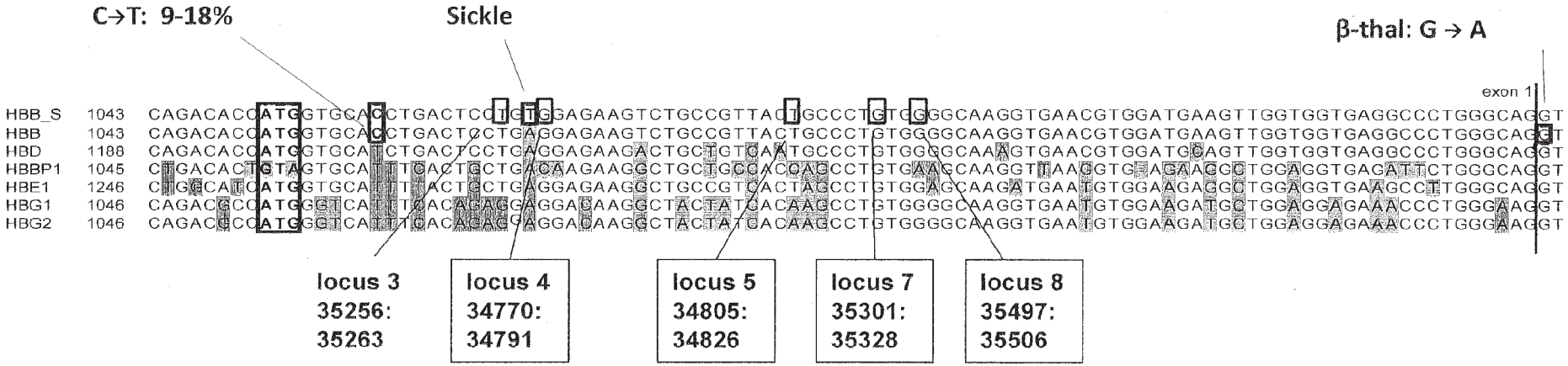
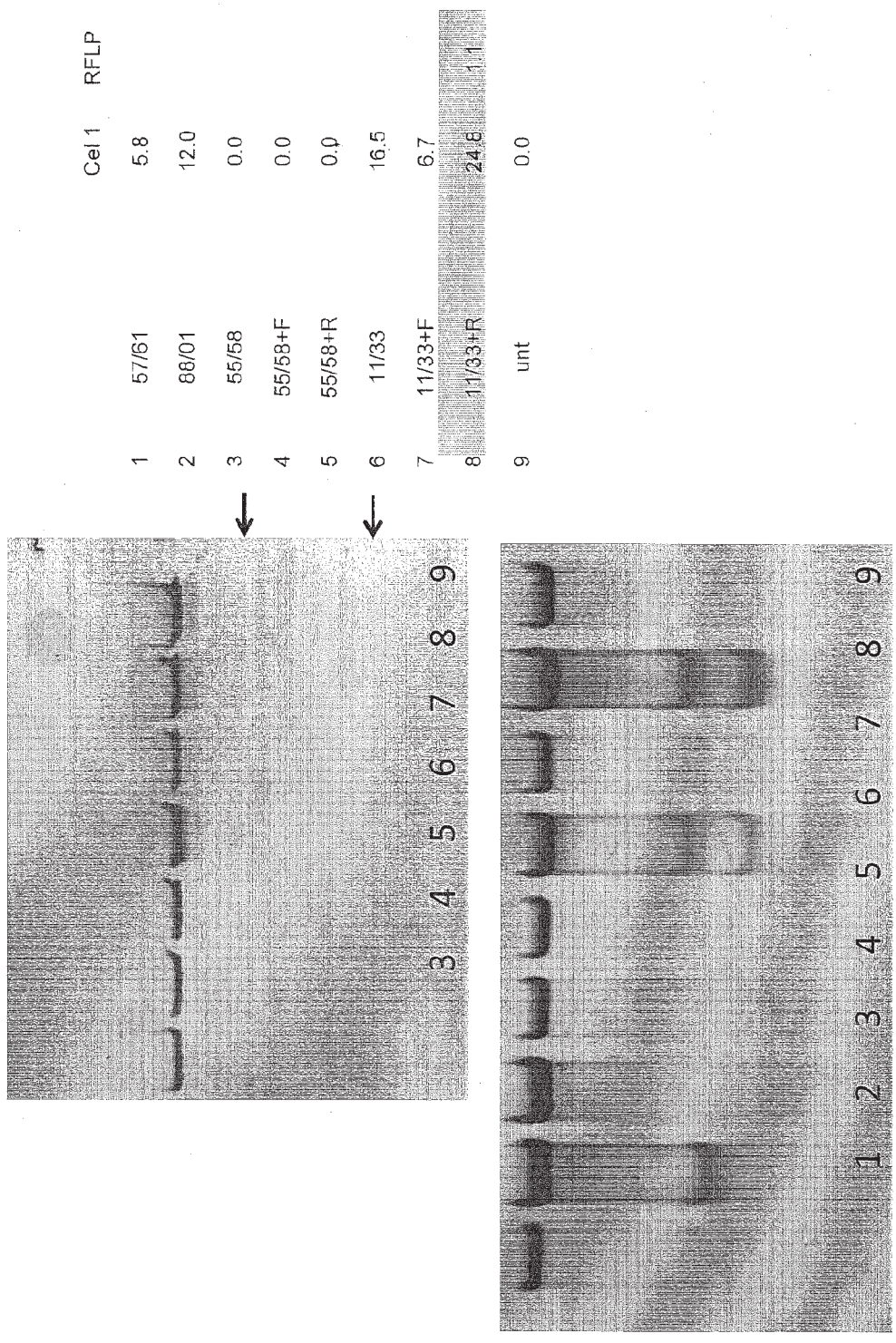


Locus	% indels, CD34 studies	
	exp 1	exp 2
3	13.3	0.0
4	0.0	0.0
5	36.8	25.6
6	42.0	23.7
7	23.2	19.9

FIGURE 1

FIGURE 2


Cel 1 RFLP
1 57/61 5.8
2 88/01 12.0
3 55/58 0.0
4 55/58+F 0.0
5 55/58+R 0.0
6 11/33 16.5
7 11/33+F 6.7
8 11/33+R 24.8
9 unt 0.0
A. RFLP
B. CEL-I
1 2 3 4 5 6 7 8 9
3 4 5 6 7 8 9

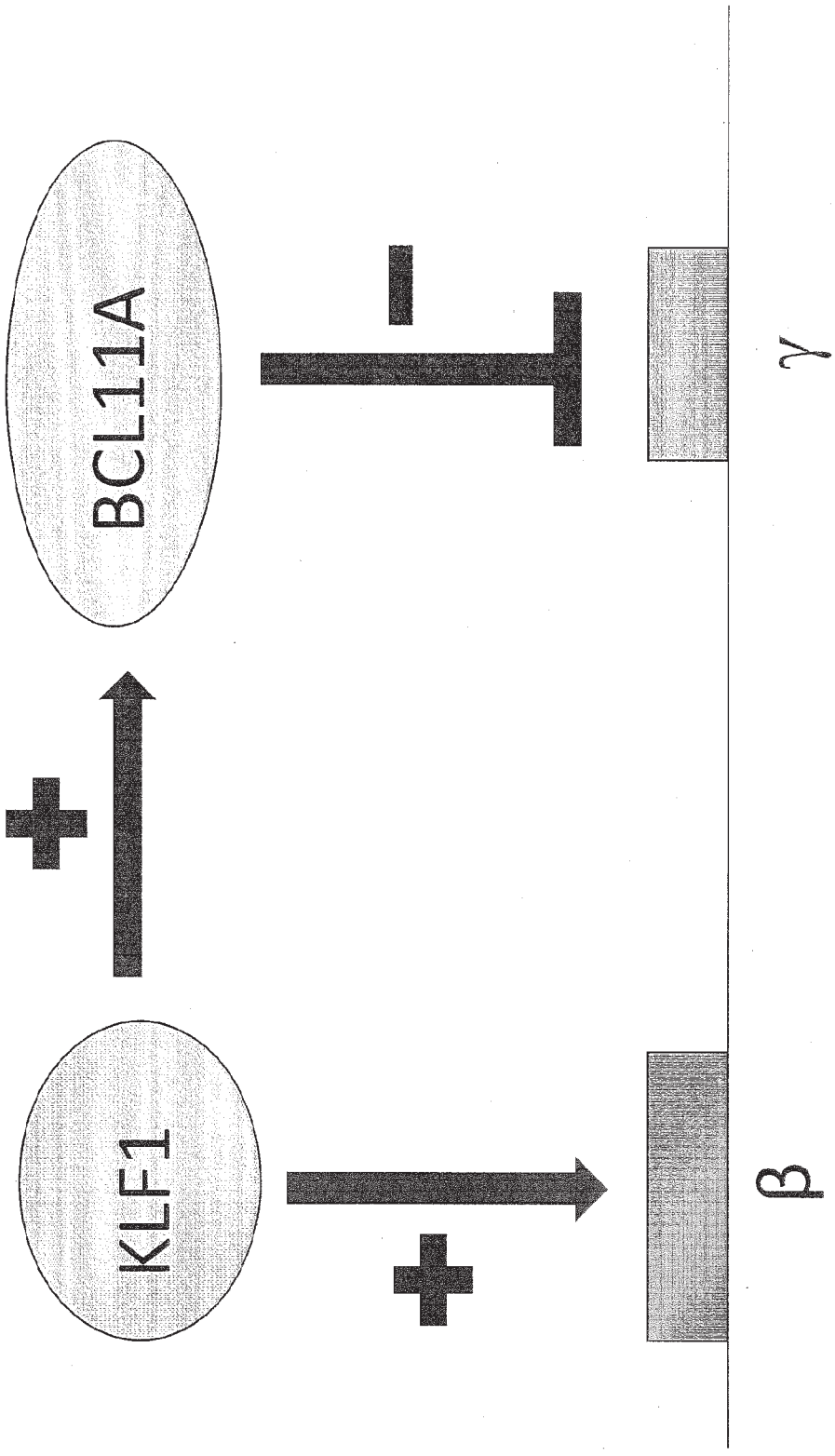


Figure 3

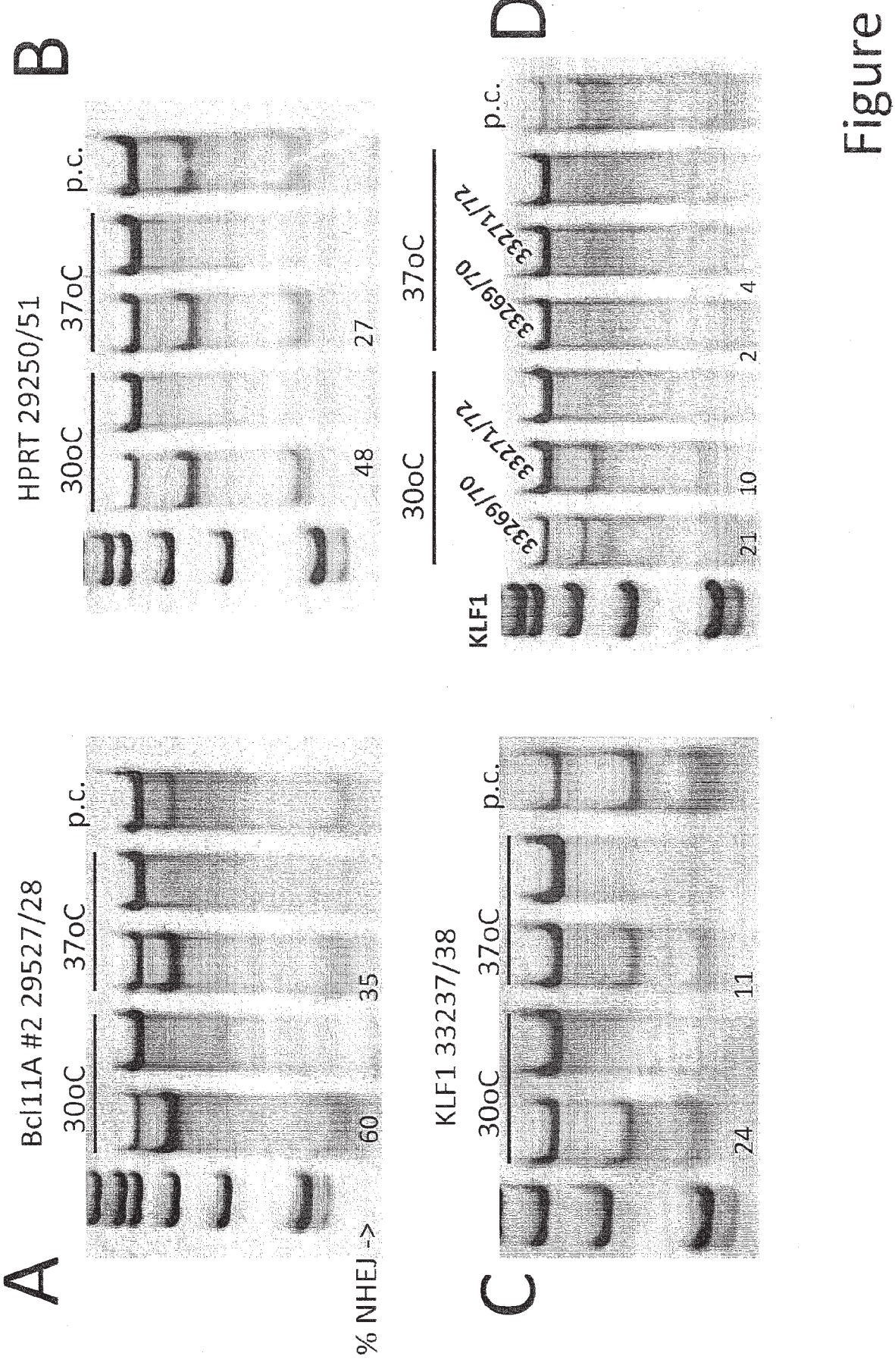

A
Bcl11A #2 29527/28
30oC
37oC
p.c.
% NHEJ ->
60
35
B
HPRT 29250/51
30oC
37oC
p.c.
48
27
C
KLF1 33237/38
30oC
37oC
p.c.
24
11
D
KLF1
30oC
37oC
33269/70
33271/72
33269/70
33271/72
p.c.
21
10
2
4

Figure 4

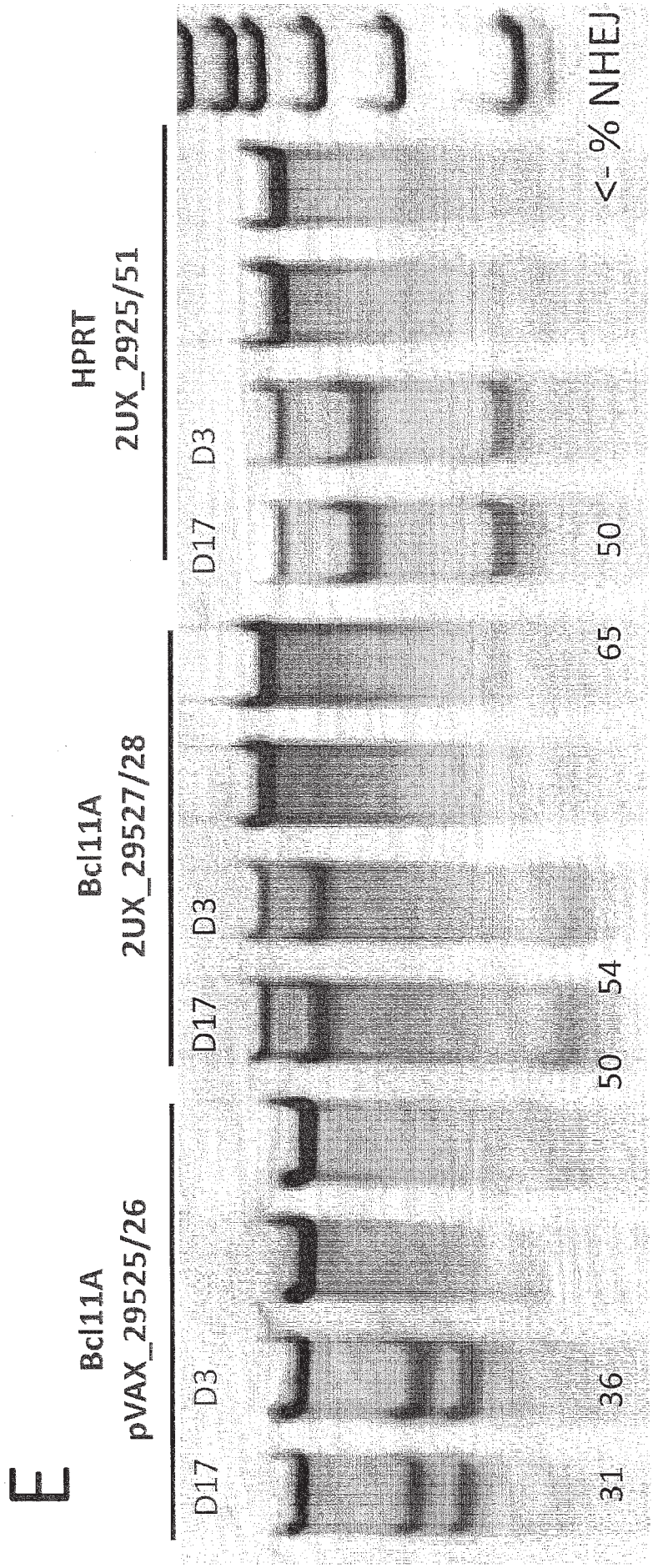

E
Bcl11A
pVAX_29525/26
D17
D3
31
36
Bcl11A
2UX_29527/28
D17
D3
50
54
65
HPRT
2UX_2925/51
D17
D3
50
<- % NHEJ

Figure 4

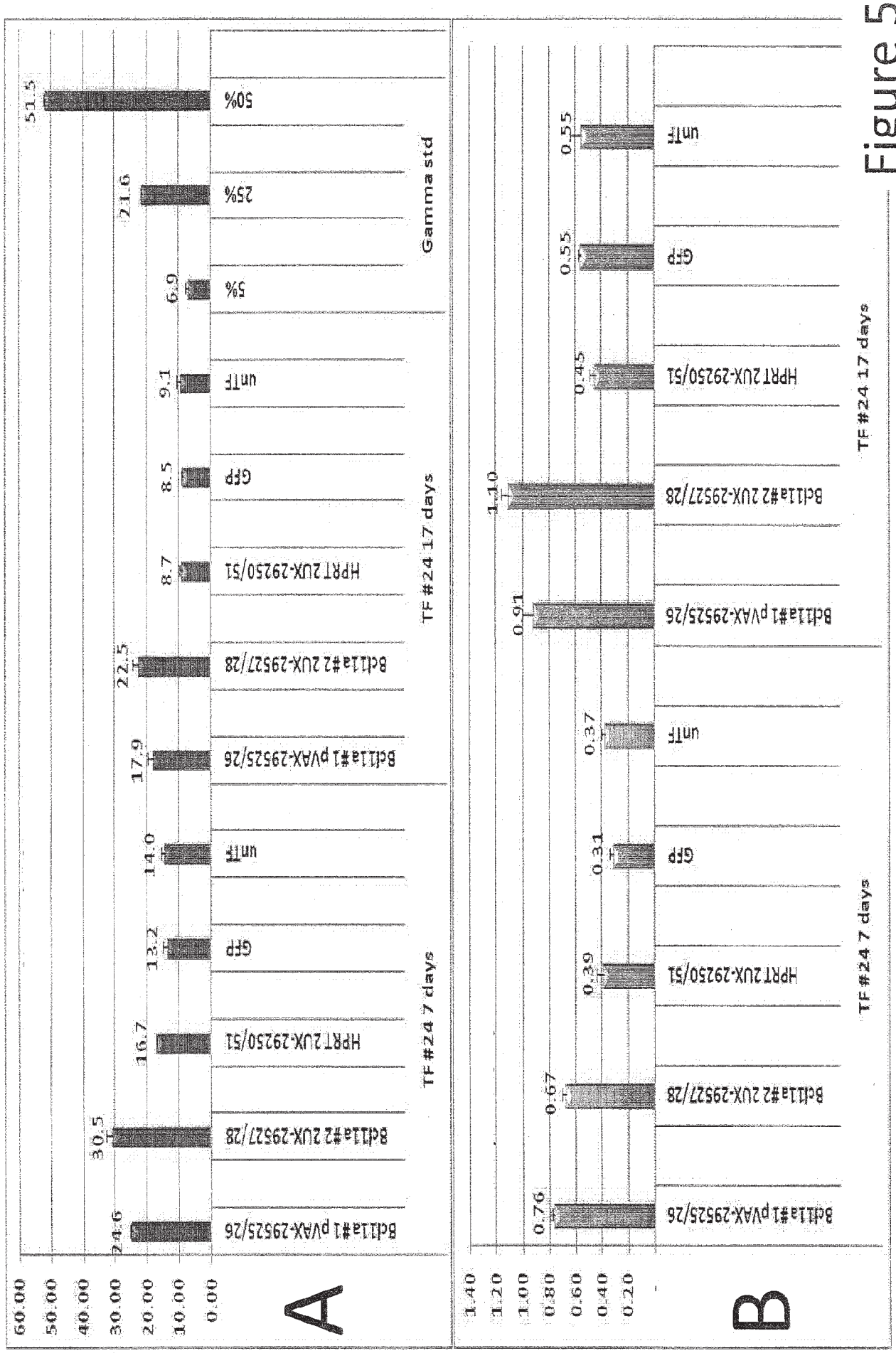
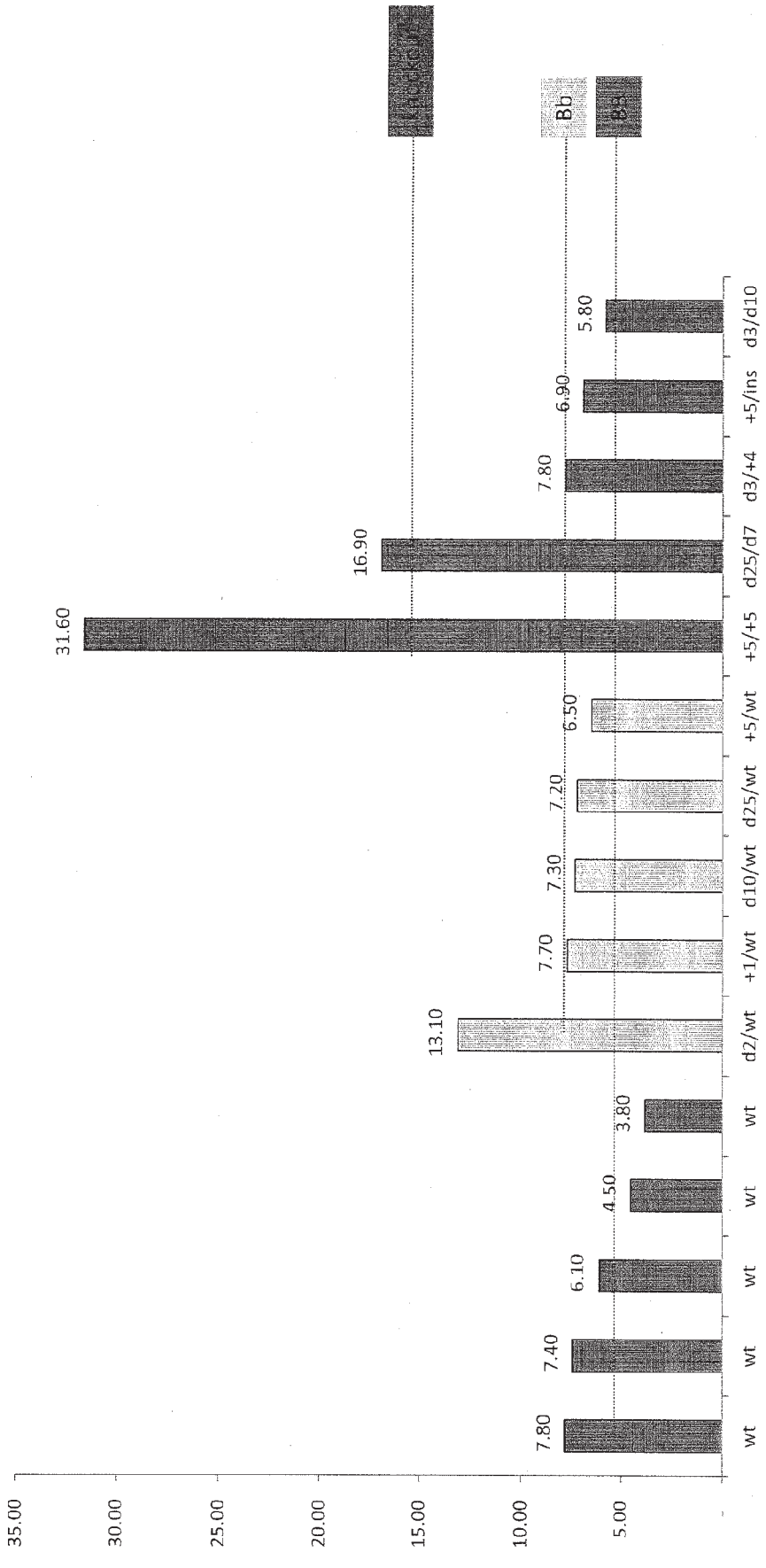

A
60.00
50.00
40.00
30.00
20.00
10.00
0.00
TF #24 7 days
TF #24 17 days
Gamma std
Bdi1a#1 pVAX-29525/26
Bdi1a#2 2UX-29527/28
HPRT 2UX-29250/51
GFP
unTF
50%
25%
5%
24.6
30.5
16.7
13.2
14.0
17.9
22.5
8.7
8.5
9.1
6.9
21.6
51.5
B
1.40
1.20
1.00
0.80
0.60
0.40
0.20
TF #24 7 days
TF #24 17 days
0.76
0.67
0.39
0.31
0.37
0.91
1.10
0.45
0.55
0.55
0.55

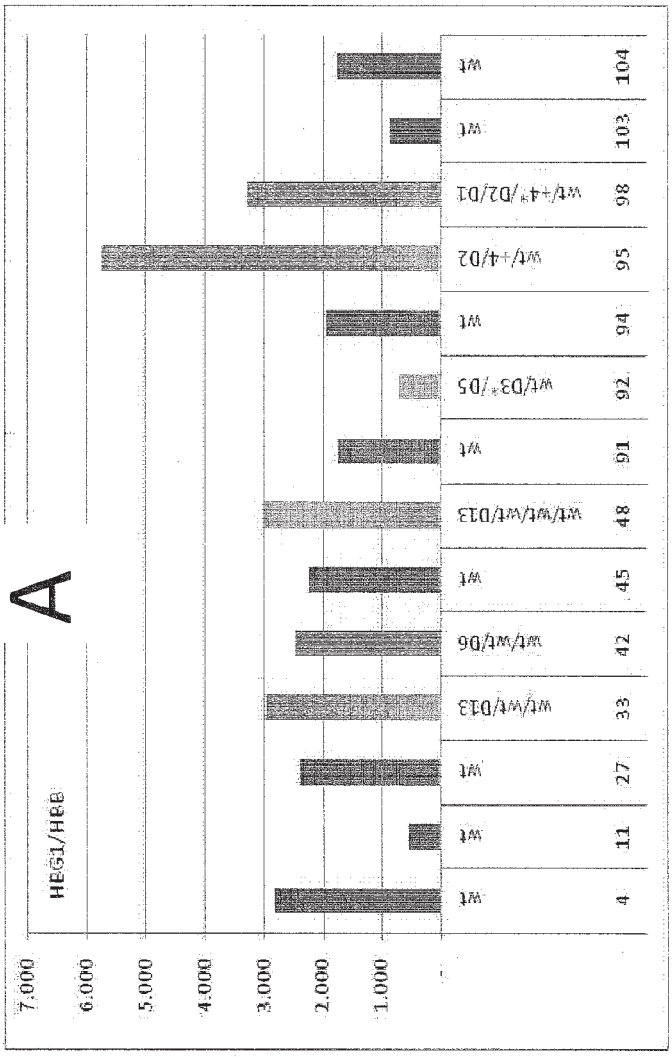
Figure 5

FIGURE 6

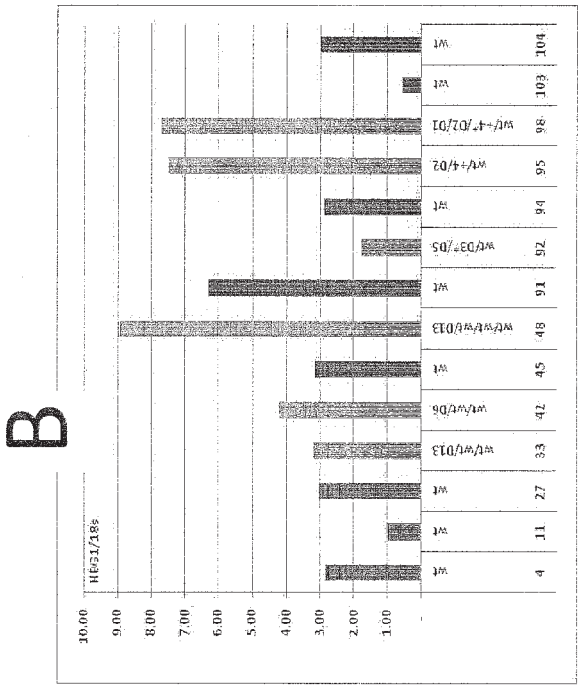

35.00
30.00
25.00
20.00
15.00
10.00
5.00
7.80
7.40
6.10
4.50
3.80
13.10
7.70
7.30
7.20
6.50
31.60
16.90
7.80
6.90
5.80
wt
wt
wt
wt
wt
d2/wt
+1/wt
d10/wt
d25/wt
+5/wt
+5/+5
d25/d7
d3/+4
+5/ins
d3/d10
Bb
Bcl11a genotype

Reference	GGCCAGCCTTGCCTTGACCAATAGCCTTGACAAGGCAAACTTGACCAATAG
wt (26)	GGCCAGCCTTGCCTTGACCAATAGCCTTGACAAGGCAAACTTGACCAATAG
Δ1bp (1)	GGCCAGCCTTGCCTTGACC-ATAGCCTTGACAAGGCAAACTTGACCAATAG
Δ4bp (1)	GGCCAGCCTTGCCTT----AATAGCCTTGACAAGGCAAACTTGACCAATAG
Δ6bp (2)	GGCCAGCCTTGCCTTGAC------CCTTGACAAGGCAAACTTGACCAATAG
Δ6bp (1)	GGCCAGCCTTGCCTTGACCAATAGC------AAGGCAAACTTGACCAATAG
Δ13bp (9)	GGCCAGCCTTGCCTTGAC-------------AAGGCAAACTTGACCAATAG
+1bp (1)	GGCCAGCCTTGCCTTGACCAAATAGCCTTGACAAGGCAAACTTGACCAATA
+3bp (1)	GGCCAGCCTTGCCTTGACCAATAGCAGCCTTGACAAGGCAAACTTGACCAA
+5bp (3)	GGCCAGCCTTGCCTTGACCAATAGAATAGCCTTGACAAGGCAAACTTGACC

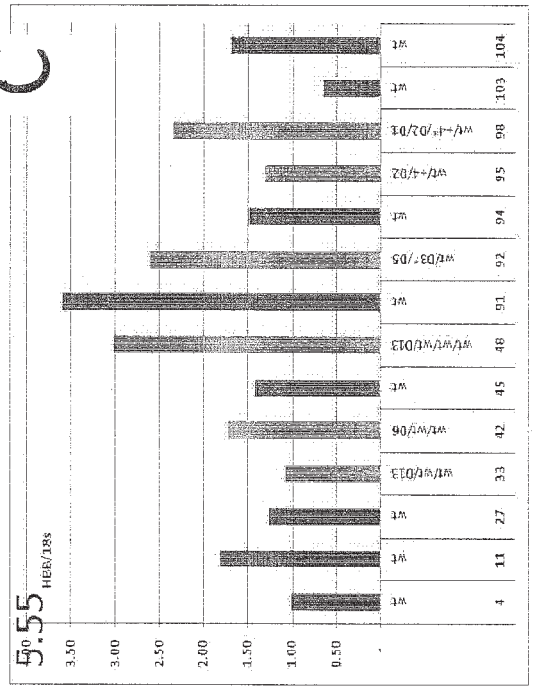
Figure 7



wt average 1.79
mut average
3.01



wt average 2.85
mut average
5.55



wt average 1.62
mut average
2.01

Figure 8

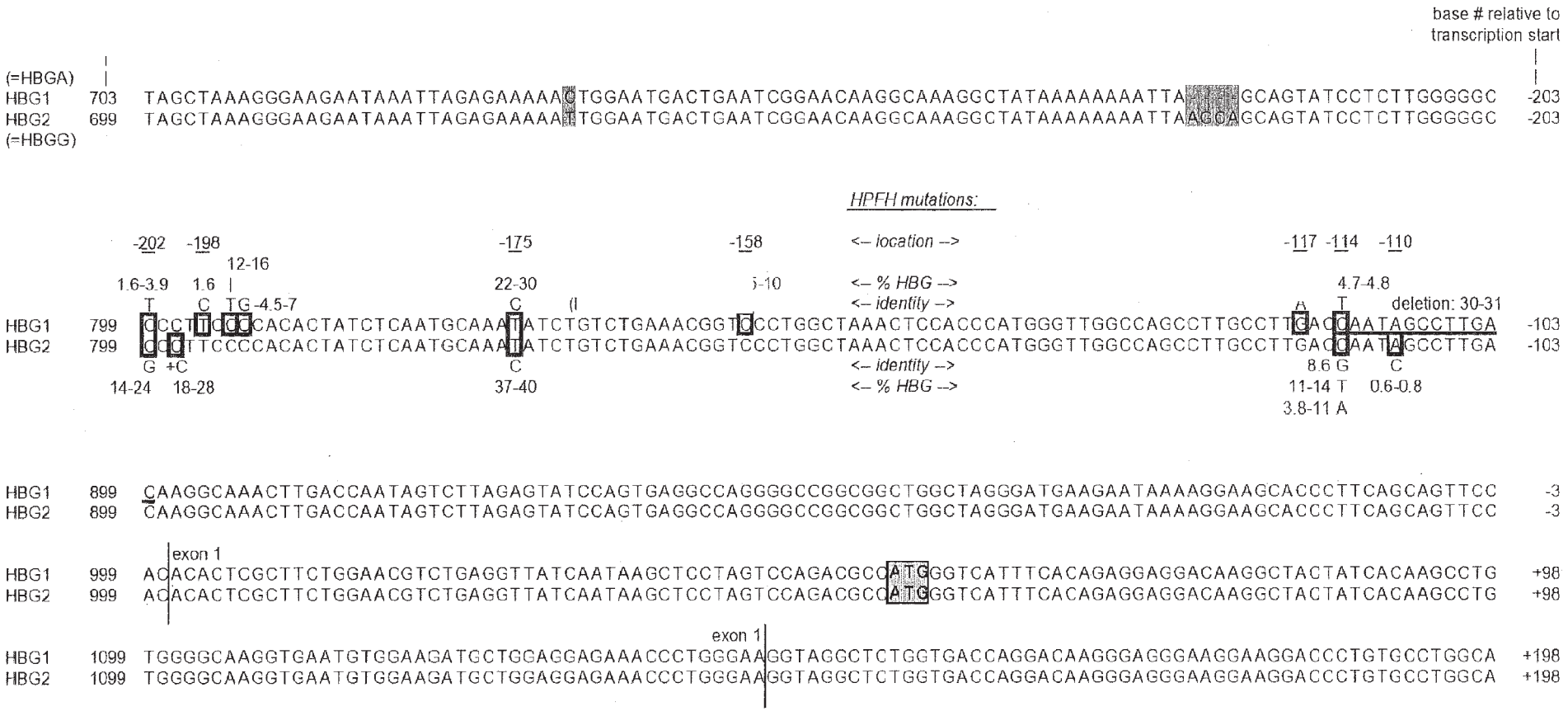
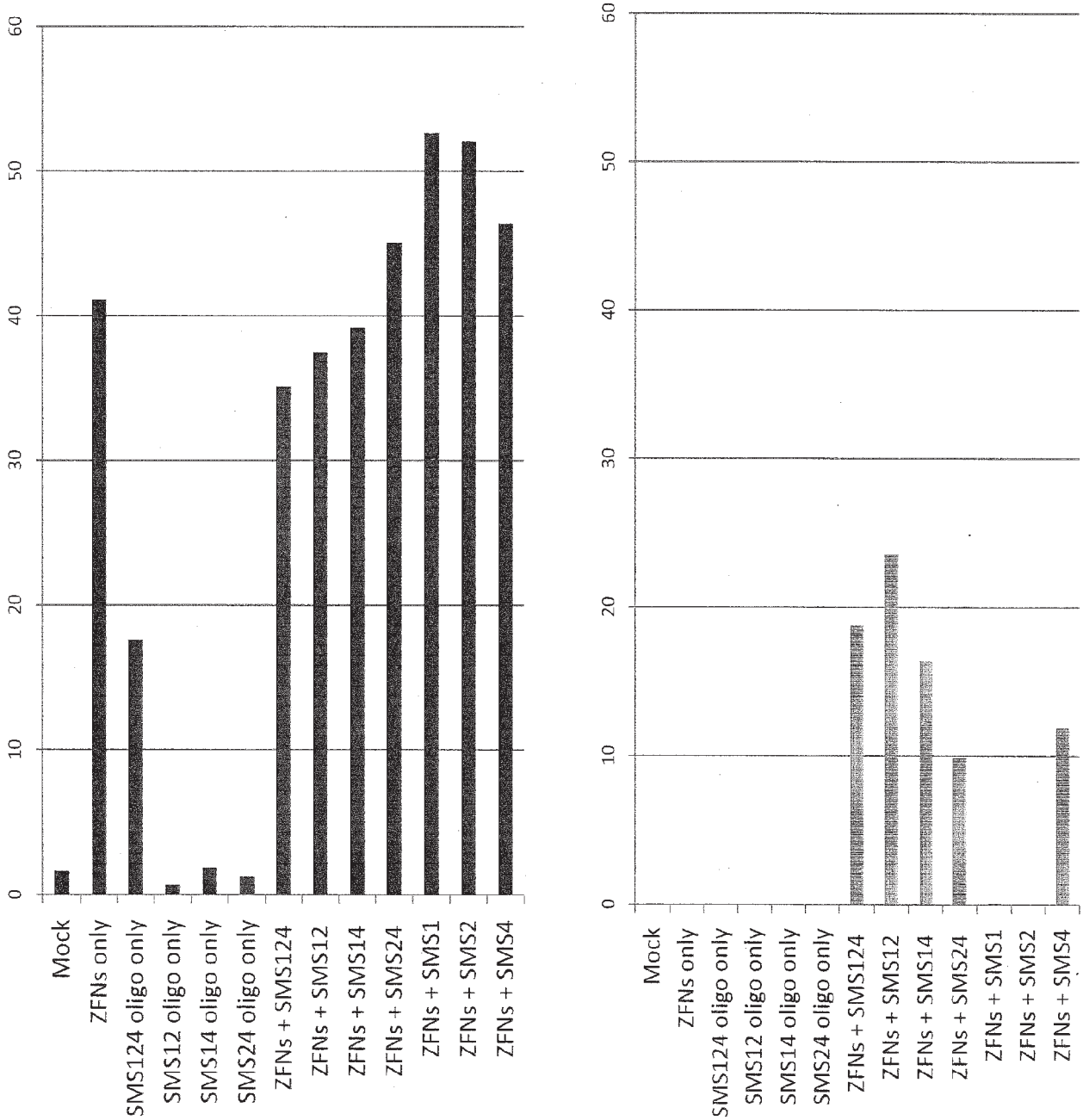

base # relative to transcription start
(=HBGA)
HBG1 703 TAGCTAAAGGGAAGAATAAATTAGAGAAAAACTGGAATGACTGAATCGGAACAAGGCAAAGGCTATAAAAAAAATTAAGCAGCAGTATCCTCTTGGGGGC -203
HBG2 699 TAGCTAAAGGGAAGAATAAATTAGAGAAAAATTGGAATGACTGAATCGGAACAAGGCAAAGGCTATAAAAAAAATTAAGCAGCAGTATCCTCTTGGGGGC -203
(=HBGG)
HPFH mutations:
-202 -198 -175 -158 <-- location --> -117 -114 -110
12-16
1.6-3.9 1.6 22-30 5-10 <-- % HBG --> 4.7-4.8
T C TG -4.5-7 C (I <-- identity --> A T deletion: 30-31
HBG1 799 CCCTTGCCCACACTATCTCAATGCAAATATCTGTCTGAAACGGTCCCTGGCTAAACTCCACCCATGGGTTGGCCAGCCTTGCCTTGACCAATAGCCTTGA -103
HBG2 799 CCCTTCCCCACACTATCTCAATGCAAATATCTGTCTGAAACGGTCCCTGGCTAAACTCCACCCATGGGTTGGCCAGCCTTGCCTTGACCAATAGCCTTGA -103
G +C C <-- identity --> 8.6 G C
14-24 18-28 37-40 <-- % HBG --> 11-14 T 0.6-0.8
3.8-11 A
HBG1 899 CAAGGCAAACTTGACCAATAGTCTTAGAGTATCCAGTGAGGCCAGGGGCCGGCGGCTGGCTAGGGATGAAGAATAAAAGGAAGCACCCTTCAGCAGTTCC -3
HBG2 899 CAAGGCAAACTTGACCAATAGTCTTAGAGTATCCAGTGAGGCCAGGGGCCGGCGGCTGGCTAGGGATGAAGAATAAAAGGAAGCACCCTTCAGCAGTTCC -3
exon 1
HBG1 999 ACACACTCGCTTCTGGAACGTCTGAGGTTATCAATAAGCTCCTAGTCCAGACGCCATGGGTCATTTCACAGAGGAGGACAAGGCTACTATCACAAGCCTG +98
HBG2 999 ACACACTCGCTTCTGGAACGTCTGAGGTTATCAATAAGCTCCTAGTCCAGACGCCATGGGTCATTTCACAGAGGAGGACAAGGCTACTATCACAAGCCTG +98
exon 1
HBG1 1099 TGGGGCAAGGTGAATGTGGAAGATGCTGGAGGAGAAACCCTGGGAAGGTAGGCTCTGGTGACCAGGACAAGGGAGGGAAGGAAGGACCCTGTGCCTGGCA +198
HBG2 1099 TGGGGCAAGGTGAATGTGGAAGATGCTGGAGGAGAAACCCTGGGAAGGTAGGCTCTGGTGACCAGGACAAGGGAGGGAAGGAAGGACCCTGTGCCTGGCA +198

Figure 9

Figure 10


NHEJ, %
A
0
10
20
30
40
50
60
Mock
ZFNs only
SMS124 oligo only
SMS12 oligo only
SMS14 oligo only
SMS24 oligo only
ZFNs + SMS124
ZFNs + SMS12
ZFNs + SMS14
ZFNs + SMS24
ZFNs + SMS1
ZFNs + SMS2
ZFNs + SMS4
Gene correction, %
B
0
10
20
30
40
50
60
Mock
ZFNs only
SMS124 oligo only
SMS12 oligo only
SMS14 oligo only
SMS24 oligo only
ZFNs + SMS124
ZFNs + SMS12
ZFNs + SMS14
ZFNs + SMS24
ZFNs + SMS1
ZFNs + SMS2
ZFNs + SMS4

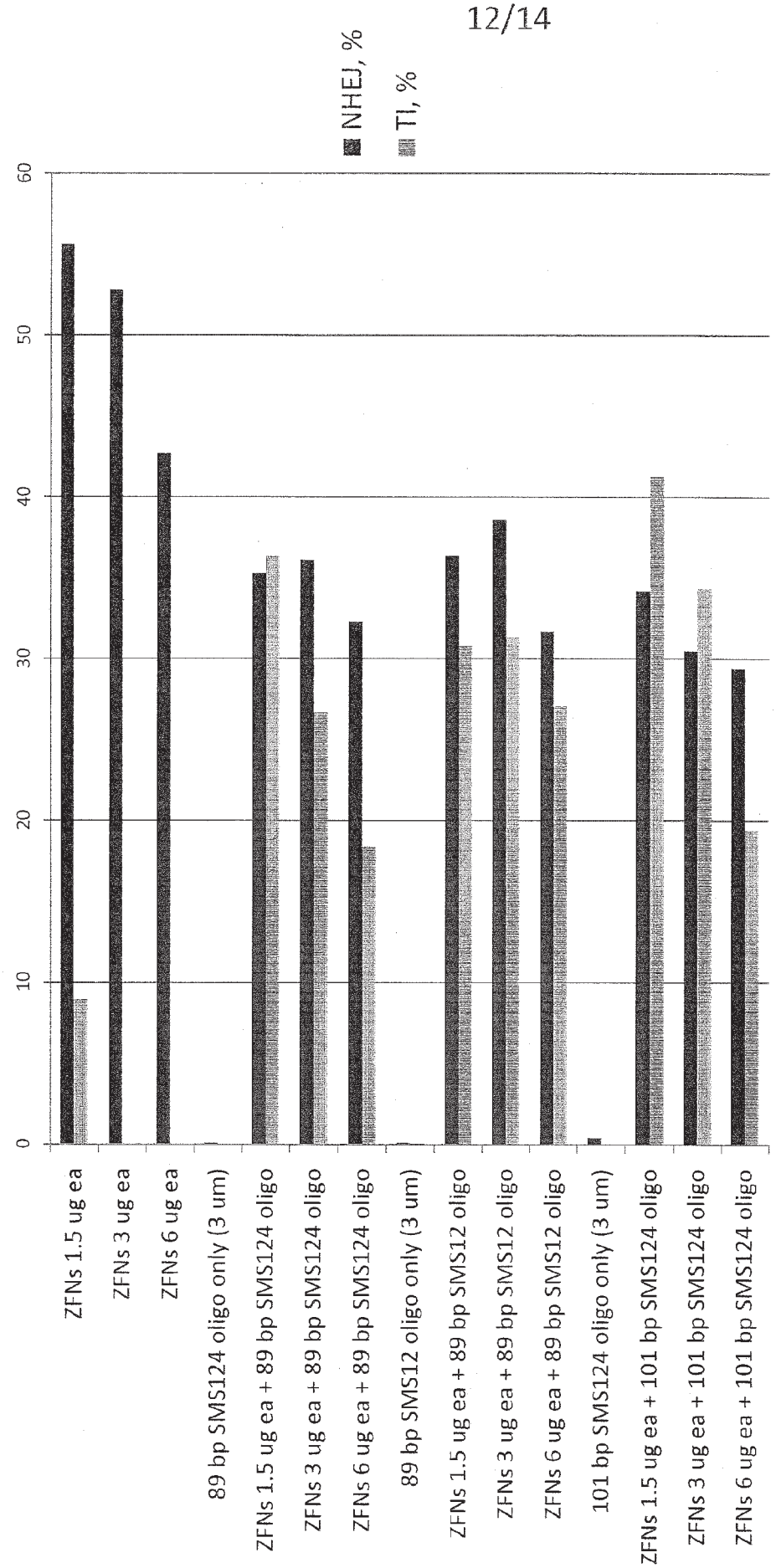

NHEJ, %
TI, %
0
10
20
30
40
50
60
ZFNs 1.5 ug ea
ZFNs 3 ug ea
ZFNs 6 ug ea
89 bp SMS124 oligo only (3 um)
ZFNs 1.5 ug ea + 89 bp SMS124 oligo
ZFNs 3 ug ea + 89 bp SMS124 oligo
ZFNs 6 ug ea + 89 bp SMS124 oligo
89 bp SMS12 oligo only (3 um)
ZFNs 1.5 ug ea + 89 bp SMS12 oligo
ZFNs 3 ug ea + 89 bp SMS12 oligo
ZFNs 6 ug ea + 89 bp SMS12 oligo
101 bp SMS124 oligo only (3 um)
ZFNs 1.5 ug ea + 101 bp SMS124 oligo
ZFNs 3 ug ea + 101 bp SMS124 oligo
ZFNs 6 ug ea + 101 bp SMS124 oligo

Figure 11

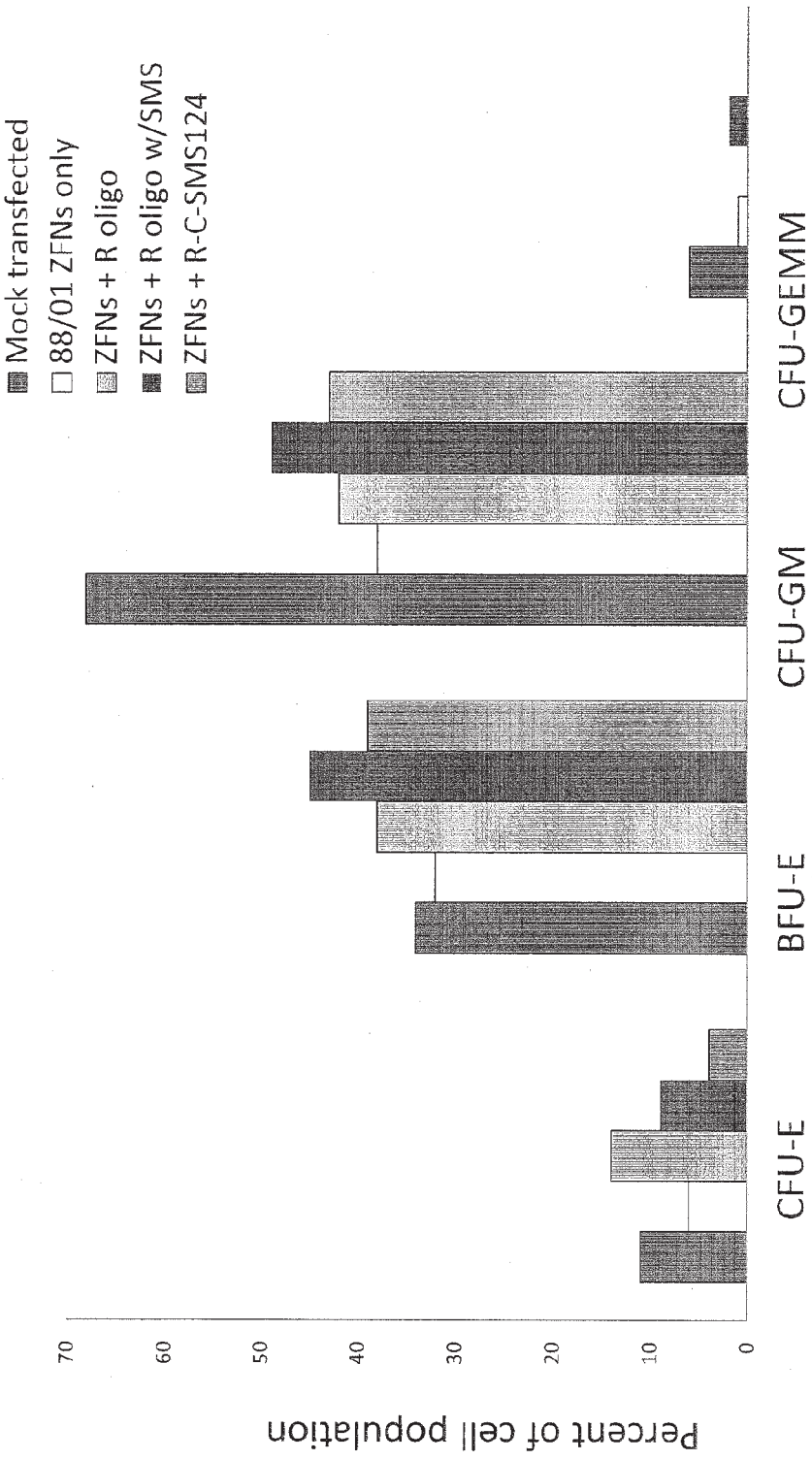
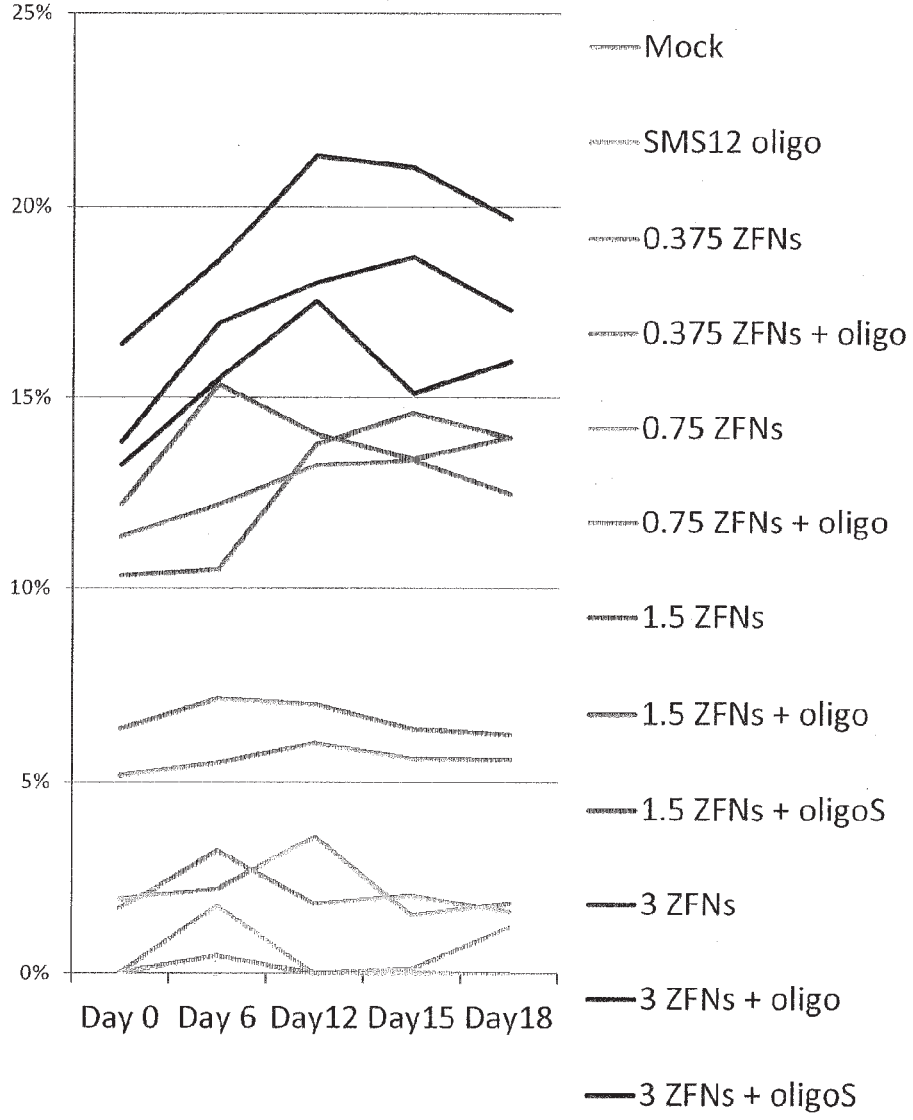
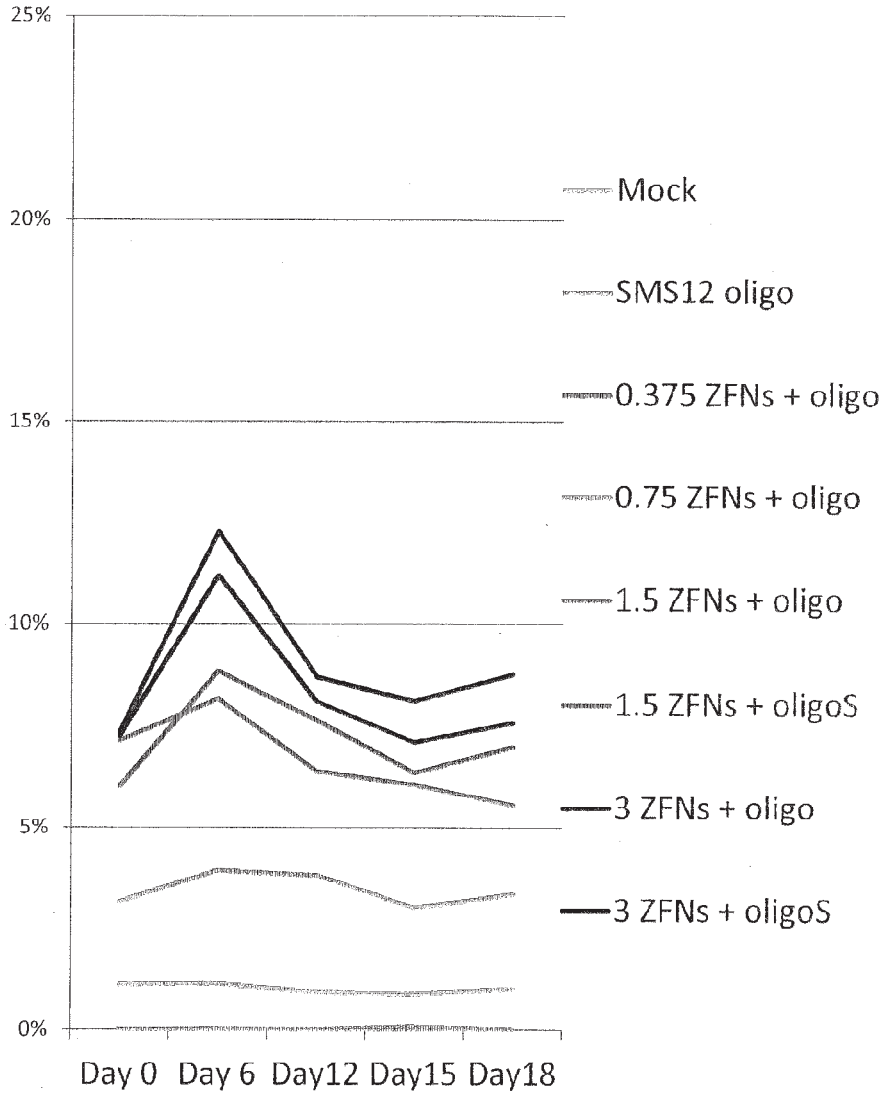

Mock transfected
88/01 ZFNs only
ZFNs + R oligo
ZFNs + R oligo w/SMS
ZFNs + R-C-SMS124
Percent of cell population
0
10
20
30
40
50
60
70
CFU-E
BFU-E
CFU-GM
CFU-GEMM

Figure 12



NHEJ, %



TI, %

Figure 13