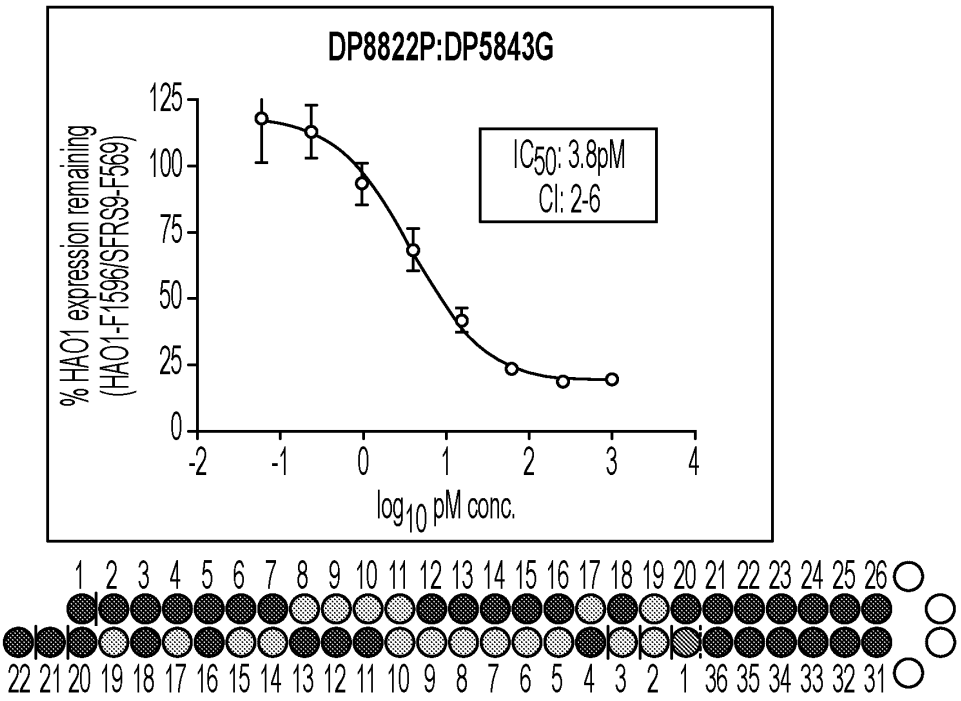

DP8822P:DP5843G
% HAO1 expression remaining (HAO1-F1596/SFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc.
IC50: 3.8pM
CI: 2-6
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 1A

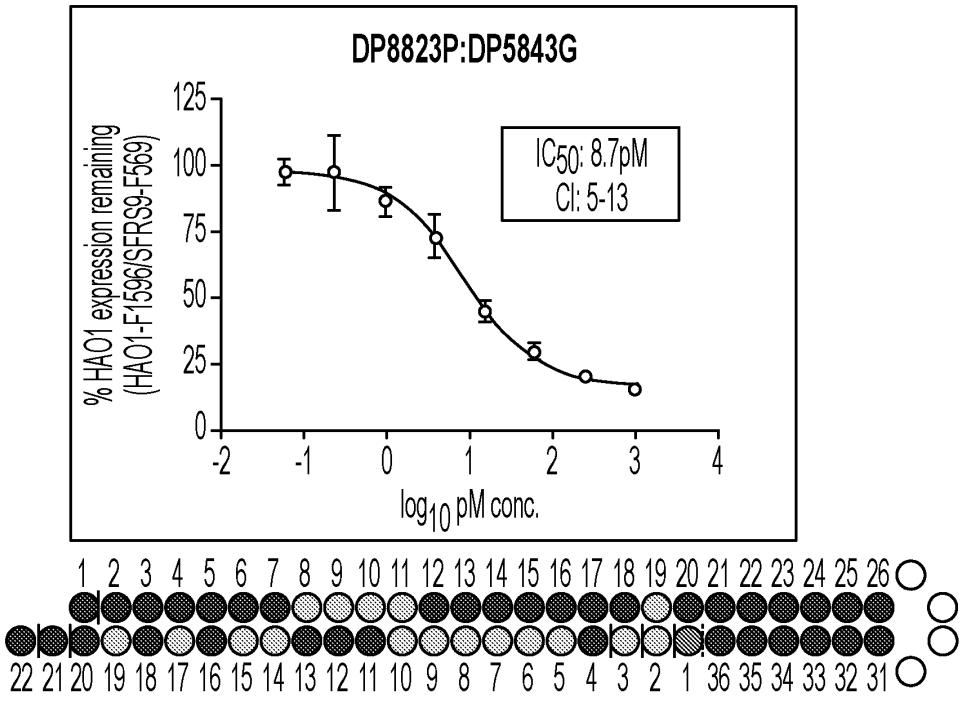
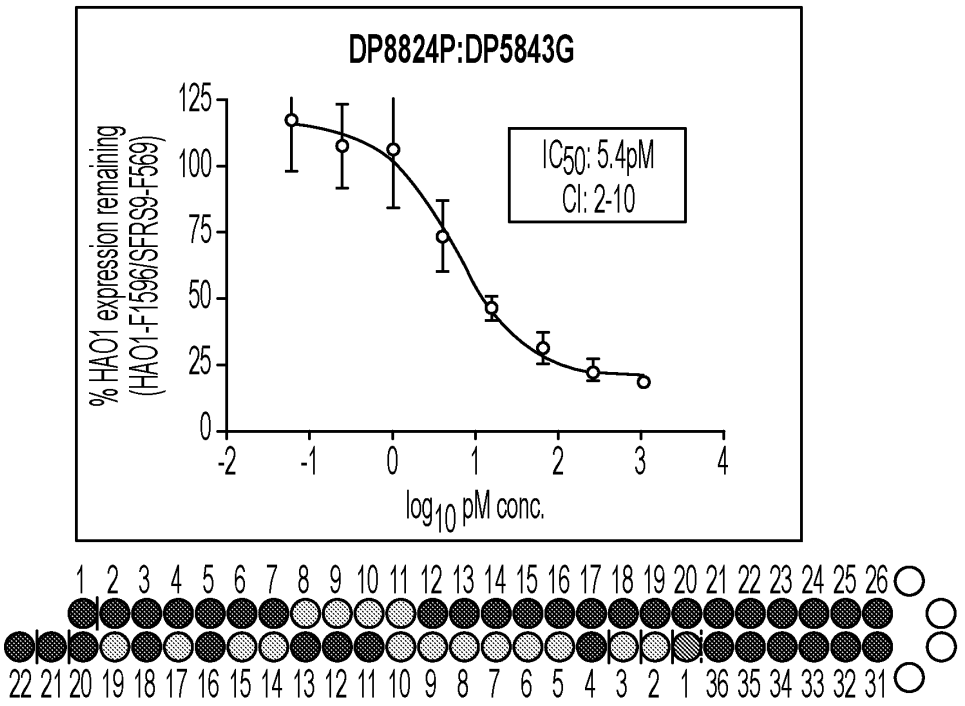

DP8823P:DP5843G
% HAO1 expression remaining (HAO1-F1596/SFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc.
IC50: 8.7pM
CI: 5-13
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 1B


DP8824P:DP5843G
% HAO1 expression remaining
(HAO1-F1596/SFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc.
IC50: 5.4pM
CI: 2-10

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 1C

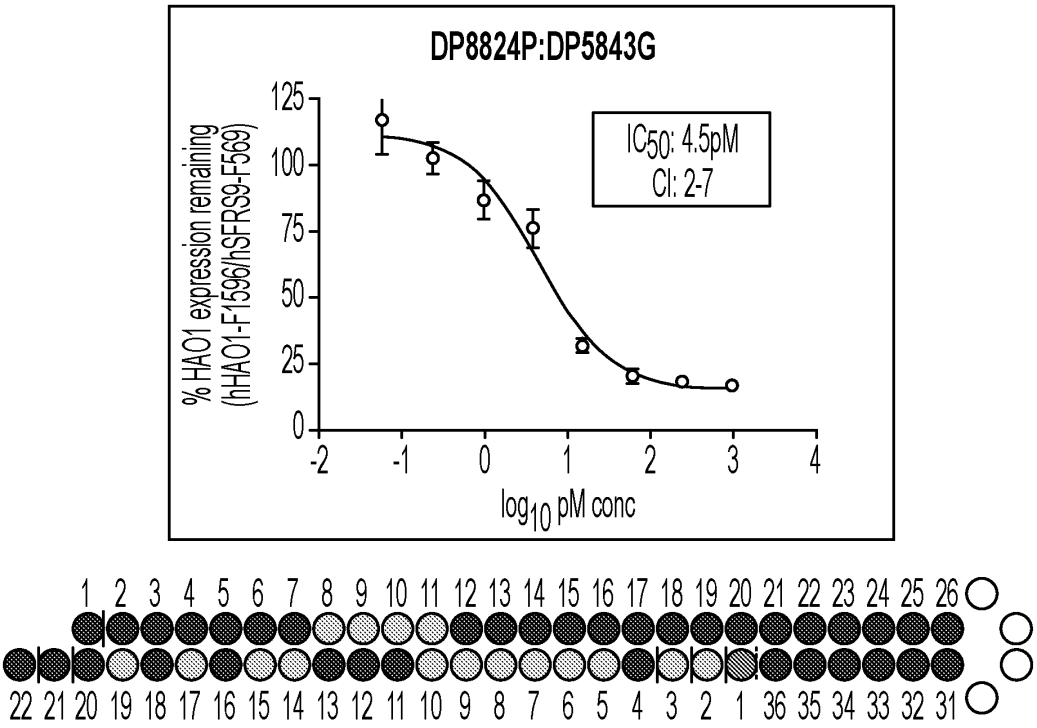

DP8824P:DP5843G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 4.5pM
CI: 2-7
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 2A

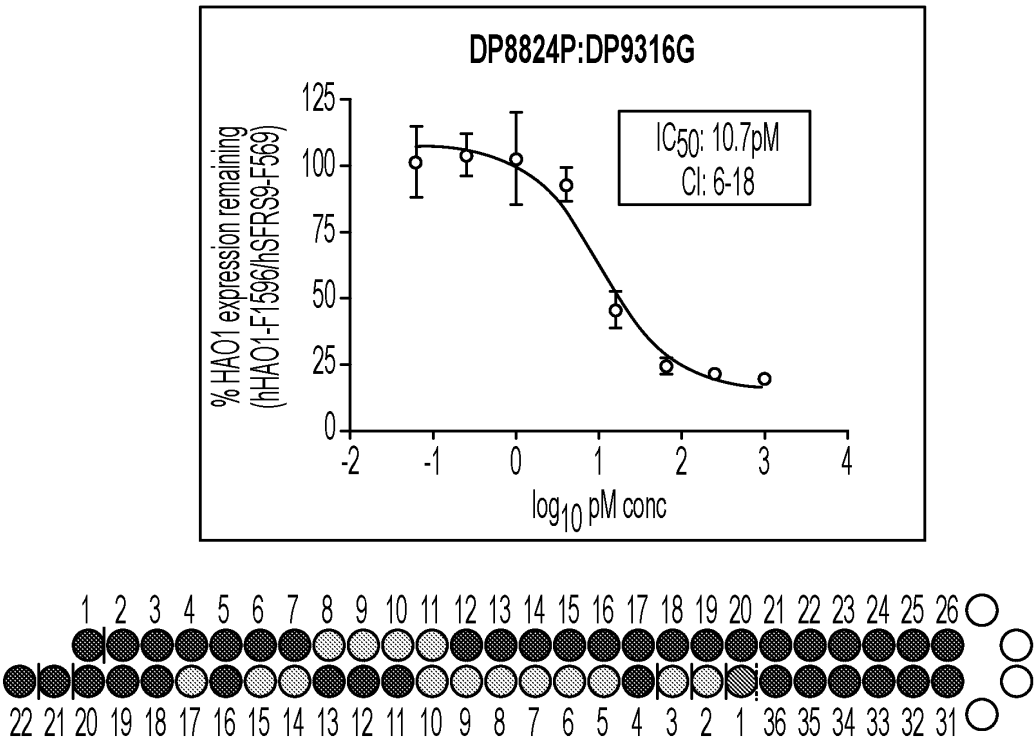
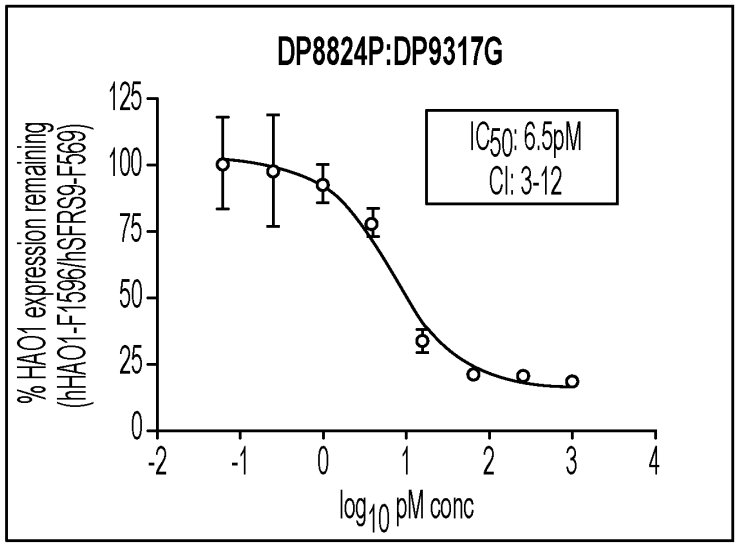

DP8824P:DP9316G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 10.7pM
CI: 6-18
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 2B


DP8824P:DP9317G
% HAO1 expression remaining
(hHAO1-F1596/hSFRS9-F569)
IC50: 6.5pM
CI: 3-12
log10 pM conc

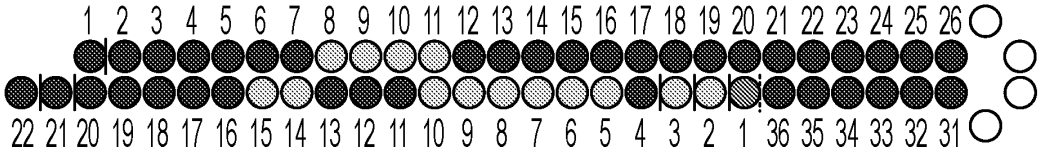
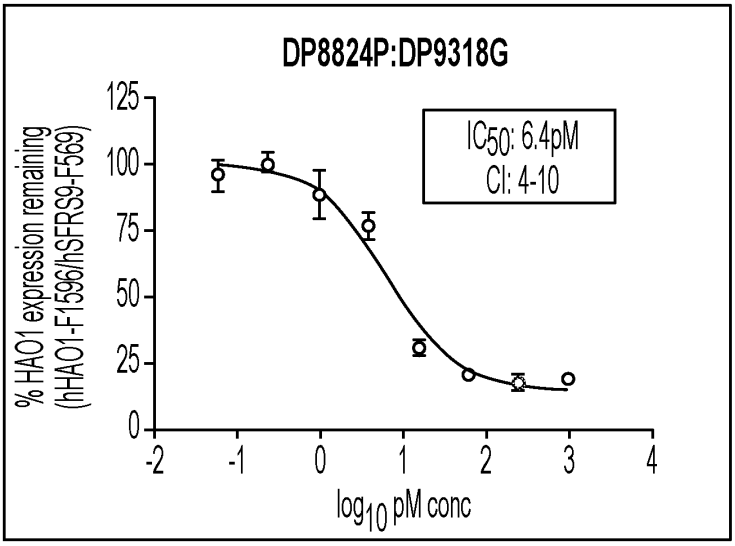

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 2C


DP8824P:DP9318G
% HAO1 expression remaining
(hHAO1-F1596/hSFRS9-F569)
IC50: 6.4pM
CI: 4-10
log10 pM conc

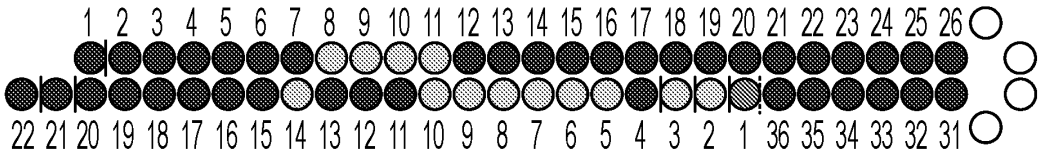

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 2D

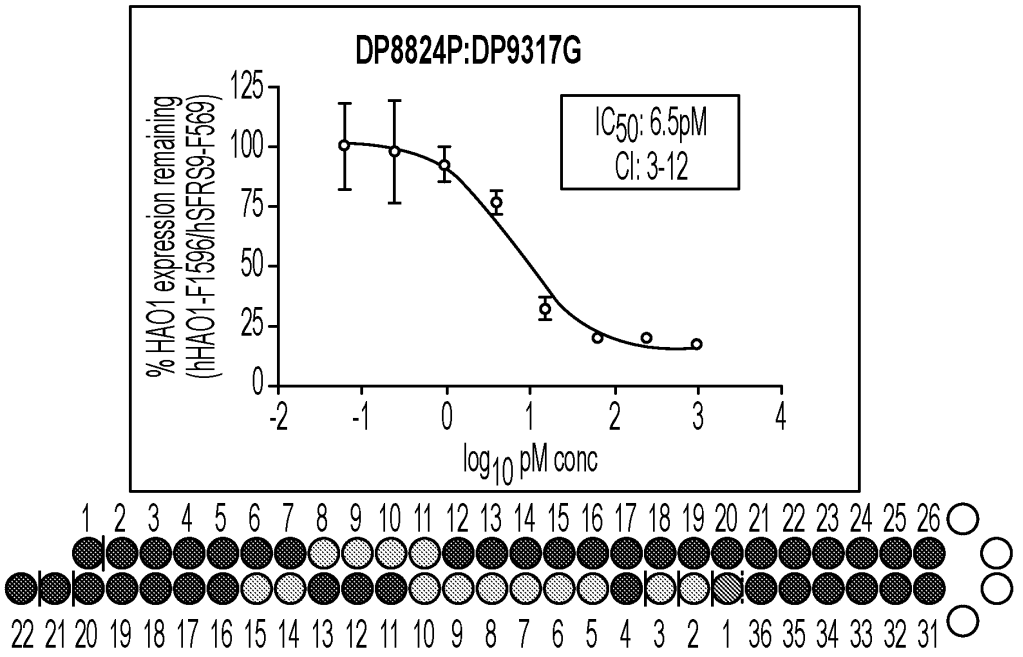

DP8824P:DP9317G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 6.5pM
CI: 3-12
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 3A

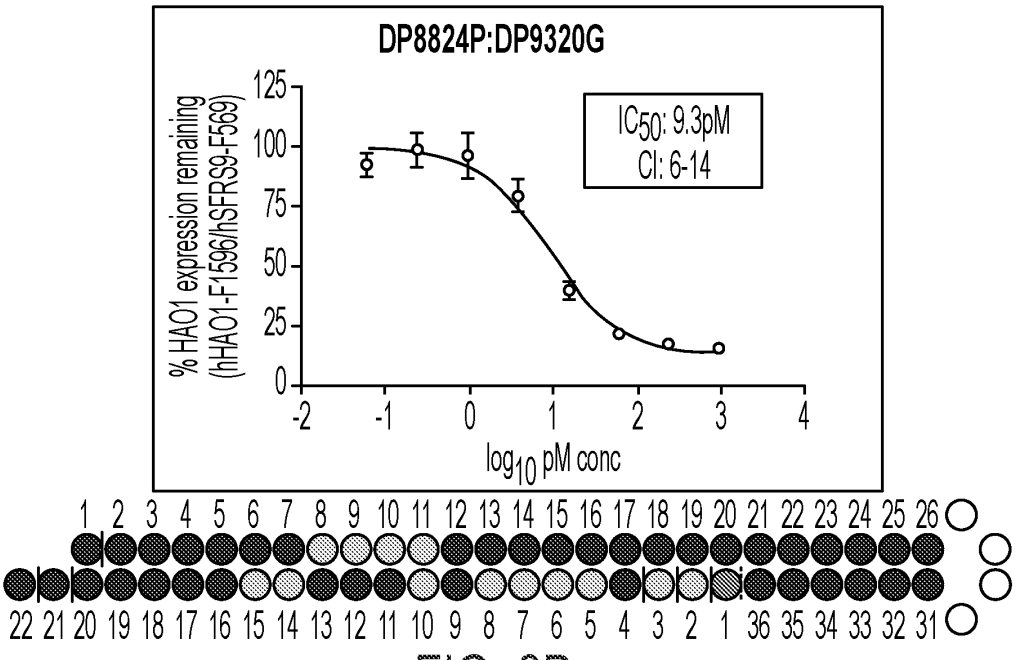

DP8824P:DP9320G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 9.3pM
CI: 6-14
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 3B

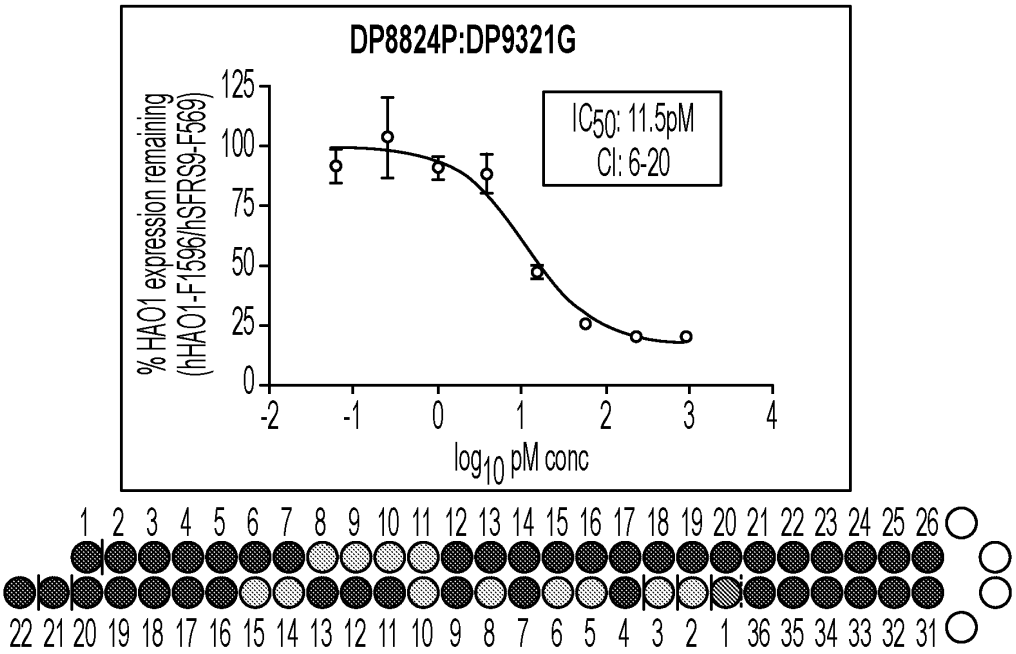

DP8824P:DP9321G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 11.5pM
CI: 6-20
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 3C

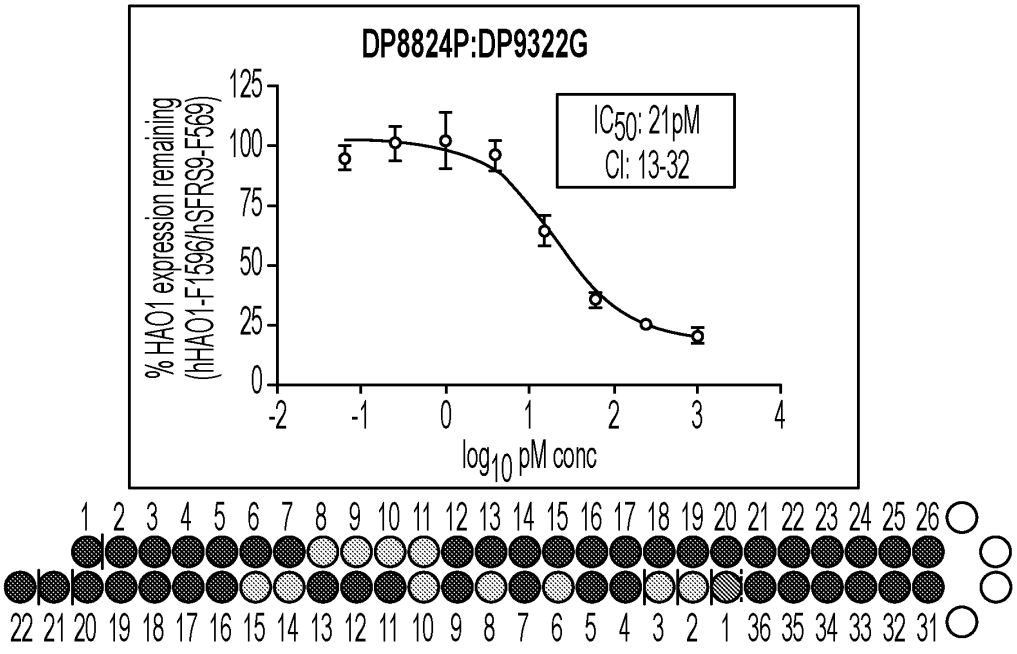

DP8824P:DP9322G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 21pM
CI: 13-32
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 3D

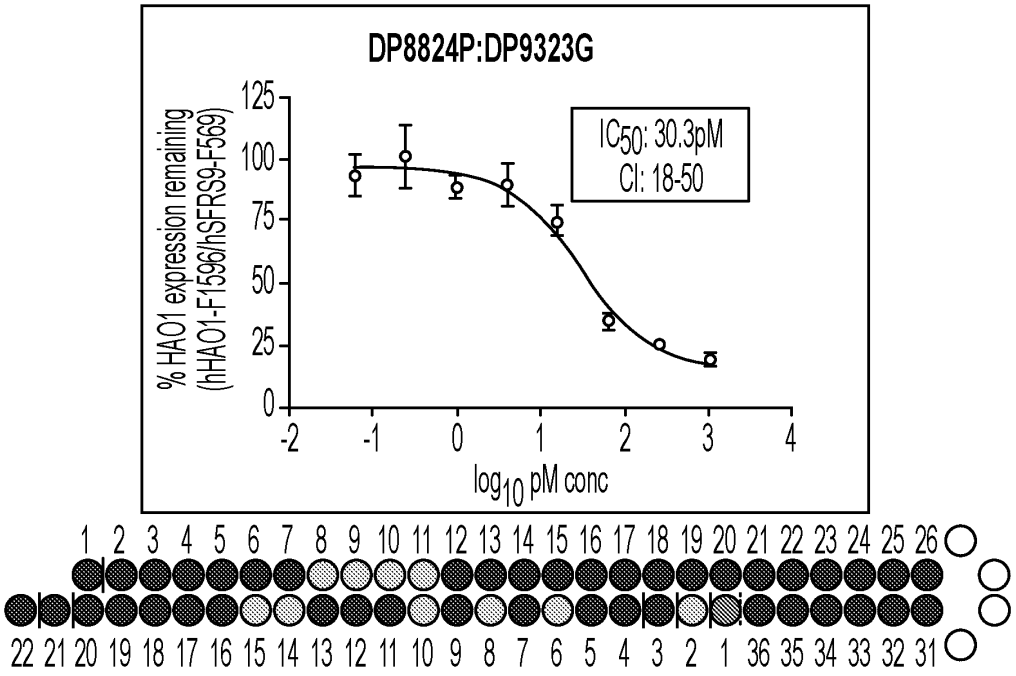

DP8824P:DP9323G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 30.3pM
CI: 18-50
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 3E

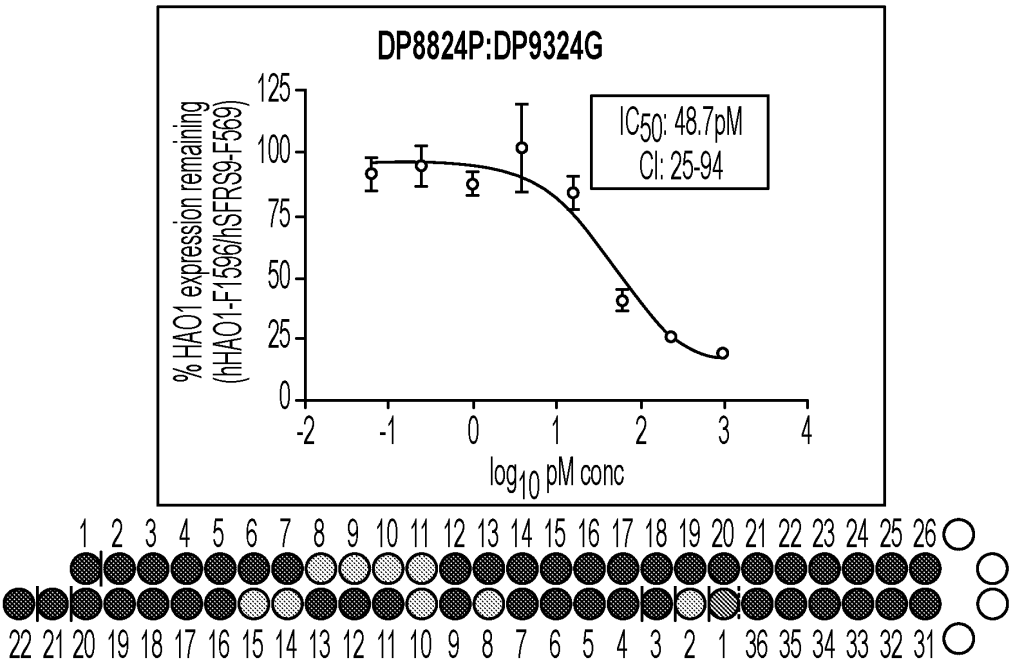

DP8824P:DP9324G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 48.7pM
CI: 25-94
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 3F

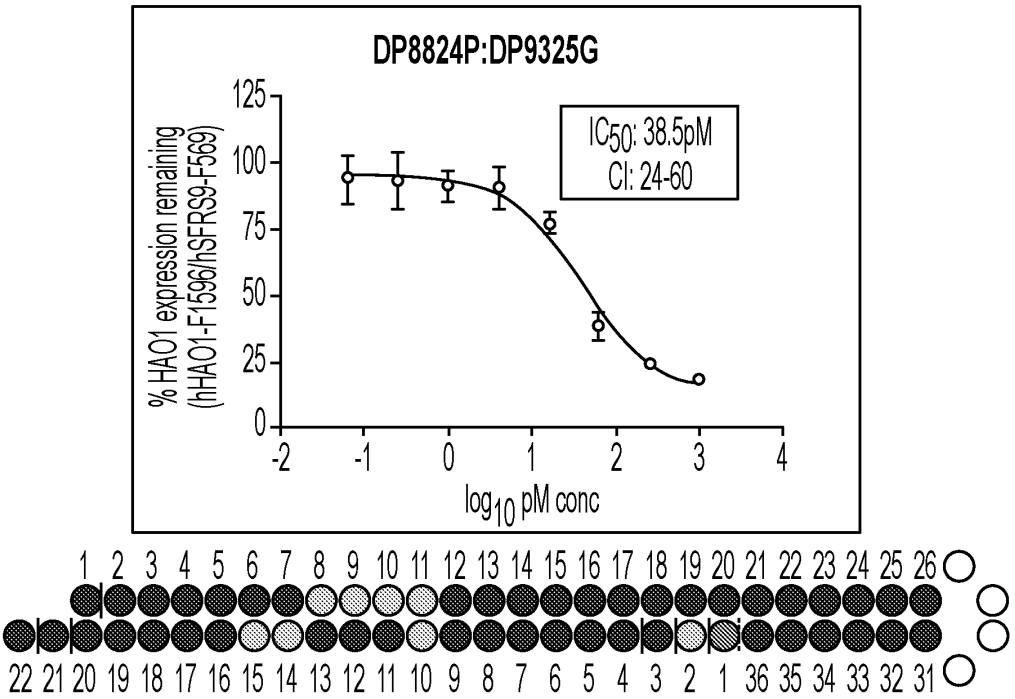

DP8824P:DP9325G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 38.5pM
CI: 24-60
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 3G

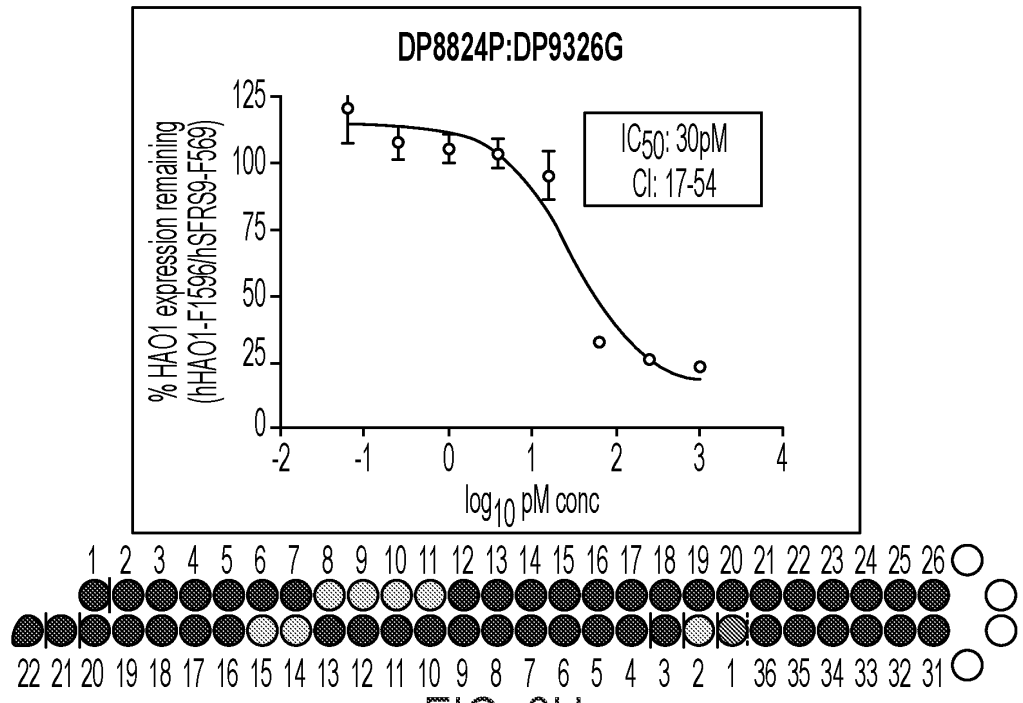

DP8824P:DP9326G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 30pM
CI: 17-54
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 3H

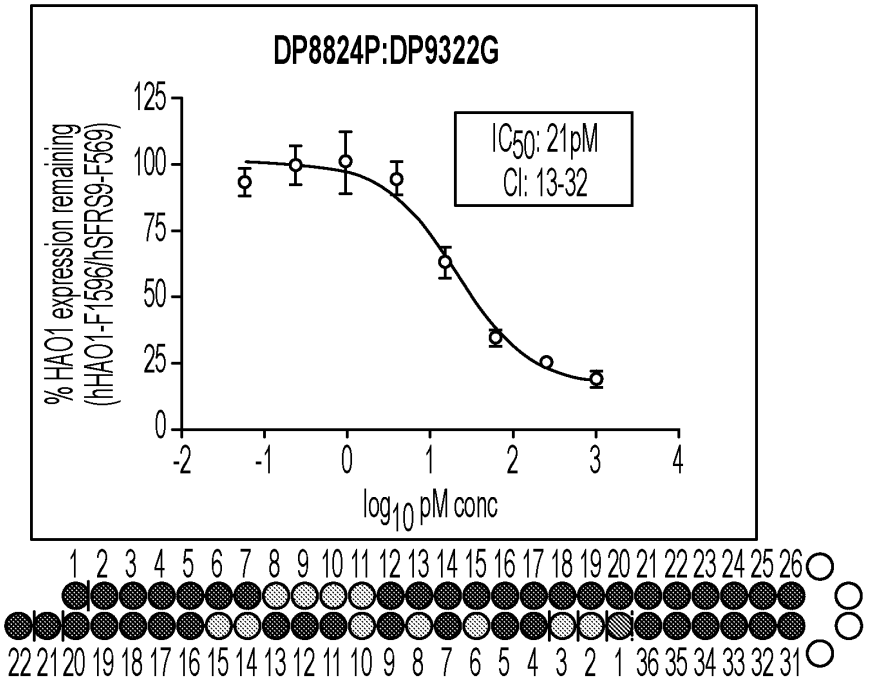

DP8824P:DP9322G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 21pM
CI: 13-32
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 4A

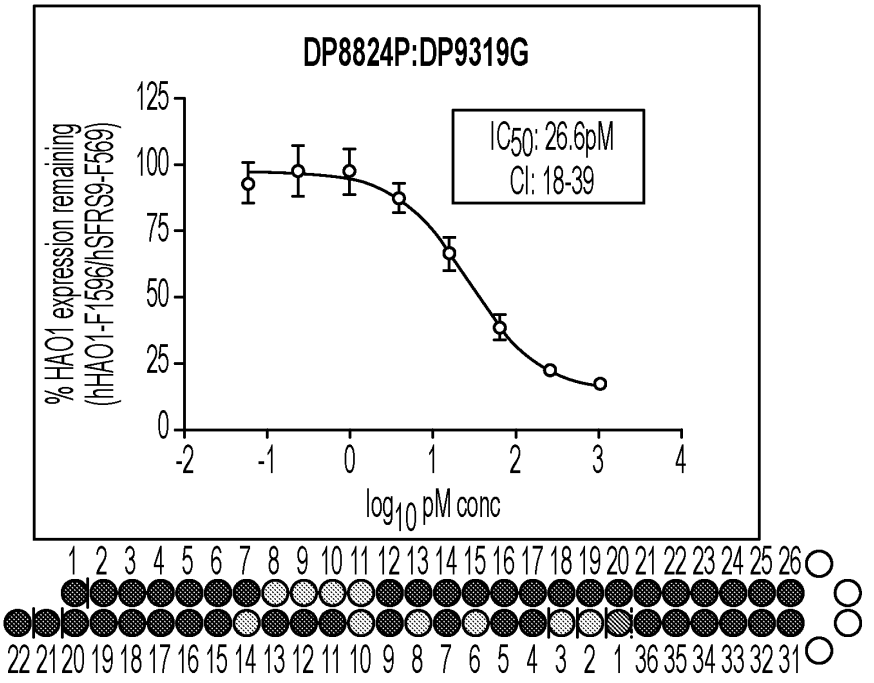

DP8824P:DP9319G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 26.6pM
CI: 18-39
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 4B

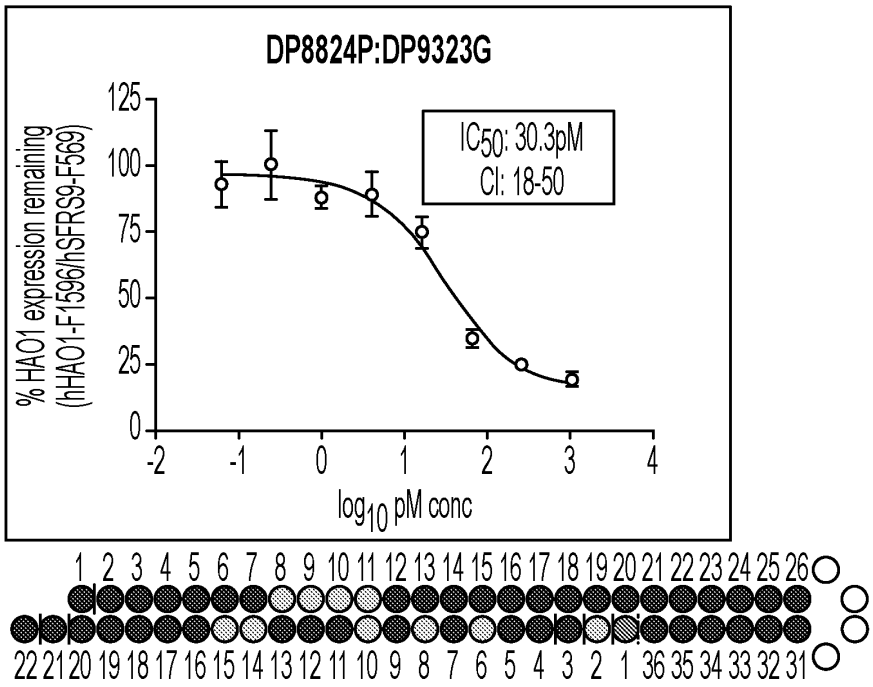

DP8824P:DP9323G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 30.3pM
CI: 18-50
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 4C

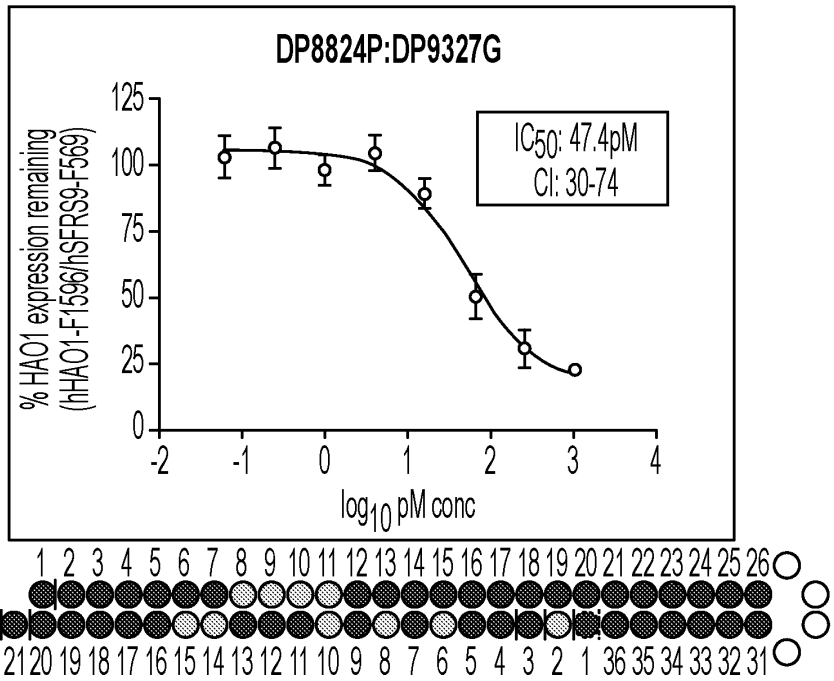

DP8824P:DP9327G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 47.4pM
CI: 30-74
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 4D

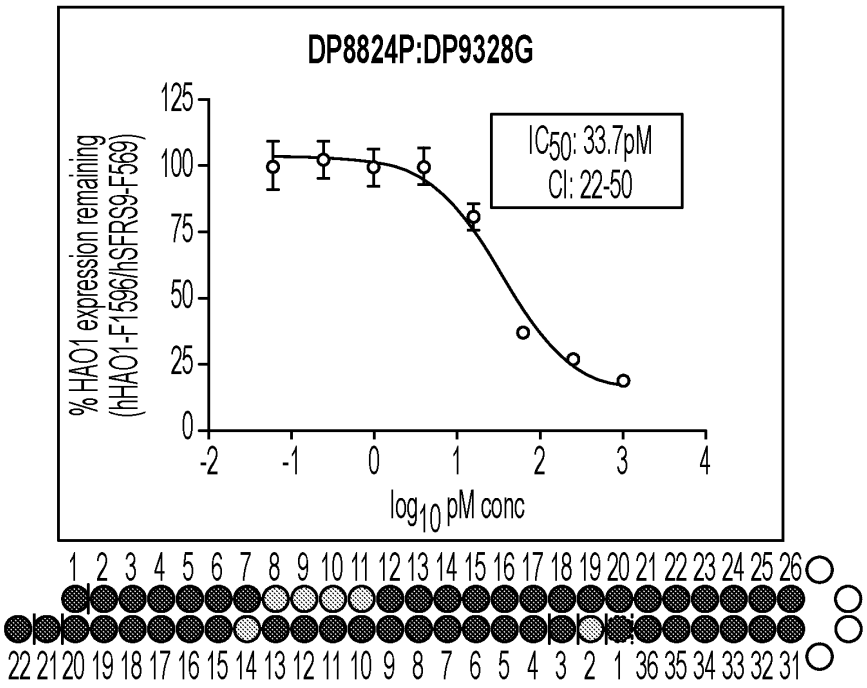

DP8824P:DP9328G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
125
100
75
50
25
0
-2
-1
0
1
2
3
4
log10 pM conc
IC50: 33.7pM
CI: 22-50
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 4E

F @ G2,14

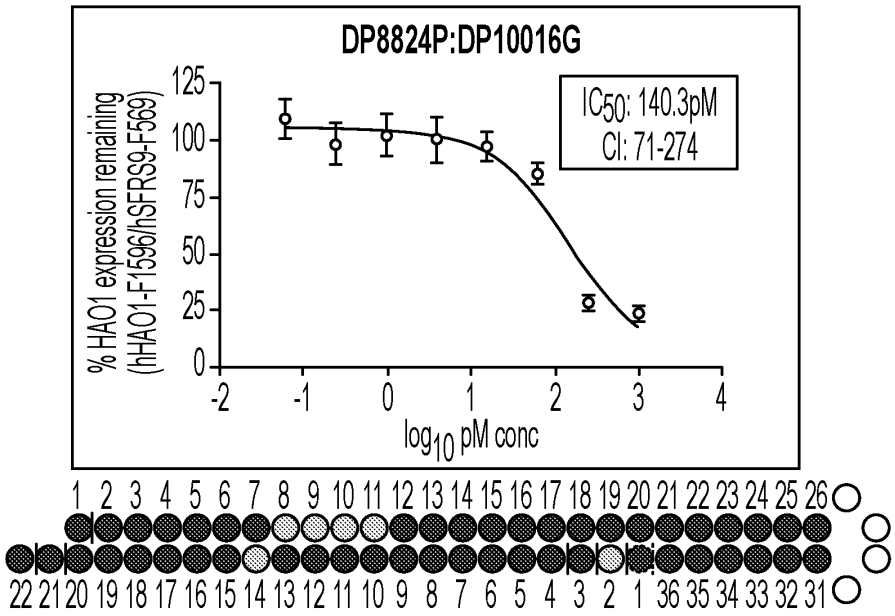


FIG. 5A

F @ G2,3,14

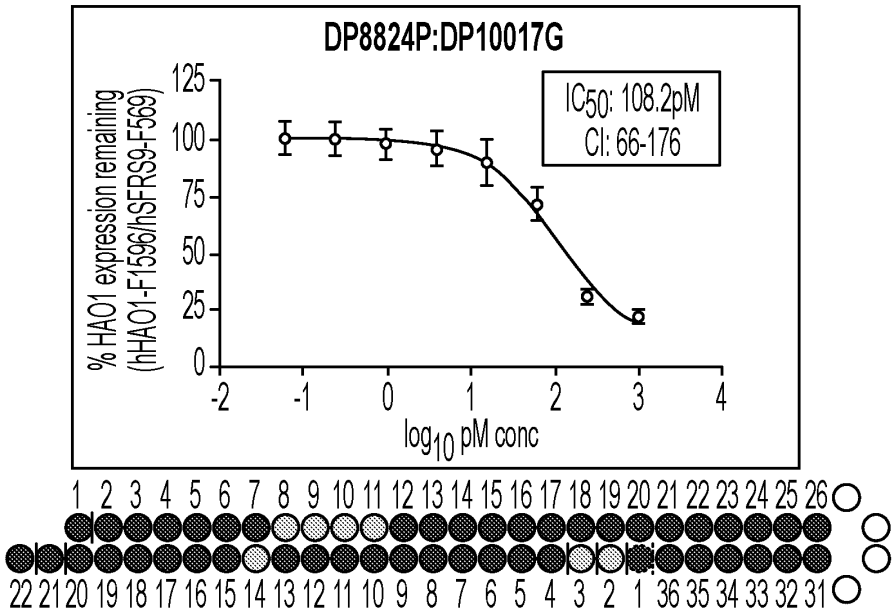


FIG. 5B

F @ G2,4,14

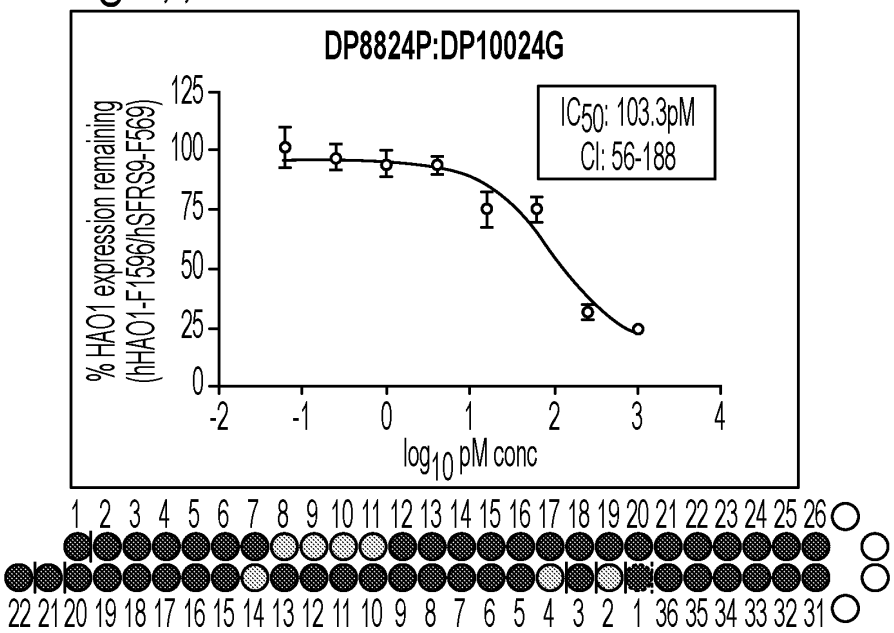


FIG. 5C

F @ G2,5,14

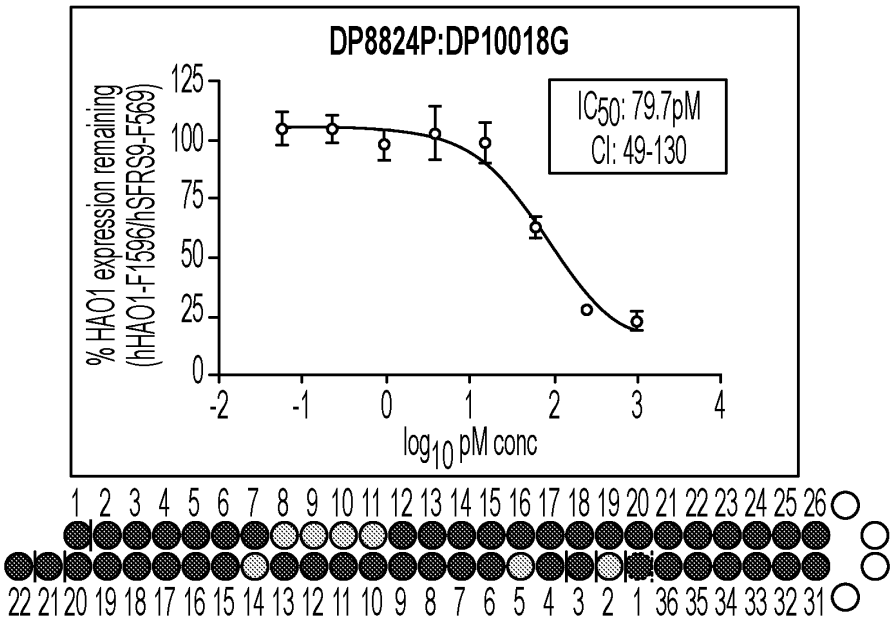


FIG. 5D

F @ G2,6,14

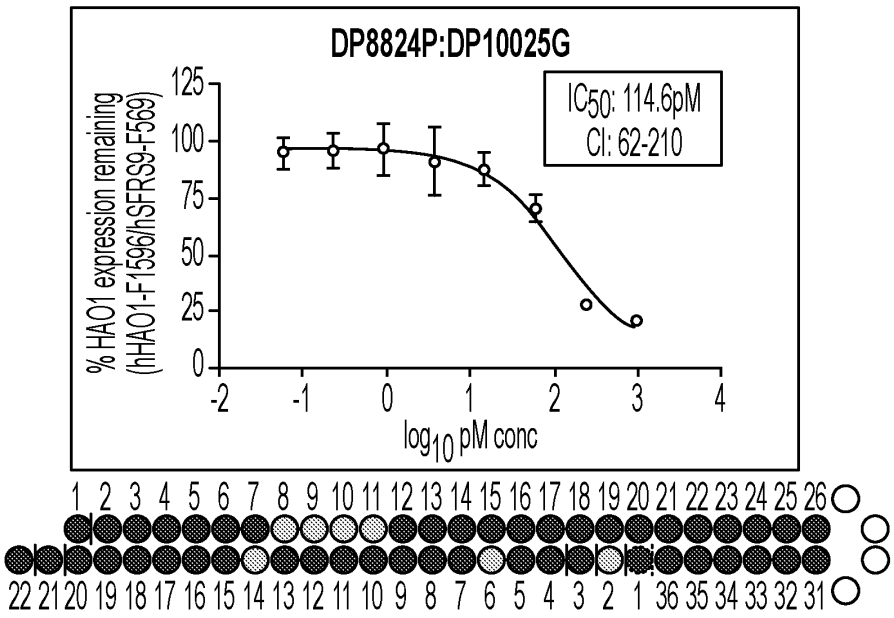


FIG. 5E

F @ G2,3,5,14

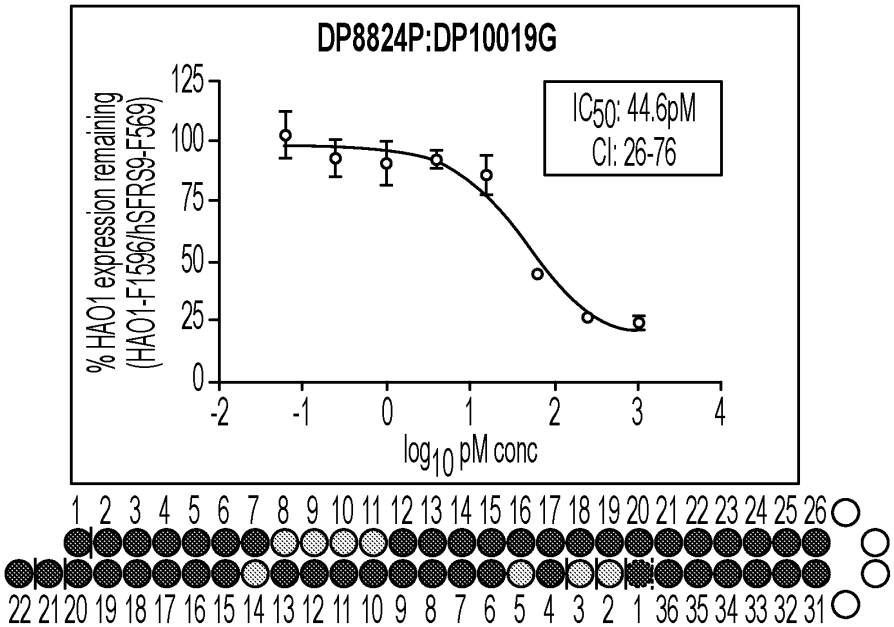


FIG. 5F

F @ G2,5,6,14

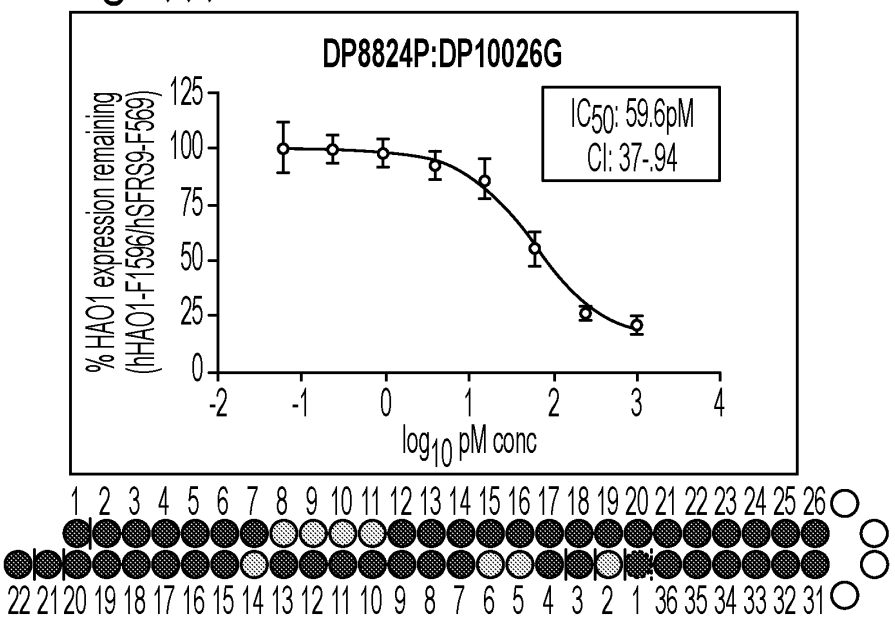


FIG. 5G

F @ G2+3,5+6,14

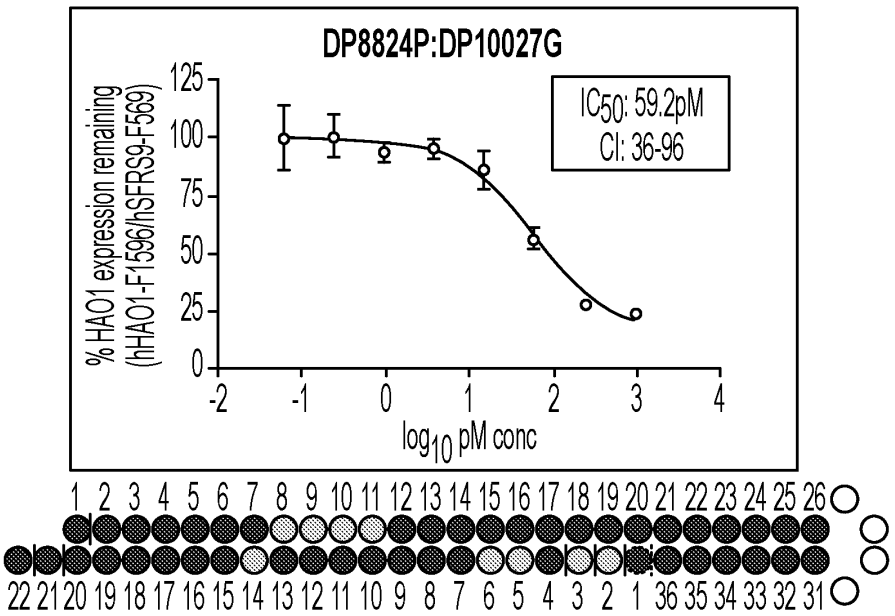


FIG. 5H

Control 1: 2'F on G1,2,3,5,14

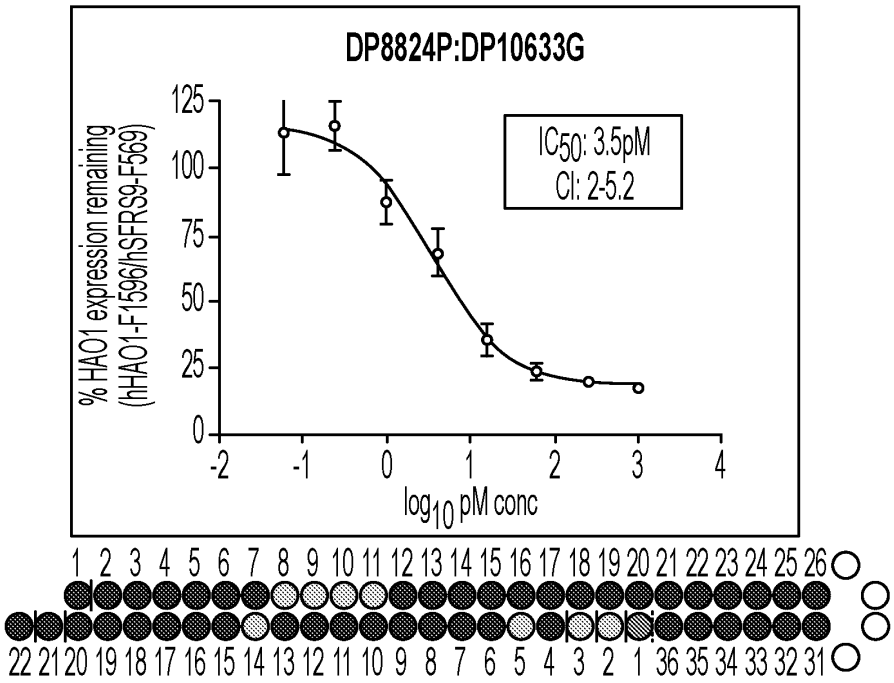


FIG. 6A

Control 2: OMe on P9
2'F on G1,2,3,5,14

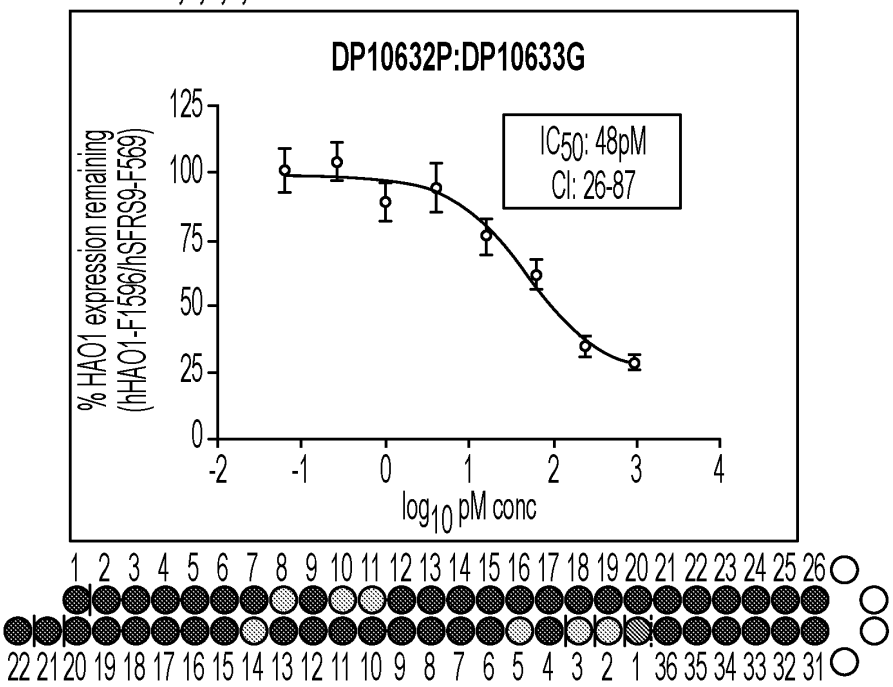


FIG. 6B

2'F on G7

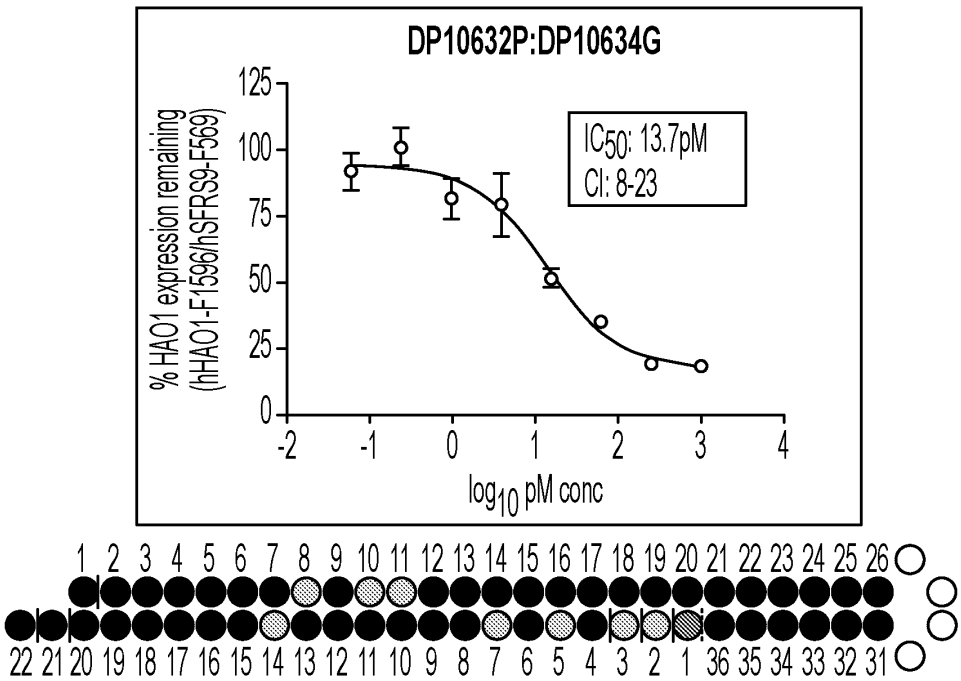


FIG. 6C

2'F on G8

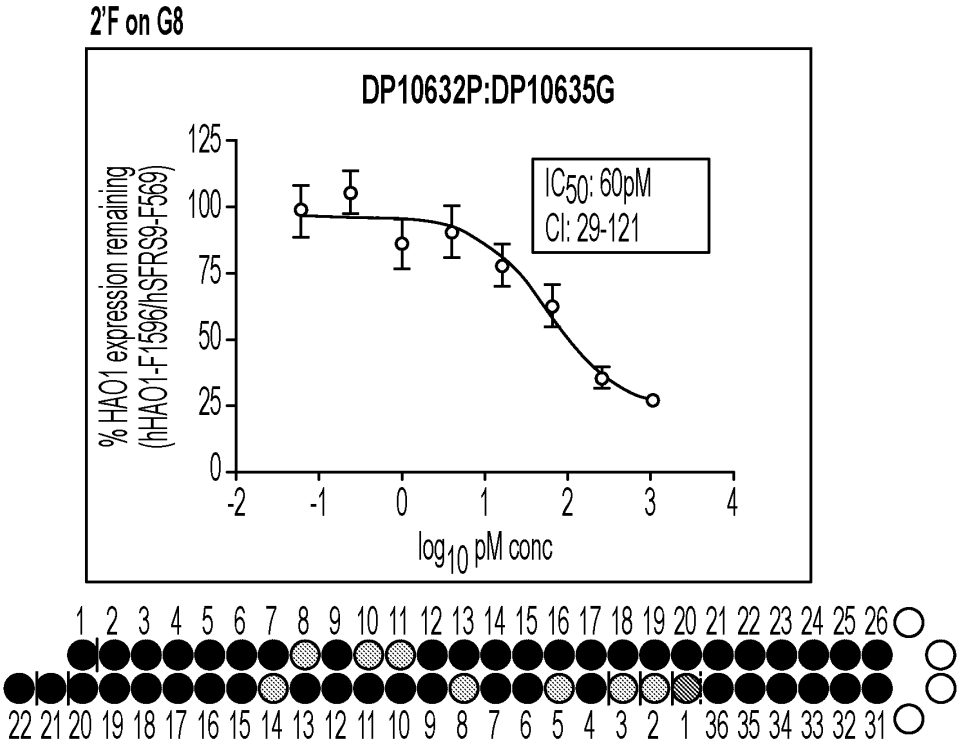


FIG. 6D

2'F on G9

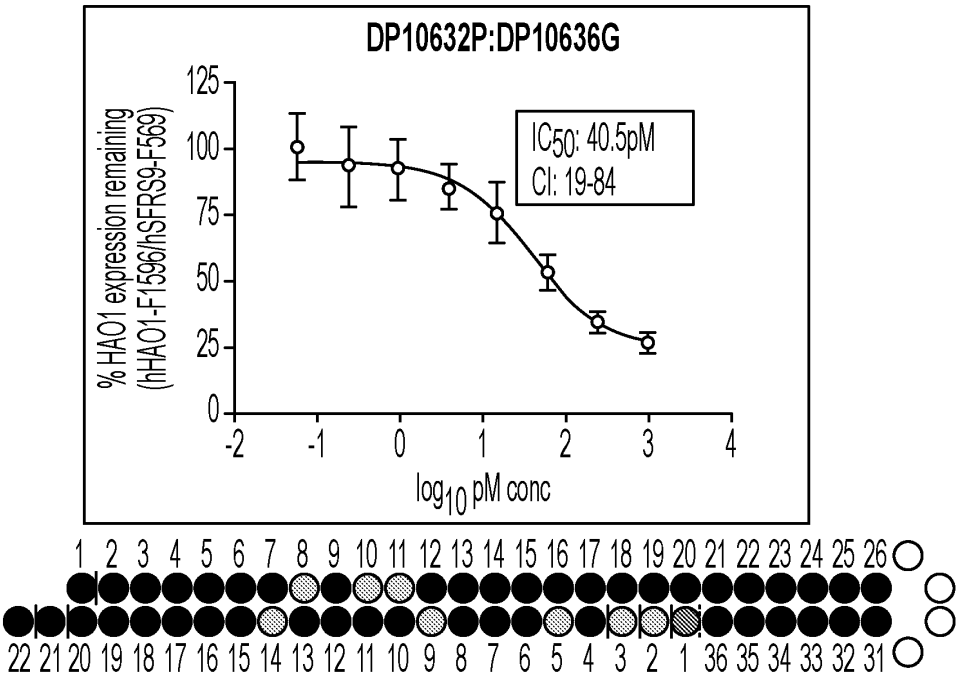


FIG. 6E

2'F on G10

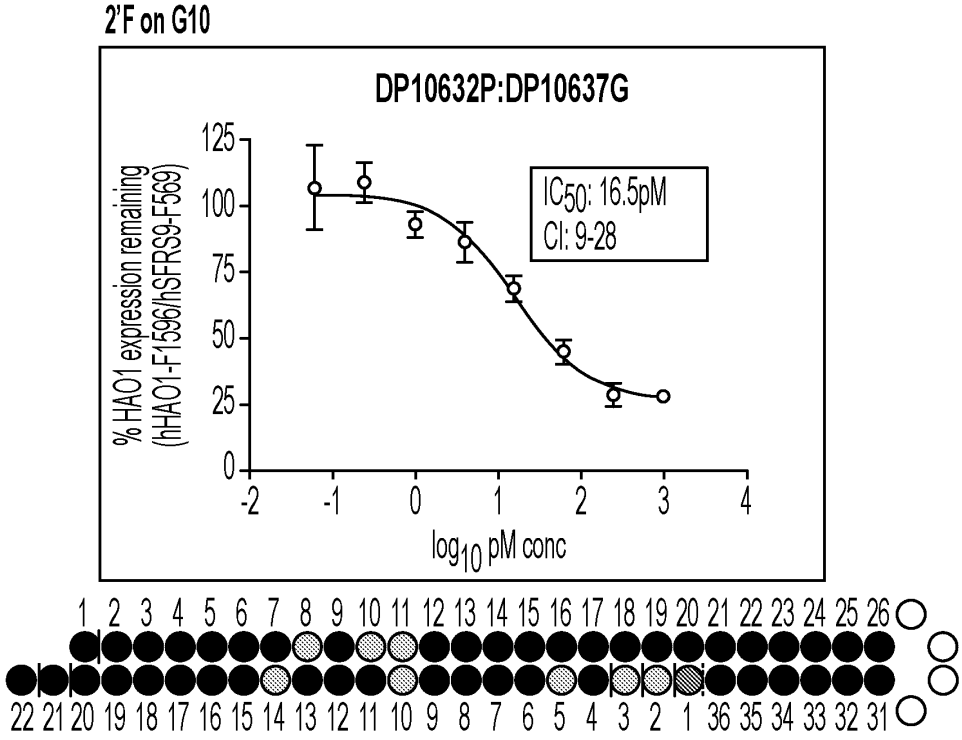
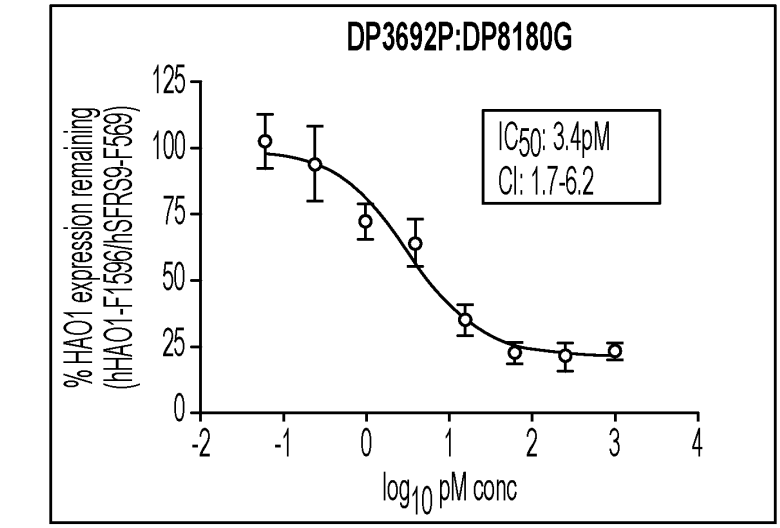


FIG. 6F

Study Control



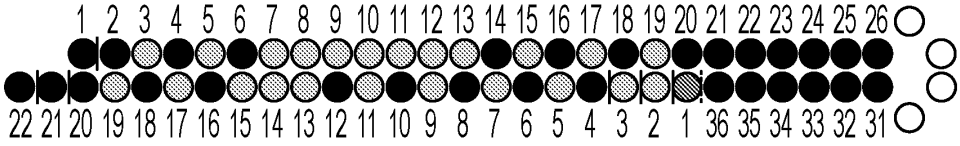
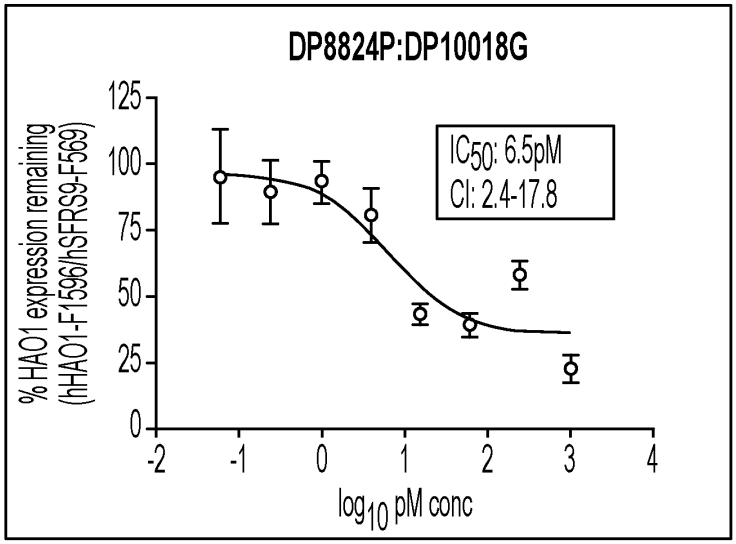


FIG. 7A

2'OMe-MOP @G1; 2'F on G2, 5, 14



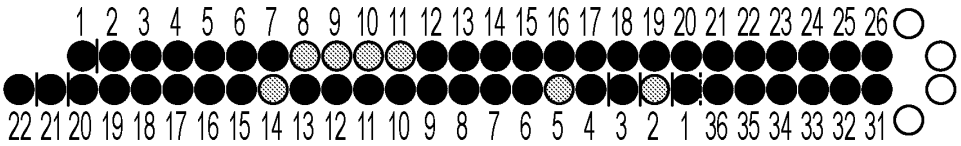


FIG. 7B

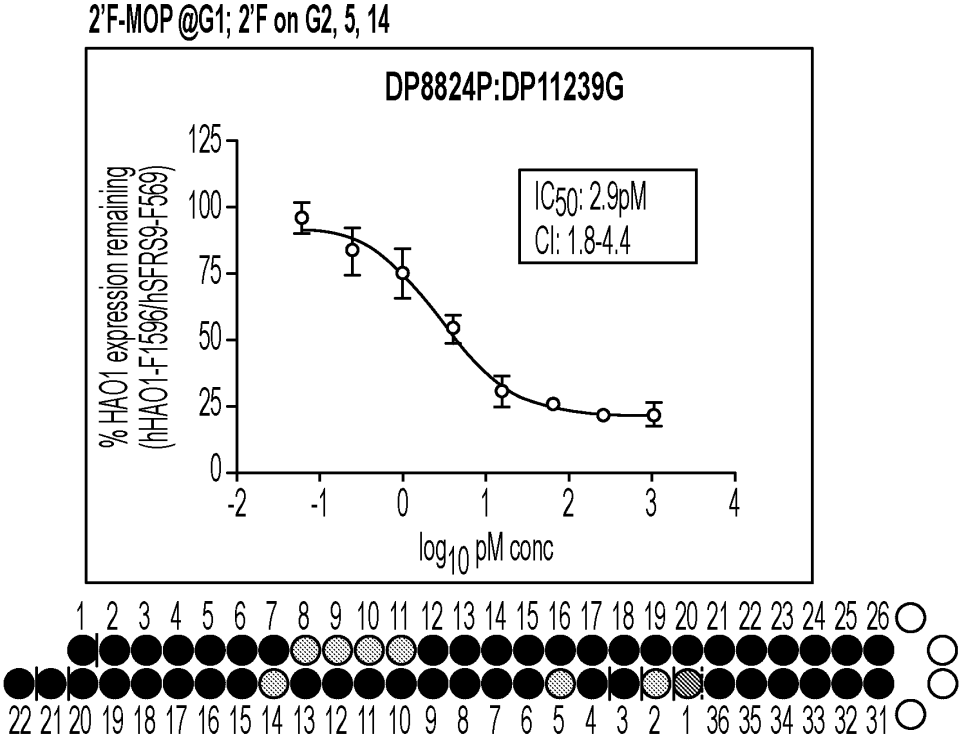

2'F-MOP @G1; 2'F on G2, 5, 14
DP8824P:DP11239G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
IC50: 2.9pM
CI: 1.8-4.4
log10 pM conc
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 7C

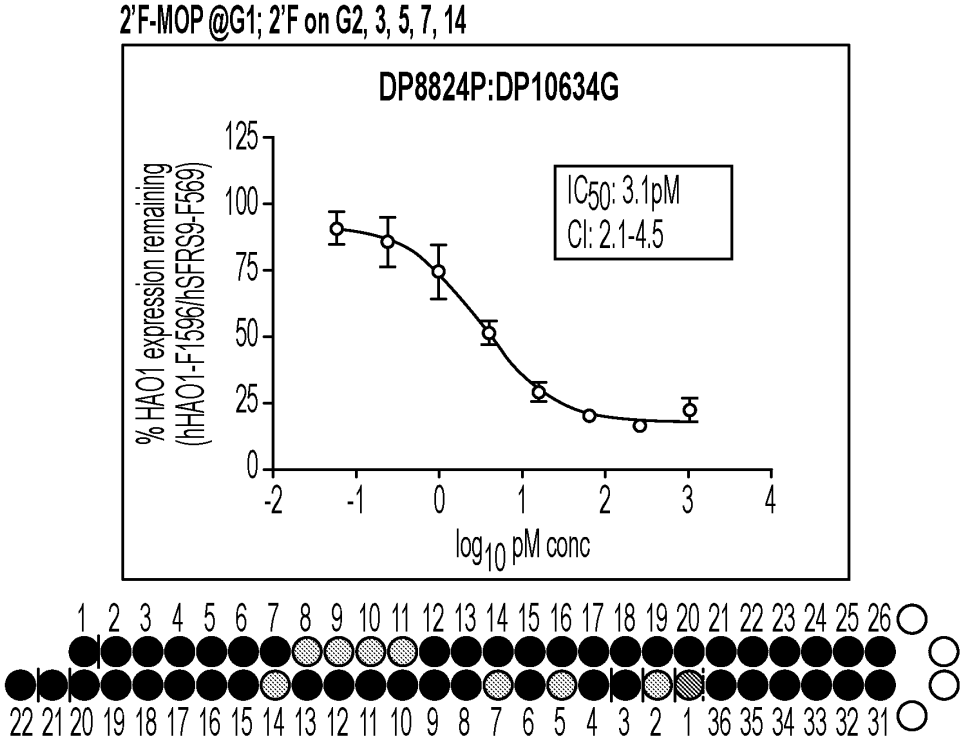

2'F-MOP @G1; 2'F on G2, 3, 5, 7, 14
DP8824P:DP10634G
% HAO1 expression remaining (hHAO1-F1596/hSFRS9-F569)
IC50: 3.1pM
CI: 2.1-4.5
log10 pM conc
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 36 35 34 33 32 31

FIG. 7D

2'F-MOP @G1; 2'F on G2, 3, 5, 10, 14

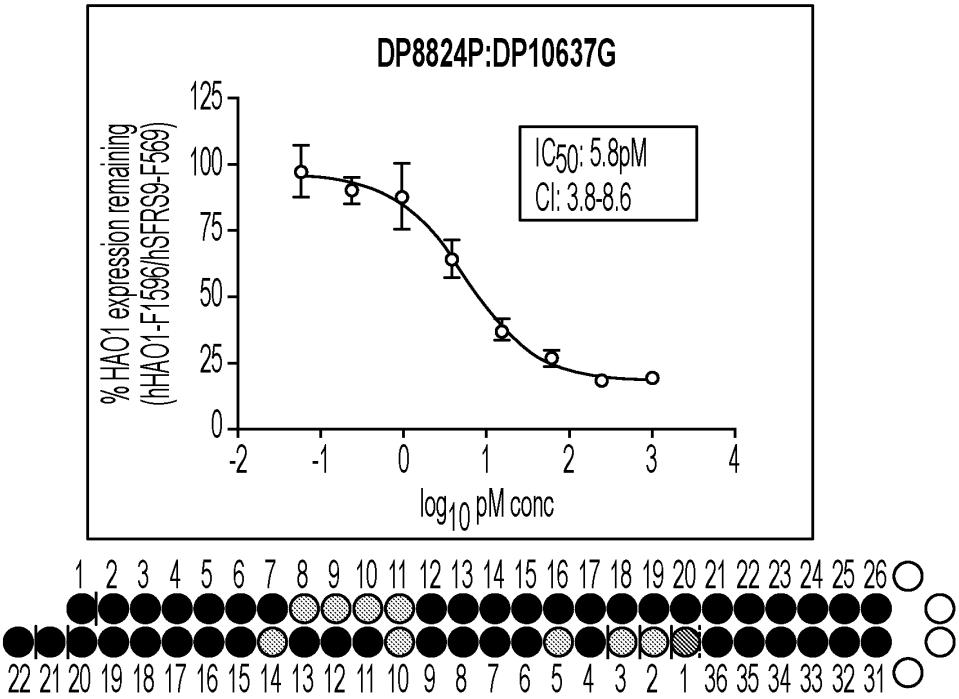
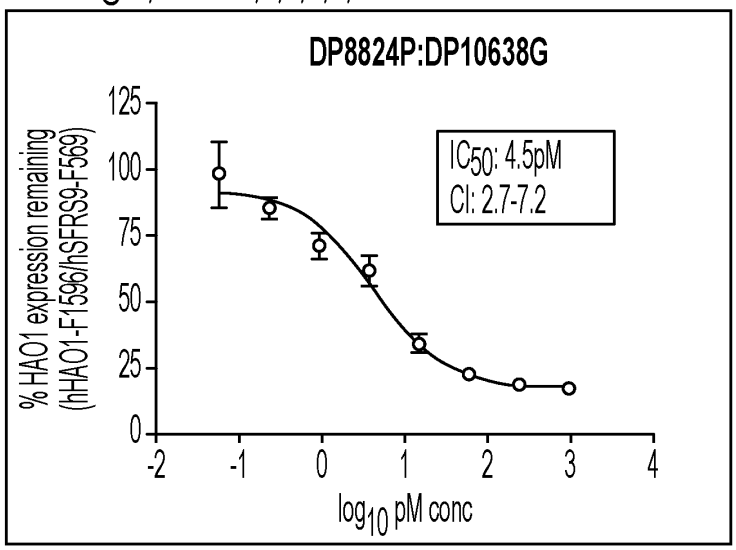


FIG. 7E

2'F-MOP @G1; 2'F on G2, 3, 5, 7, 9, 14



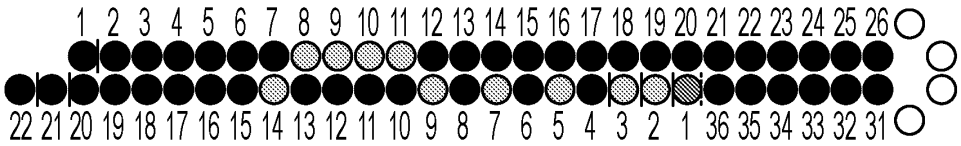


FIG. 7F

2'F-MOP @G1; 2'F on G2, 3, 5, 7, 10, 14

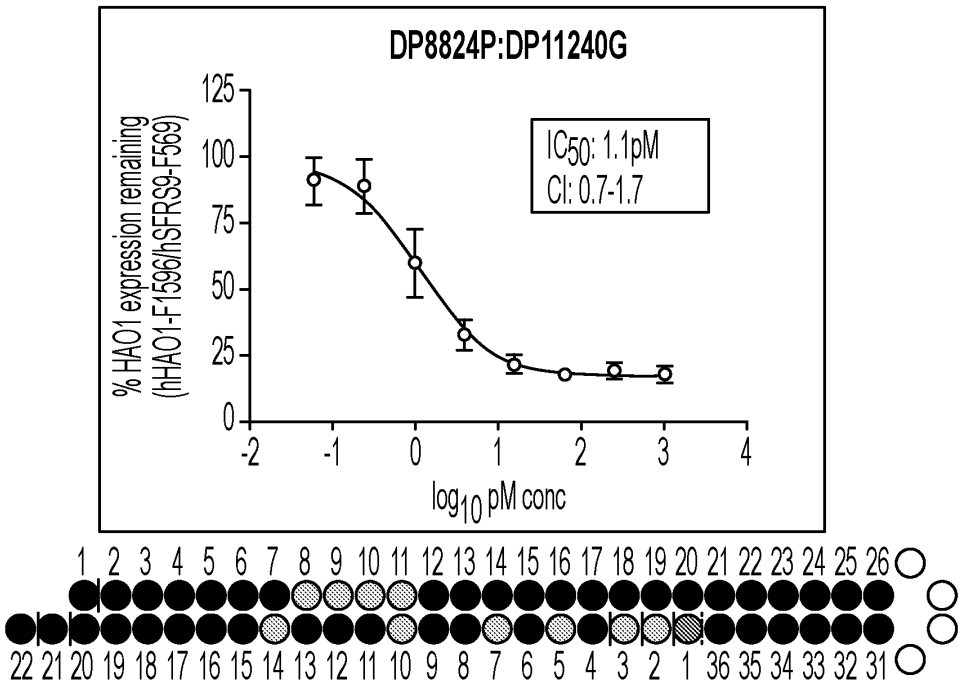


FIG. 7G

2'F-MOP @G1; 2'F on G2, 3, 5, 7, 10, 14

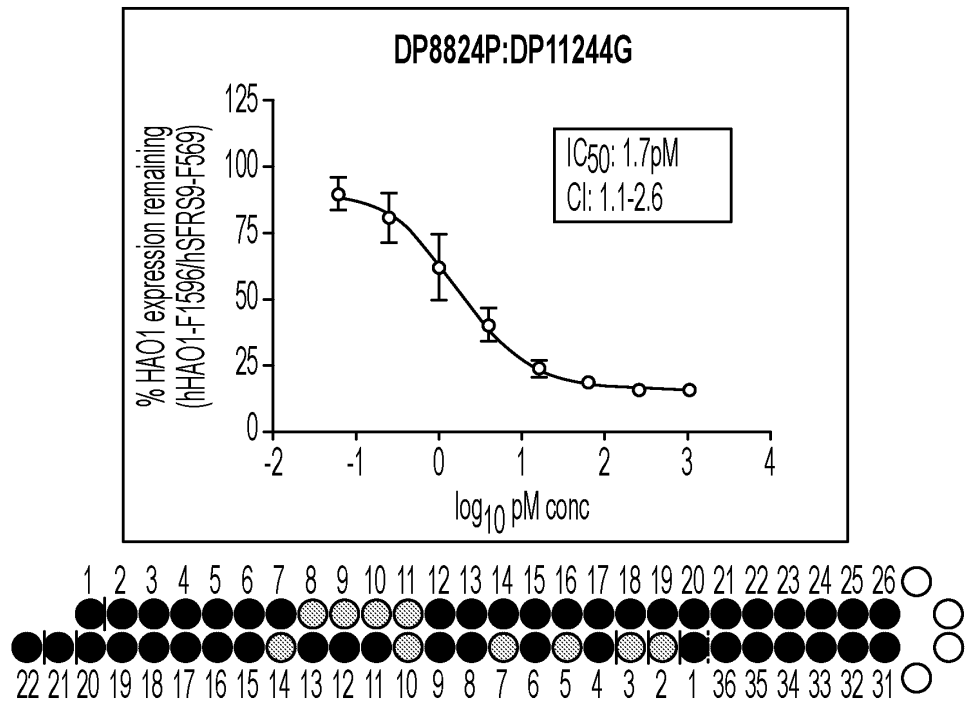


FIG. 7H

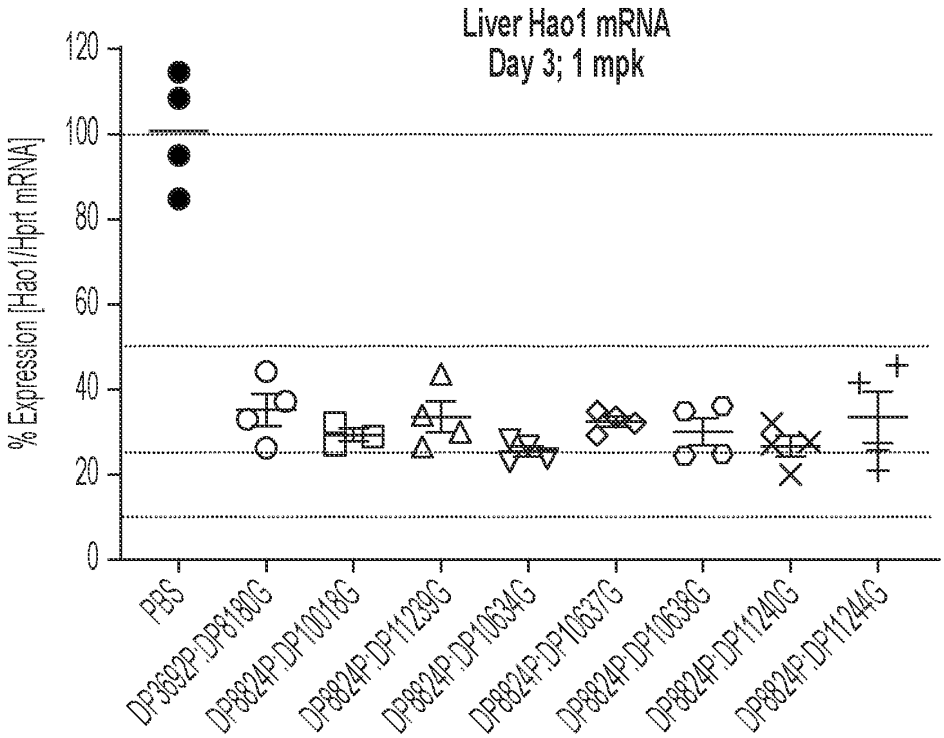

Liver Hao1 mRNA
Day 3; 1 mpk
% Expression [Hao1/Hprt mRNA]
120
100
80
60
40
20
0
PBS
DP3692P:DP8180G
DP8824P:DP10018G
DP8824P:DP11239G
DP8824P:DP10634G
DP8824P:DP10637G
DP8824P:DP10638G
DP8824P:DP11240G
DP8824P:DP11244G

FIG. 7I

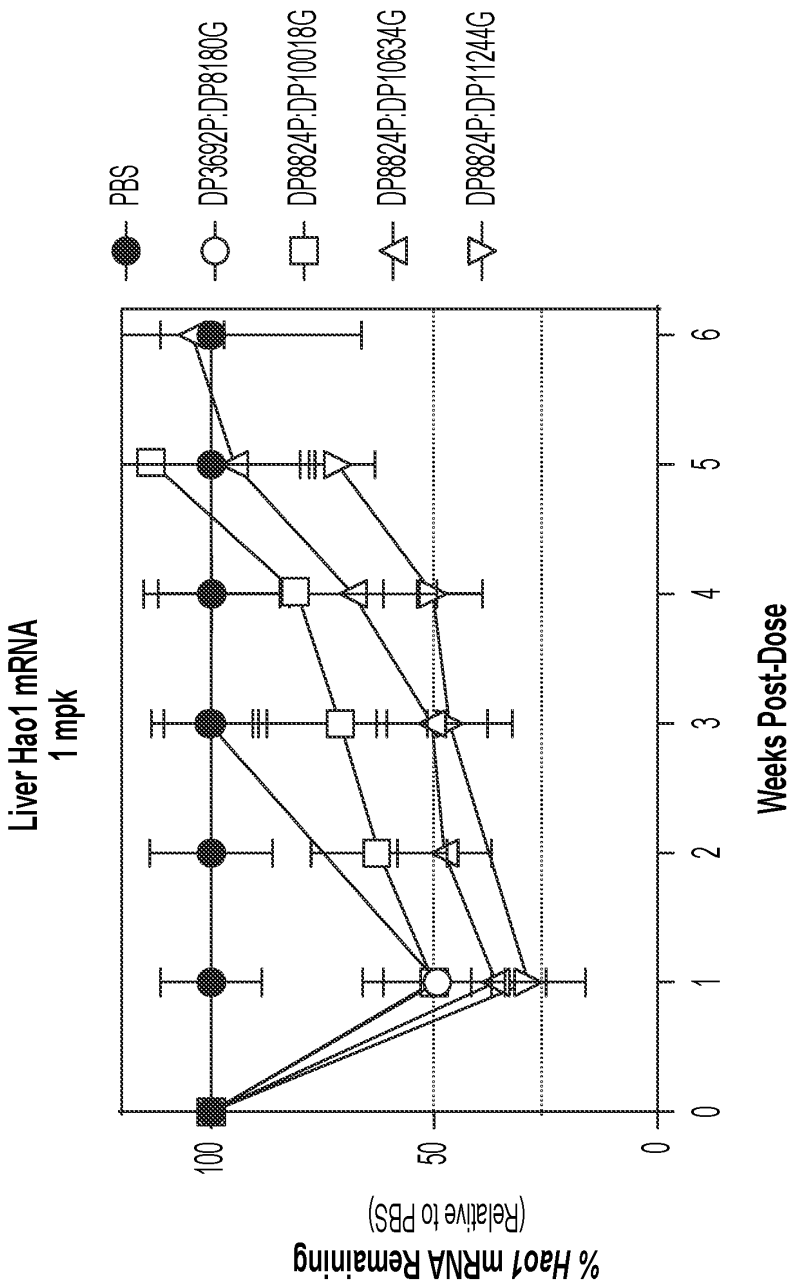

PBS
DP3692P:DP8180G
DP8824P:DP10018G
DP8824P:DP10634G
DP8824P:DP11244G
Liver Hao1 mRNA
1 mpk
% Hao1 mRNA Remaining
(Relative to PBS)
100
50
0
0
1
2
3
4
5
6
Weeks Post-Dose

FIG. 8

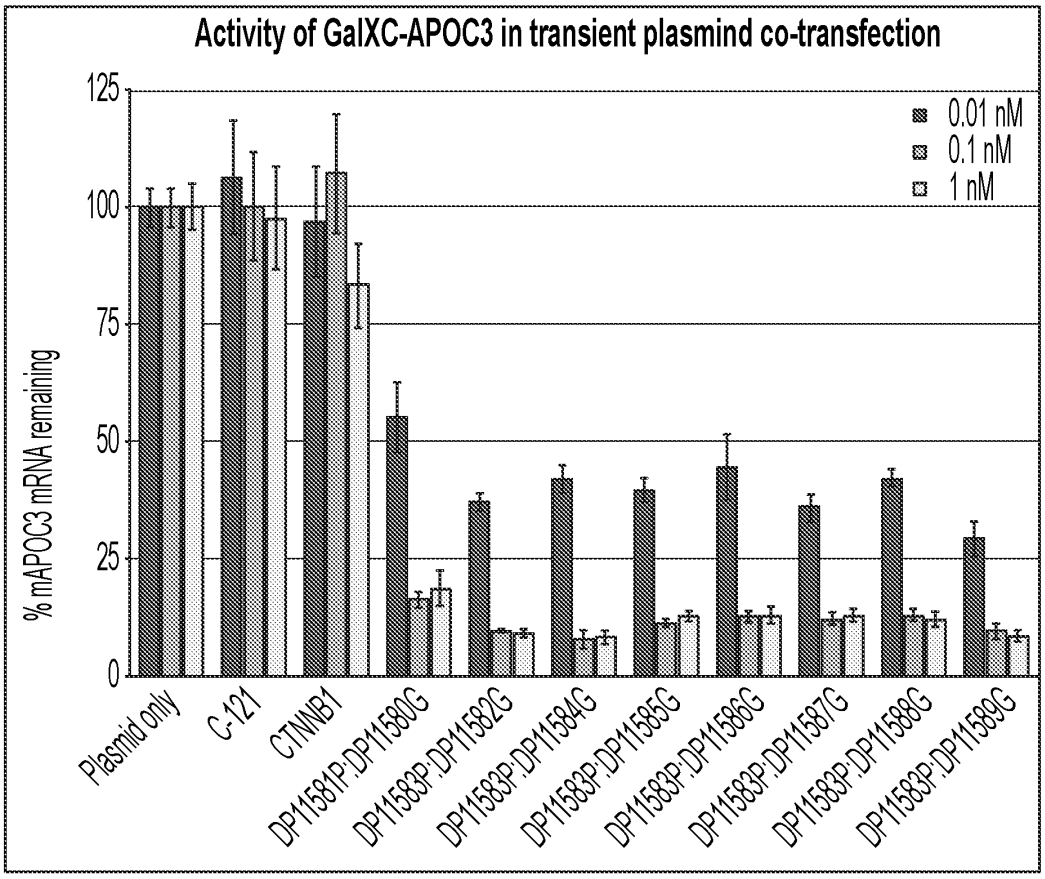

Activity of GalXC-APOC3 in transient plasmind co-transfection
% mAPOC3 mRNA remaining
125
100
75
50
25
0
0.01 nM
0.1 nM
1 nM
Plasmid only
C-121
CTNNB1
DP11581P:DP11580G
DP11583P:DP11582G
DP11583P:DP11584G
DP11583P:DP11585G
DP11583P:DP11586G
DP11583P:DP11587G
DP11583P:DP11588G
DP11583P:DP11589G

FIG. 9A

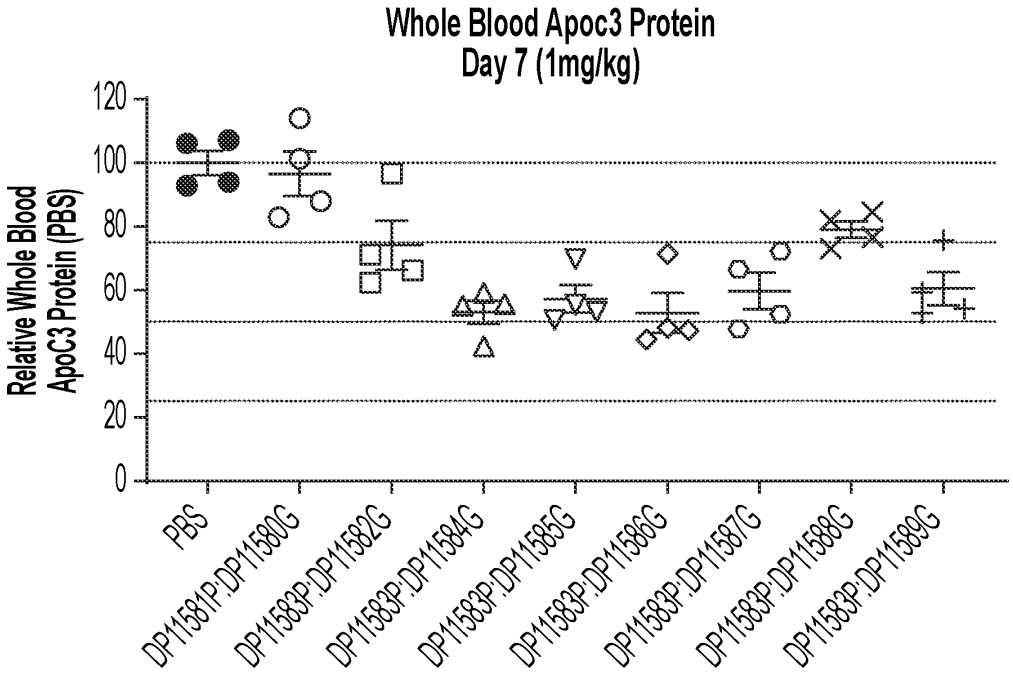

Whole Blood Apoc3 Protein
Day 7 (1mg/kg)
Relative Whole Blood ApoC3 Protein (PBS)
120
100
80
60
40
20
0
PBS
DP11581P:DP11580G
DP11583P:DP11582G
DP11583P:DP11584G
DP11583P:DP11585G
DP11583P:DP11586G
DP11583P:DP11587G
DP11583P:DP11588G
DP11583P:DP11589G

FIG. 9B

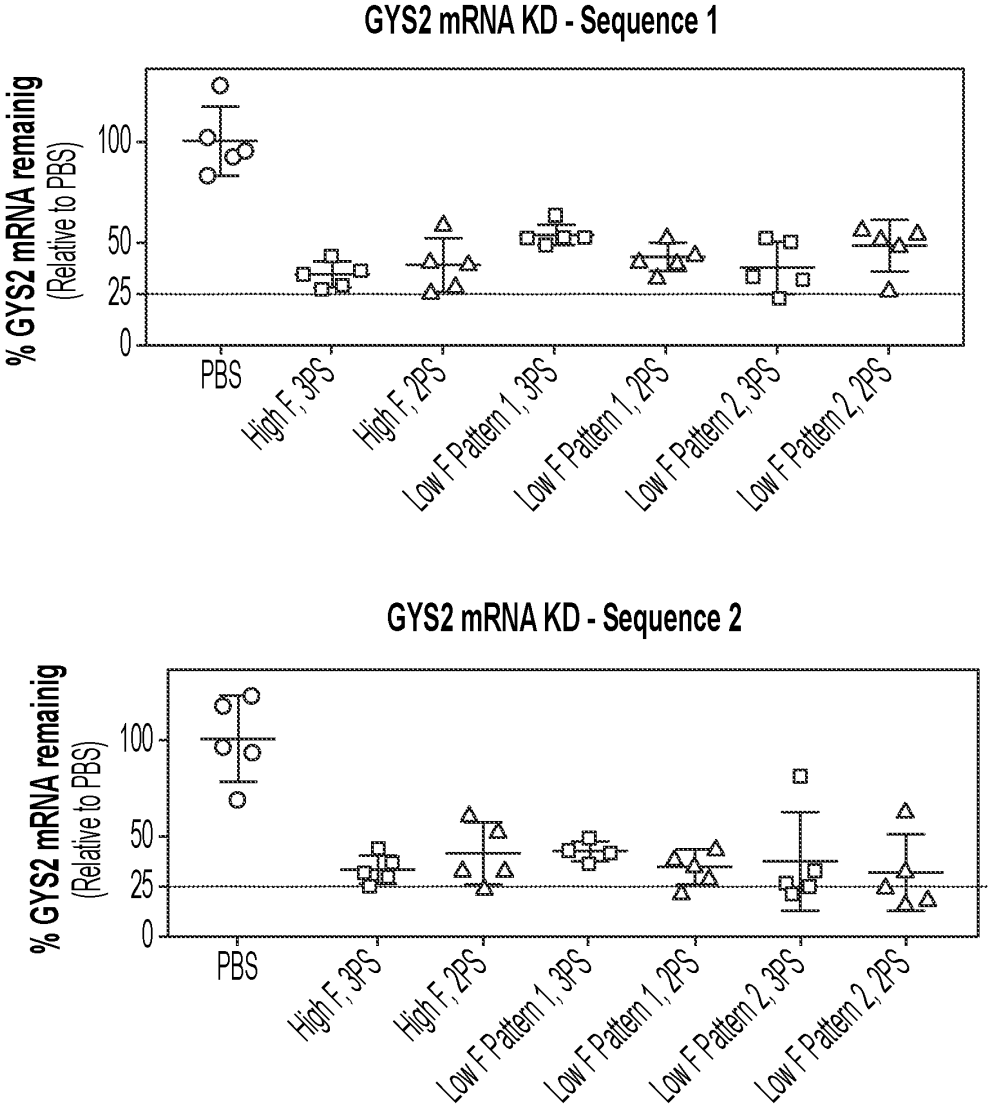

GYS2 mRNA KD - Sequence 1
% GYS2 mRNA remainig
(Relative to PBS)
100
50
25
0
PBS
High F, 3PS
High F, 2PS
Low F Pattern 1, 3PS
Low F Pattern 1, 2PS
Low F Pattern 2, 3PS
Low F Pattern 2, 2PS
GYS2 mRNA KD - Sequence 2
% GYS2 mRNA remainig
(Relative to PBS)
100
50
25
0
PBS
High F, 3PS
High F, 2PS
Low F Pattern 1, 3PS
Low F Pattern 1, 2PS
Low F Pattern 2, 3PS
Low F Pattern 2, 2PS

FIG. 10

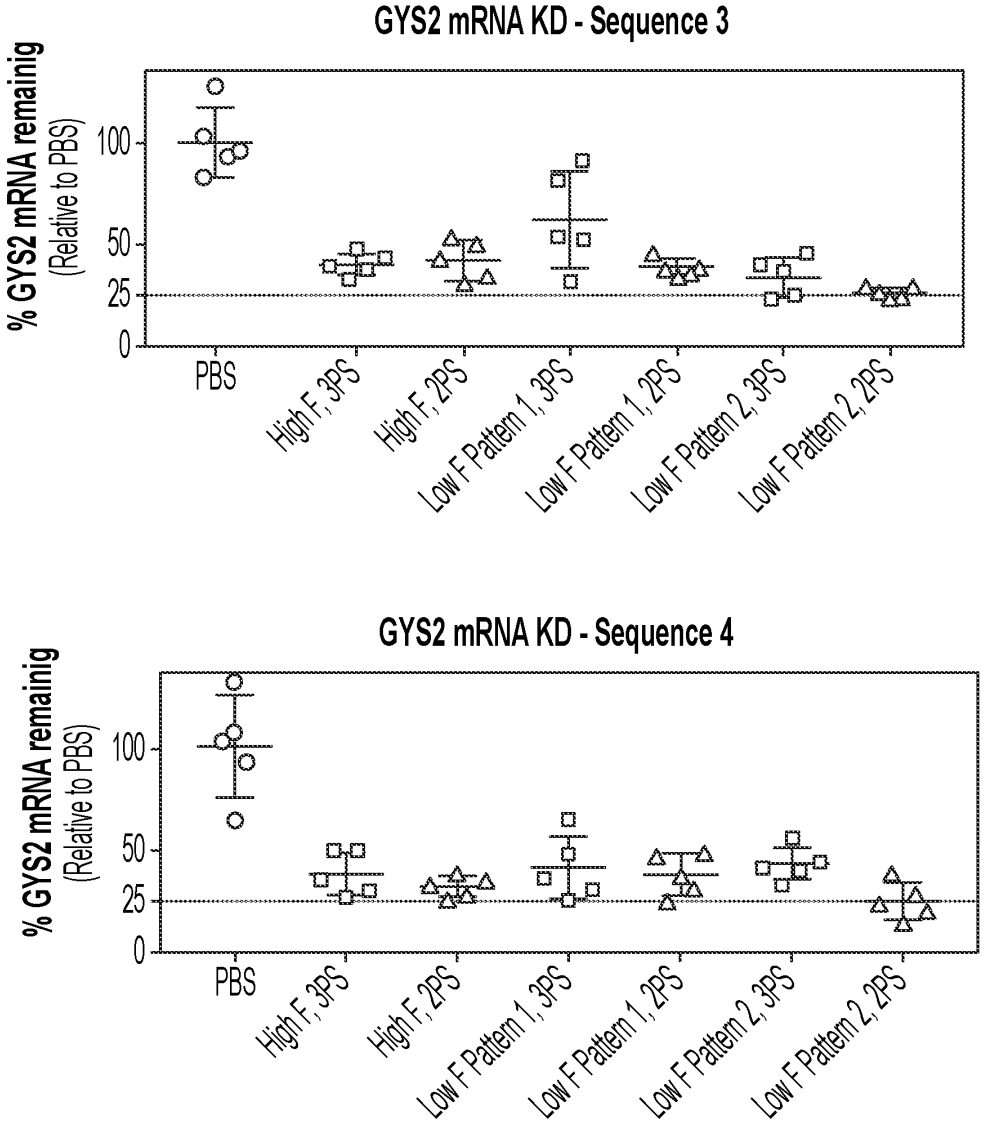

GYS2 mRNA KD - Sequence 3
% GYS2 mRNA remainig
(Relative to PBS)
100
50
25
0
a
PBS
High F, 3PS
High F, 2PS
Low F Pattern 1, 3PS
Low F Pattern 1, 2PS
Low F Pattern 2, 3PS
Low F Pattern 2, 2PS
GYS2 mRNA KD - Sequence 4
% GYS2 mRNA remainig
(Relative to PBS)
100
50
25
0
PBS
High F, 3PS
High F, 2PS
Low F Pattern 1, 3PS
Low F Pattern 1, 2PS
Low F Pattern 2, 3PS
Low F Pattern 2, 2PS

FIG. 10 CONT.