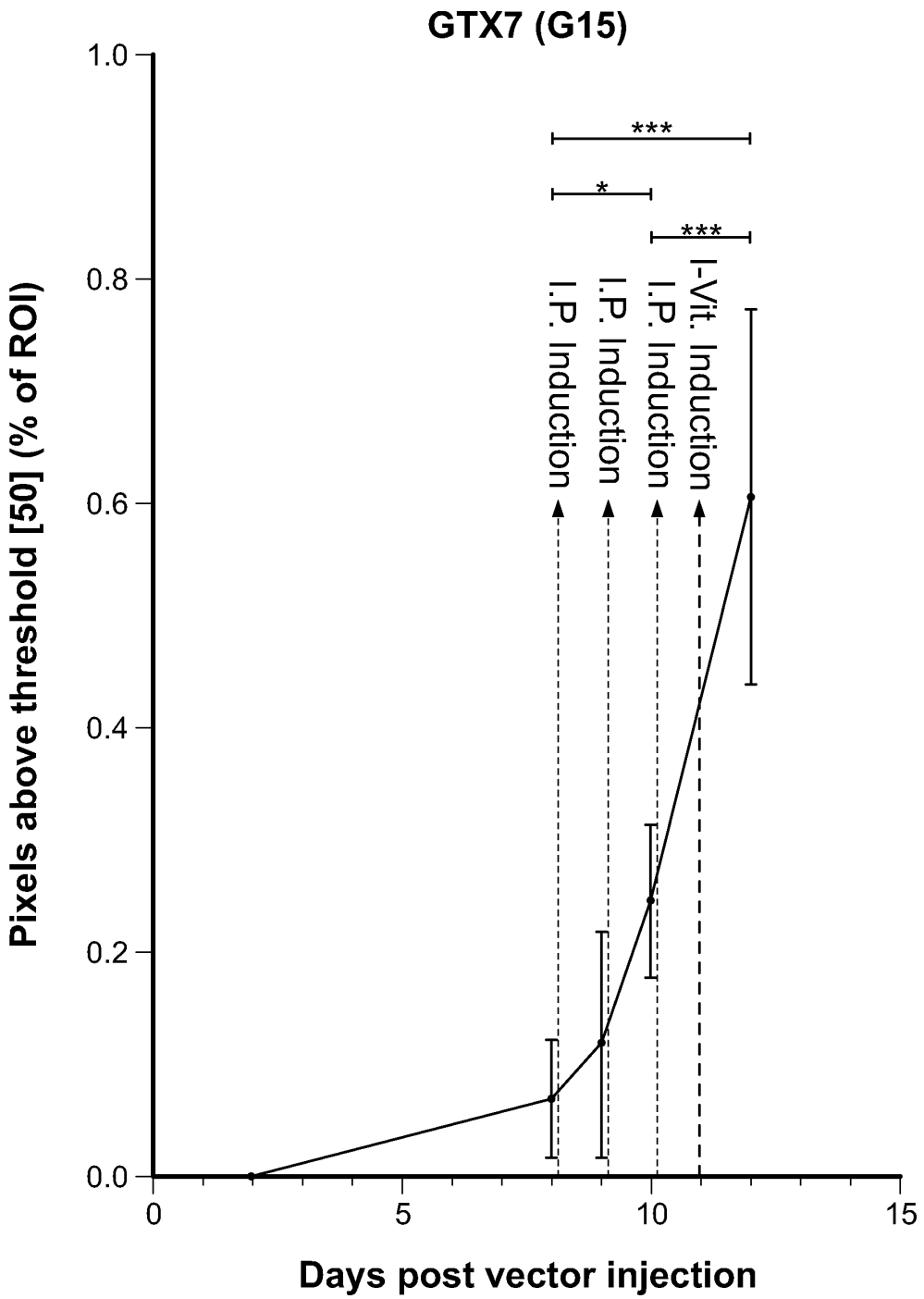

GTX7 (G15)
Pixels above threshold [50] (% of ROI)
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
Days post vector injection
***
*
***
I.P. Induction
I.P. Induction
I.P. Induction
I-Vit. Induction

Fig. 13c

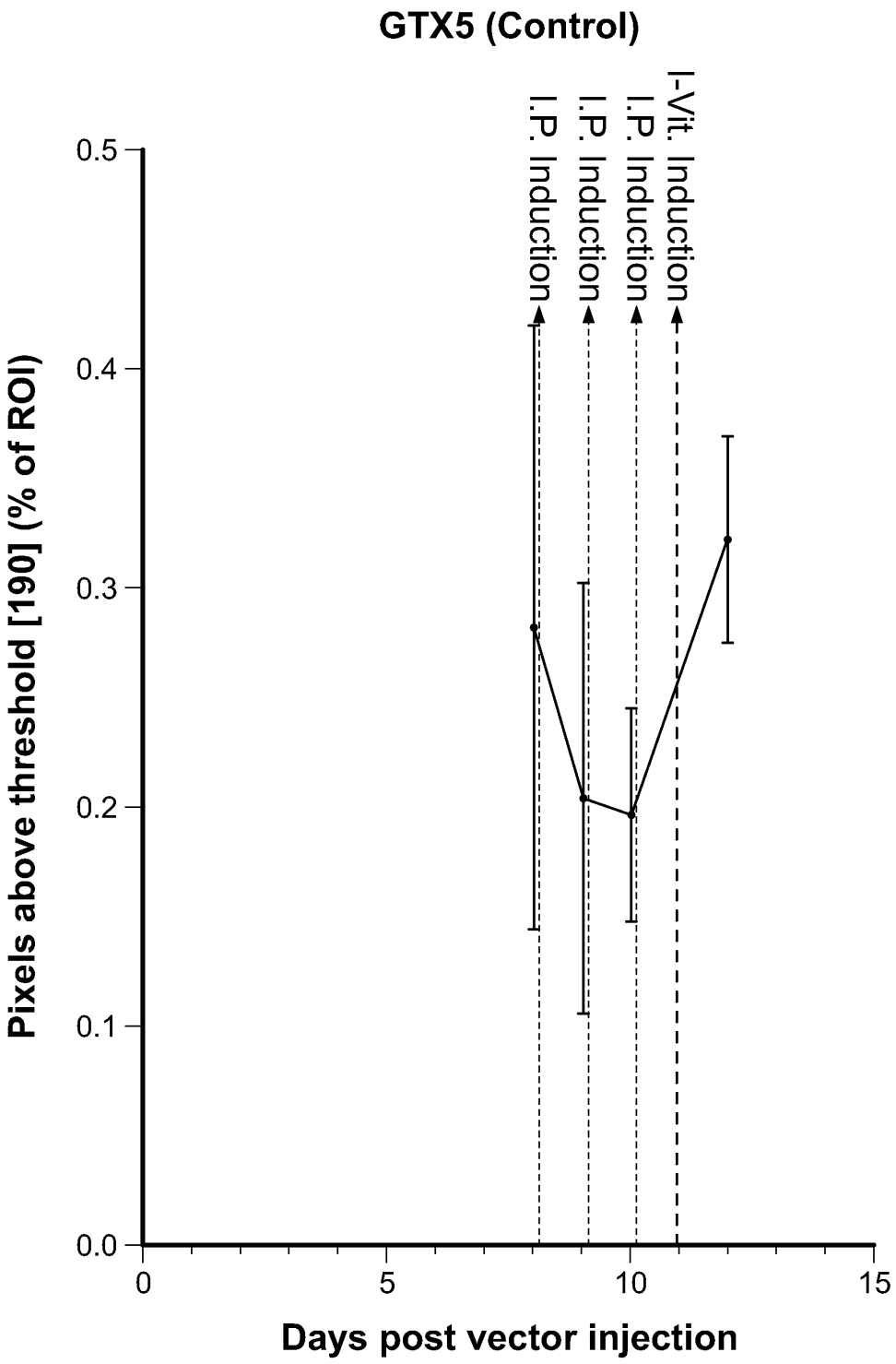

GTX5 (Control)
I.P. Induction
I.P. Induction
I.P. Induction
I-Vit. Induction
Pixels above threshold [190] (% of ROI)
0.5
0.4
0.3
0.2
0.1
0.0
0
5
10
15
Days post vector injection

Fig. 13d