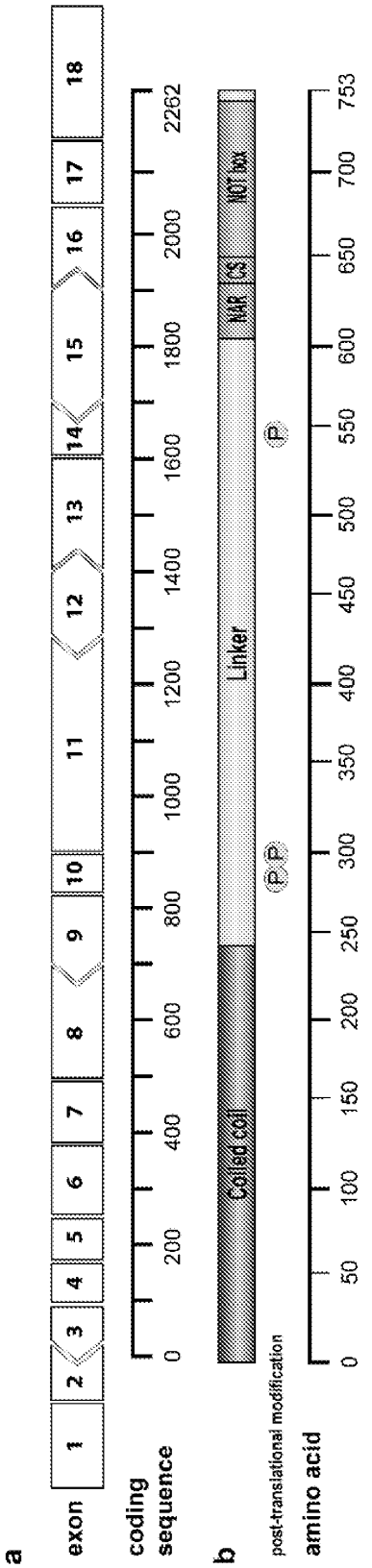

a
exon
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
coding sequence
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2262
b
Coiled coil
Linker
NAR
CS
NOT box
P
P
P
post-translational modification
amino acid
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
753

Figure 1

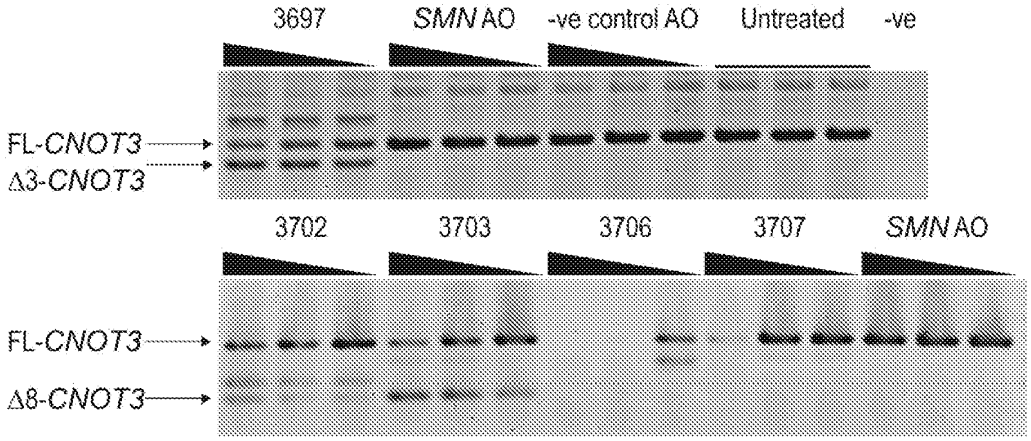


Figure 2A

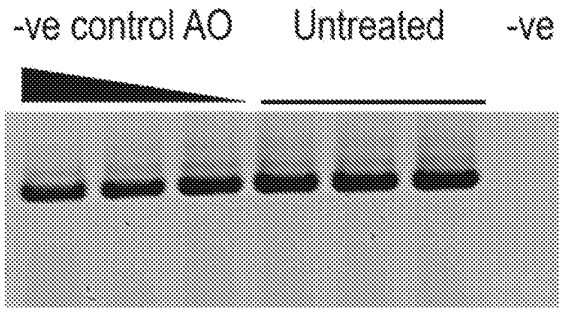


Figure 2B

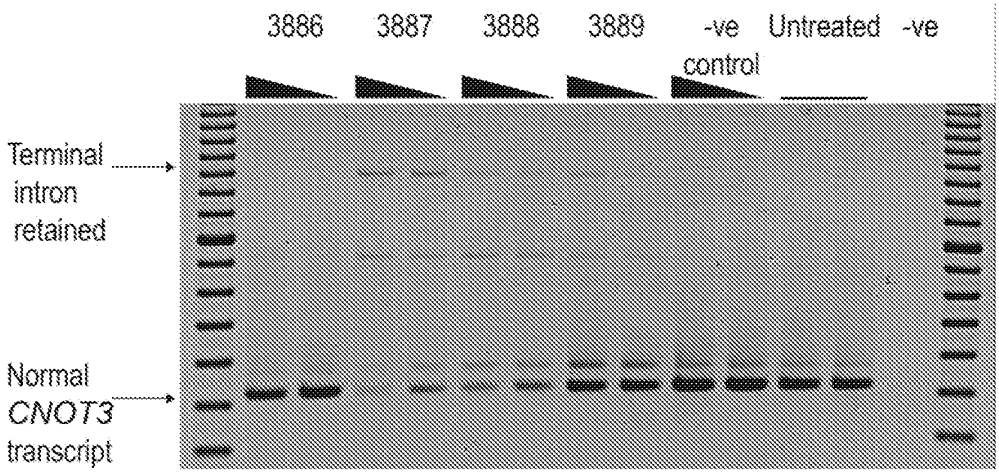

3886
3887
3888
3889
-ve control
Untreated
-ve
Terminal intron retained
Normal CNOT3 transcript

Figure 3

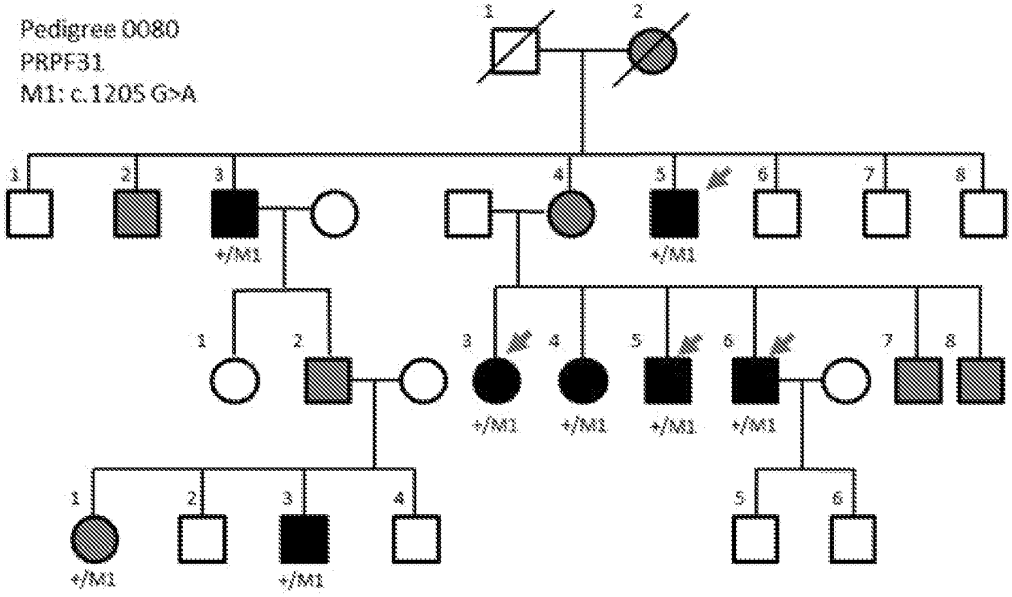


Figure 4A

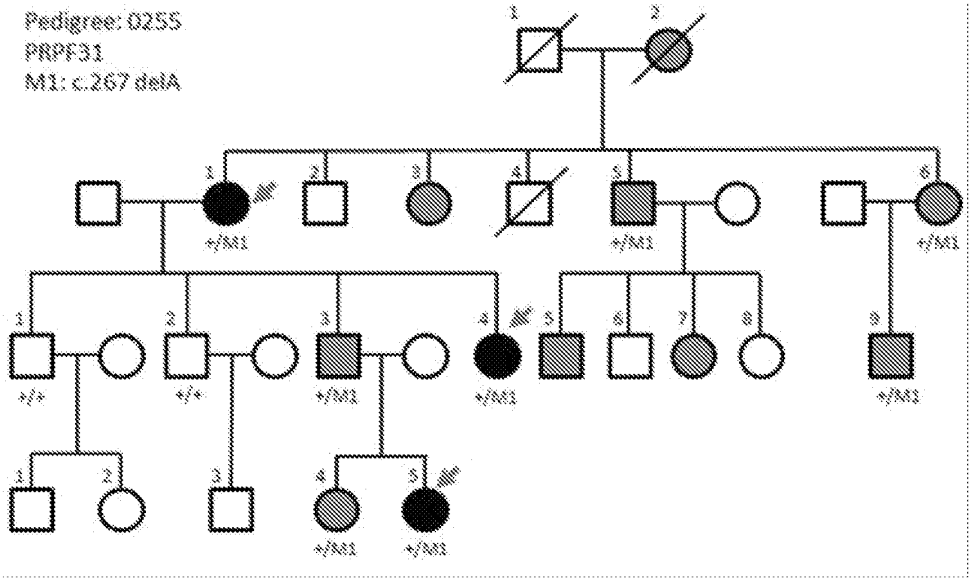


Figure 4B

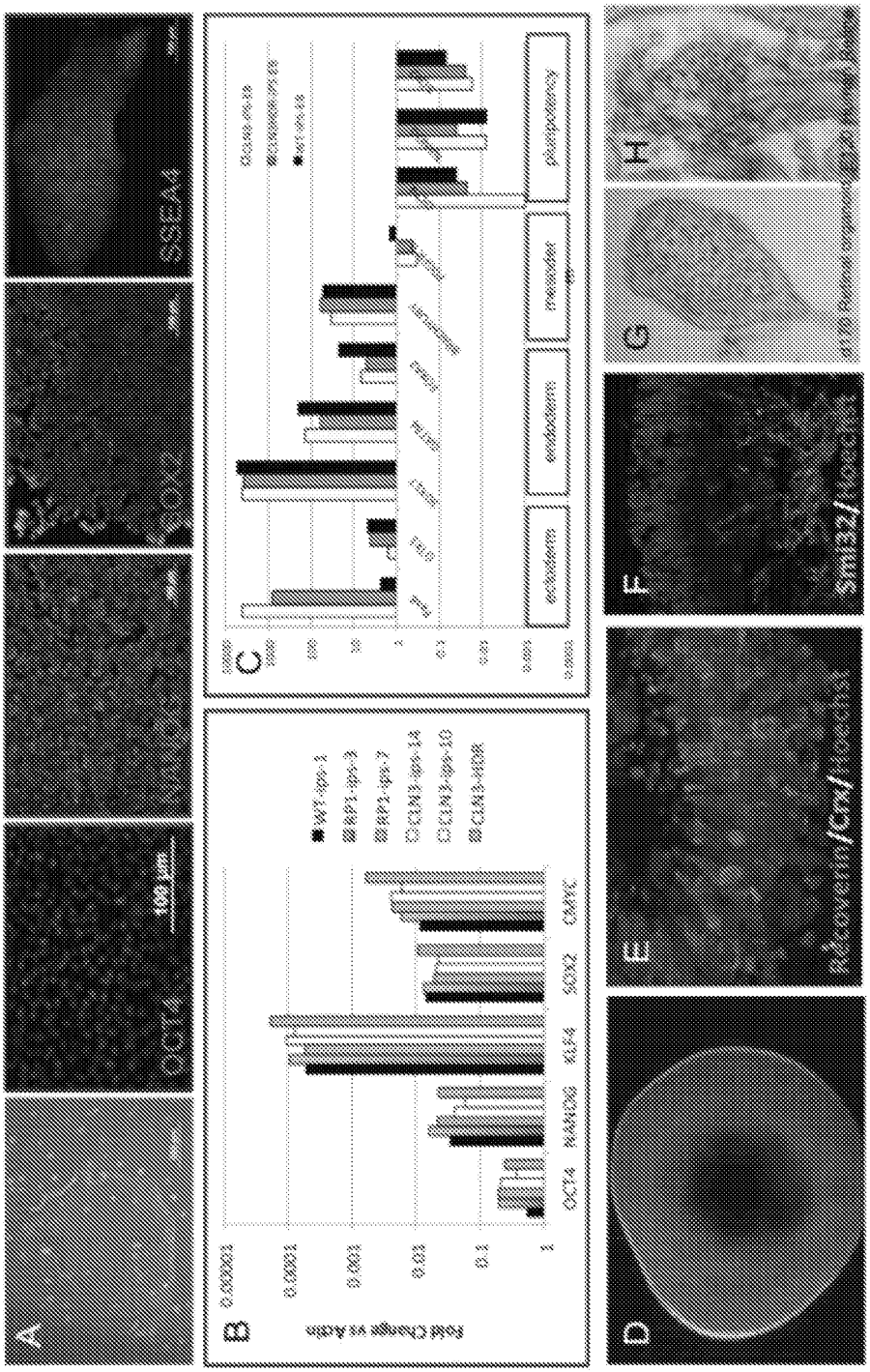

A
OCT4
100 µm
SSEA4
B
Fold Change vs Adult
0.00001
0.0001
0.001
0.01
0.1
1
WT-sp-1
WT-sp-2
WT-sp-7
CDM3-sp-13
CDM3-sp-10
CDM3-sp-8
OCT4
NANOG
KLF4
SOX2
CMYC
C
ectoderm
endoderm
mesoderm
pluripotency
D
E
Caveolin/Cav1 Integrin β1
F
Sm32/Hoechst
G
H

Figure 5

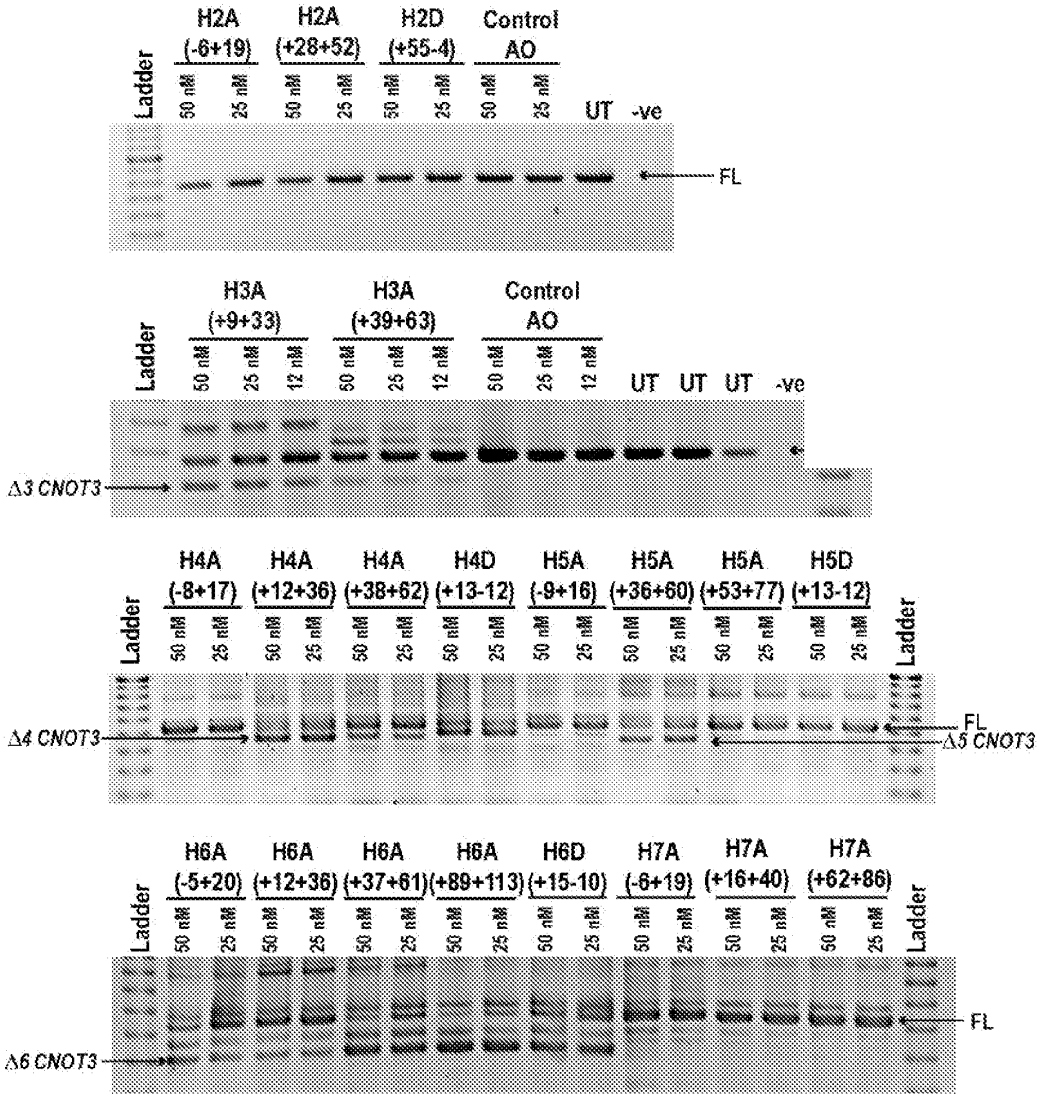

H2A (-6+19)
H2A (+28+52)
H2D (+55-4)
Control AO
Ladder
50 nM
25 nM
UT
-ve
FL
H3A (+9+33)
H3A (+39+63)
Control AO
12 nM
Δ3 CNOT3
H4A (-8+17)
H4A (+12+36)
H4A (+38+62)
H4D (+13-12)
H5A (-9+16)
H5A (+36+60)
H5A (+53+77)
H5D (+13-12)
Δ4 CNOT3
Δ5 CNOT3
H6A (-5+20)
H6A (+12+36)
H6A (+37+61)
H6A (+89+113)
H6D (+15-10)
H7A (-6+19)
H7A (+16+40)
H7A (+62+86)
Δ6 CNOT3

Figure 6A

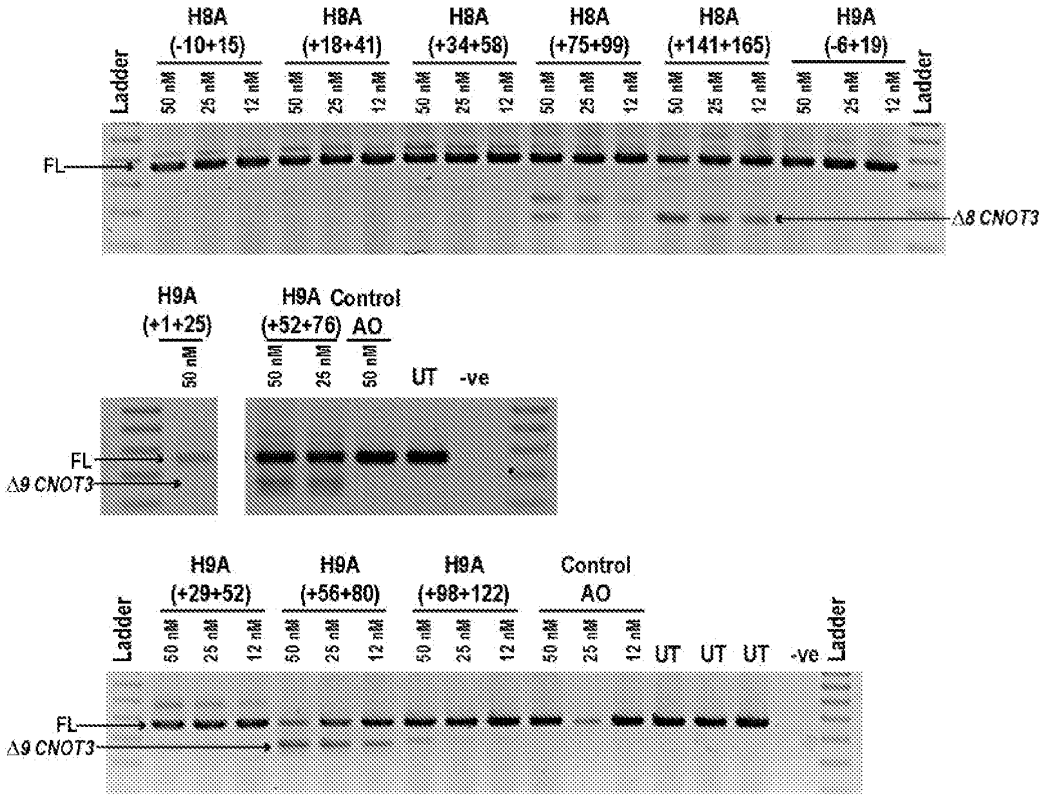

H8A (-10+15)
H8A (+18+41)
H8A (+34+58)
H8A (+75+99)
H8A (+141+165)
H9A (-6+19)
Ladder
50 nM
25 nM
12 nM
FL
Δ8 CNOT3
H9A (+1+25)
H9A (+52+76)
Control AO
UT
-ve
Δ9 CNOT3
H9A (+29+52)
H9A (+56+80)
H9A (+98+122)
Control AO

Figure 6B

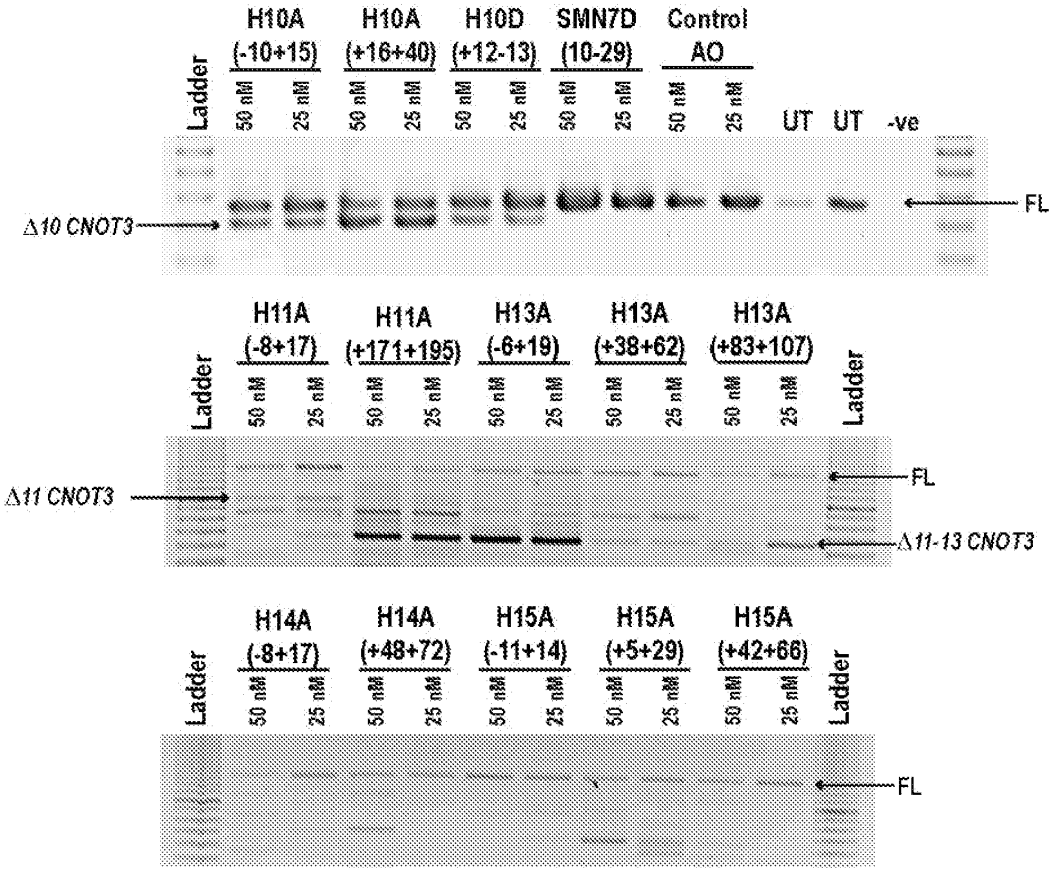

H10A (-10+15)
H10A (+16+40)
H10D (+12-13)
SMN7D (10-29)
Control AO
Ladder
50 nM
25 nM
UT
UT
-ve
Δ10 CNOT3
FL
H11A (-8+17)
H11A (+171+195)
H13A (-6+19)
H13A (+38+62)
H13A (+83+107)
Ladder
Δ11 CNOT3
FL
Δ11-13 CNOT3
H14A (-8+17)
H14A (+48+72)
H15A (-11+14)
H15A (+5+29)
H15A (+42+66)
Ladder
FL

Figure 7A

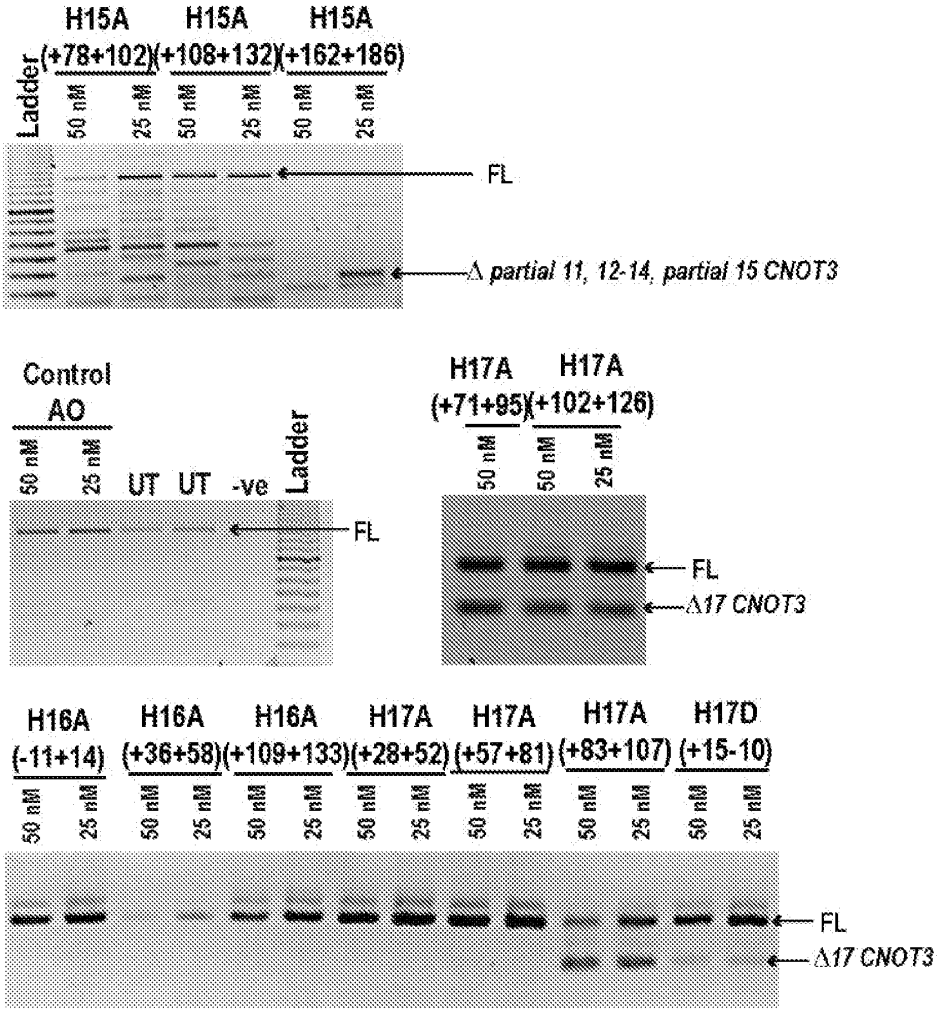

H15A (+78+102)
H15A (+108+132)
H15A (+162+186)
Ladder
50 nM
25 nM
FL
Δ partial 11, 12-14, partial 15 CNOT3
Control AO
UT
UT
-ve
Ladder
H17A (+71+95)
H17A (+102+126)
Δ17 CNOT3
H16A (-11+14)
H16A (+36+58)
H16A (+109+133)
H17A (+28+52)
H17A (+57+81)
H17A (+83+107)
H17D (+15-10)

Figure 7B

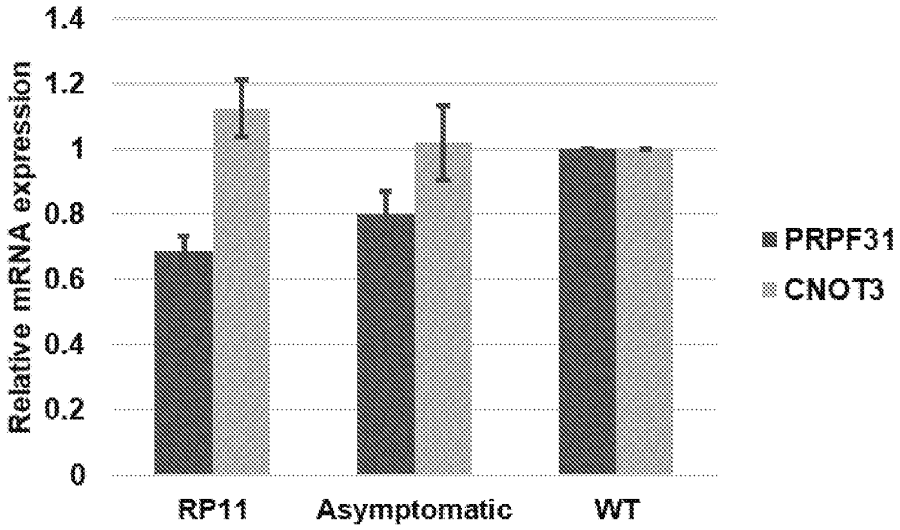


Figure 8a

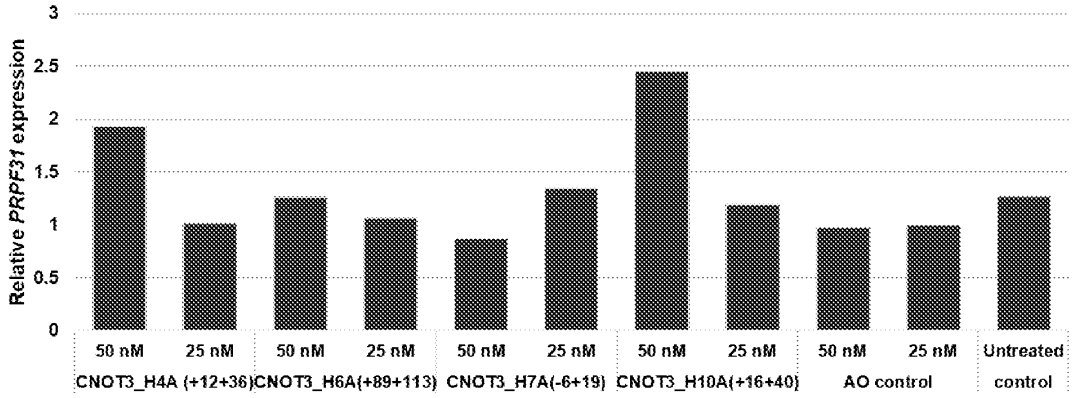


Figure 8b

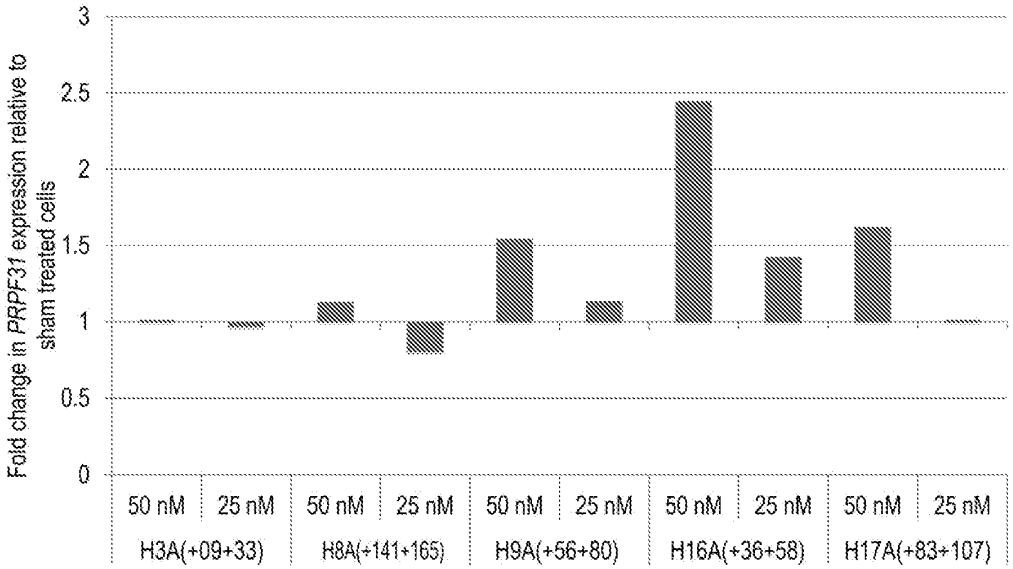

Fold change in PRPF31 expression relative to sham treated cells
3
2.5
2
1.5
1
0.5
0
50 nM
25 nM
50 nM
25 nM
50 nM
25 nM
50 nM
25 nM
50 nM
25 nM
H3A(+09+33)
H8A(+141+165)
H9A(+56+80)
H16A(+36+58)
H17A(+83+107)

Figure 8c

a

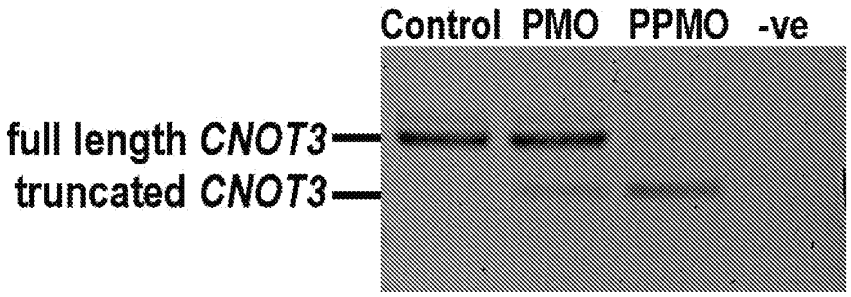


Figure 9A

b

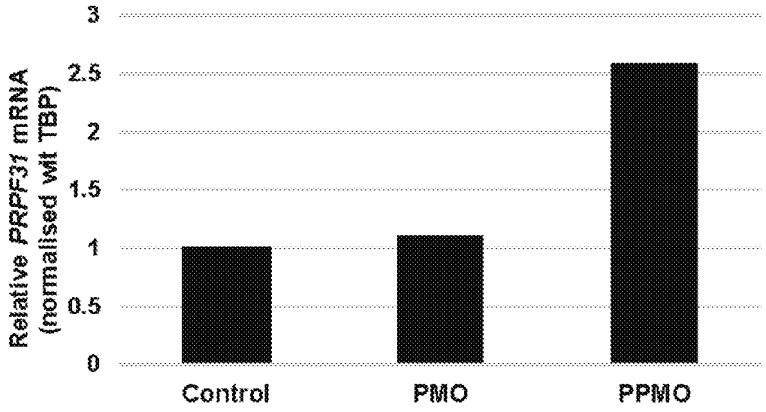


Figure 9B

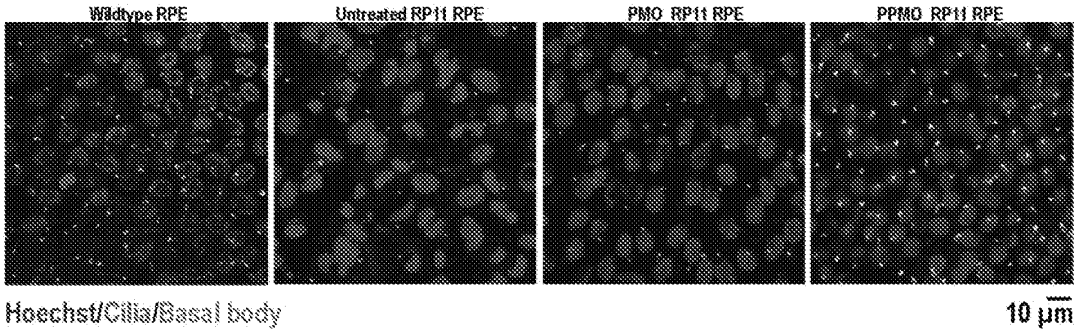


Figure 10A

b

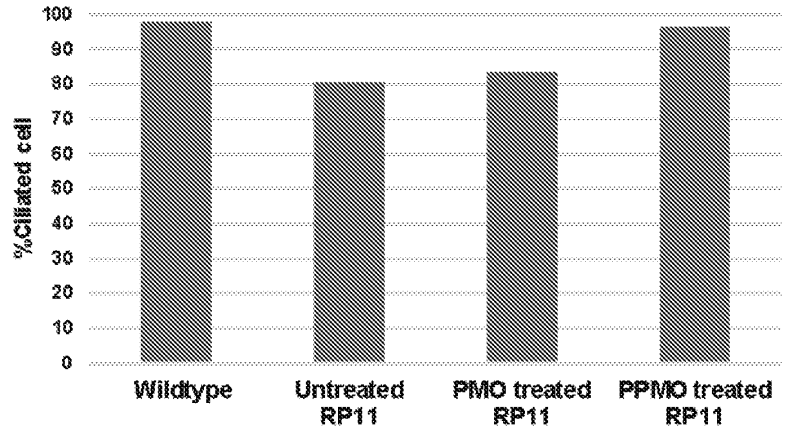


Figure 10B

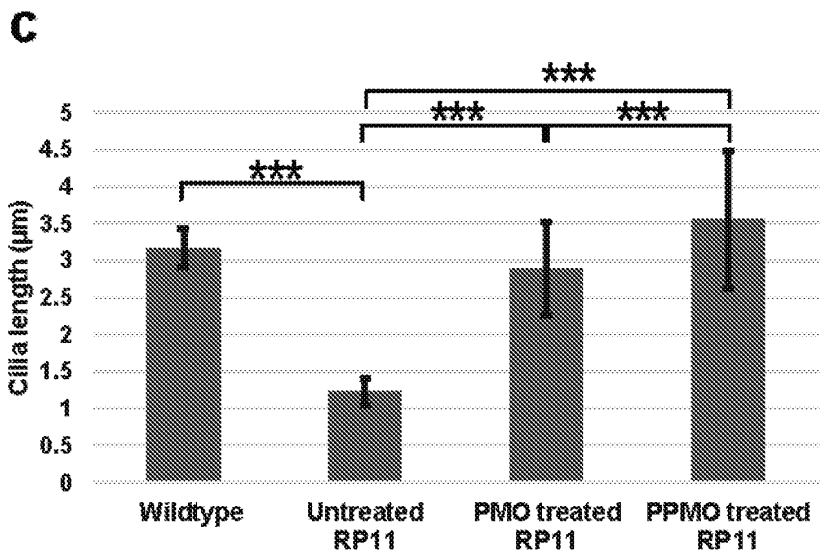

C
***
***
***
***
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
Cilia length (µm)
Wildtype
Untreated RP11
PMO treated RP11
PPMO treated RP11

Figure 10C