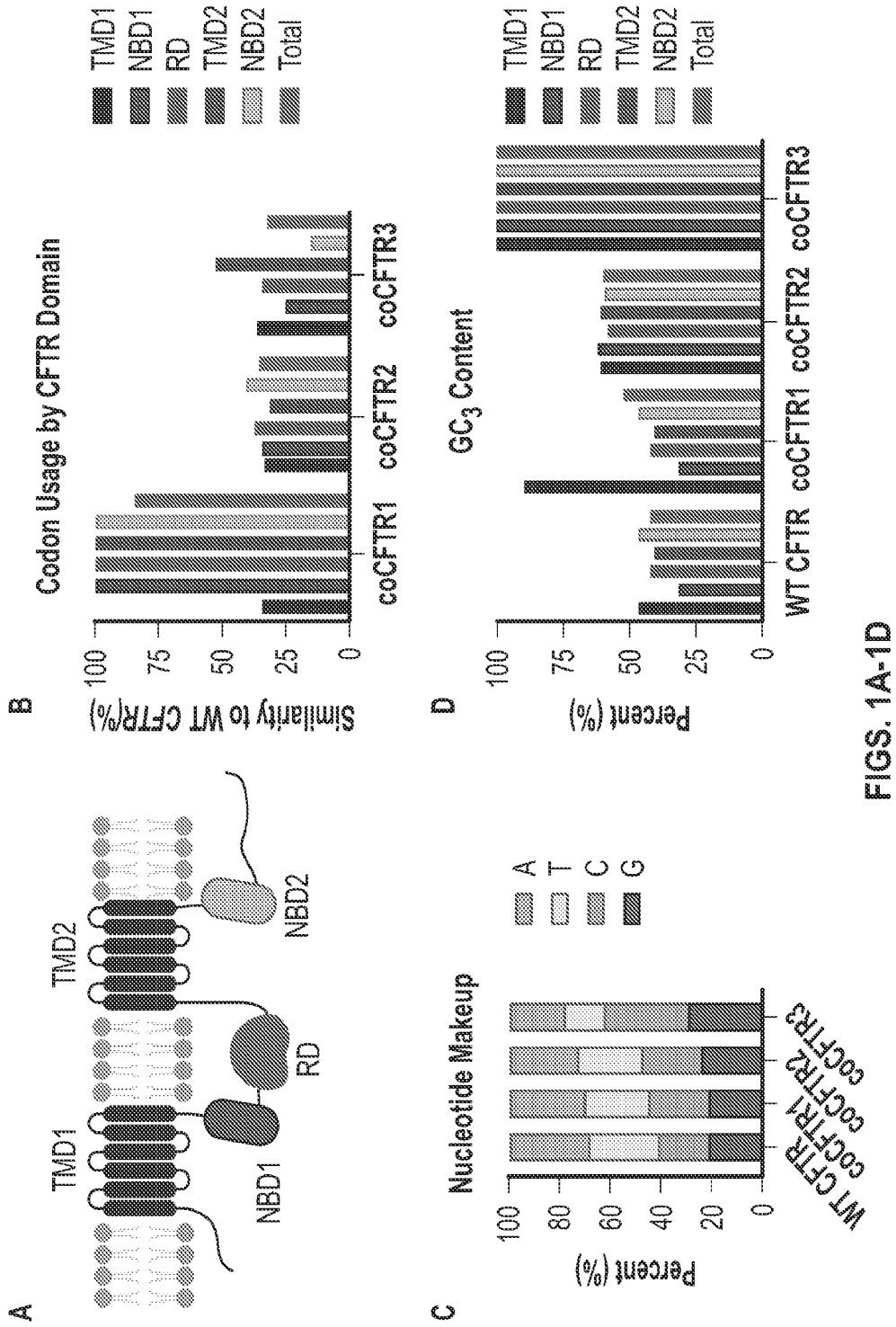
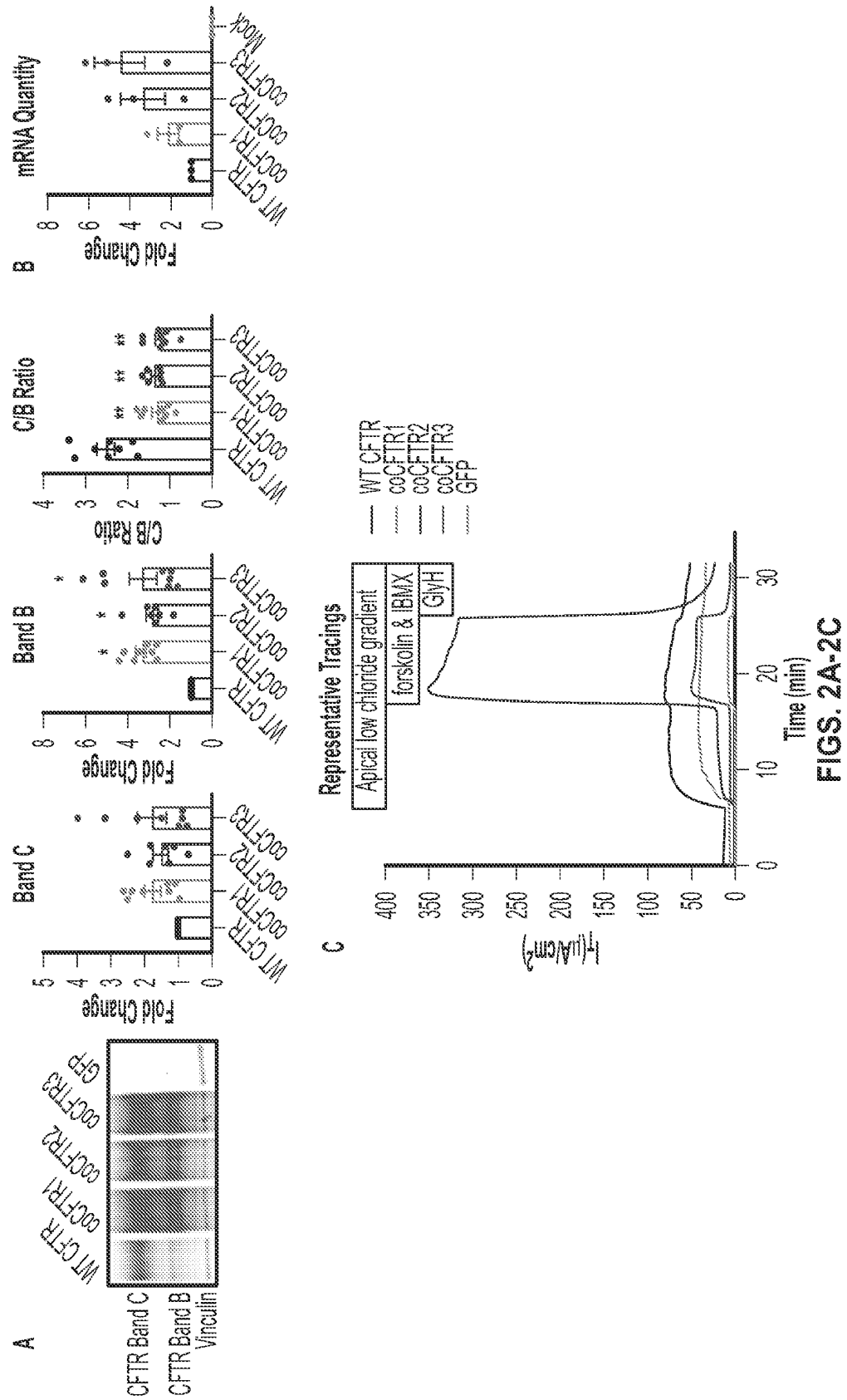
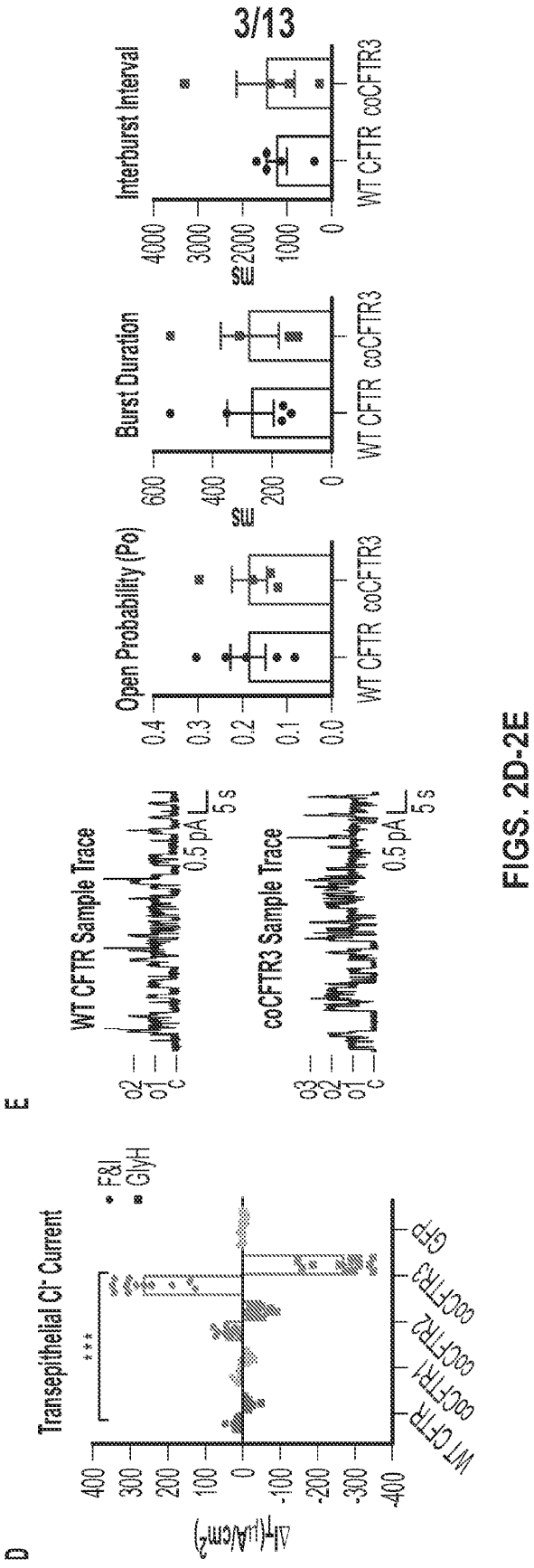

A
TMD1
TMD2
NBD1
RD
NBD2
B
Codon Usage by CFTR Domain
TMD1
NBD1
RD
TMD2
NBD2
Total
Similarity to WT CFTR(%)
100
75
50
25
0
coCFTR1
coCFTR2
coCFTR3
C
Nucleotide Makeup
A
T
C
G
Percent (%)
100
80
60
40
20
0
WT CFTR
coCFTR1
coCFTR2
coCFTR3
D
GC3 Content
TMD1
NBD1
RD
TMD2
NBD2
Total
Percent (%)
100
75
50
25
0
WT CFTR
coCFTR1
coCFTR2
coCFTR3

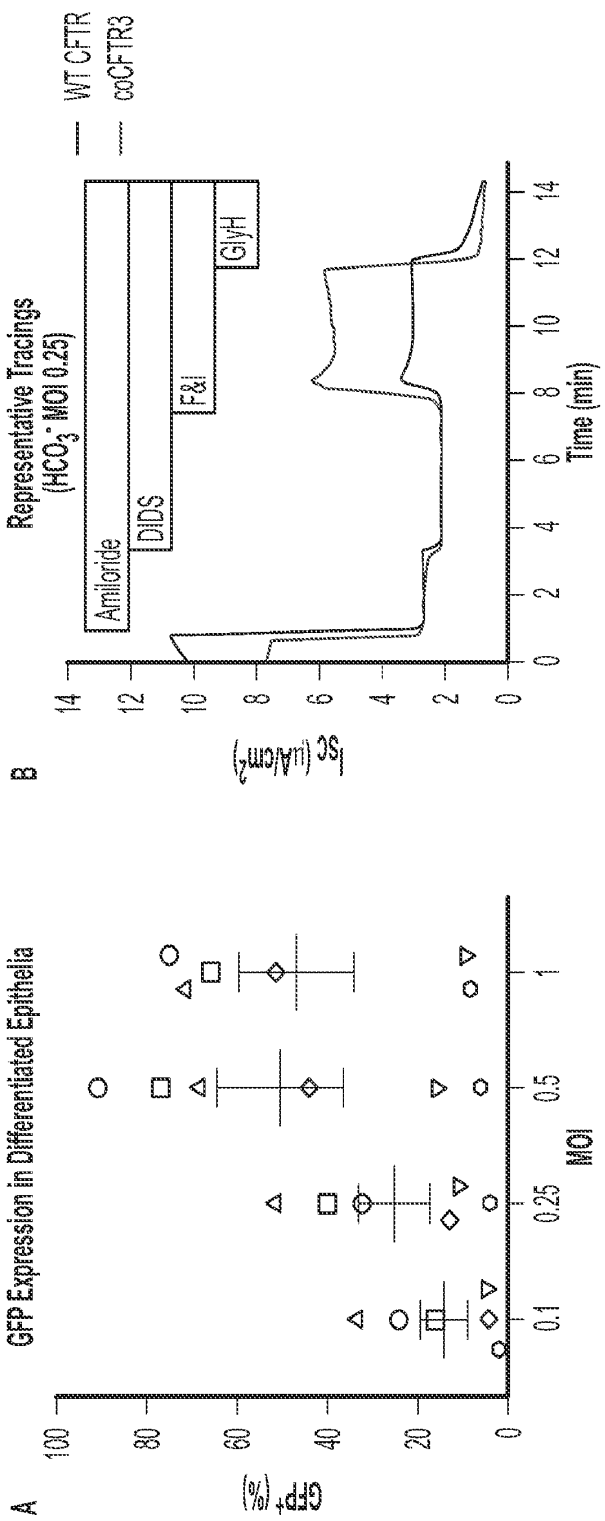
FIGS. 1A-1D


A
CFTR Band C
CFTR Band B
Vinculin
WT CFTR
ΔΔCFTR1
ΔΔCFTR2
ΔΔCFTR3
GFP
Band C
Fold Change
Band B
Fold Change
C/B Ratio
C/B Ratio
B
mRNA Quantity
Fold Change
Mock
C
Representative Tracings
Apical low chloride gradient
forskolin & IBMX
GlyH
WT CFTR
ΔΔCFTR1
ΔΔCFTR2
ΔΔCFTR3
GFP
Time (min)

FIGS. 2A-2C


D
Transepithelial Cl- Current
F&I
Gly/H
ΔIsc(μA/cm²)
400
300
200
100
0
-100
-200
-300
-400
***
WT CFTR
coCFTR1
coCFTR2
coCFTR3
GP
E
WT CFTR Sample Trace
o2
o1
c
0.5 pA
5 s
coCFTR3 Sample Trace
o3
o2
o1
c
0.5 pA
5 s
Open Probability (Po)
0.4
0.3
0.2
0.1
0.0
WT CFTR coCFTR3
Burst Duration
600
400
200
0
WT CFTR coCFTR3
Interburst Interval
4000
3000
2000
1000
0
WT CFTR coCFTR3

FIGS. 2D-2E



FIGS. 3A and 3B

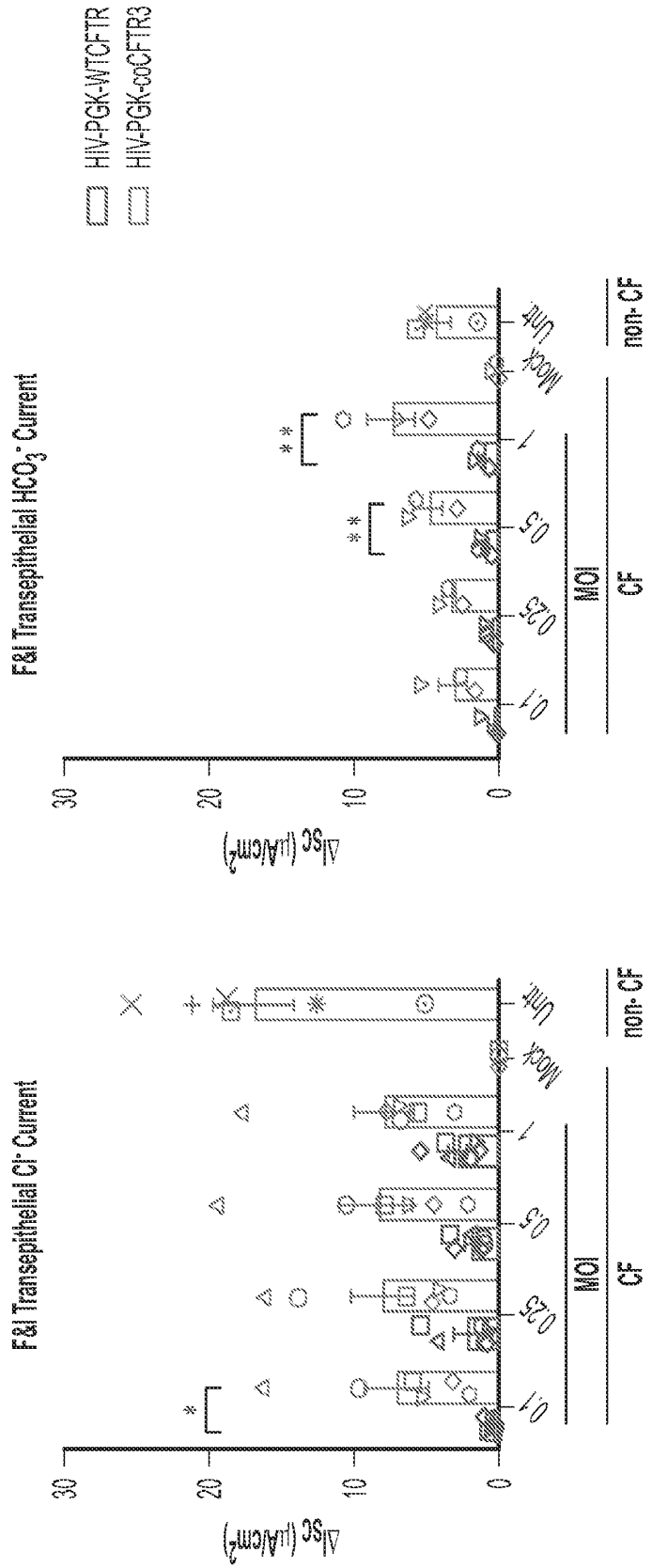

HIV-PGK-WTCFTR
HIV-PGK-coCFTR3
F&I Transepithelial HCO_3^- Current
F&I Transepithelial Cl^- Current
ΔI_{SC} ($\mu A/cm^2$)
0
10
20
30
0.1
0.25
0.5
1
MOI
CF
Mock
Unt.
non-CF
*
**

FIG. 3C

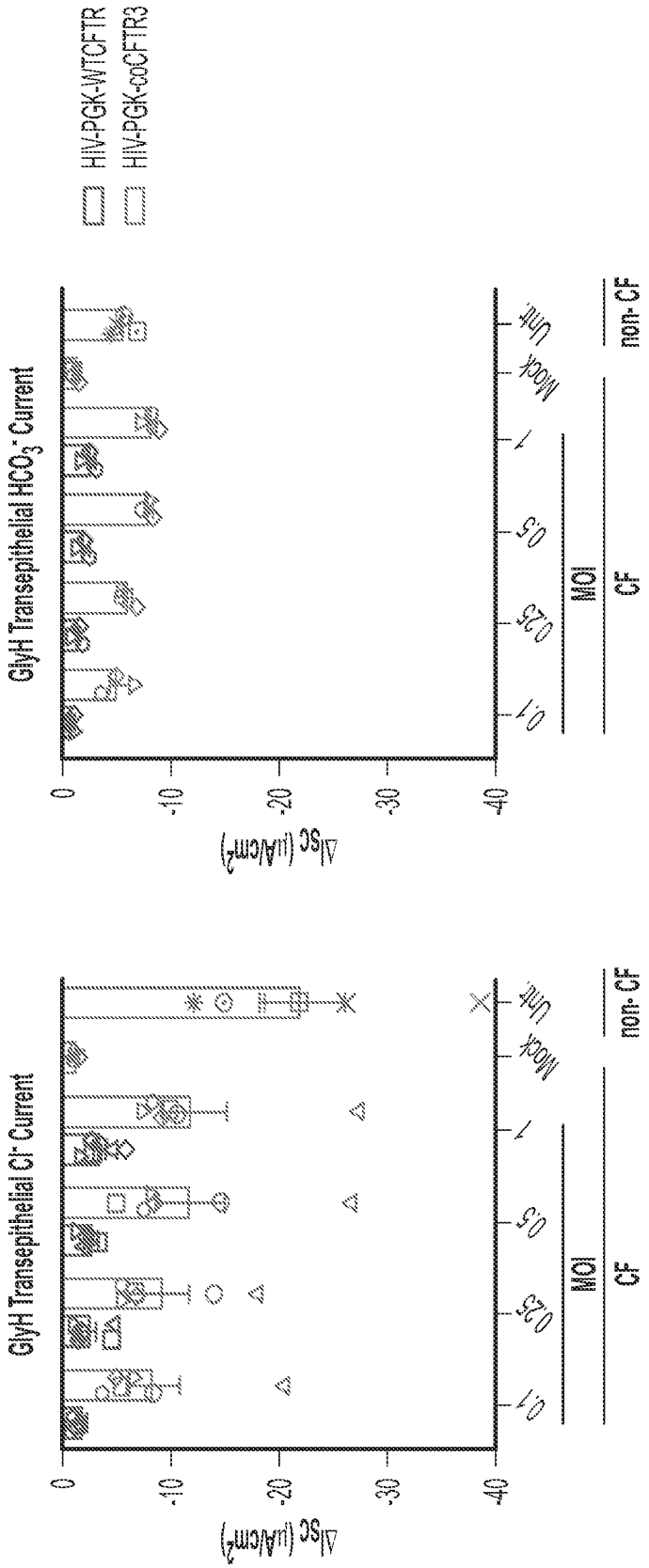

HIV-PGK-WTCFTR
HIV-PGK-coCFTR3
GlyH Transepithelial HCO_3^- Current
GlyH Transepithelial Cl^- Current
ΔI_{SC} ($\mu A/cm^2$)
0
-10
-20
-30
-40
MOI
0.1
0.25
0.5
1
Mock
Unk.
CF
non-CF

FIG. 3D

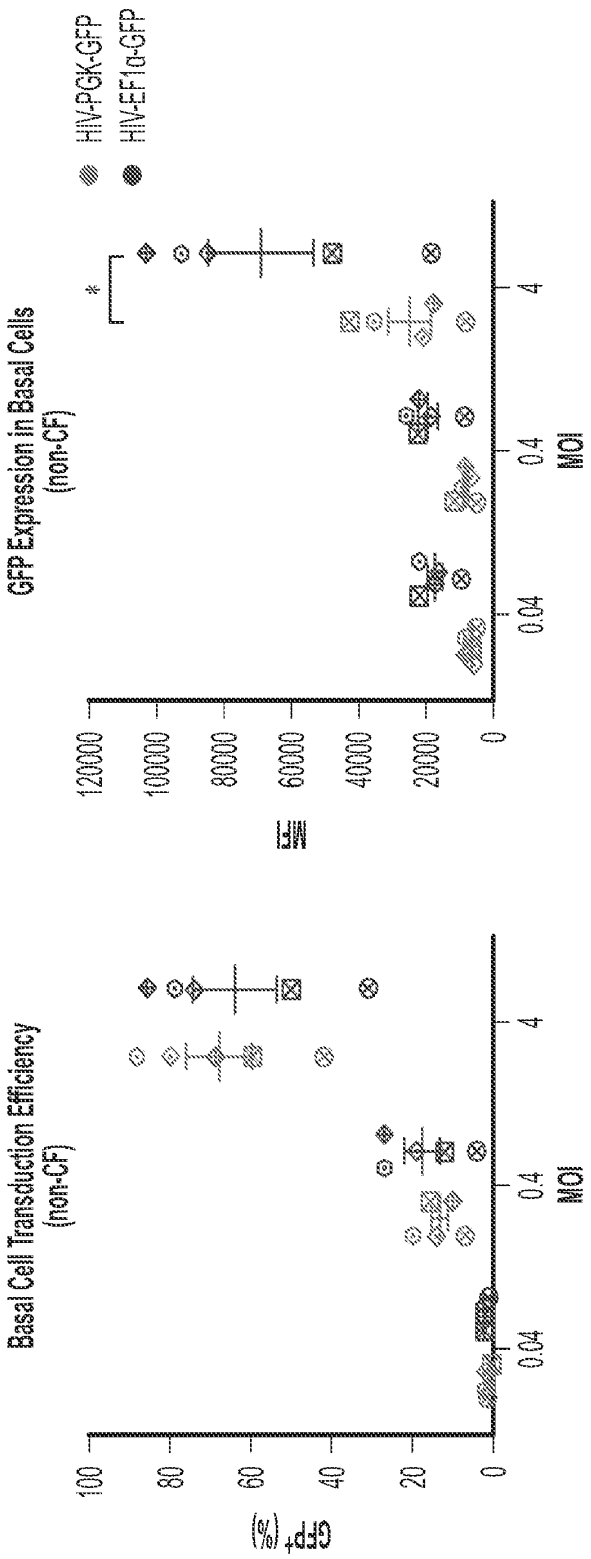

HIV-PGK-GFP
HIV-EF1α-GFP
GFP Expression in Basal Cells (non-CF)
MFI
120000
100000
80000
60000
40000
20000
0
*
0.04
0.4
4
MOI
Basal Cell Transduction Efficiency (non-CF)
GFP+ (%)
100
80
60
40
20
0
0.04
0.4
4
MOI

FIG. 4A

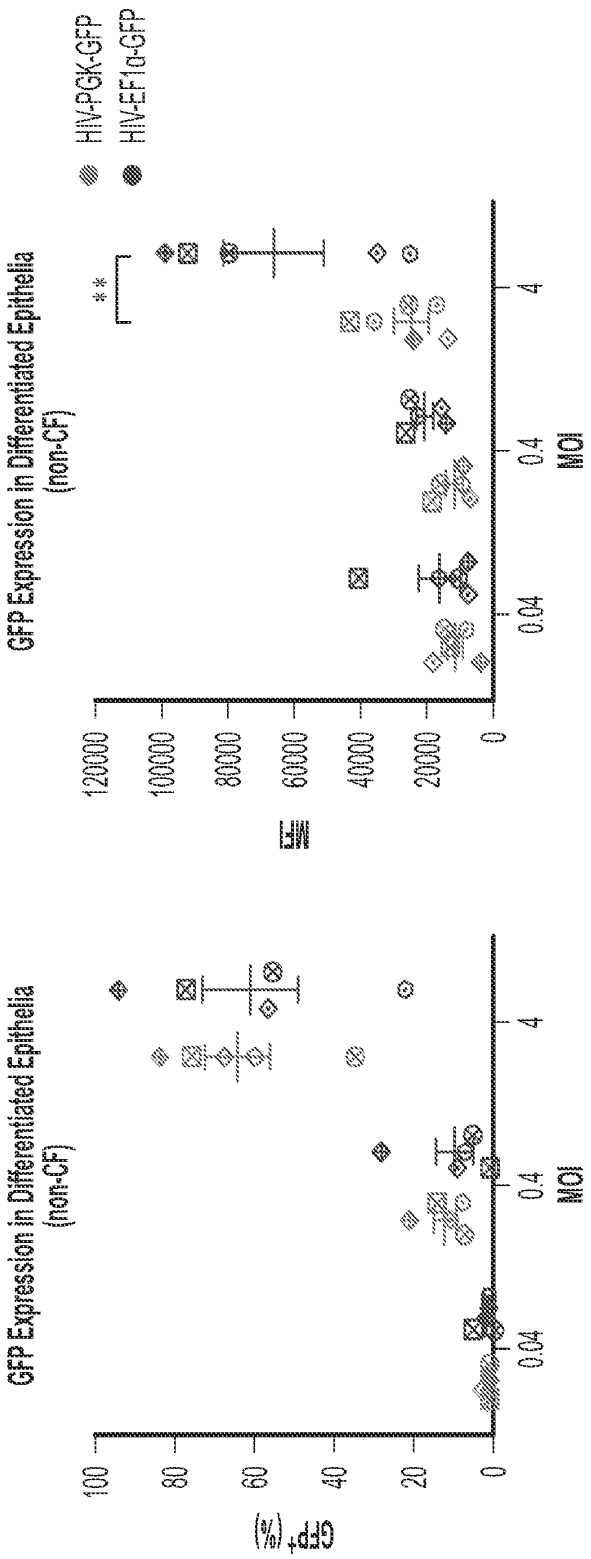

GFP Expression in Differentiated Epithelia
(non-CF)
HIV-PGK-GFP
HIV-EF1α-GFP
**
MFI
MOI
GFP Expression in Differentiated Epithelia
(non-CF)
GFP+ (%)
MOI

FIG. 4B

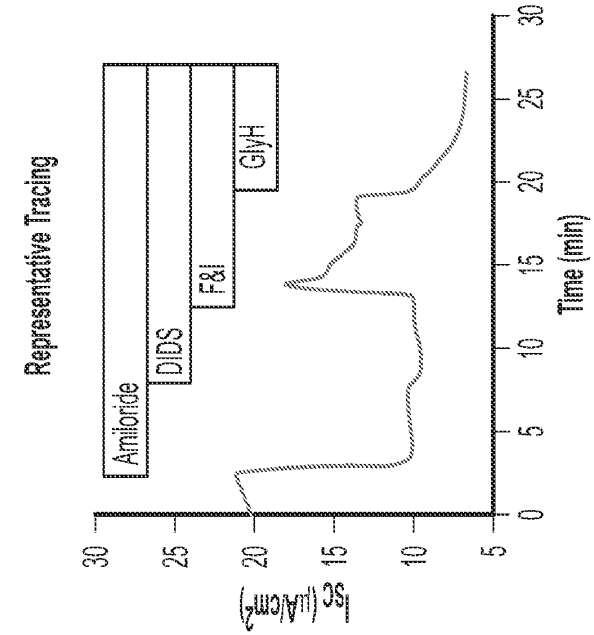

Representative Tracing
Amiloride
DIDS
F&I
GlyH
I_{SC} (μA/cm²)
Time (min)

FIG. 4D

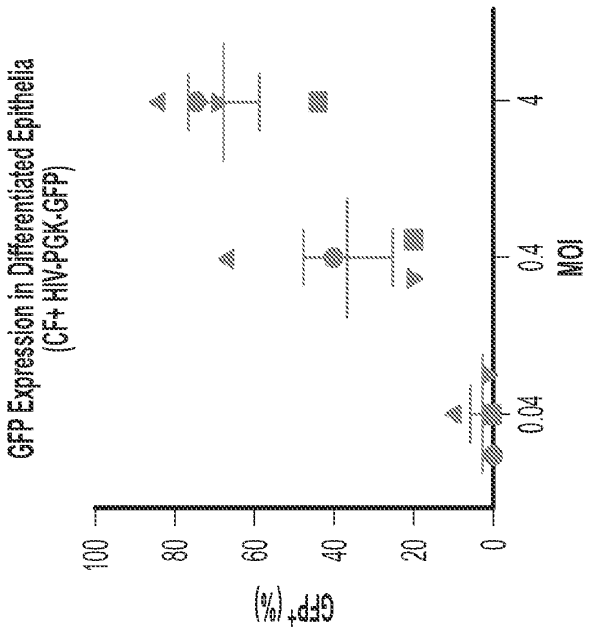

GFP Expression in Differentiated Epithelia
(CF+ HIV-PGK-GFP)
GFP⁺ (%)
MOI

FIG. 4C

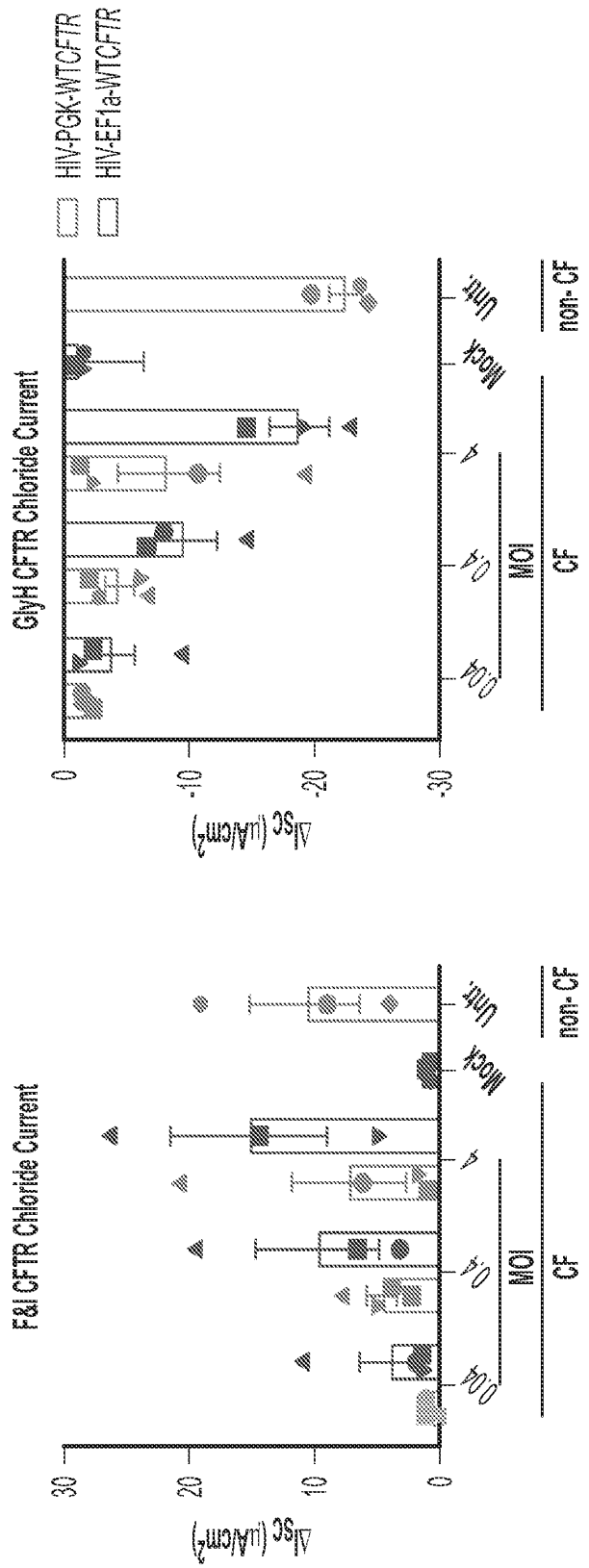

HIV-PGK-WTCFTR
HIV-EF1a-WTCFTR
GlyH CFTR Chloride Current
F&I CFTR Chloride Current
ΔIsc (μA/cm²)
0
-10
-20
-30
30
20
10
0
Untr.
Mock
4
0.4
0.04
MOI
CF
non-CF

FIG. 4E

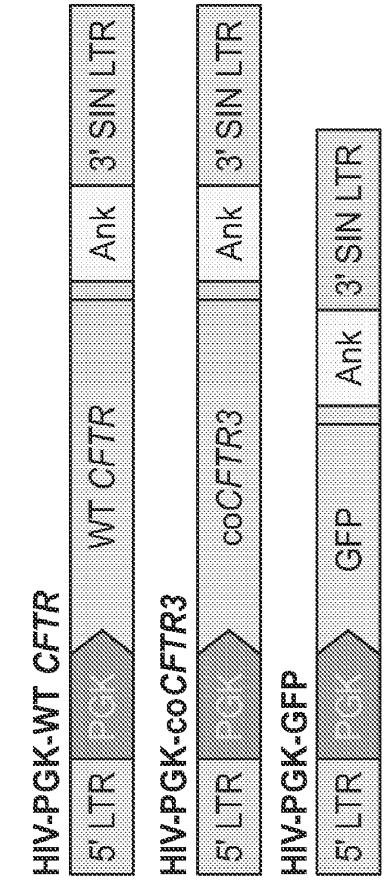

HIV-PGK-WT CFTR
5' LTR
PGK
WT CFTR
Ank
3' SIN LTR
HIV-PGK-coCFTR3
5' LTR
PGK
coCFTR3
Ank
3' SIN LTR
HIV-PGK-GFP
5' LTR
PGK
GFP
Ank
3' SIN LTR

FIG. 5A

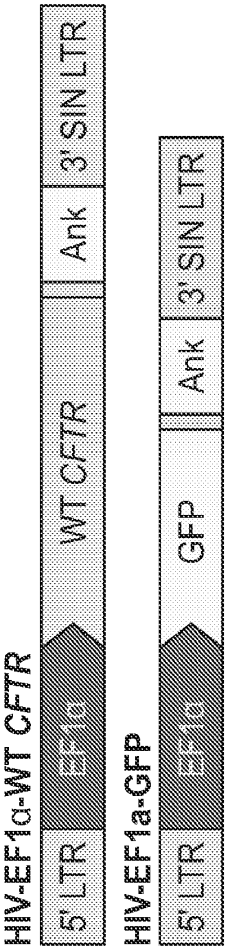
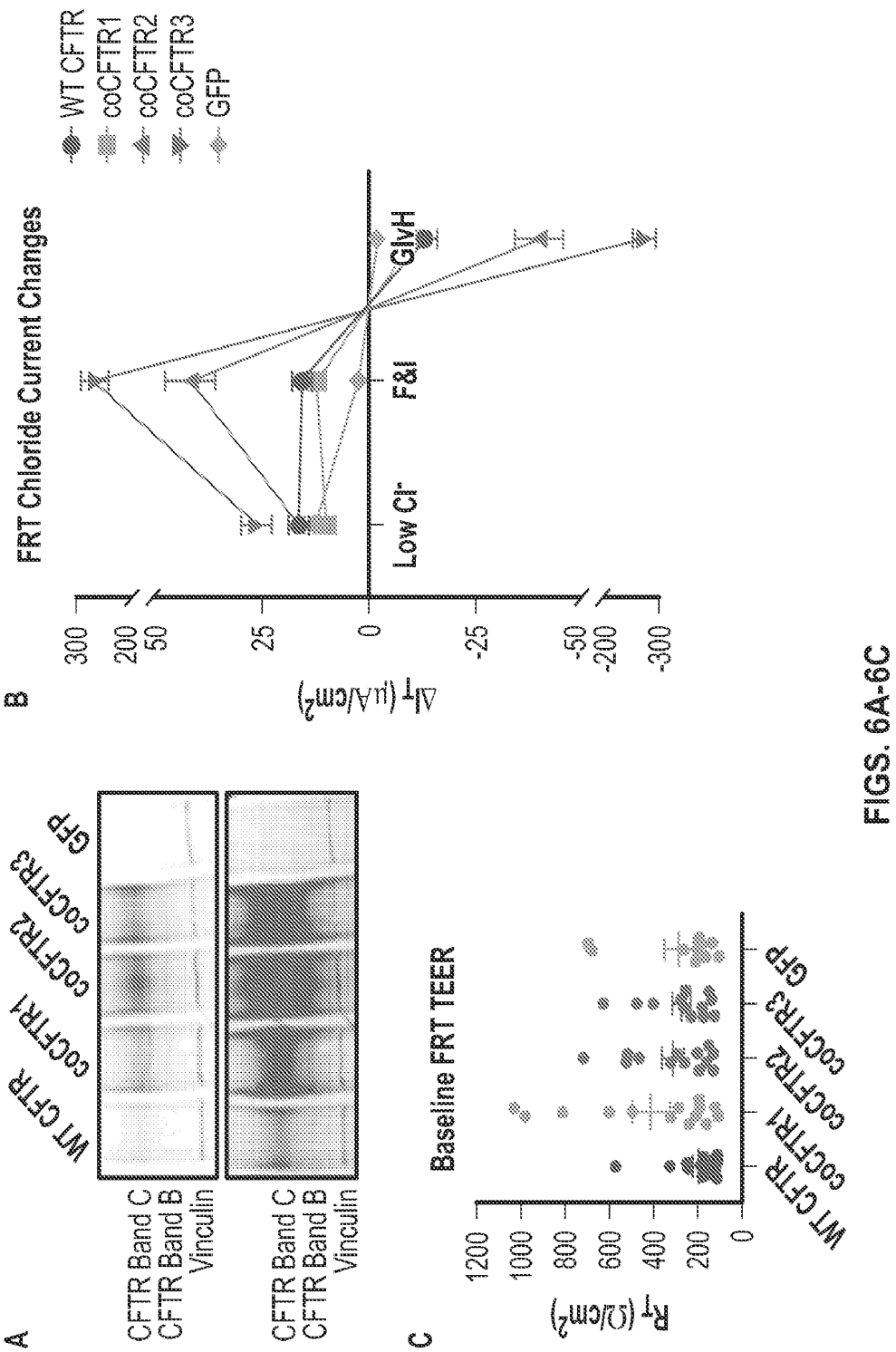
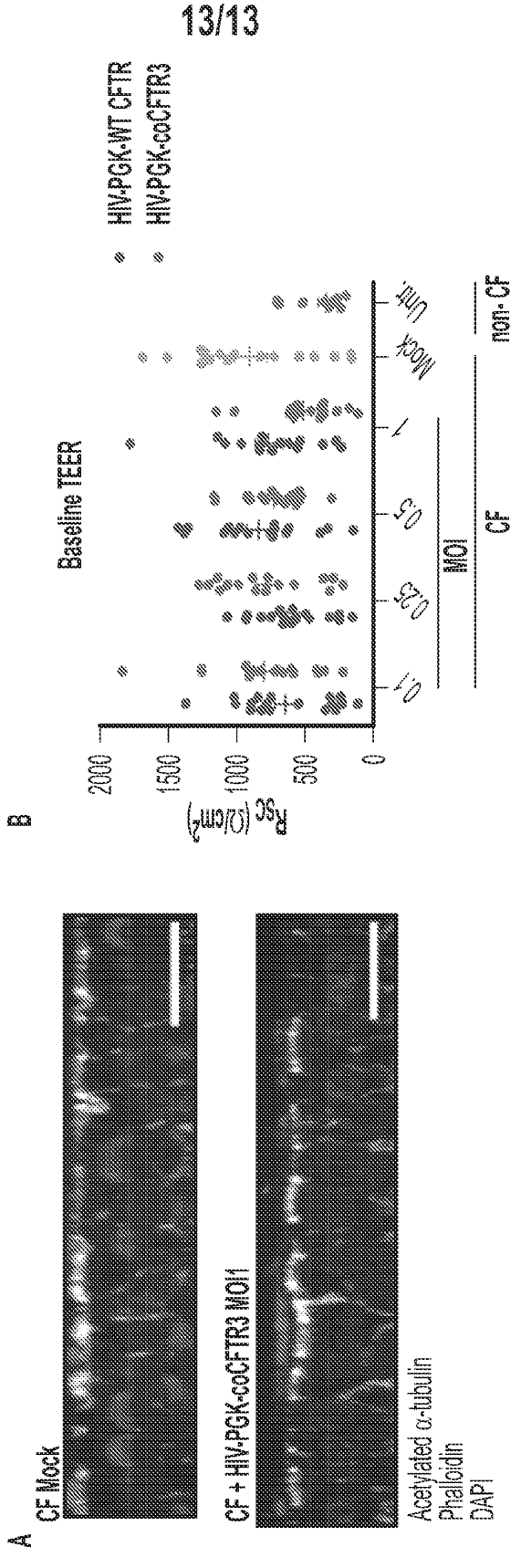

HIV-EF1α-WT CFTR
5' LTR
EF1α
WT CFTR
Ank
3' SIN LTR
HIV-EF1a-GFP
5' LTR
EF1α
GFP
Ank
3' SIN LTR

FIG. 5B


A
WT CFTR
coCFTR1
coCFTR2
coCFTR3
GFP
CFTR Band C
CFTR Band B
Vinculin
CFTR Band C
CFTR Band B
Vinculin
B
FRT Chloride Current Changes
WT CFTR
coCFTR1
coCFTR2
coCFTR3
GFP
Low Cl-
F&I
GlyH
300
200
50
25
0
-25
-50
-200
-300
ΔIT (μA/cm2)
C
Baseline FRT TEER
1200
1000
800
600
400
200
0
RT (Ω/cm2)
WT CFTR
coCFTR1
coCFTR2
coCFTR3
GFP

FIGS. 6A-6C



FIGS. 7A and 7B