

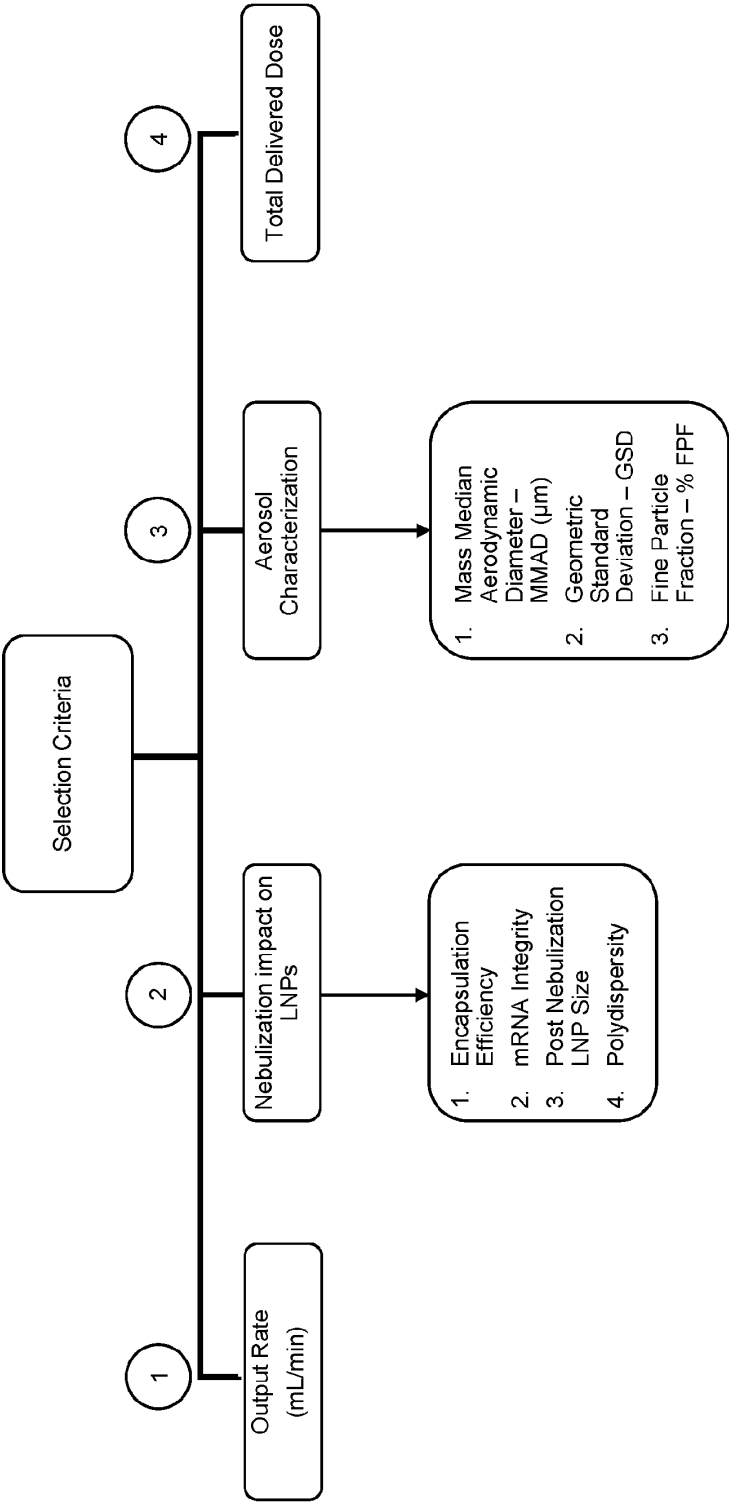


FIG. 1

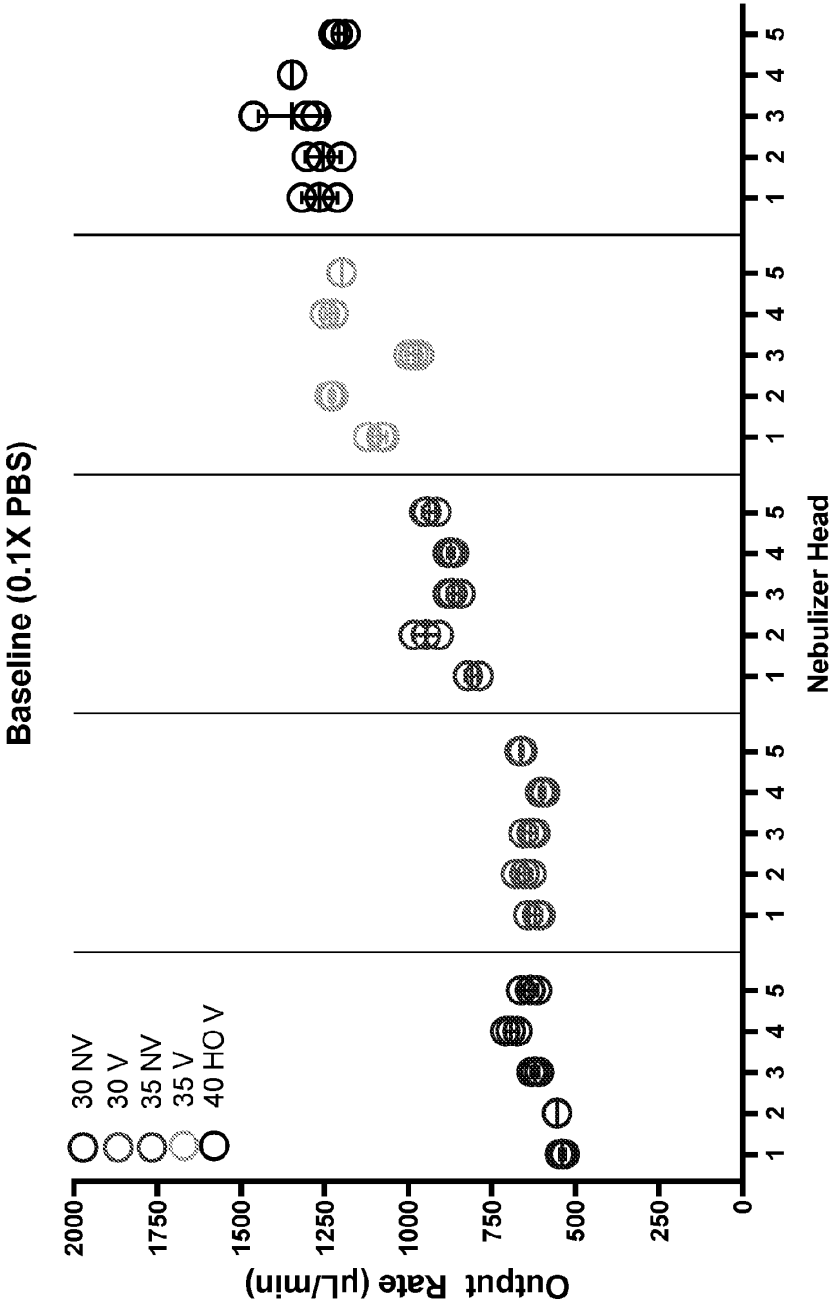
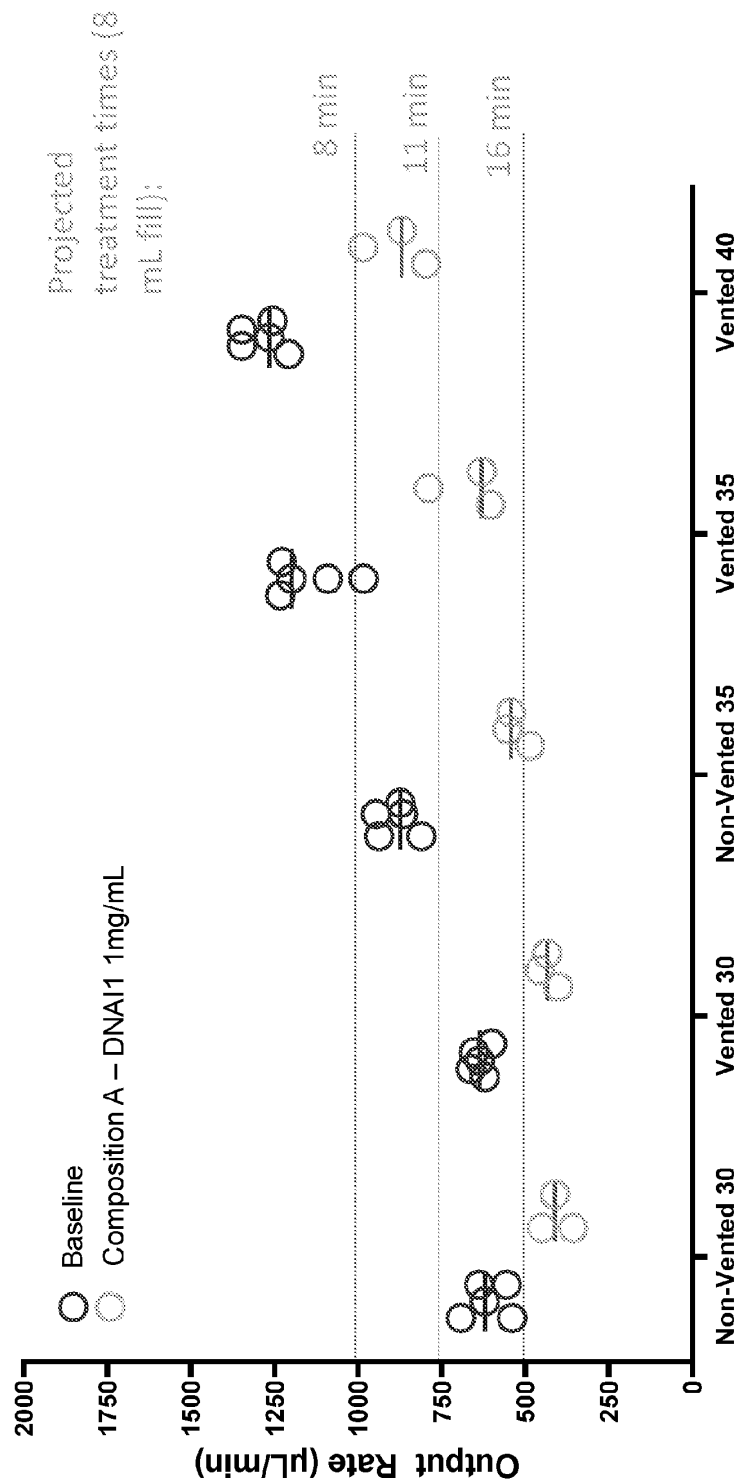


FIG. 2



○ Each circle represents an average of 3 replicates for each of the 5 aerosol heads

○ Each circle represents an average of 3 replicates for slow, median & fast aerosol heads

FIG. 3

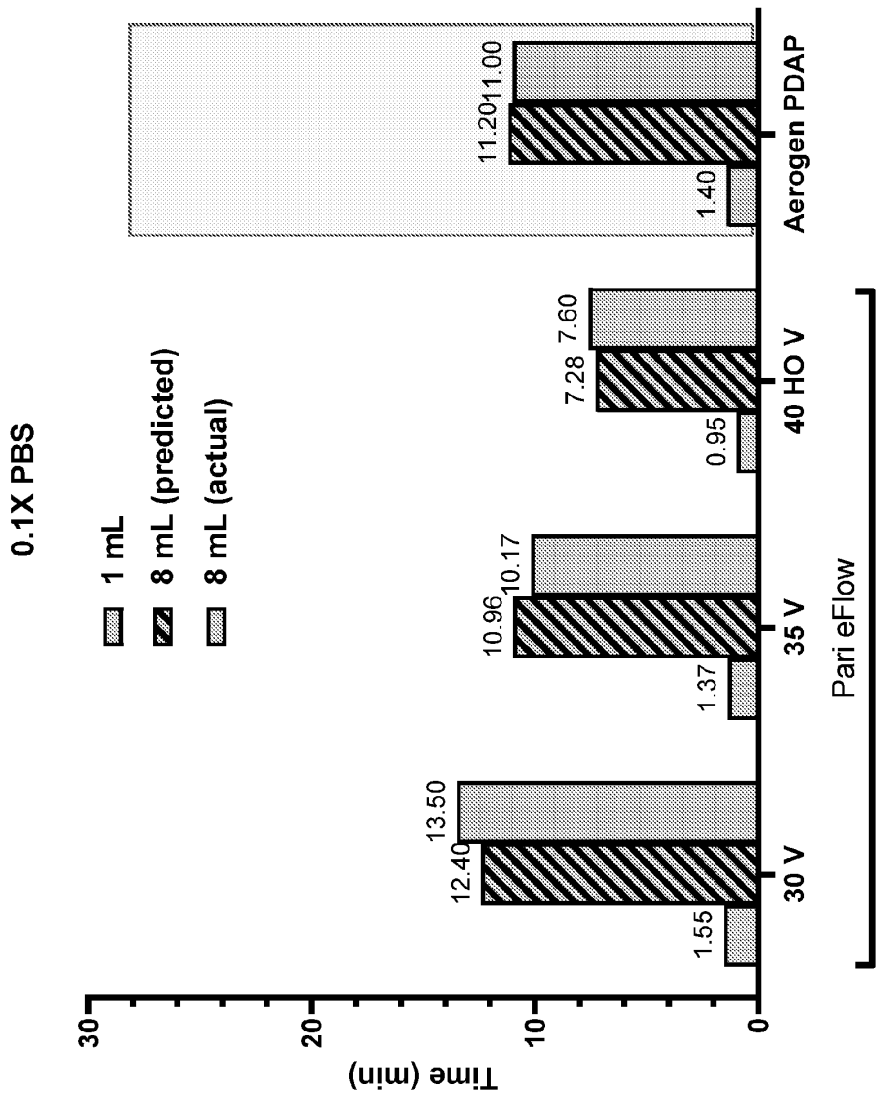


FIG. 4A

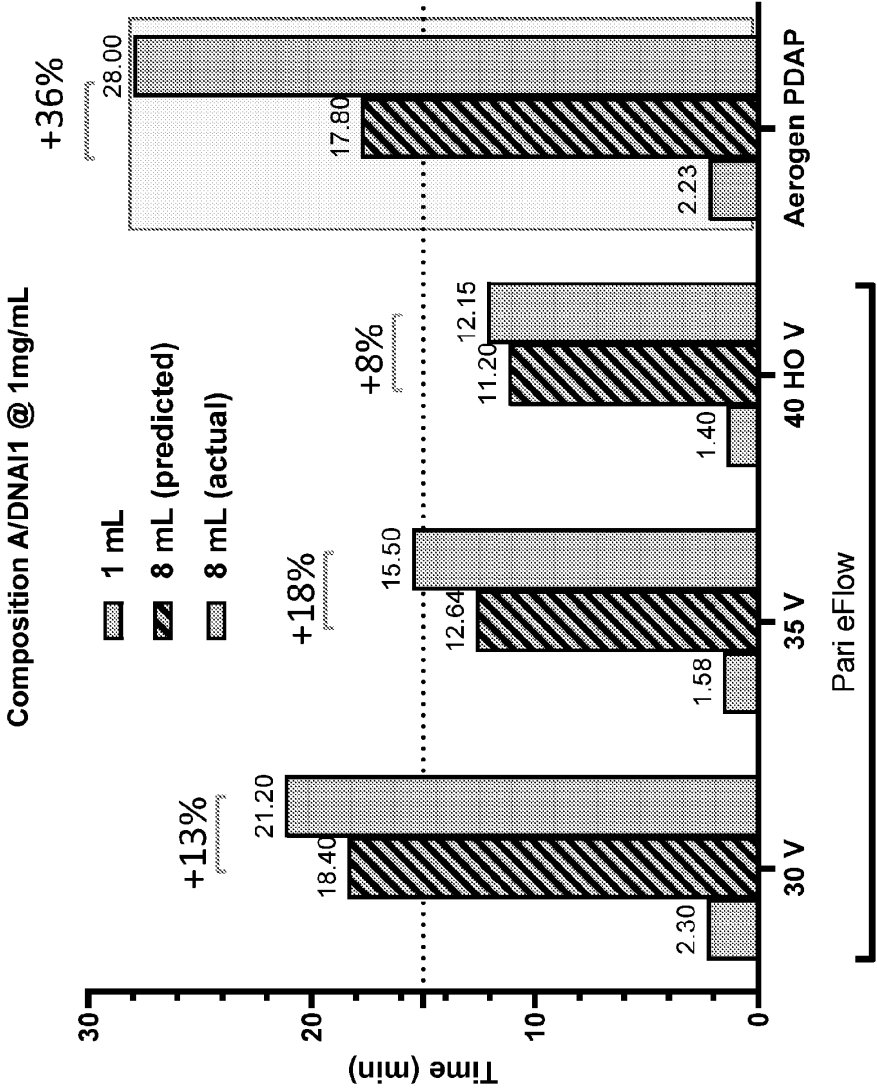


FIG. 4B

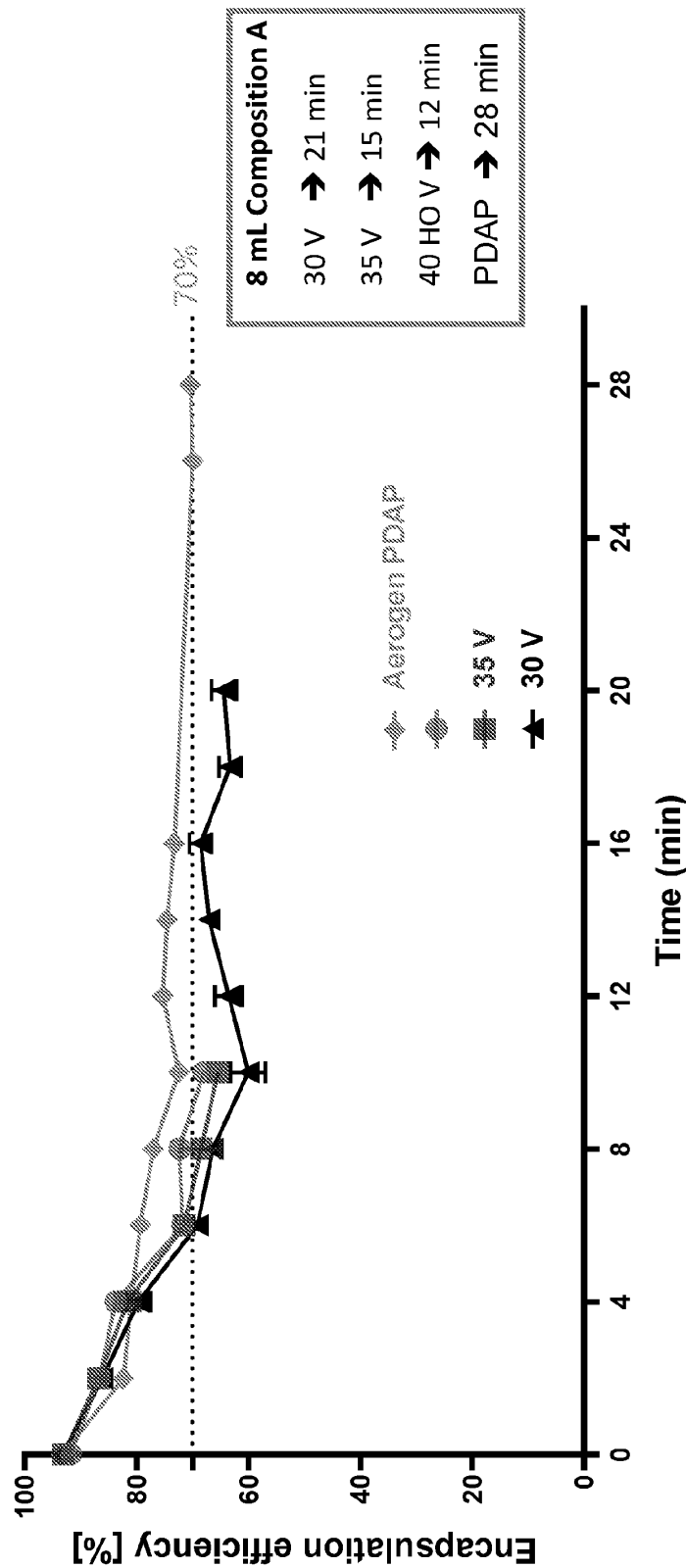


FIG. 5

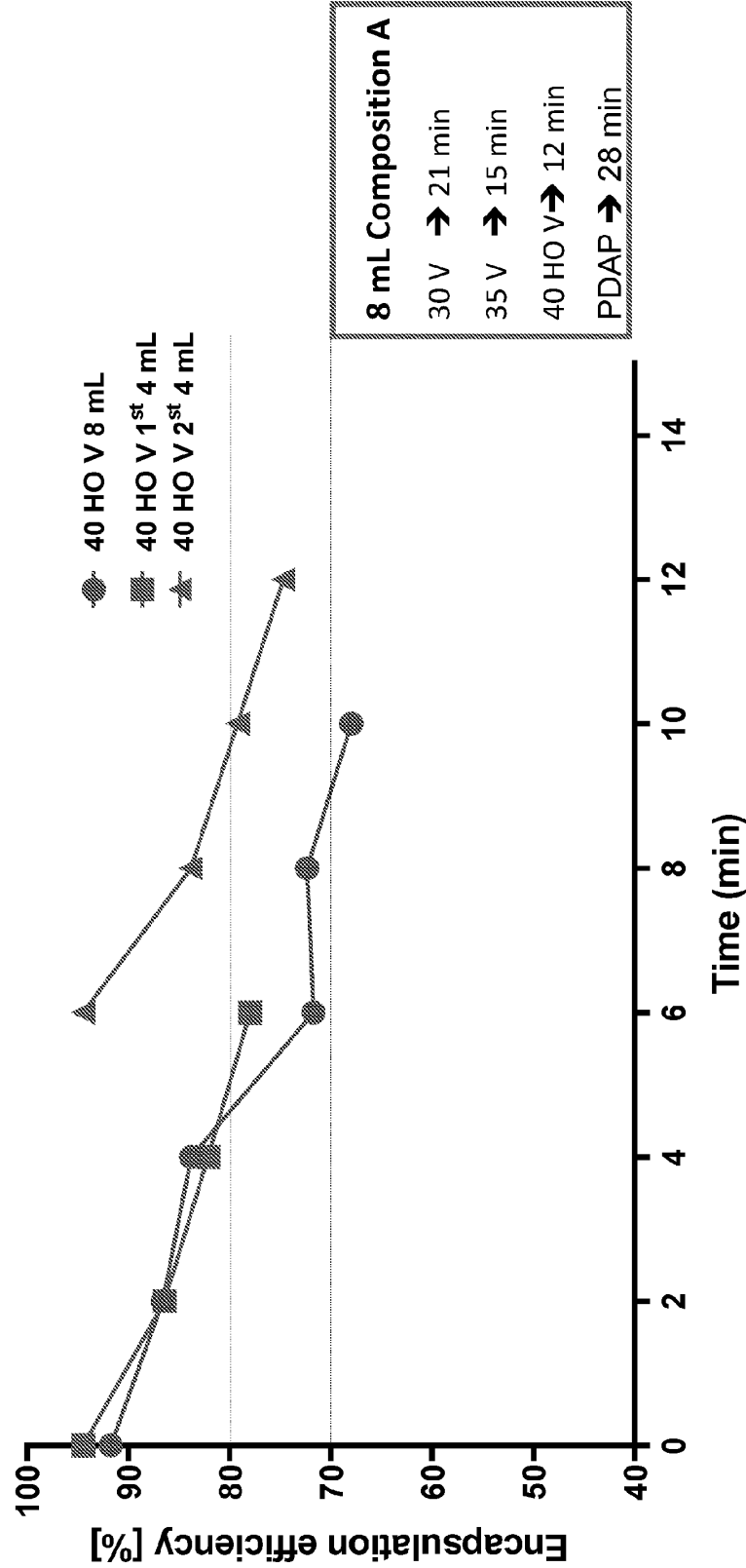


FIG. 6

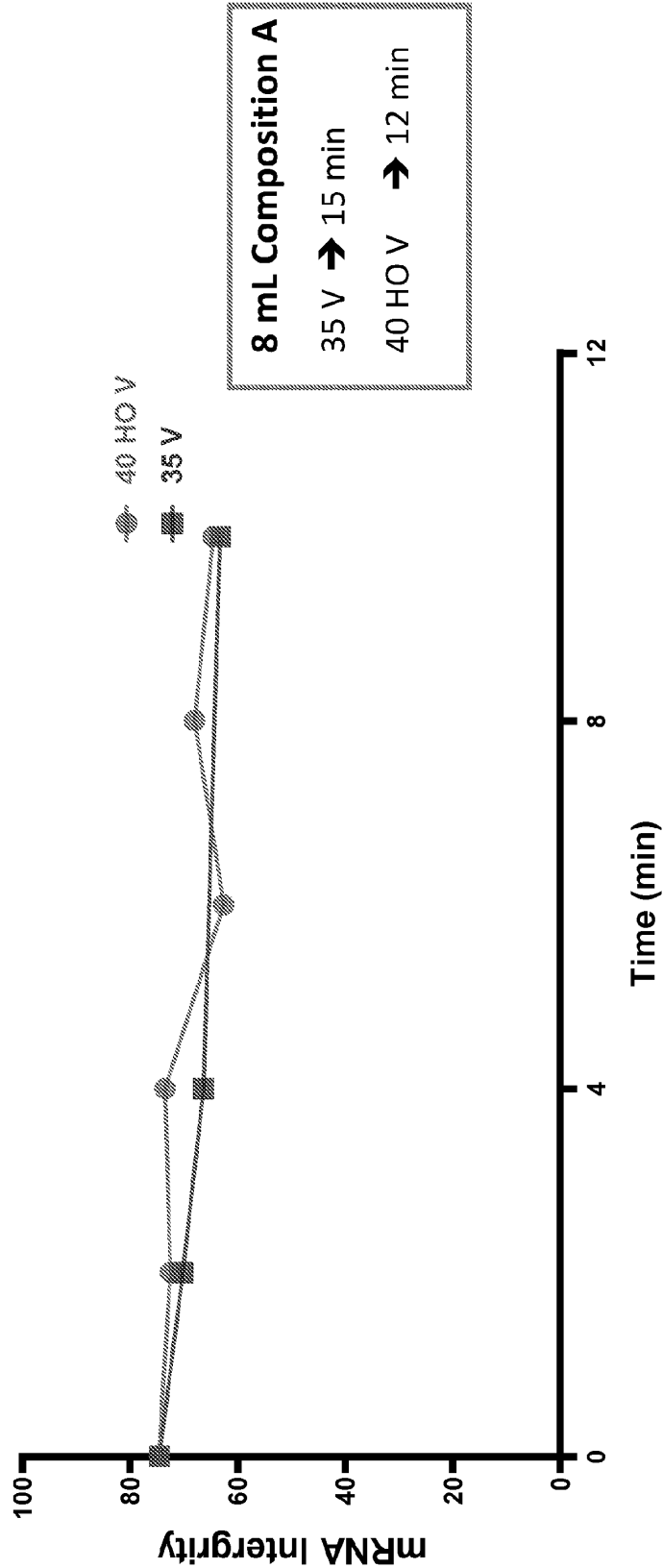


FIG. 7

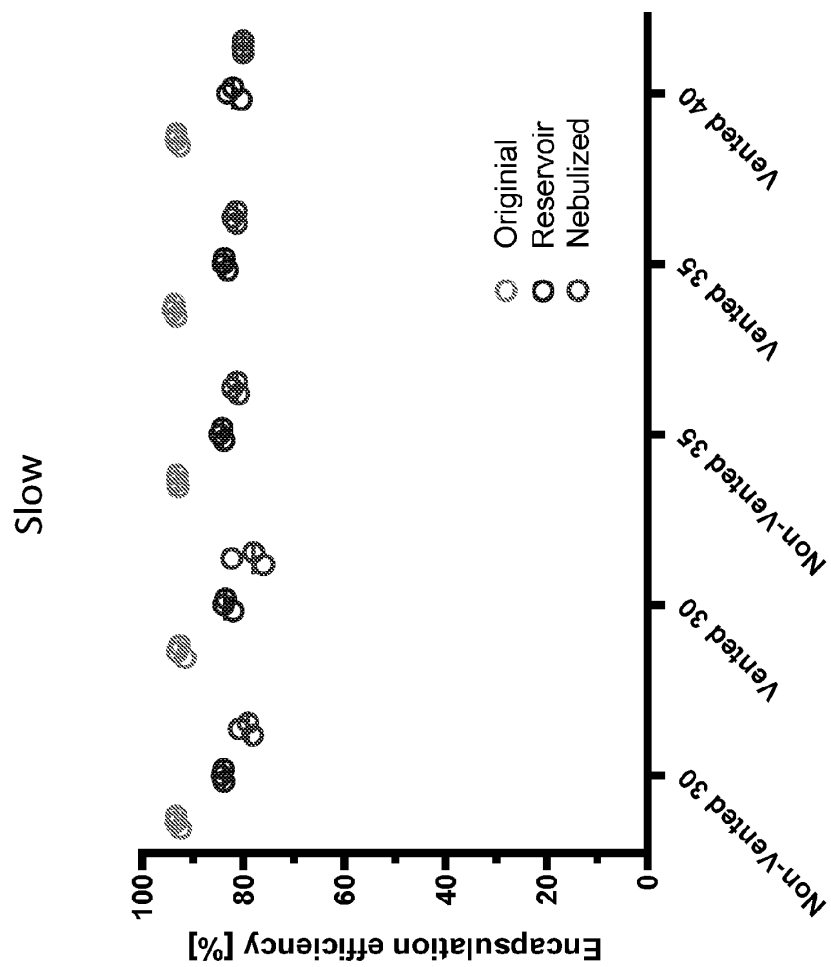


FIG. 8A

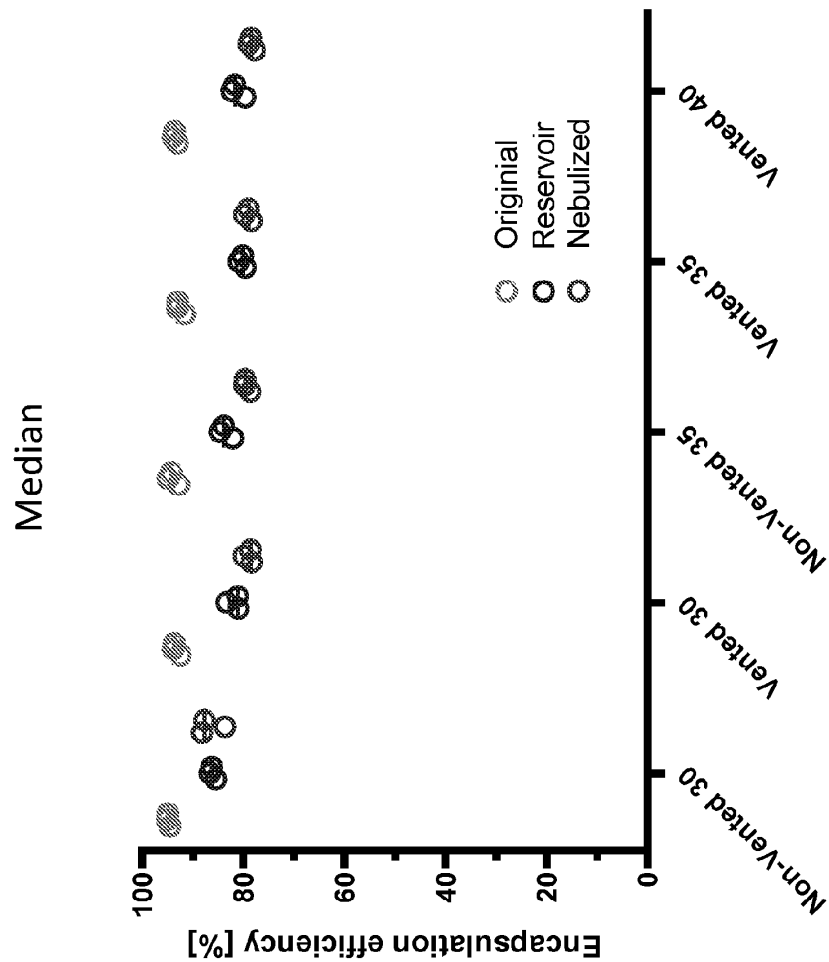


FIG. 8B

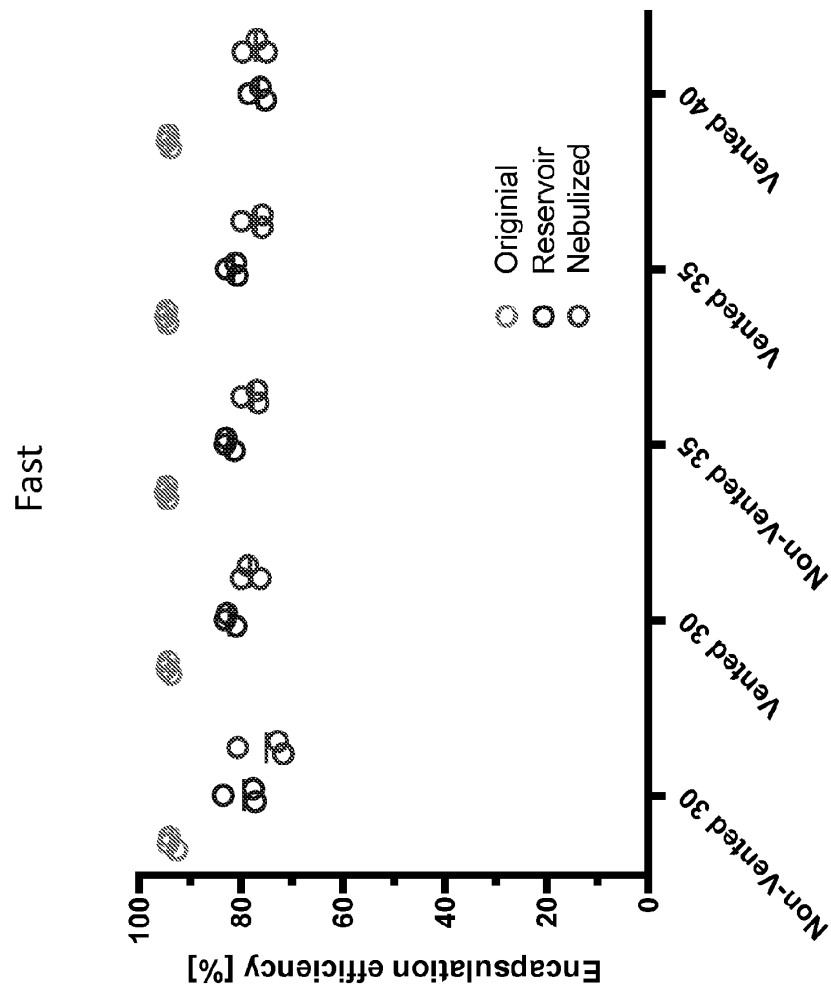


FIG. 8C

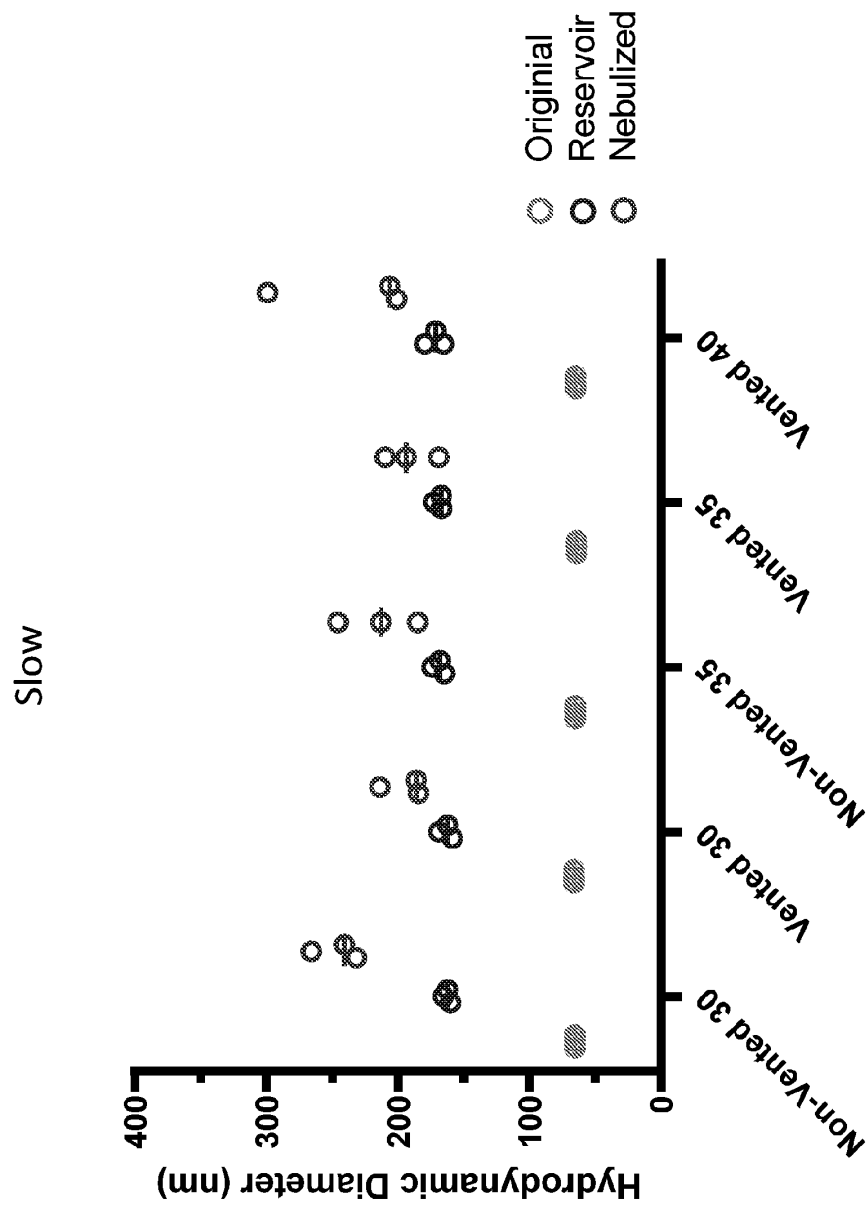


FIG. 9A

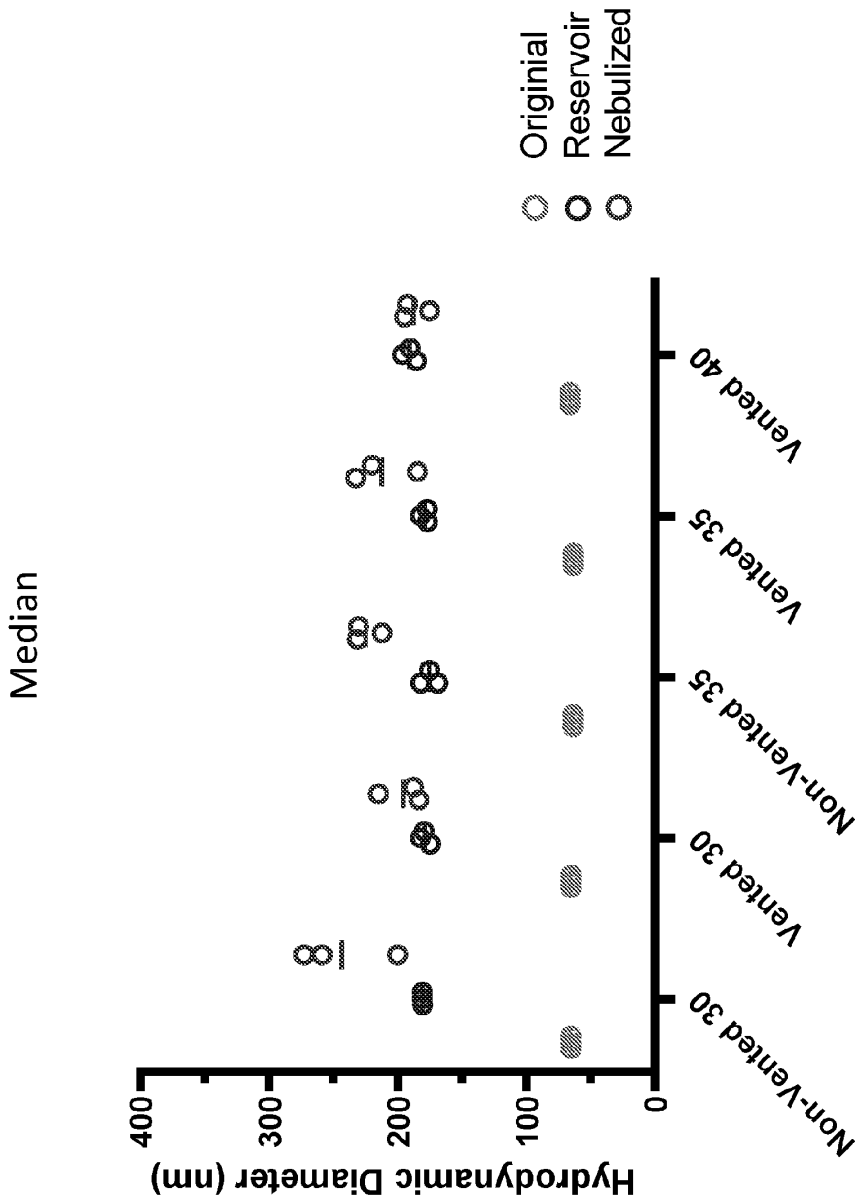


FIG. 9B

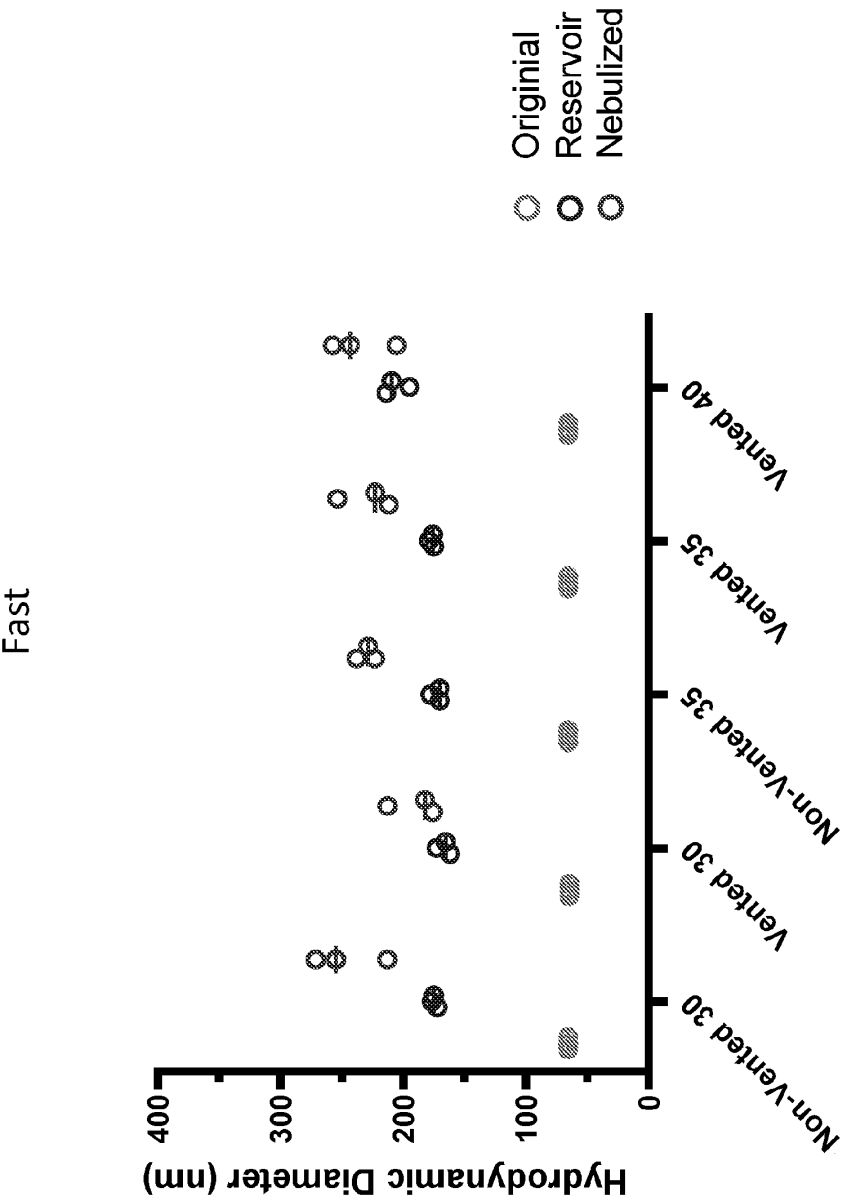


FIG. 9C

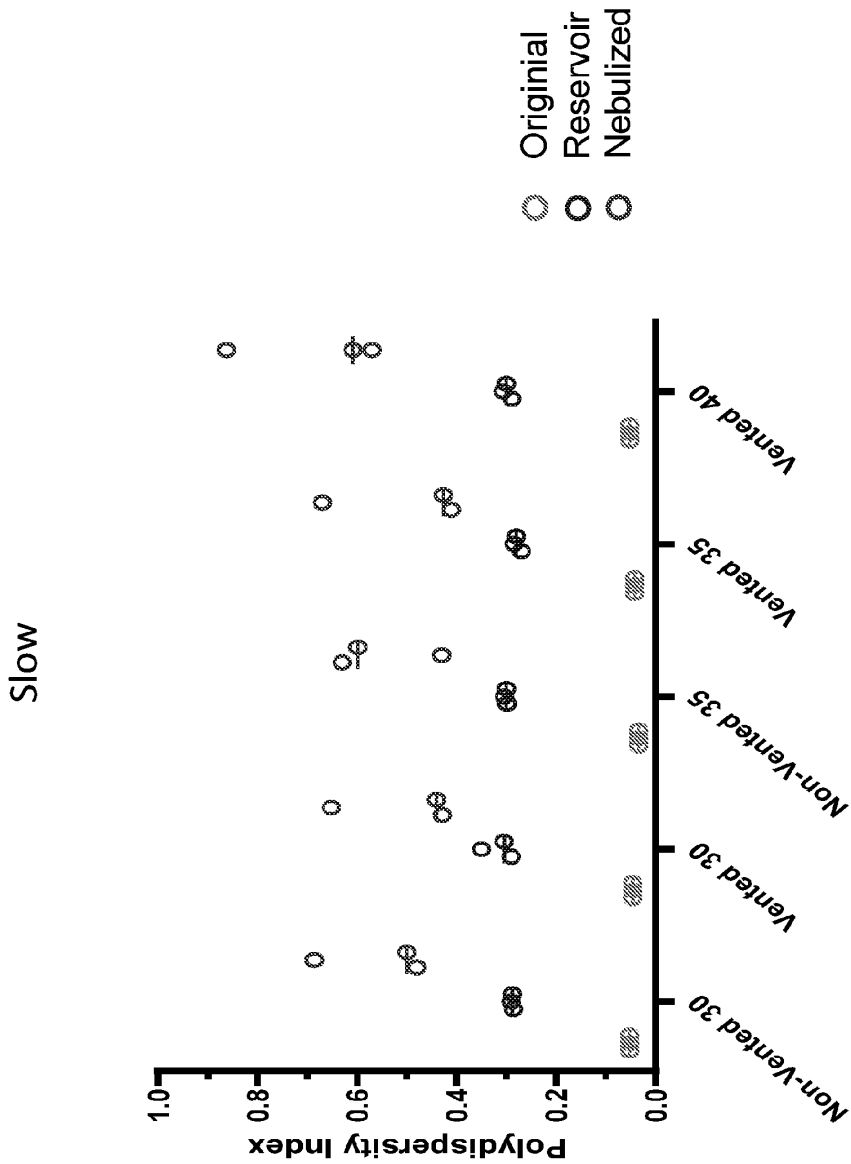


FIG. 10A

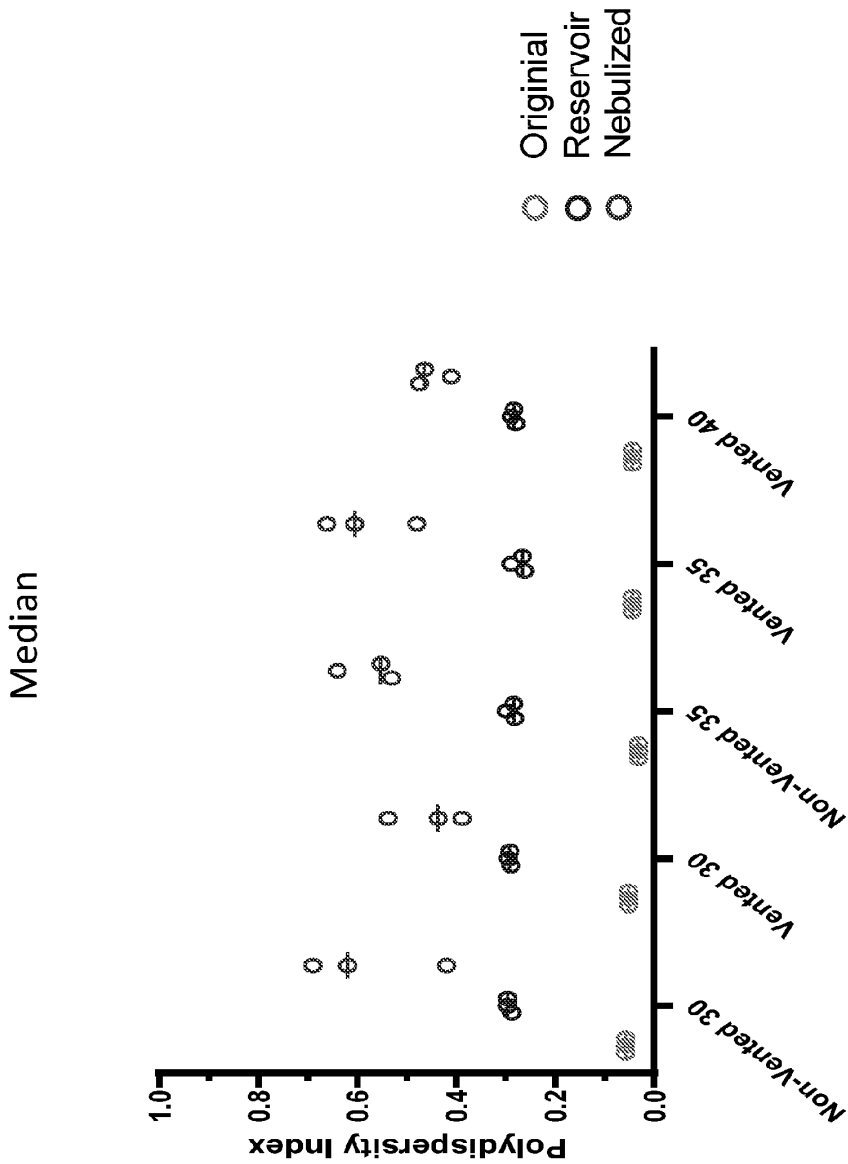


FIG. 10B

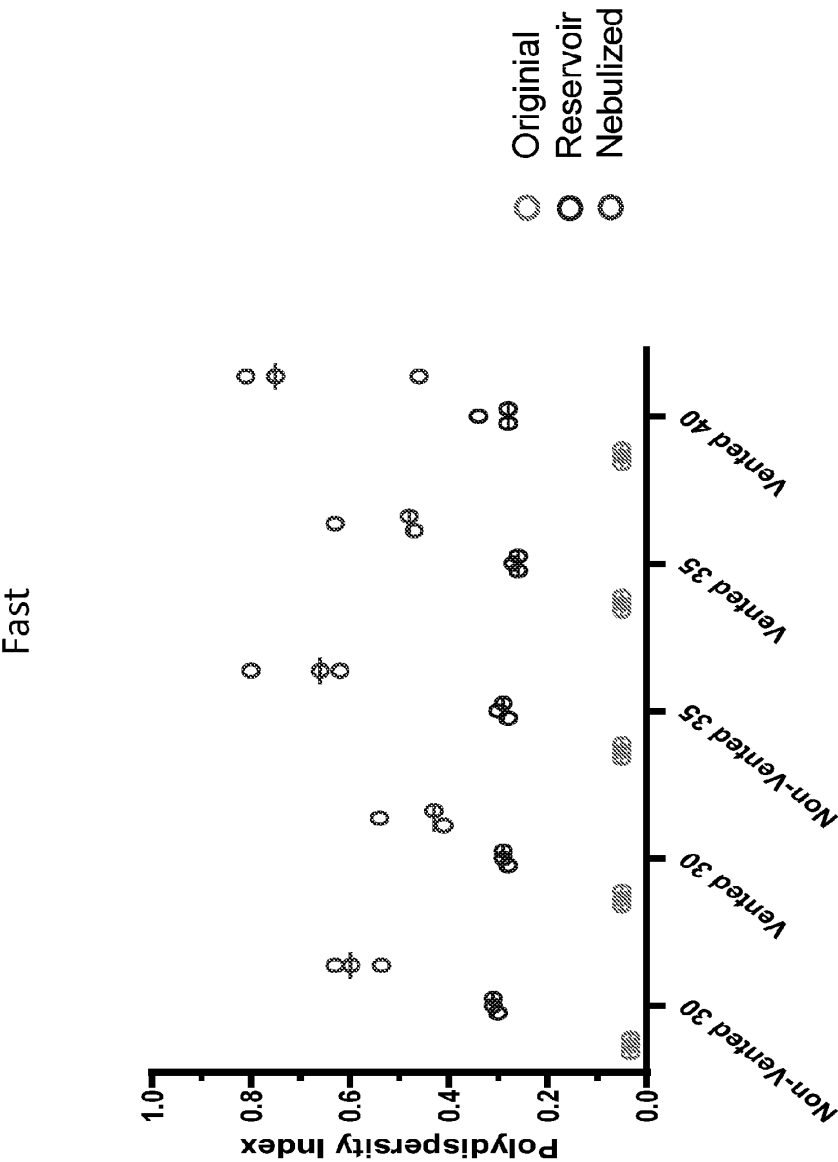


FIG. 10C

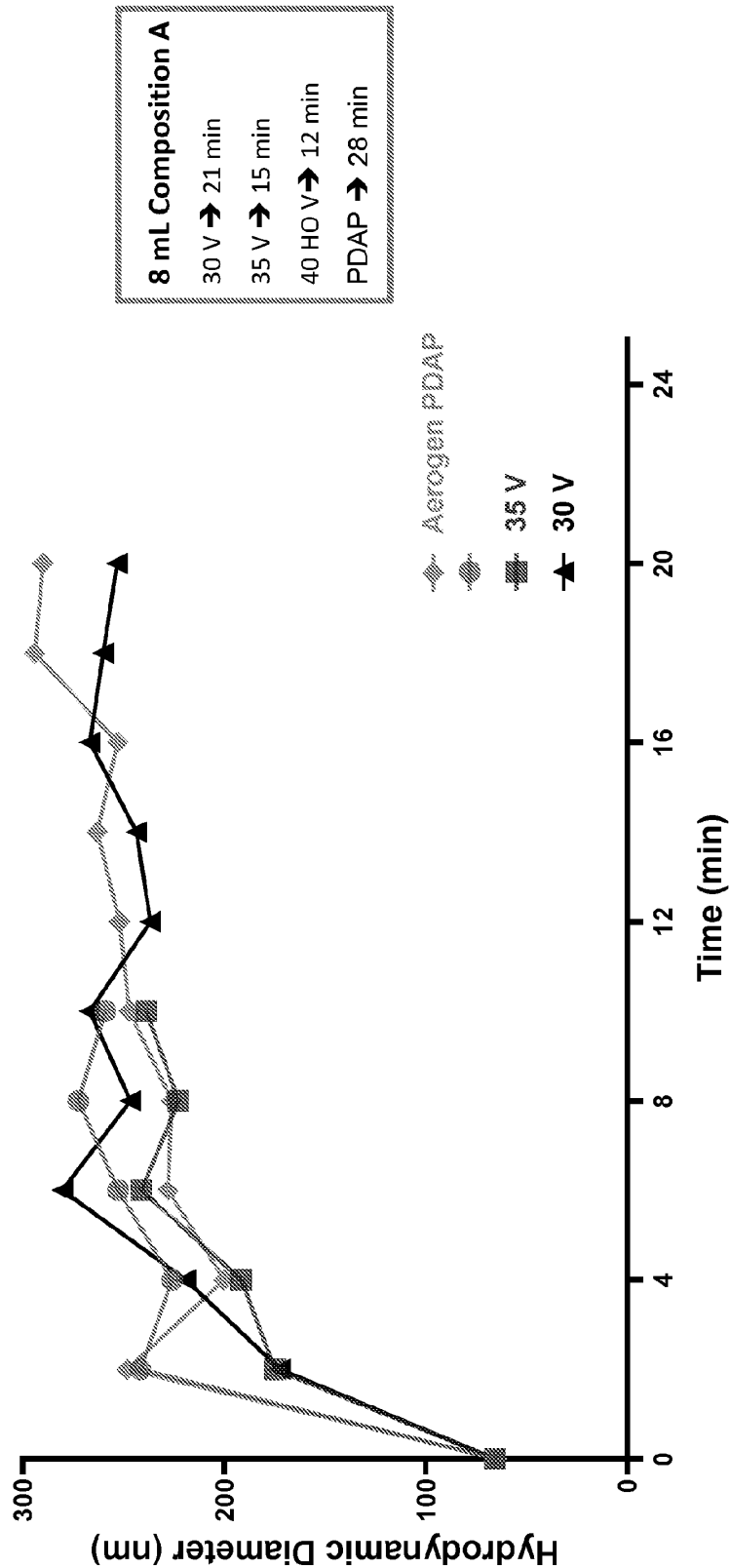


FIG. 11

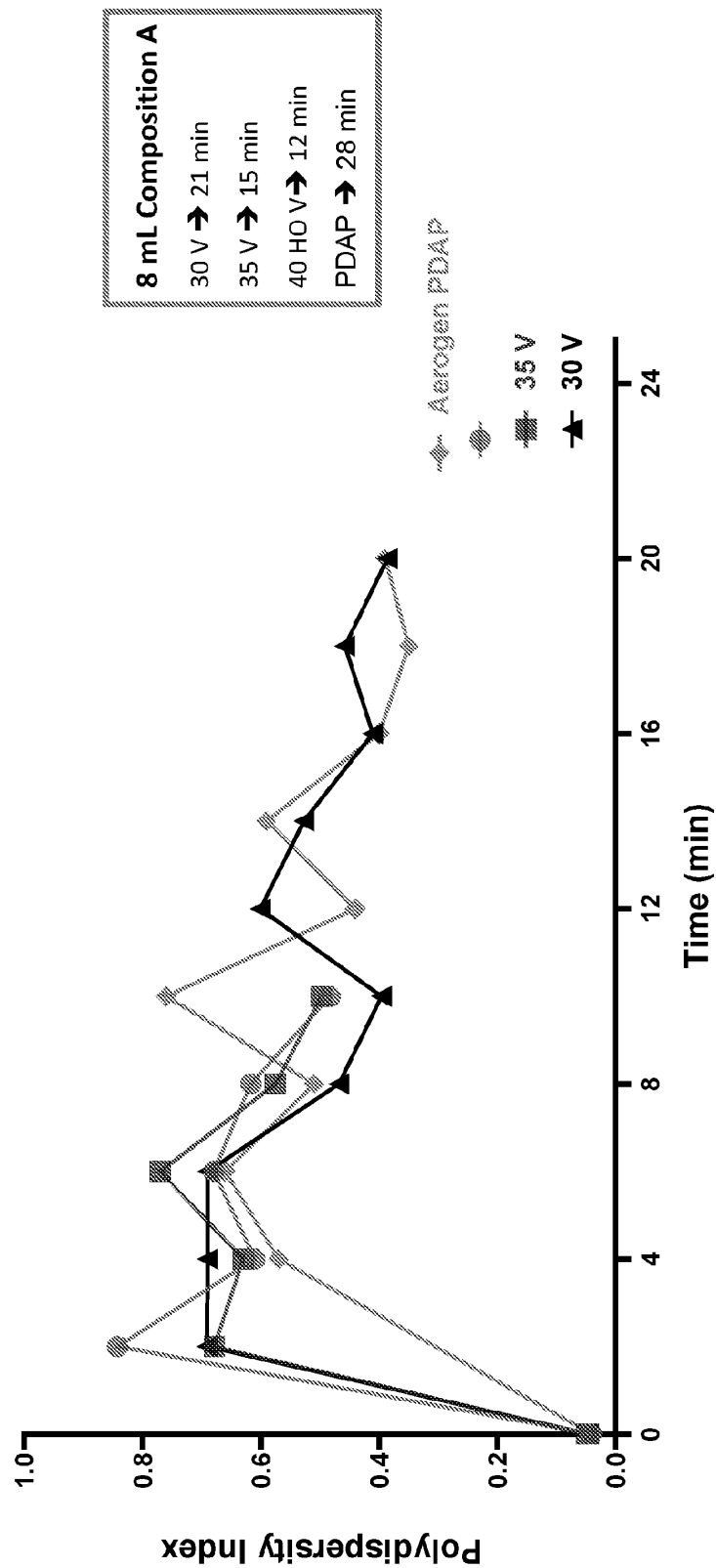


FIG. 12

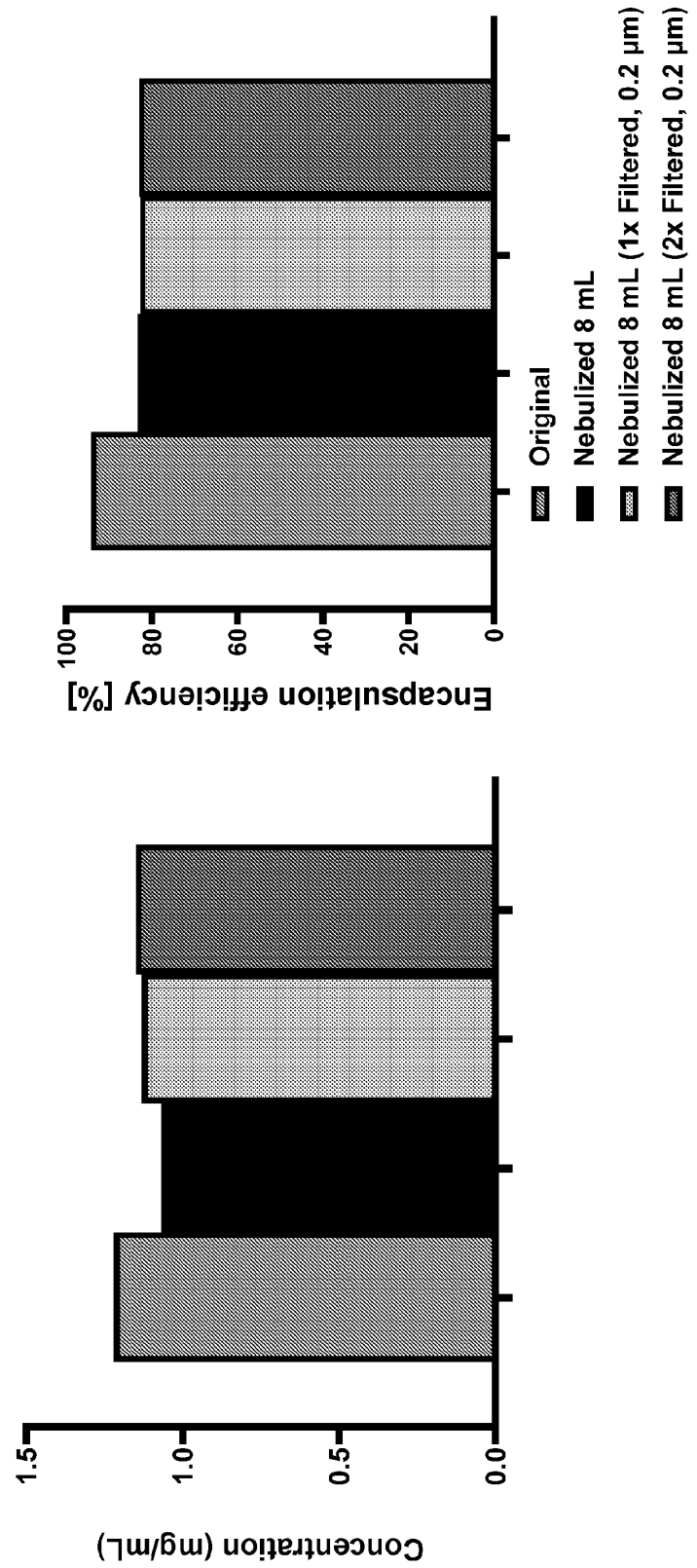


FIG. 13A

FIG. 13B

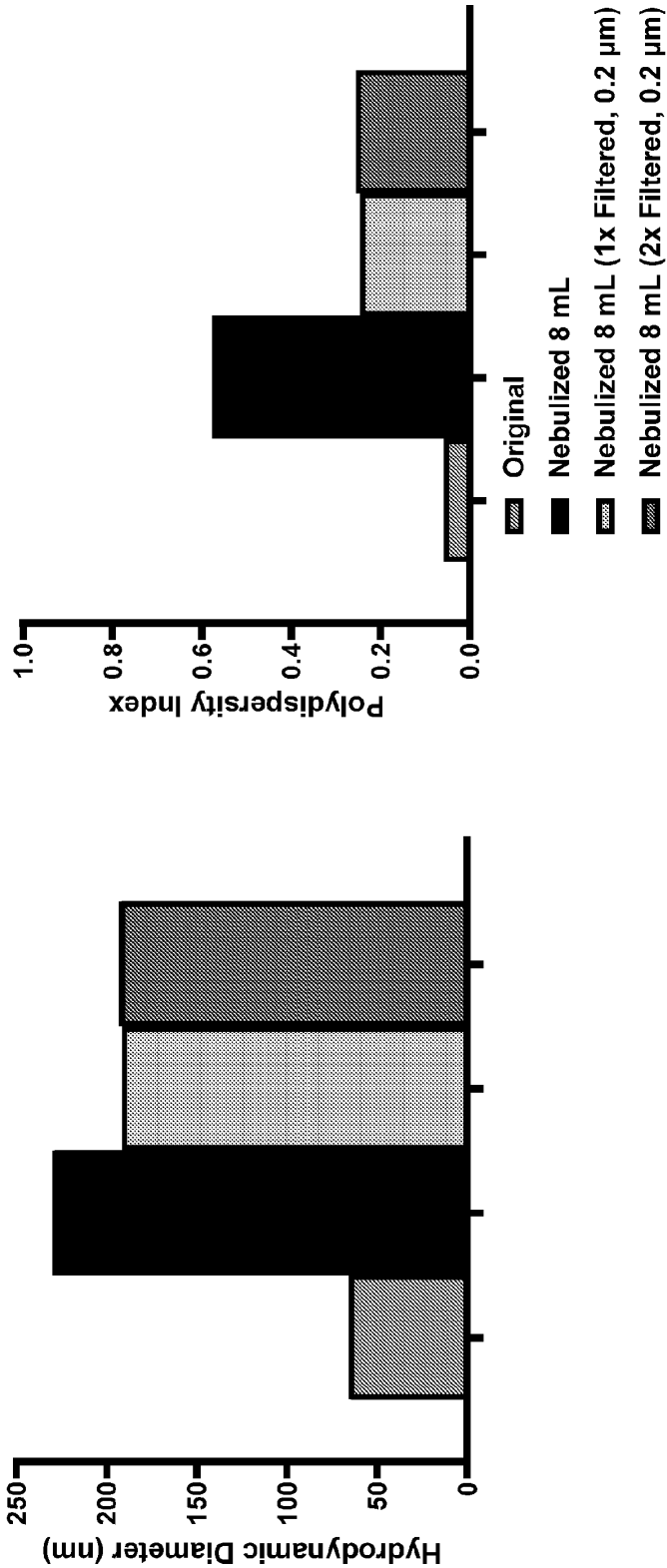


FIG. 13C

FIG. 13D

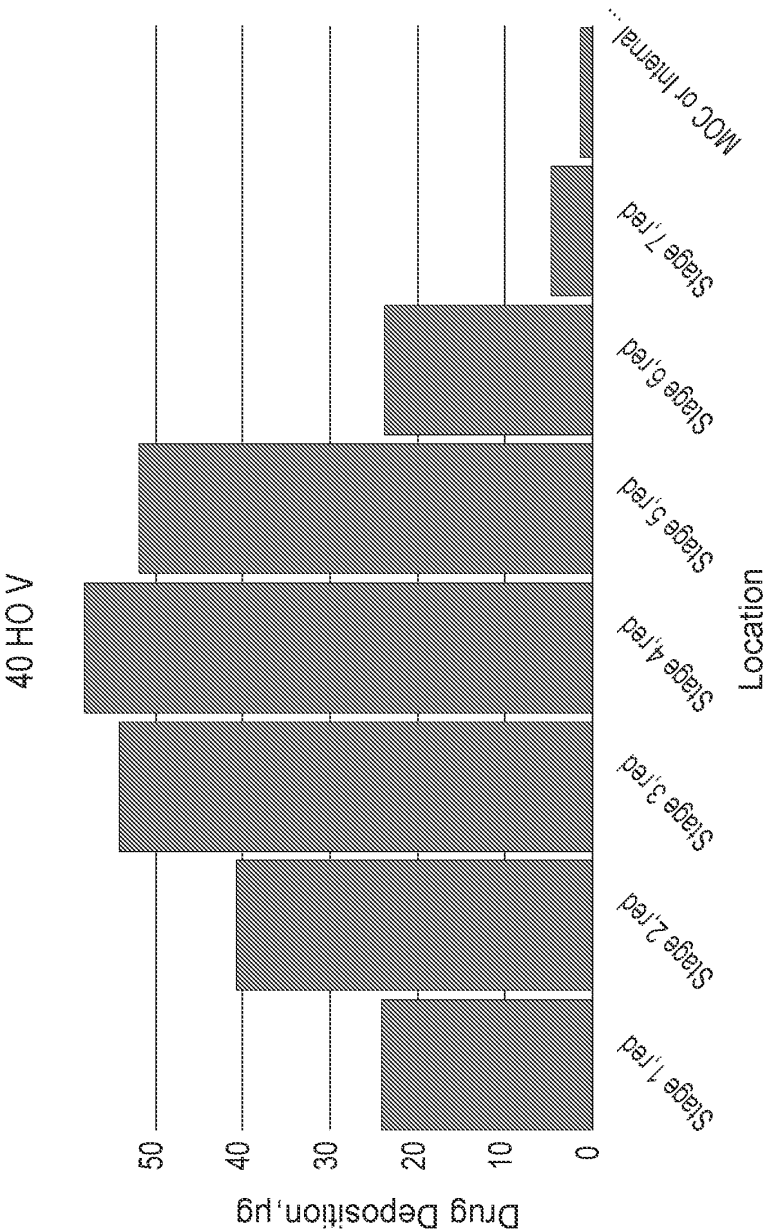


FIG. 14A

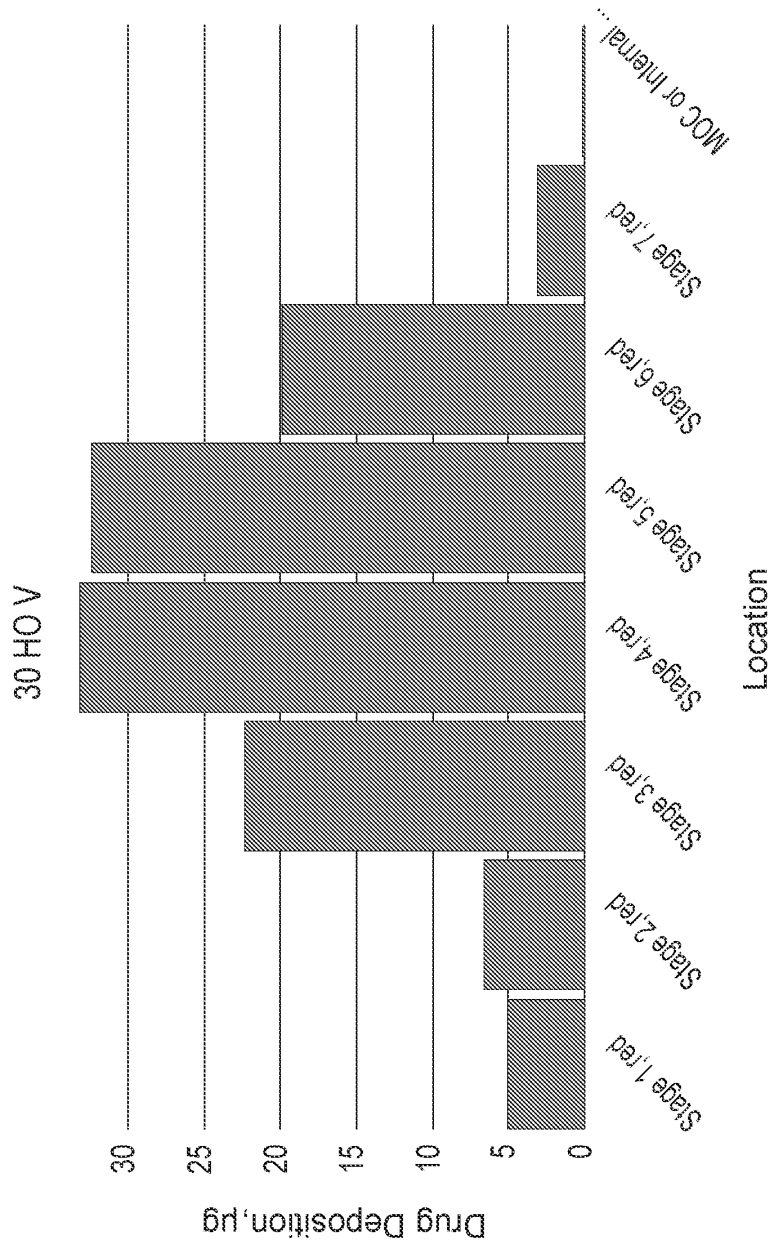
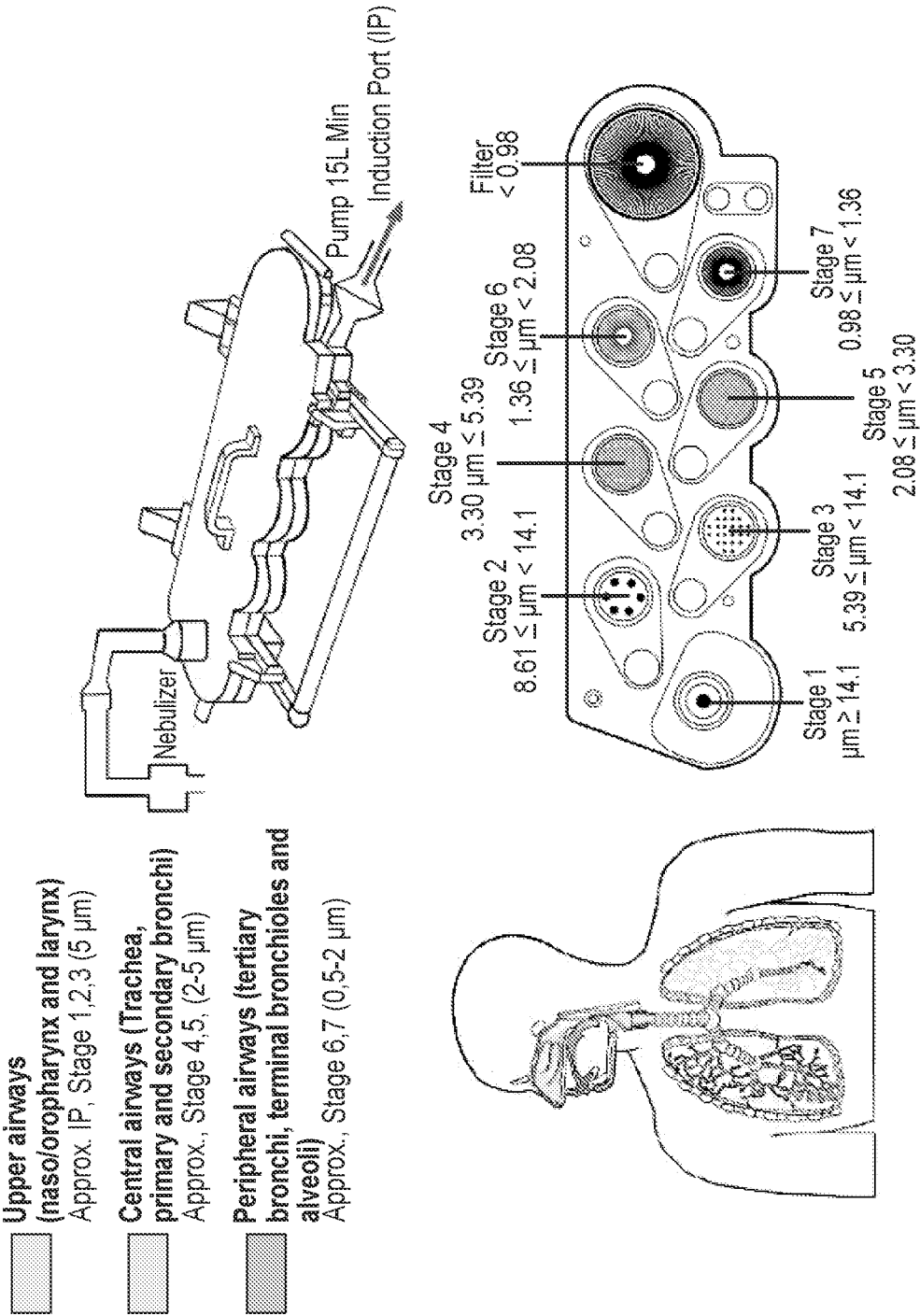


FIG. 14B



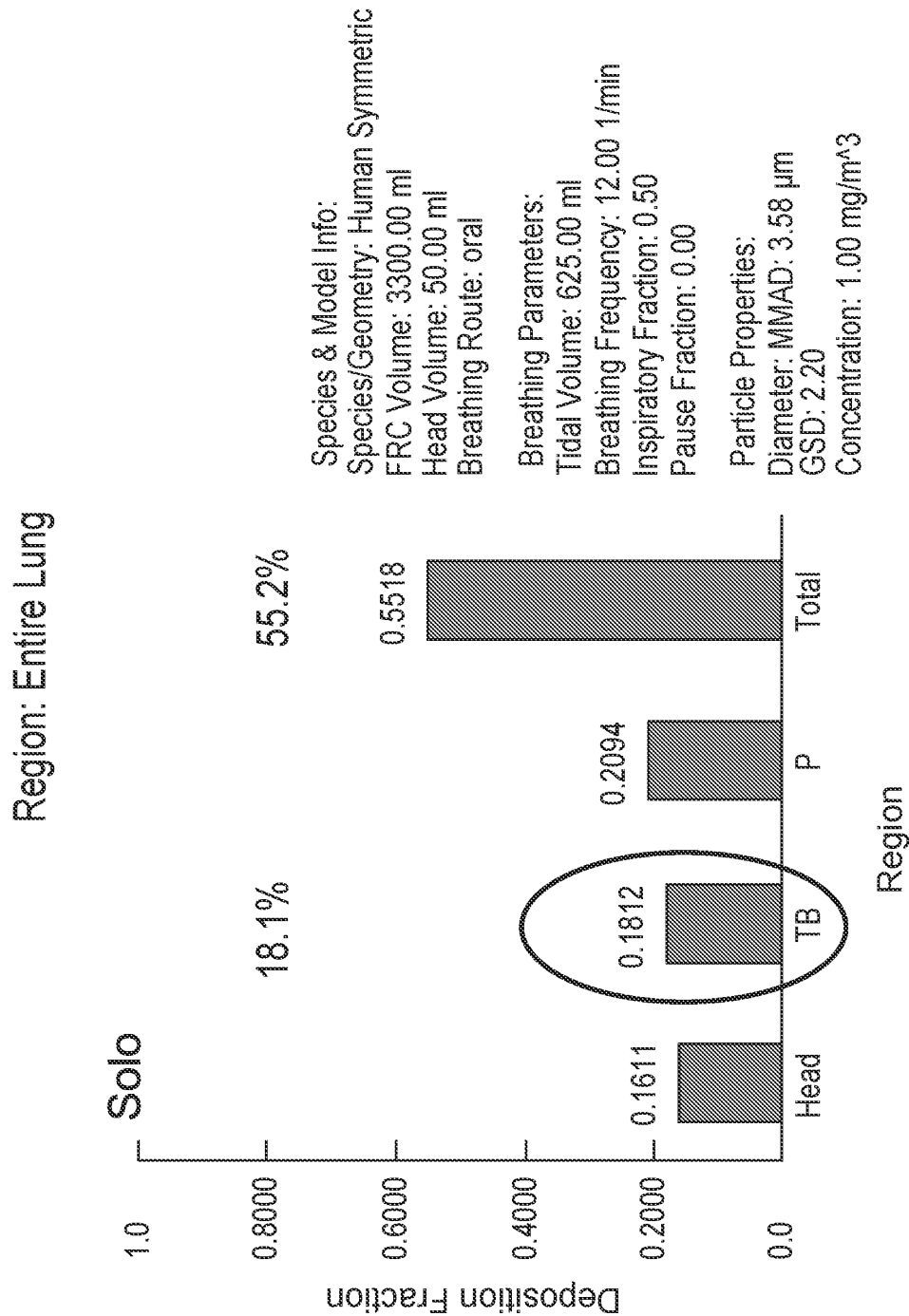


FIG. 15A

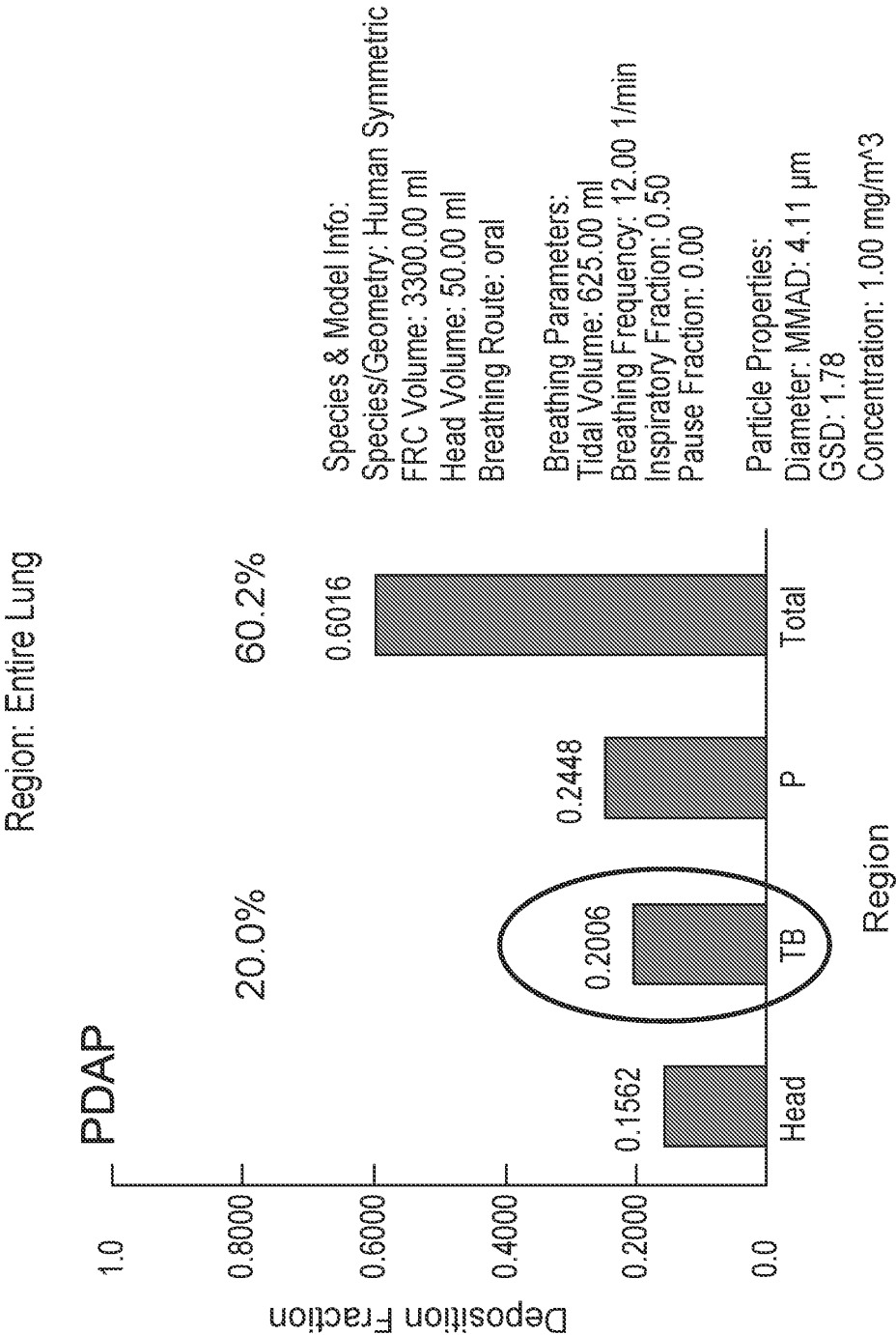


FIG. 15B



FIG. 16A

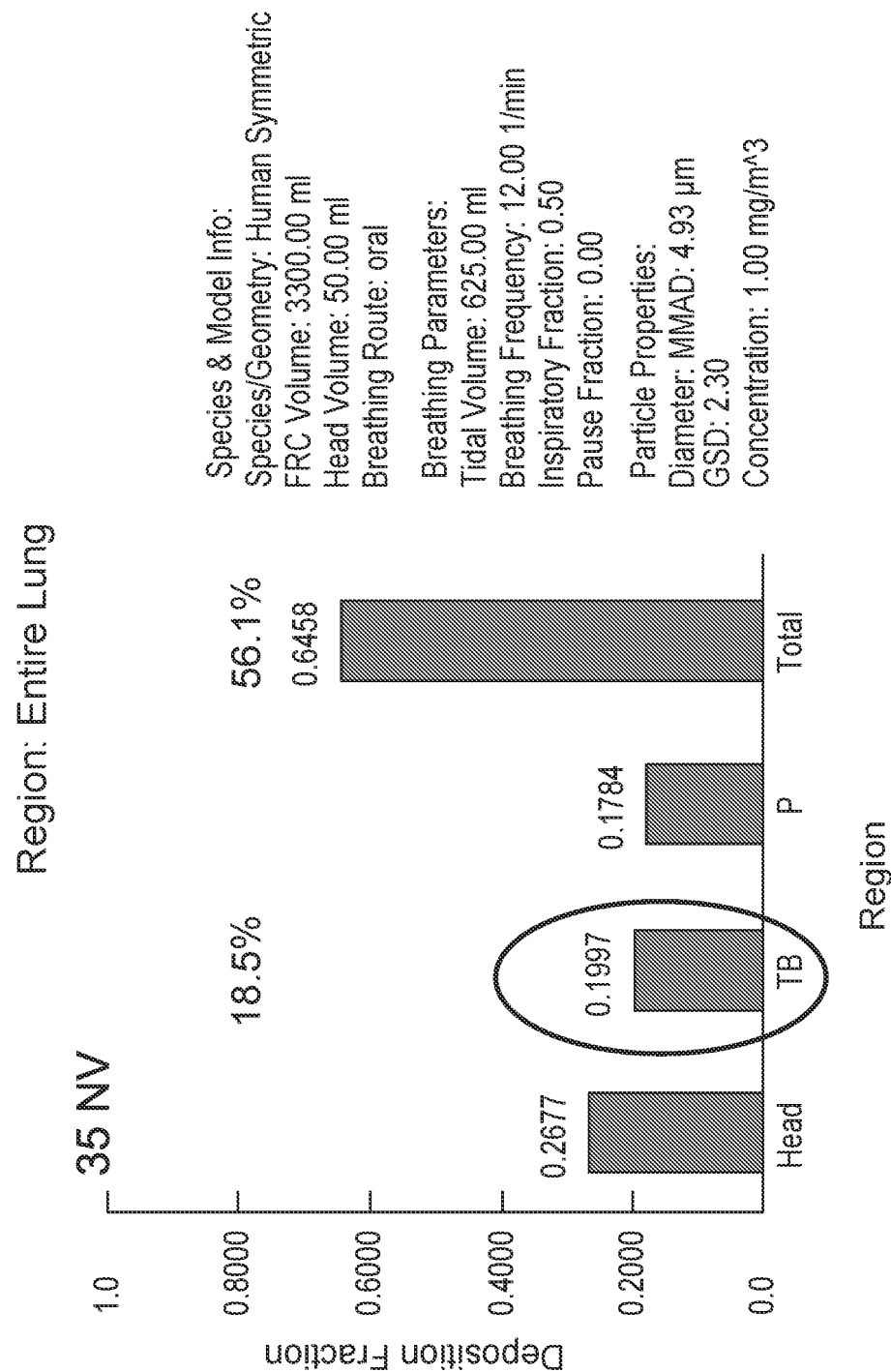


FIG. 16B

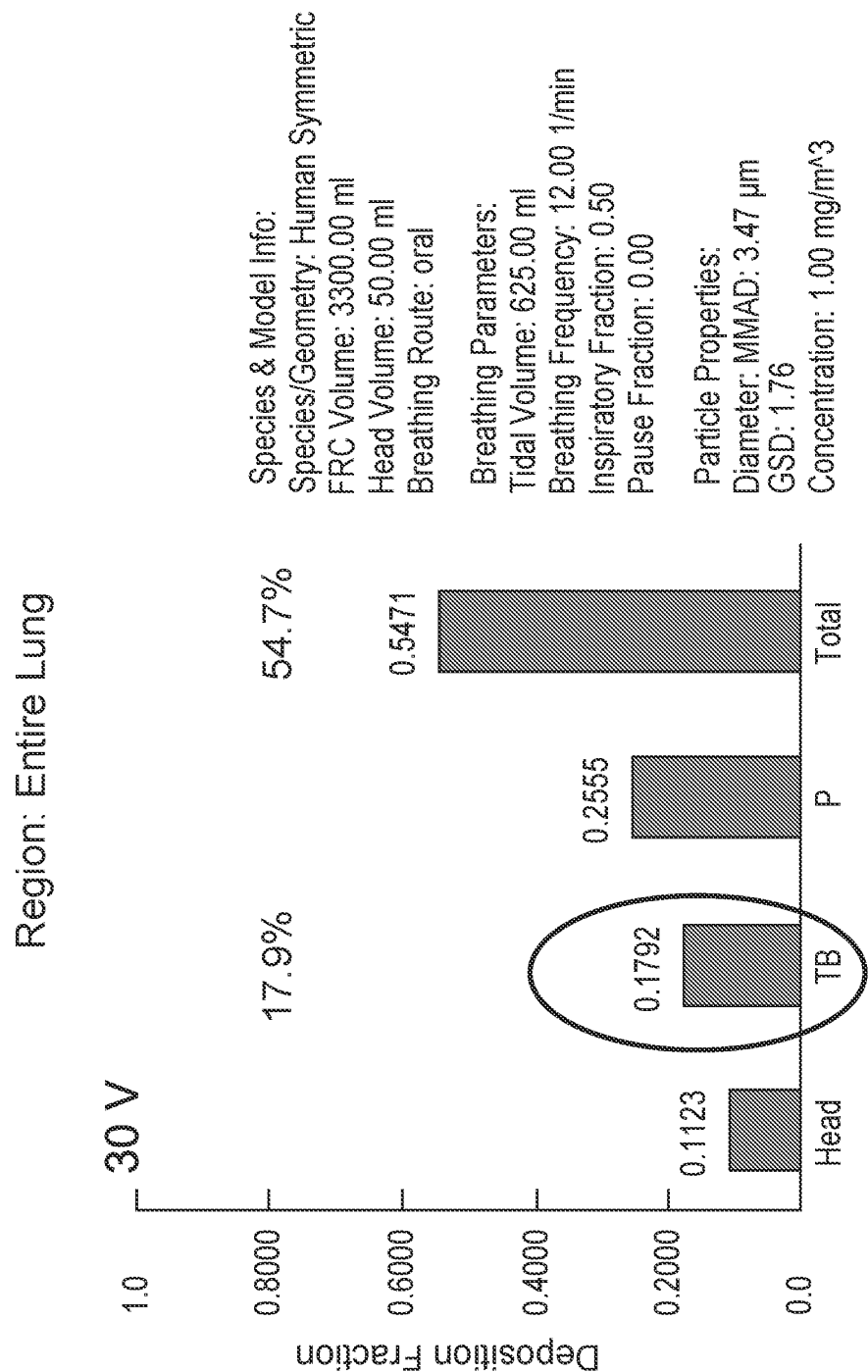


FIG. 16C

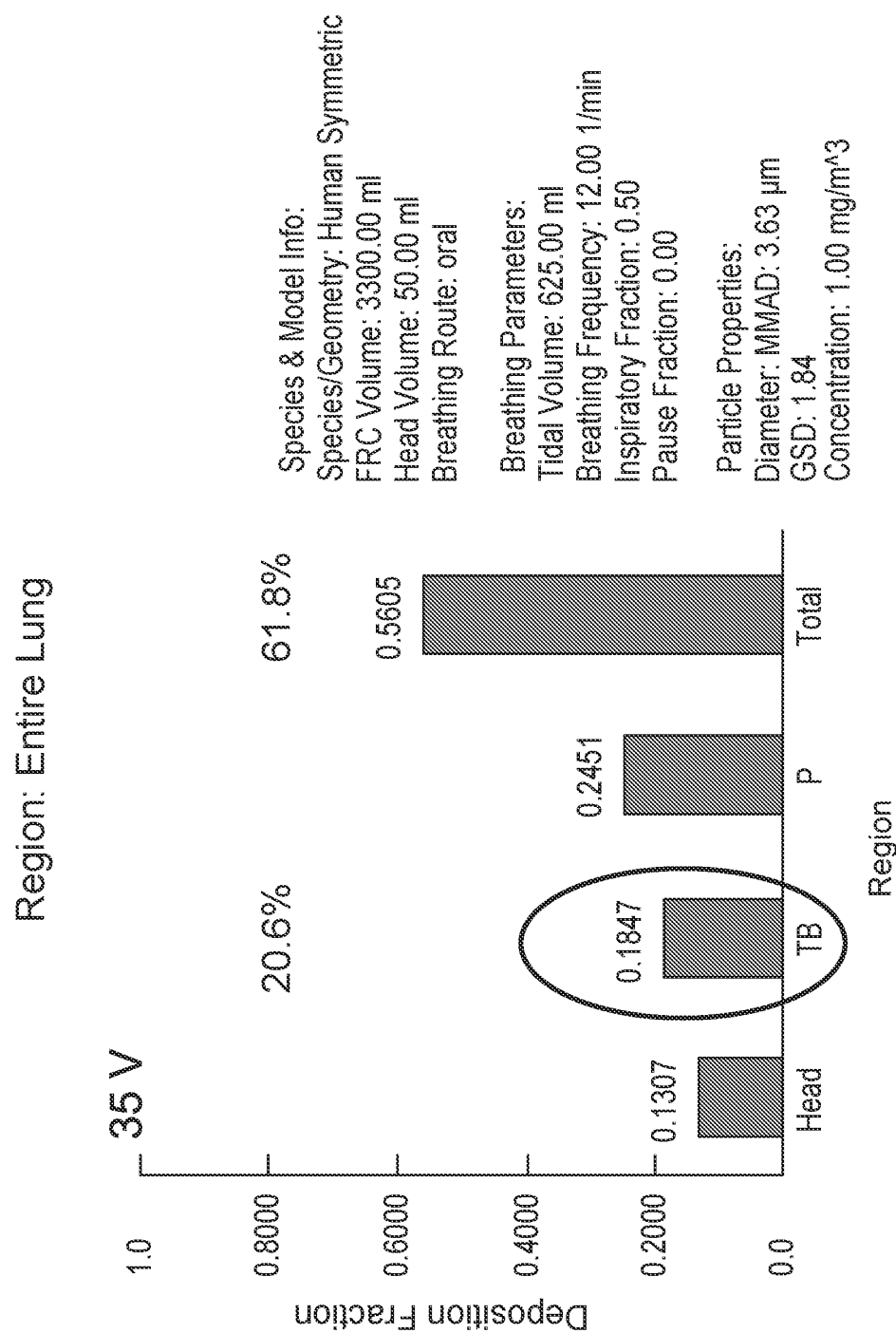


FIG. 16D

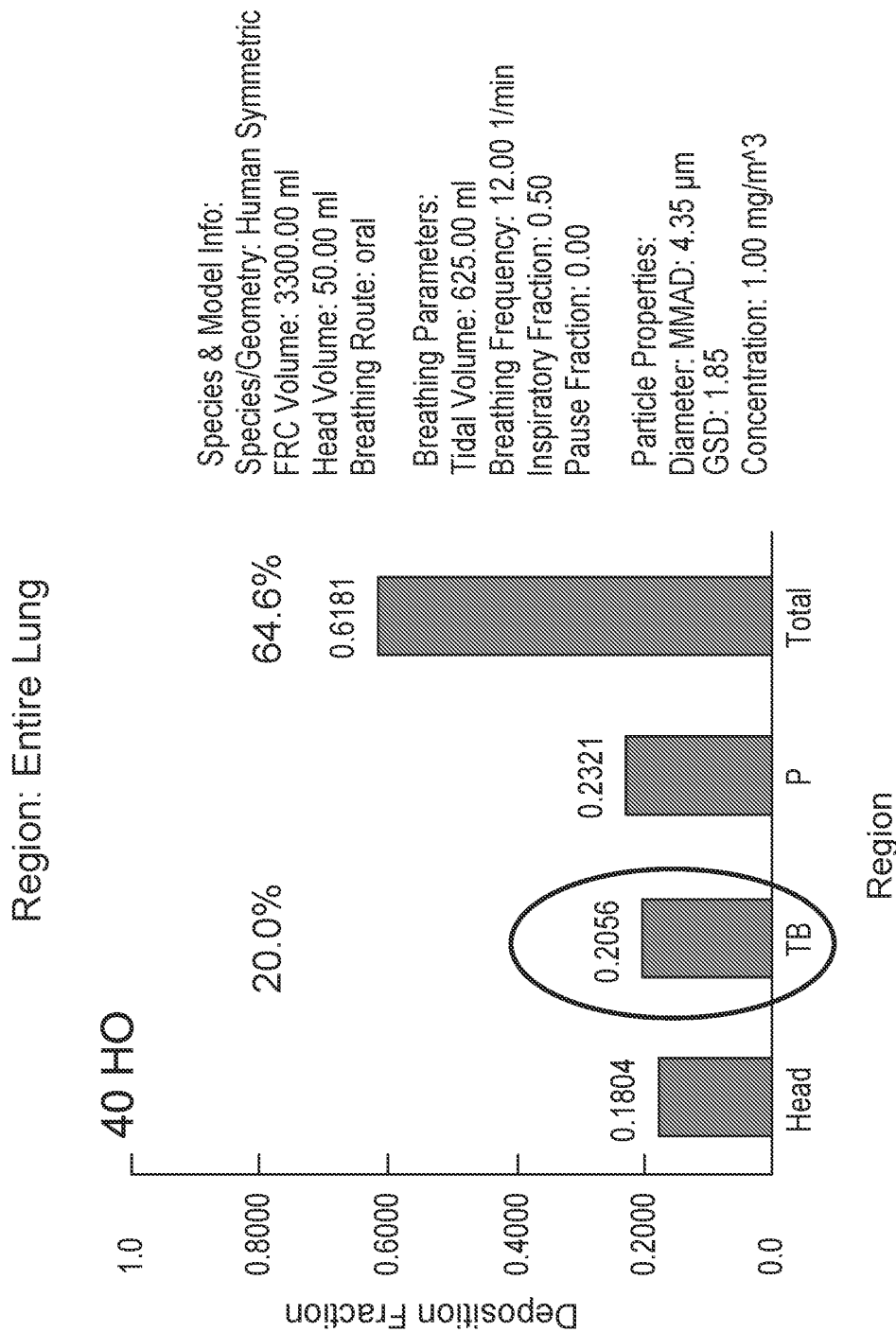


FIG. 16E

Percent recovery of lipids using different extraction solutions and volume

	Exp 1	Exp 2	Exp 3	Exp 4	Exp 5
Extraction solution	Water / Isopropanol (20:80 v/v)	Water / Isopropanol (40:60 v/v)	Water / Isopropanol (40:60 v/v)	Water / Isopropanol (40:60 v/v)	50 mM ammonium acetate / Isopropanol (40:60 v/v)
Extraction volume	4 mL	4 mL	8 mL	8 mL	8 mL
Extraction time	30 min	30 min	30 min	60 min	60 min
14:0 EPC	65.52 ± 0.32	72.84 ± 1.39	83.08 ± 1.80	88.41 ± 1.05	94.65 ± 2.38
4A3-SC7	85.52 ± 0.92	93.31 ± 2.97	102.51 ± 0.37	102.93 ± 0.59	95.74 ± 3.52
Cholesterol	90.71 ± 2.37	95.64 ± 2.01	102.34 ± 1.47	103.51 ± 1.20	95.78 ± 1.16
DMG-PEG2k	84.46 ± 3.15	90.45 ± 1.72	101.89 ± 0.58	103.37 ± 1.52	96.47 ± 1.27
DOPE	90.23 ± 3.30	95.96 ± 1.67	102.07 ± 0.88	104.71 ± 2.90	97.59 ± 1.43

FIG. 17A

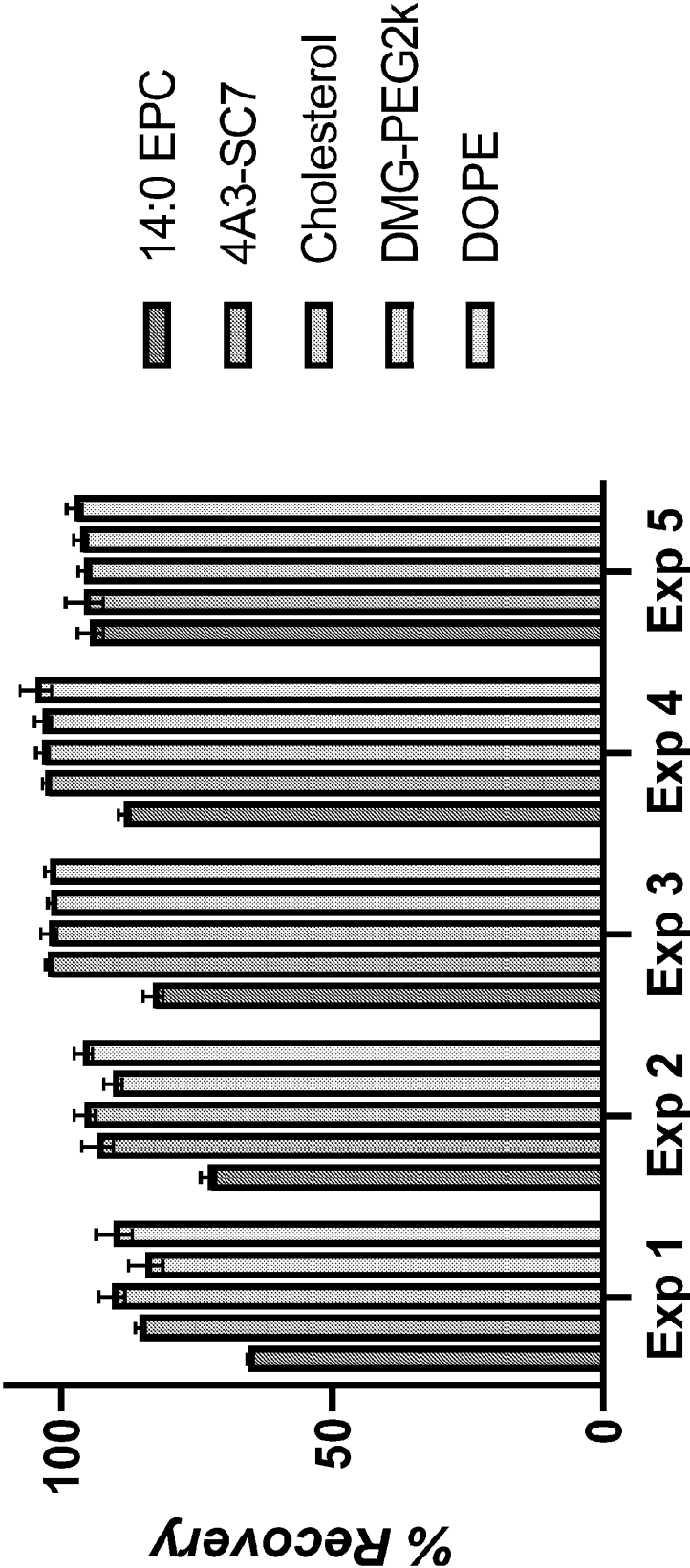


FIG. 17B

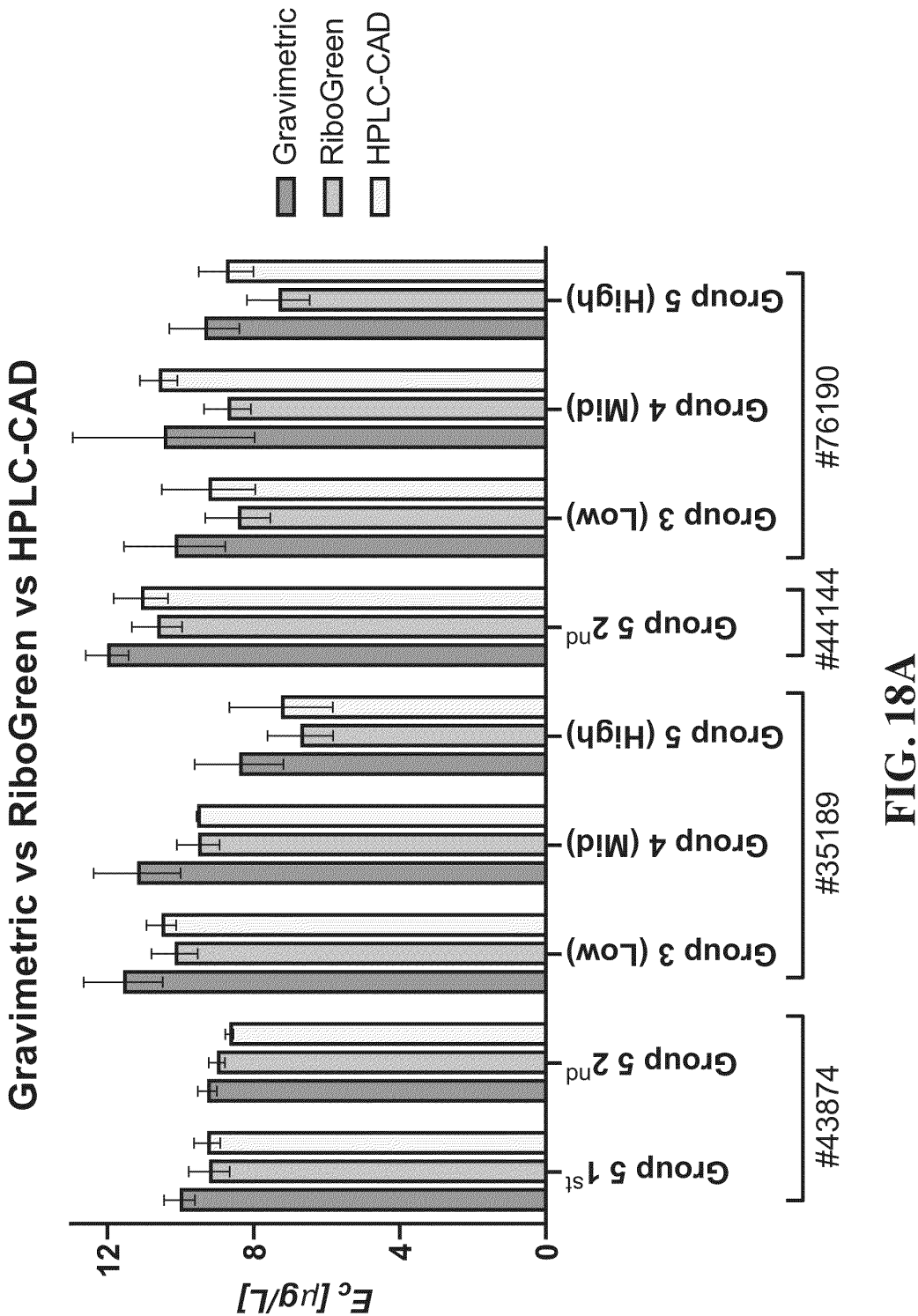


FIG. 18A

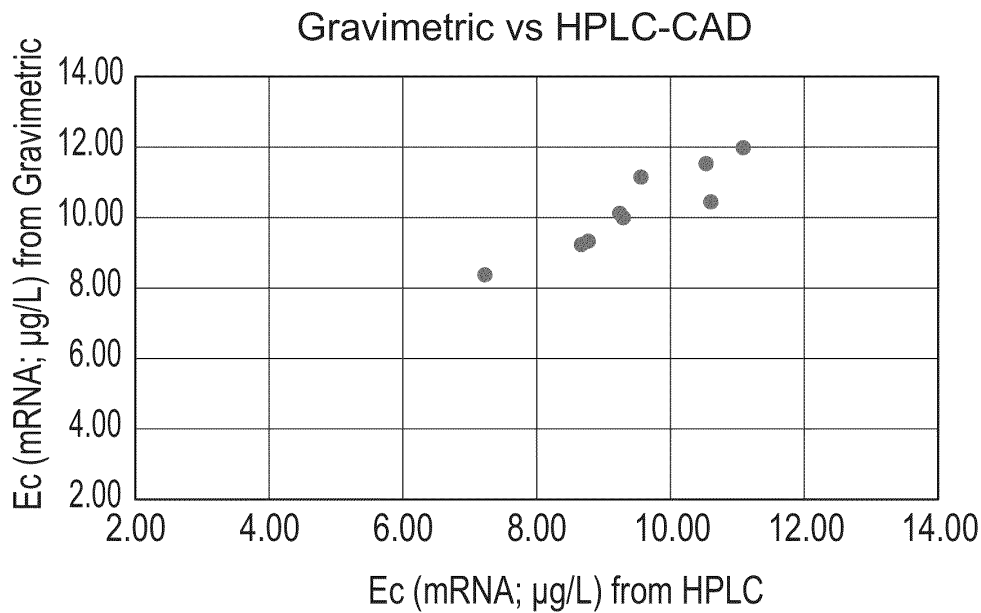


FIG. 18B

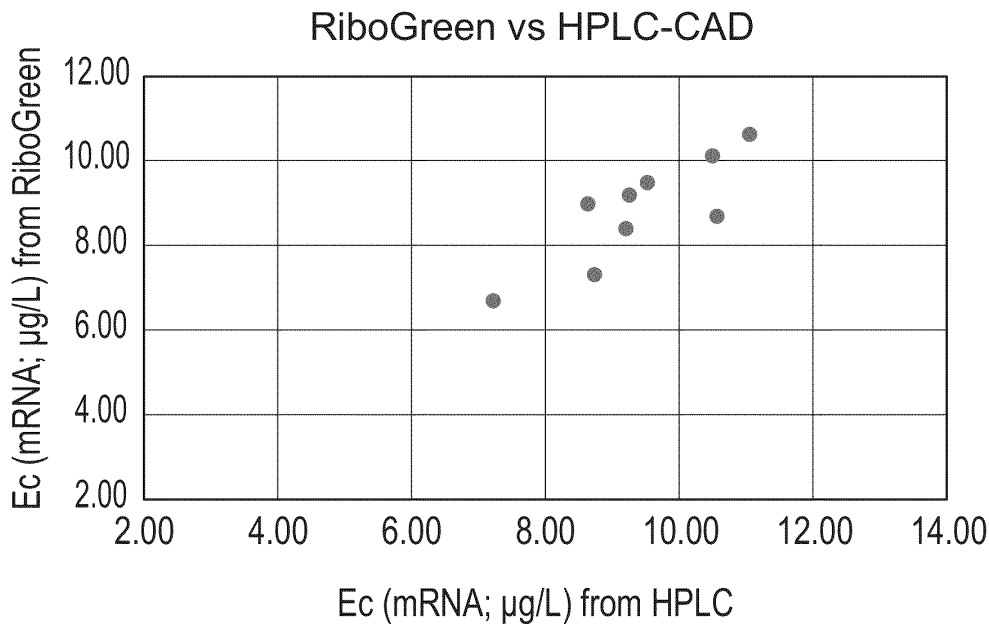


FIG. 18C



FIG. 19A



FIG. 19B

Storage Condition	Exp 6		Exp 7	
	4 °C for 24 hours		-80 °C for 24 hours	
14:0 EPC	95.77 ± 3.25		97.22 ± 0.90	
4A3-SC7	94.59 ± 1.63		97.05 ± 2.27	
Cholesterol	96.21 ± 1.54		96.04 ± 1.65	
DMG-PEG2k	96.24 ± 1.08		96.78 ± 2.64	
DOPE	94.68 ± 1.16		94.69 ± 1.87	

FIG. 20A

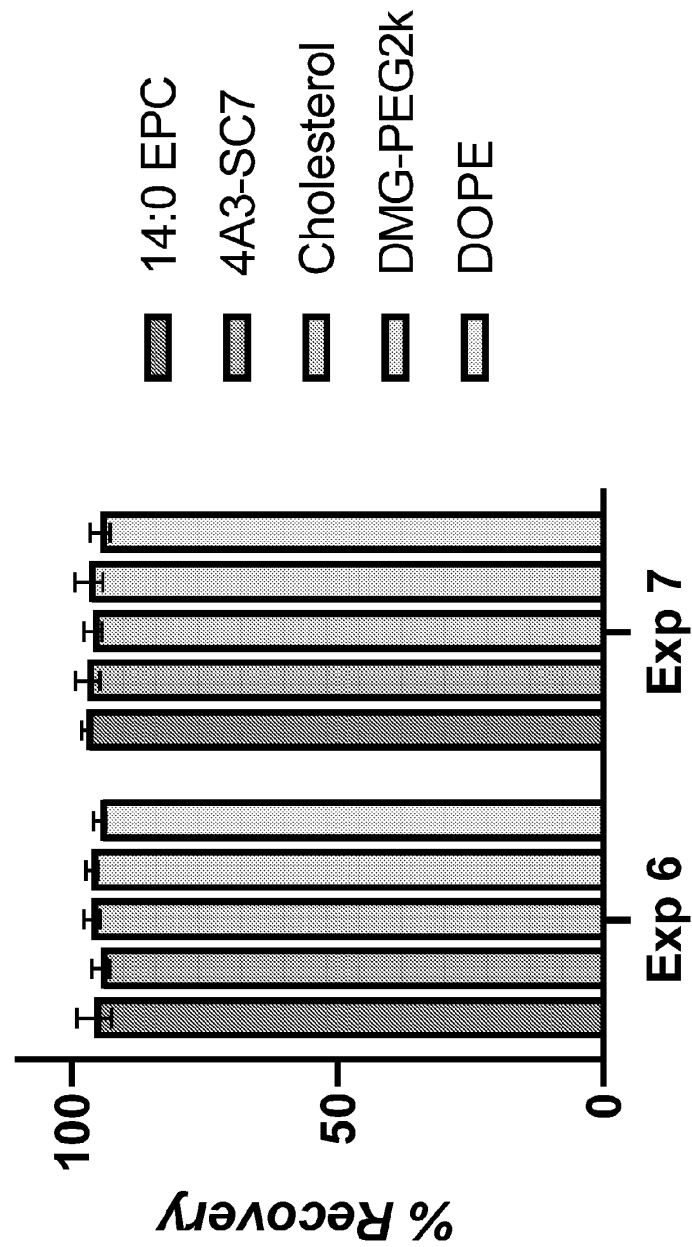


FIG. 20B

Extraction solution	50 mM ammonium acetate / Isopropanol (40:60 v/v)
Extraction volume	8 mL
Extraction time	60 min
4A3-SC7	100.66 ± 0.10
DODAP	99.87 ± 0.28
Cholesterol	98.09 ± 0.30
DMG-PEG2k	99.14 ± 0.31
DOPE	98.59 ± 0.64

FIG. 21A

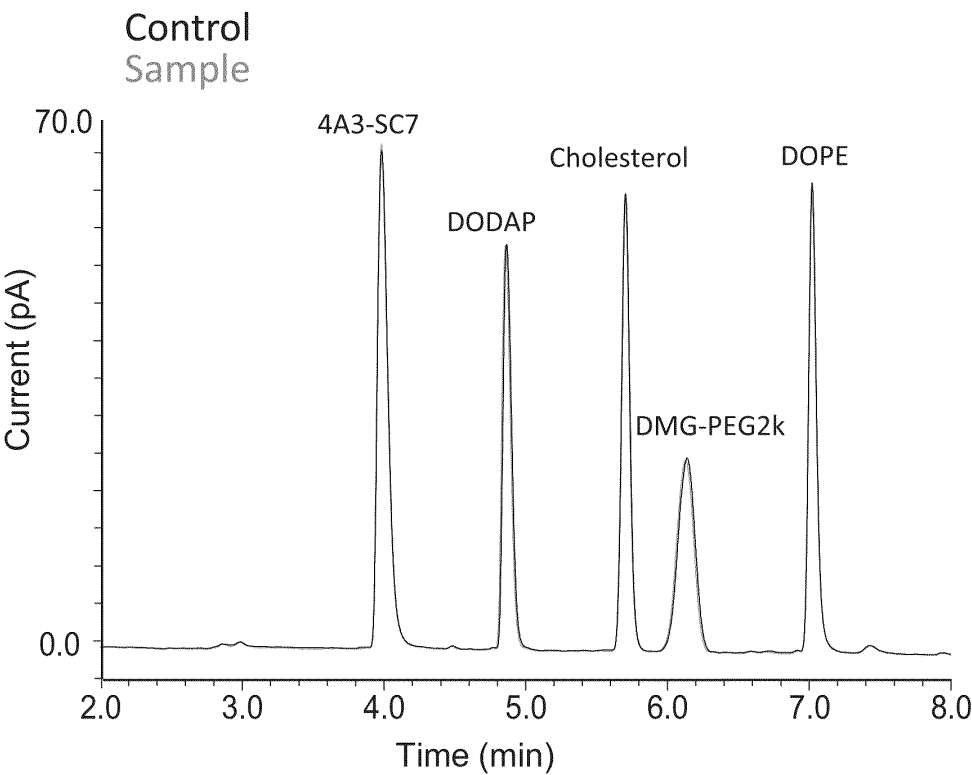


FIG. 21B

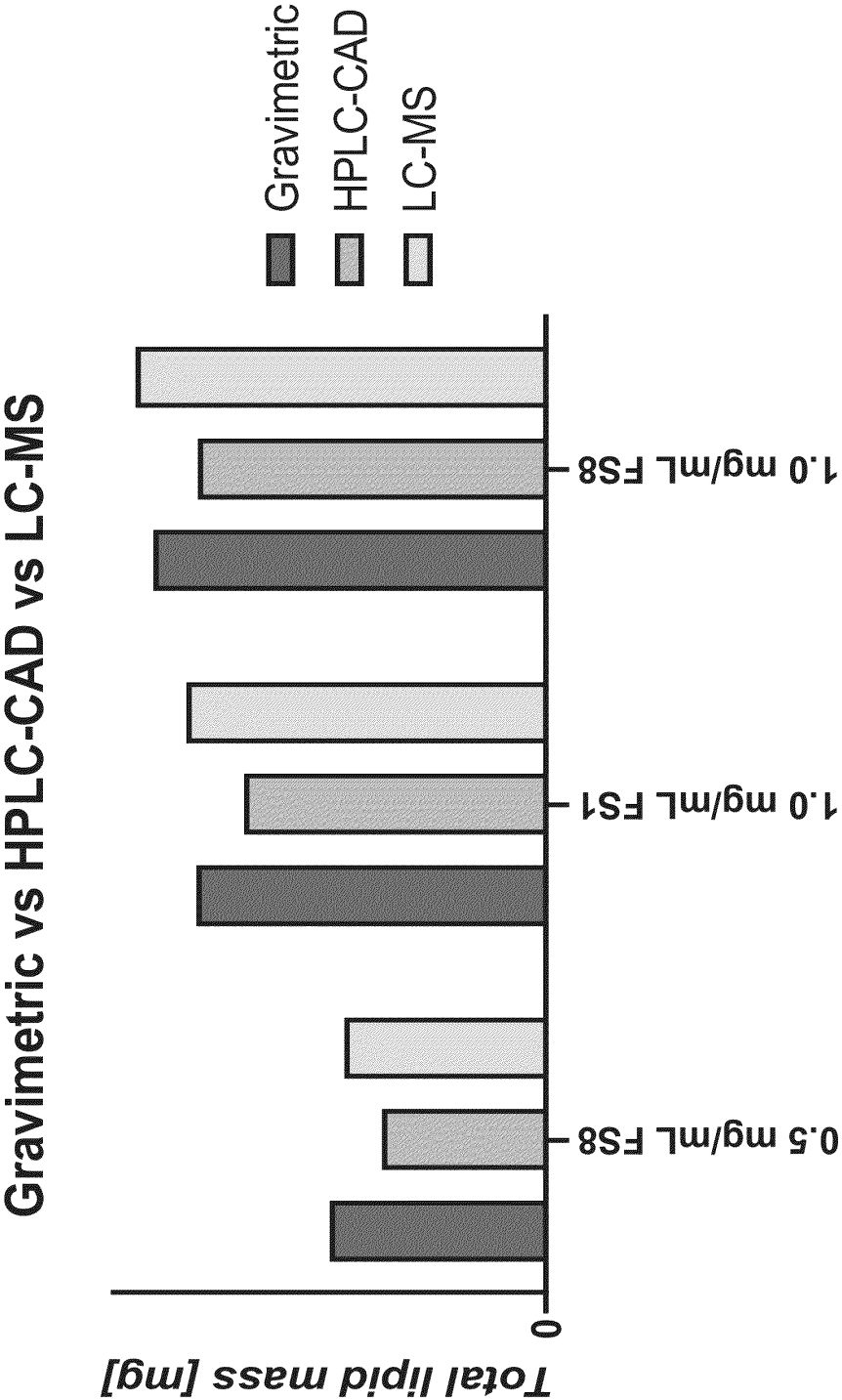


FIG. 21C

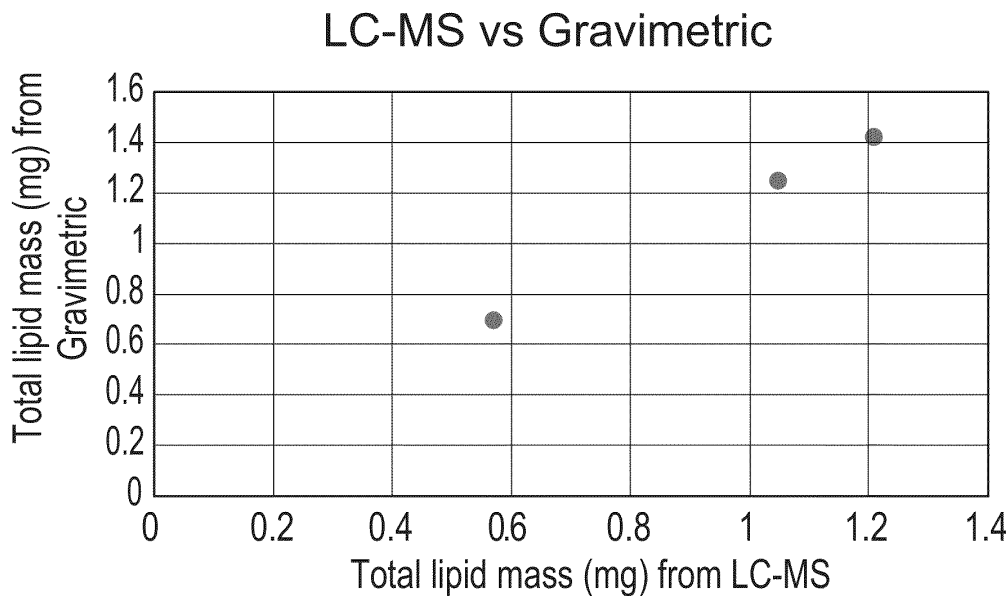


FIG. 21D

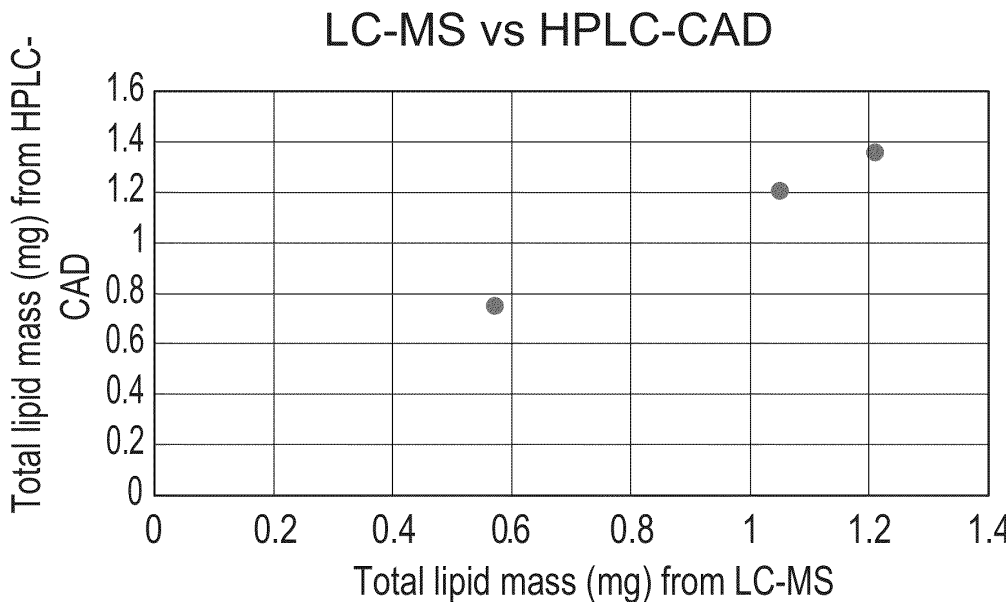


FIG. 21E

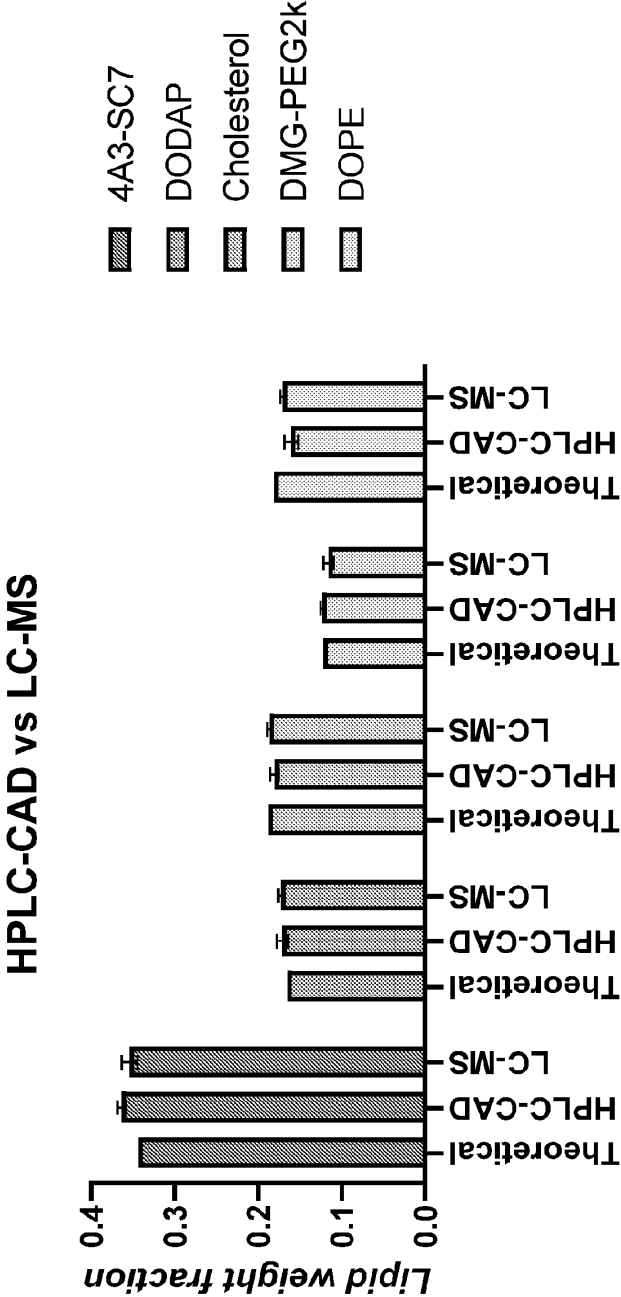


FIG. 22

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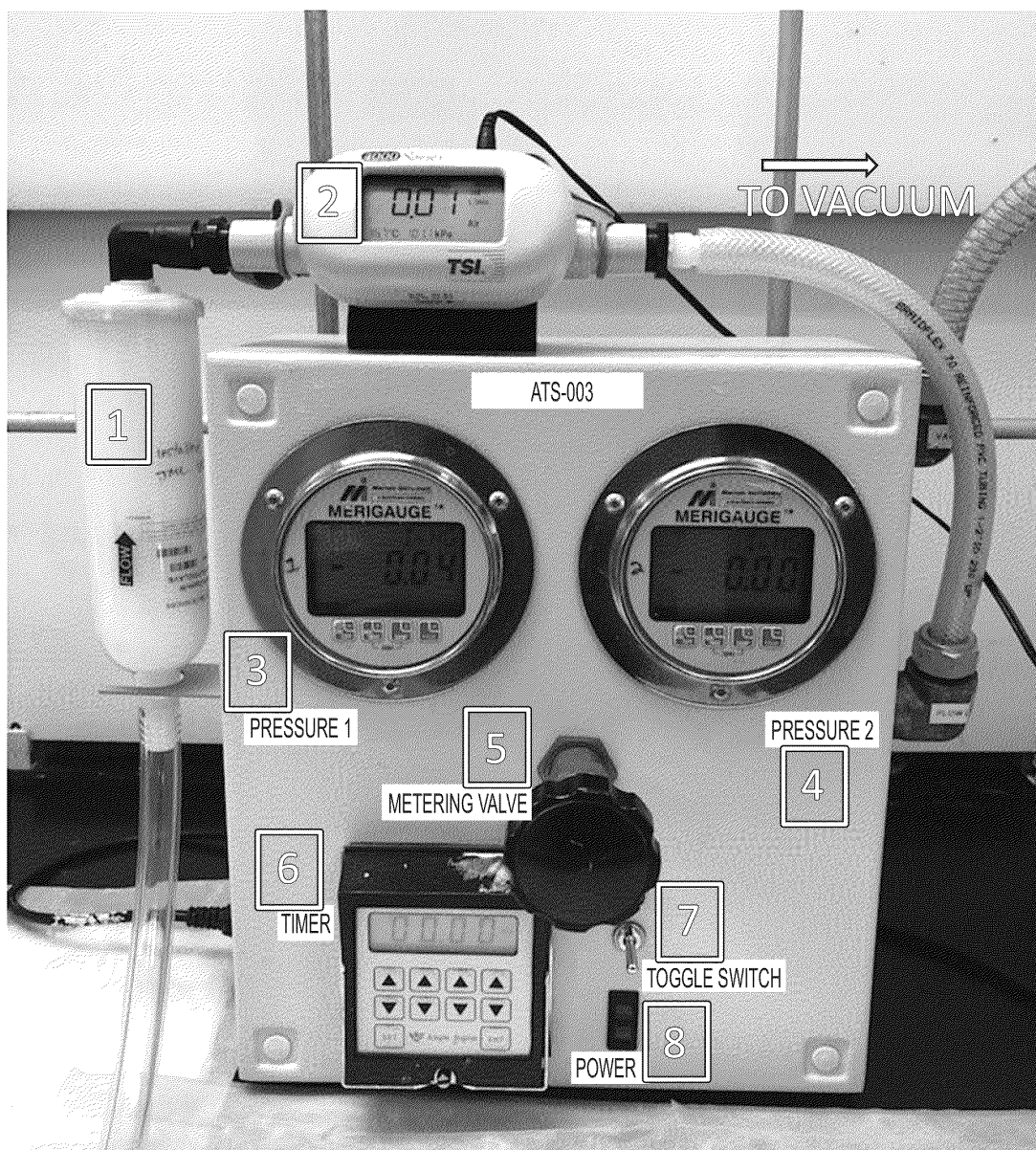


FIG. 23

SUBSTITUTE SHEET (RULE 26)

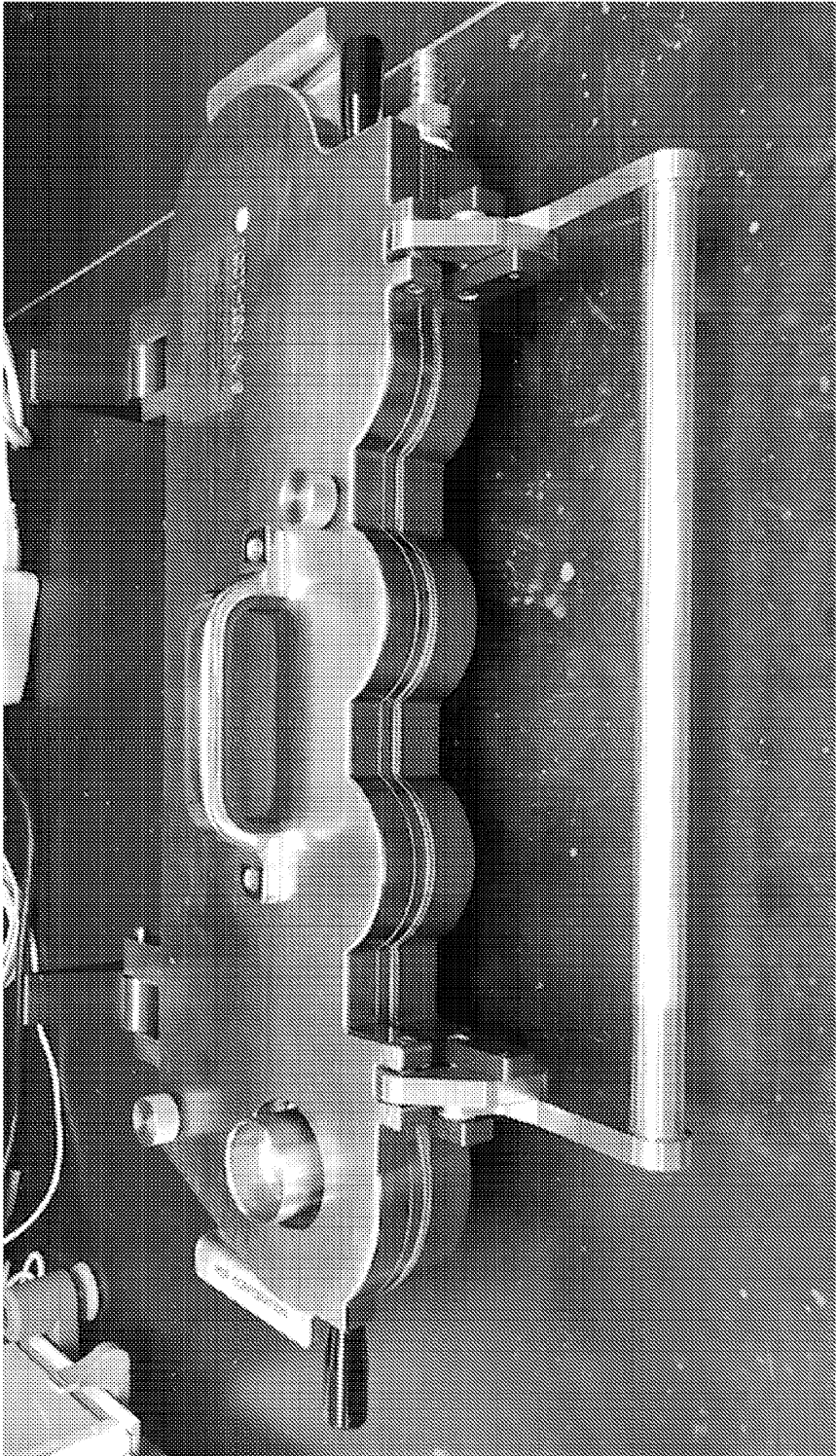


FIG. 24A

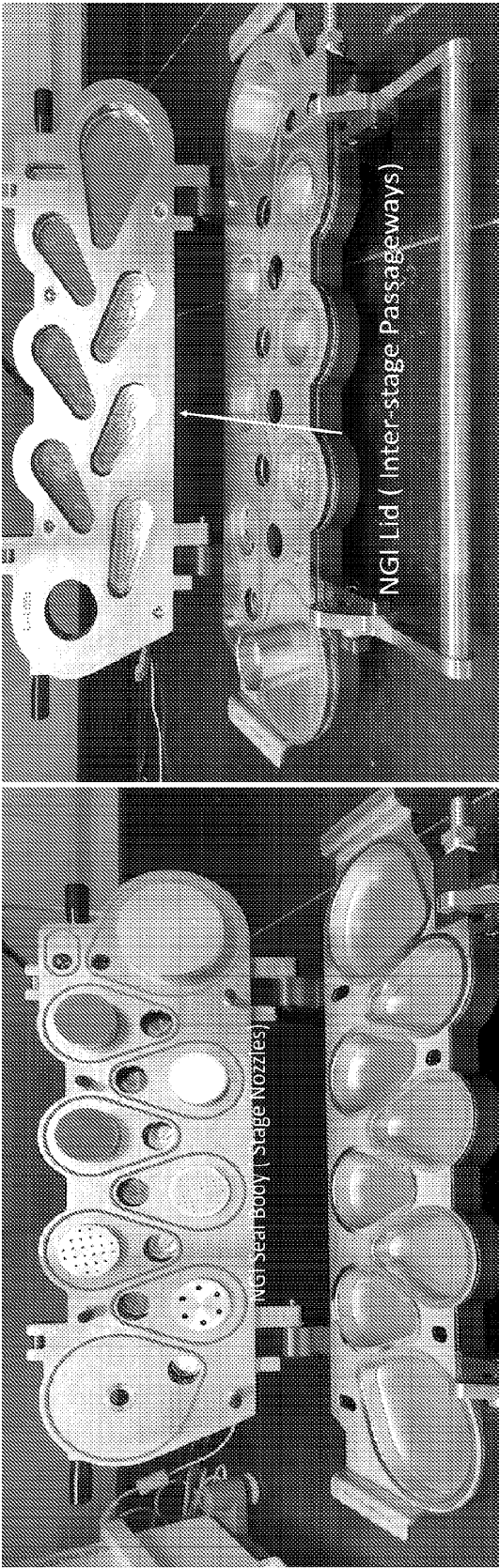


FIG. 24C

FIG. 24B

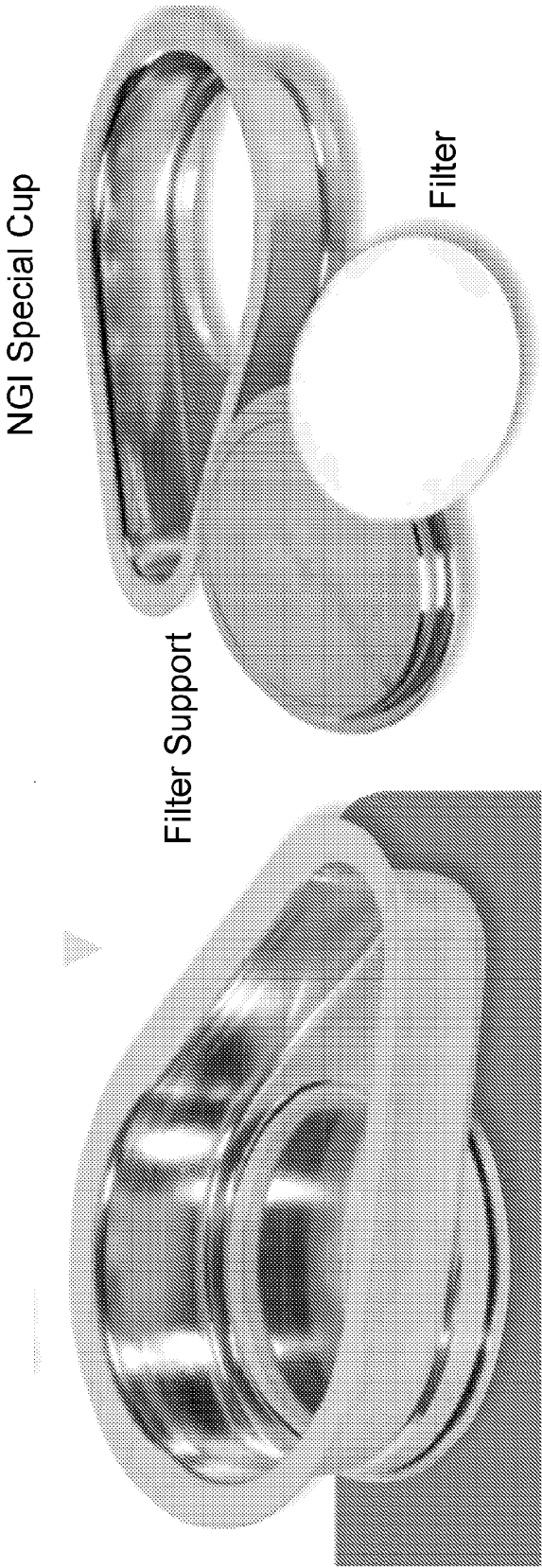


FIG. 25A

FIG. 25B

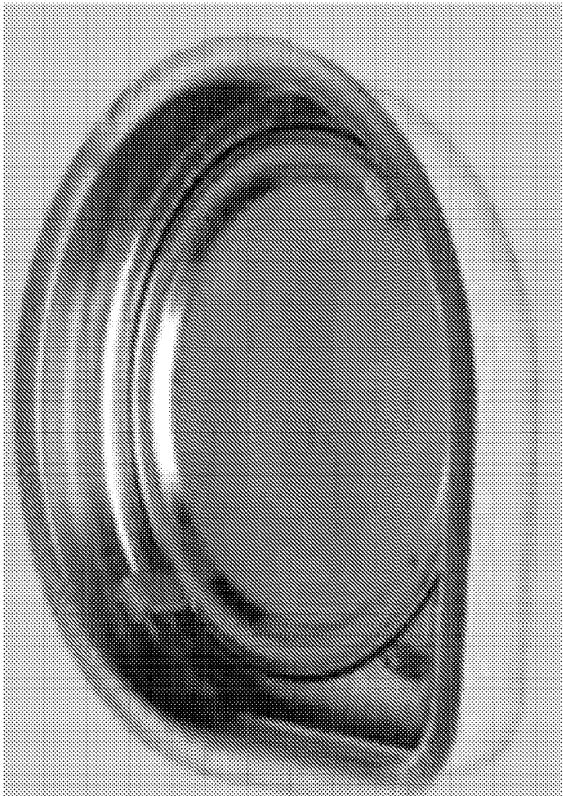


FIG. 26B

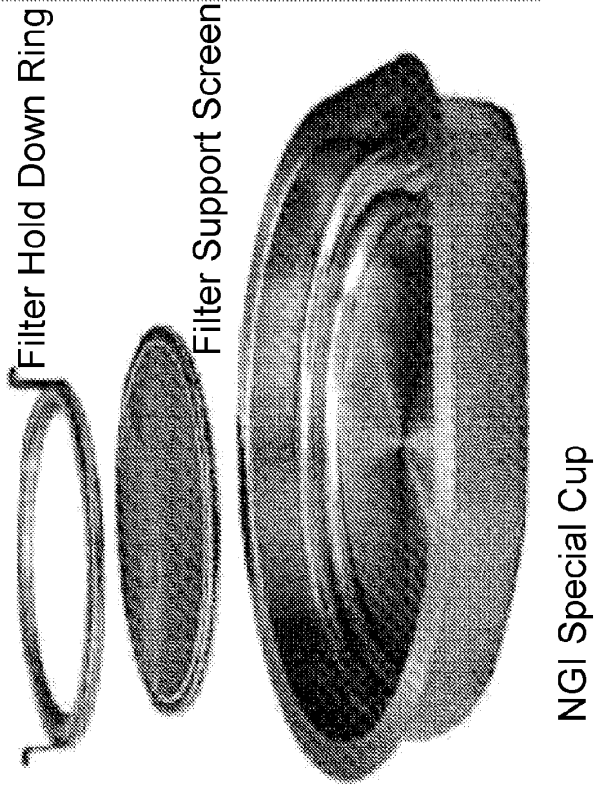


FIG. 26A



FIG. 27

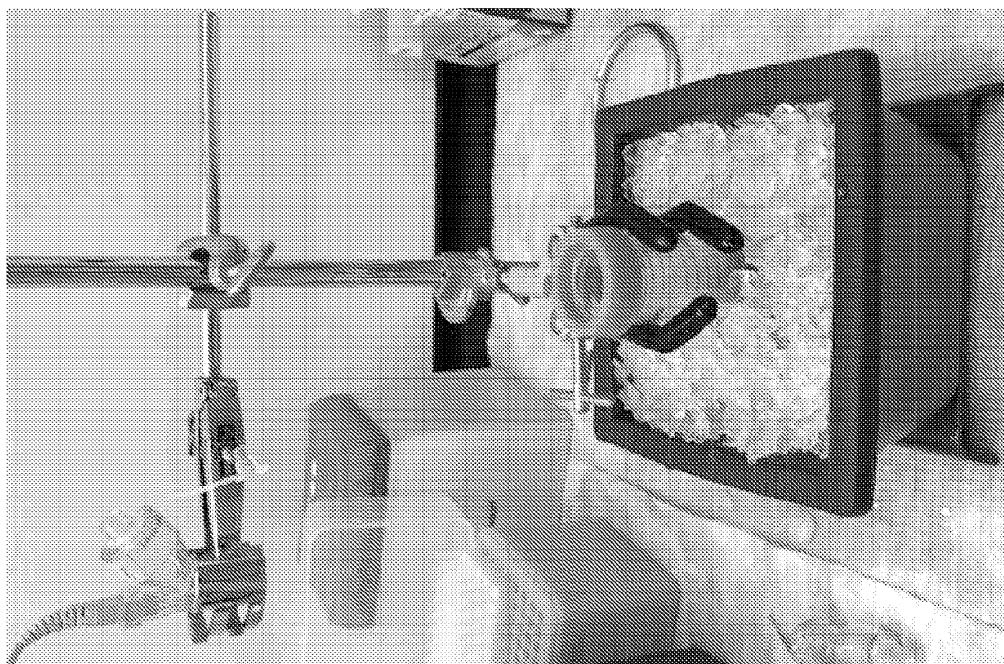


FIG. 28B

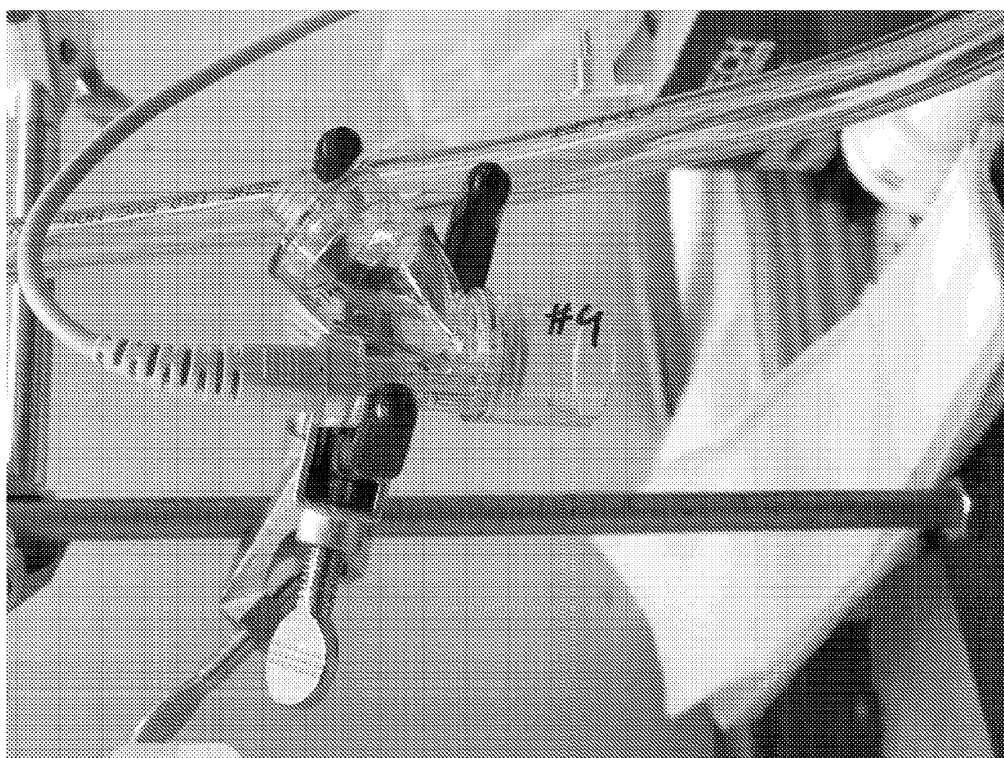


FIG. 28A

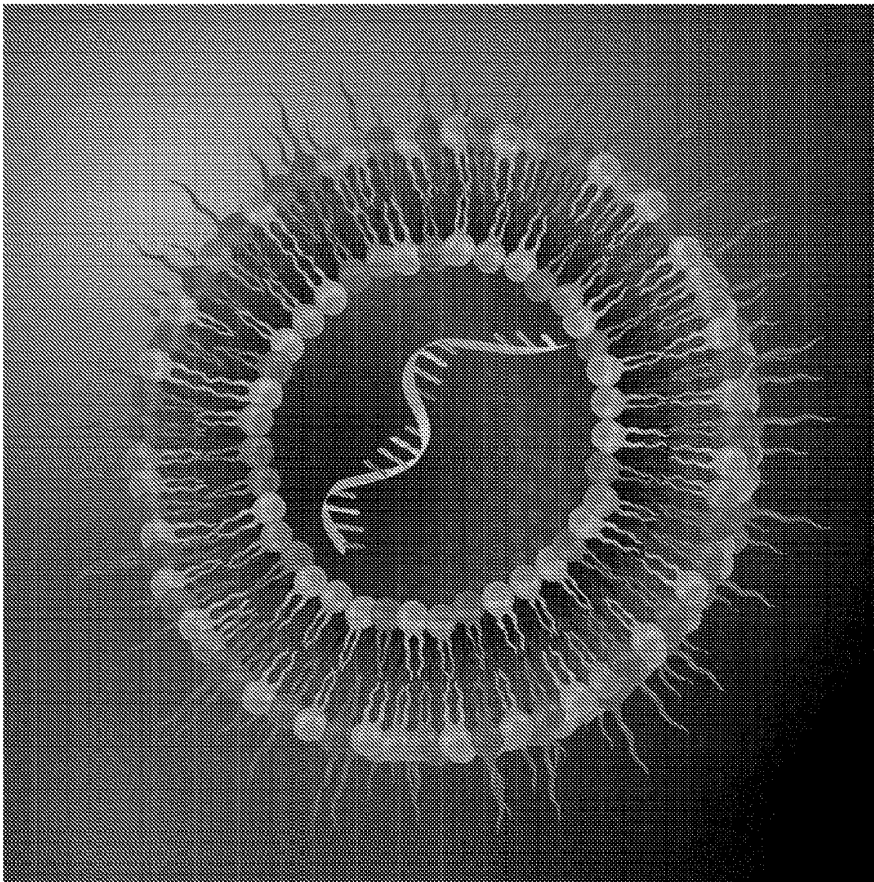


FIG.29

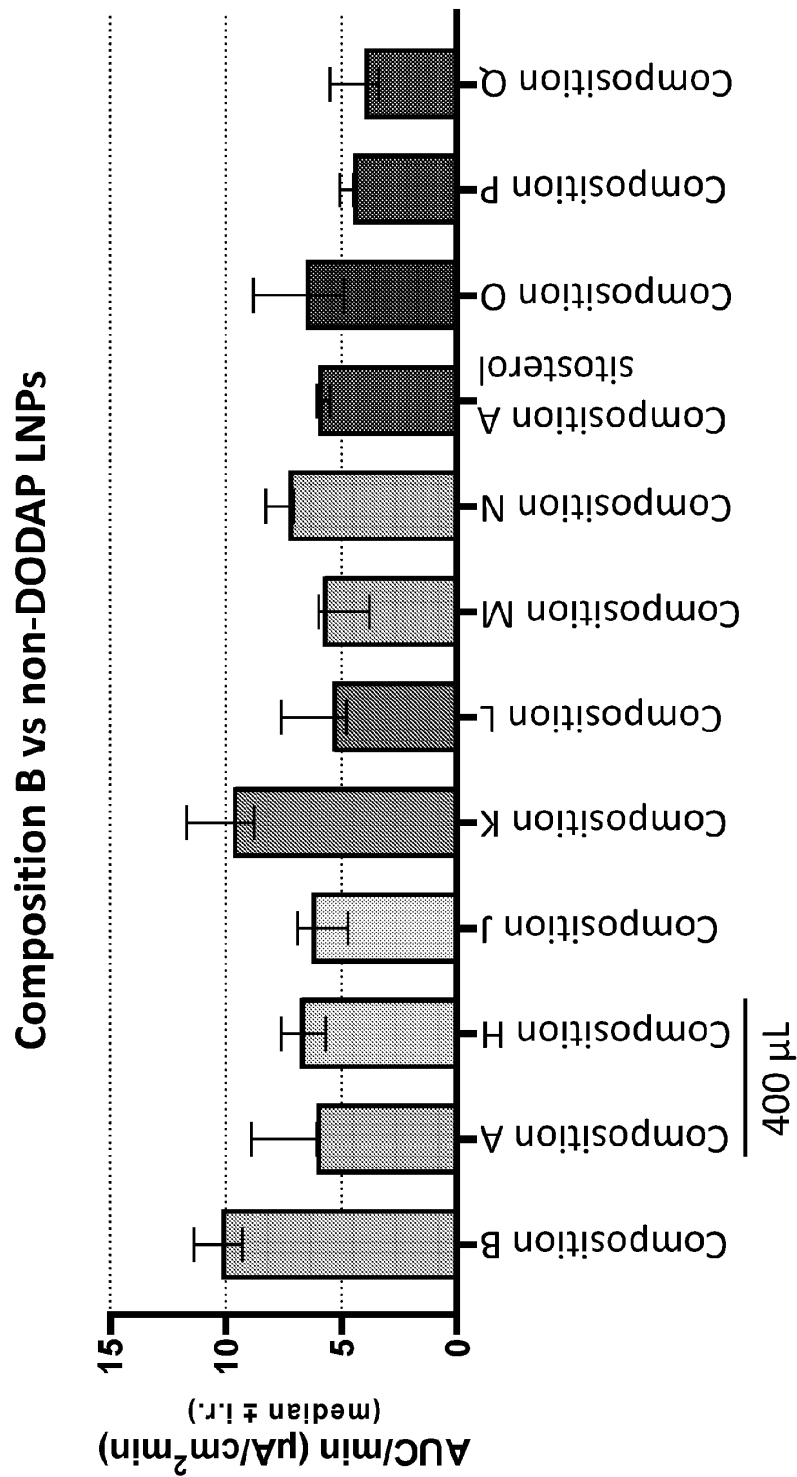


FIG. 30

Composition B vs DODAP variants
in 1x PBS

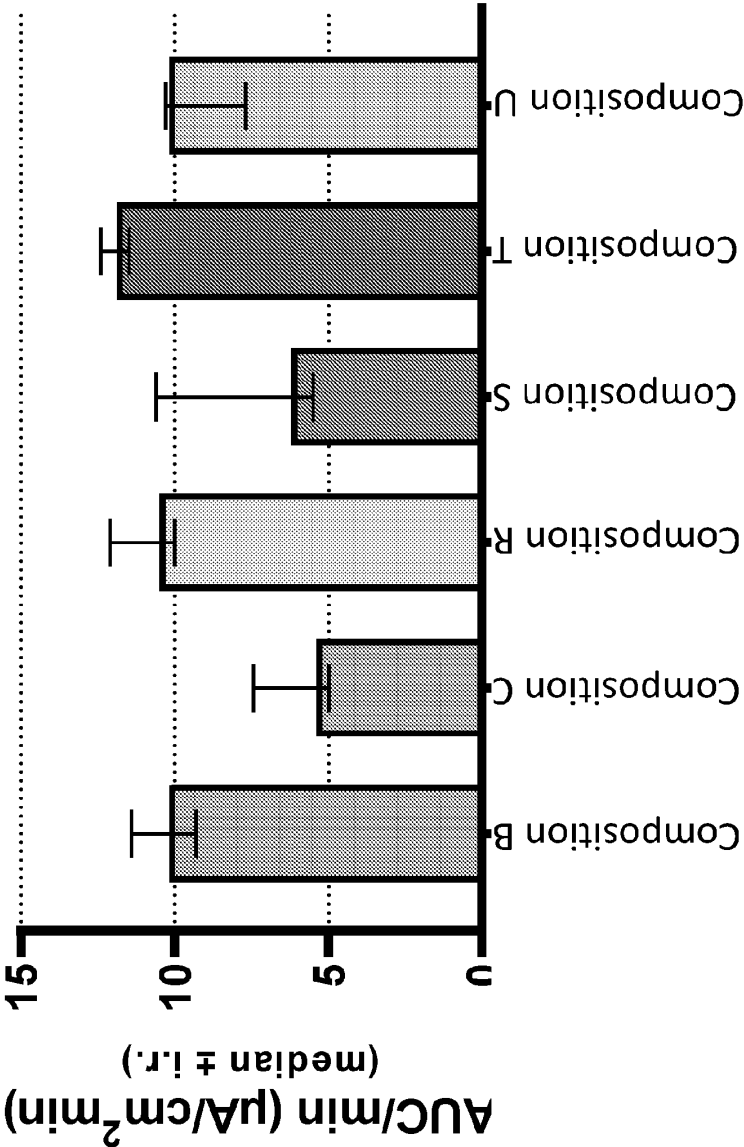


FIG. 31

Composition B
buffer screening

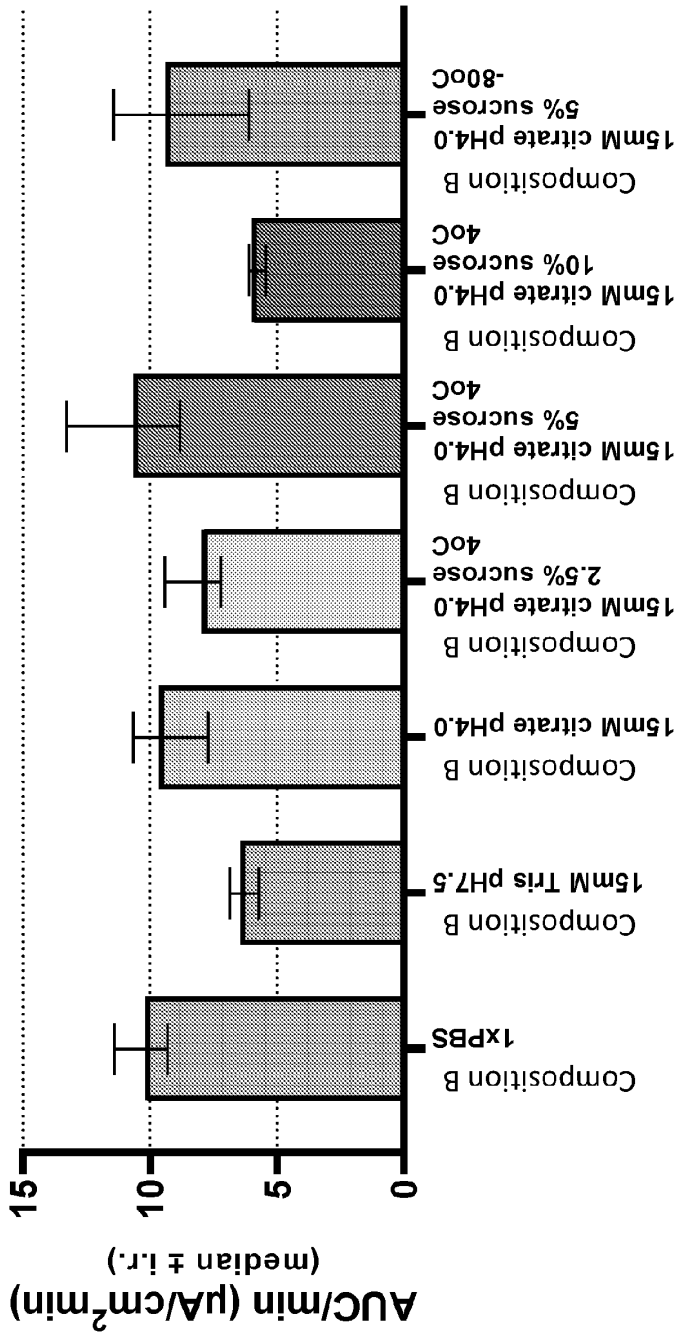


FIG. 32

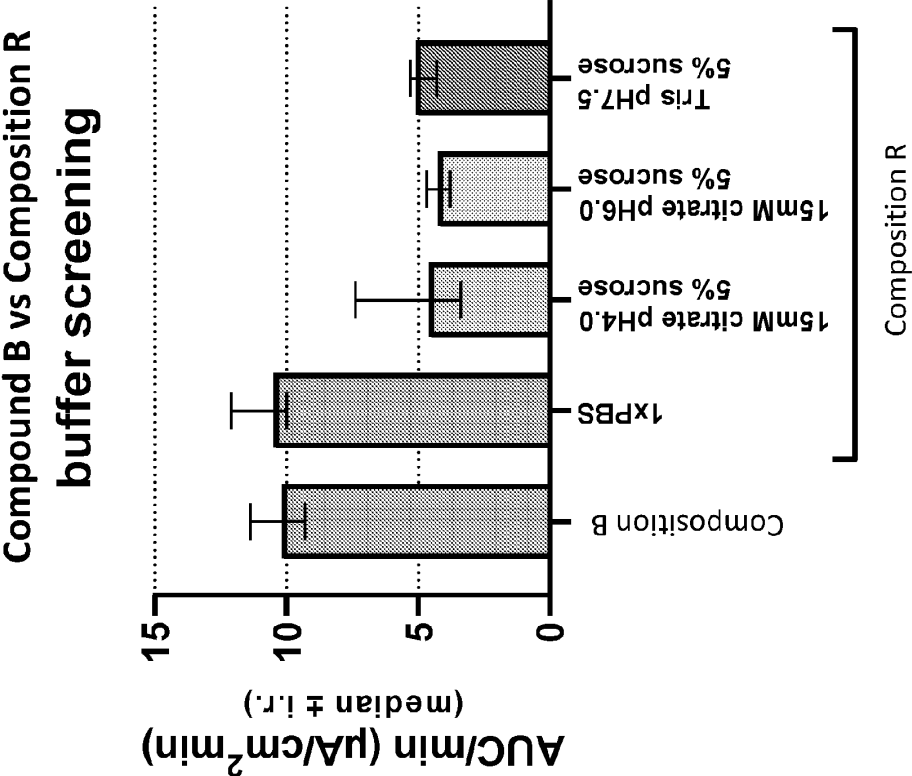


FIG. 33A

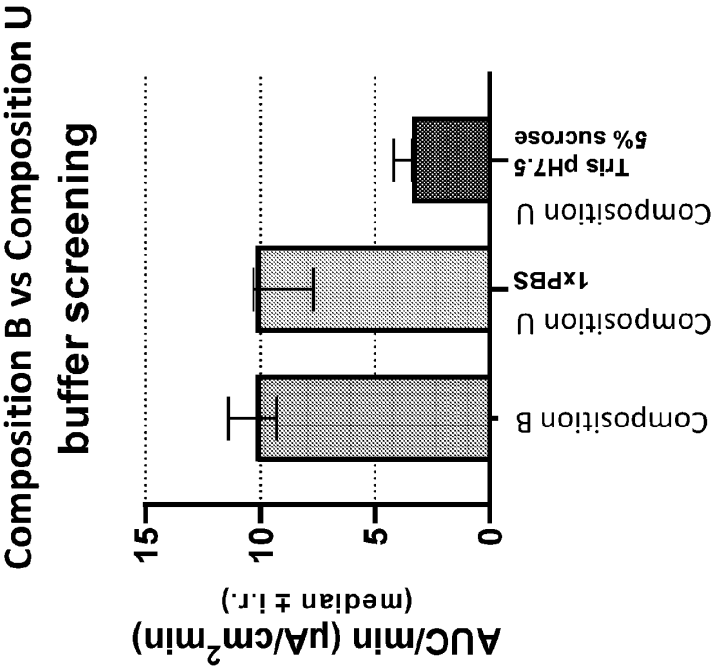


FIG. 33B

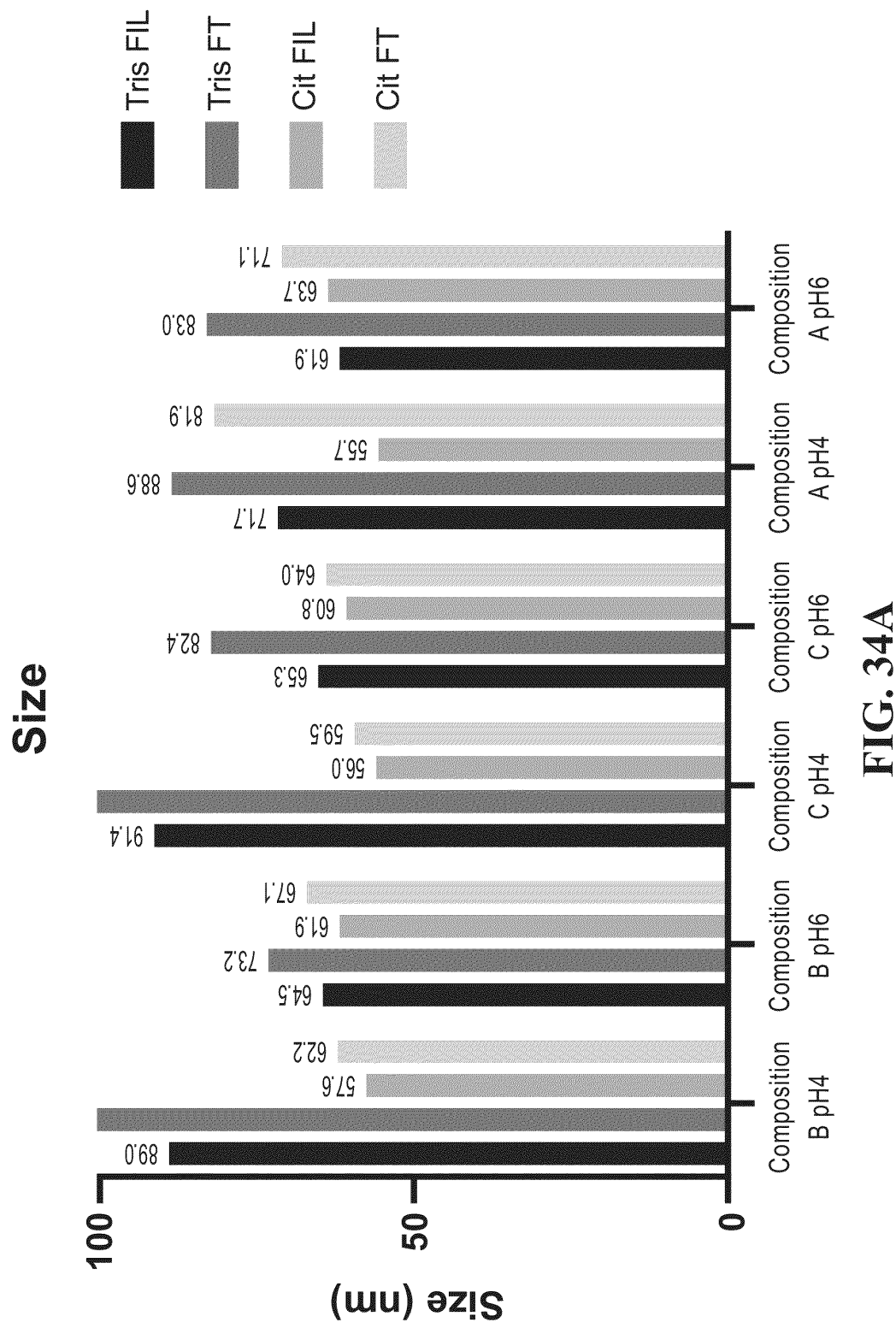


FIG. 34A

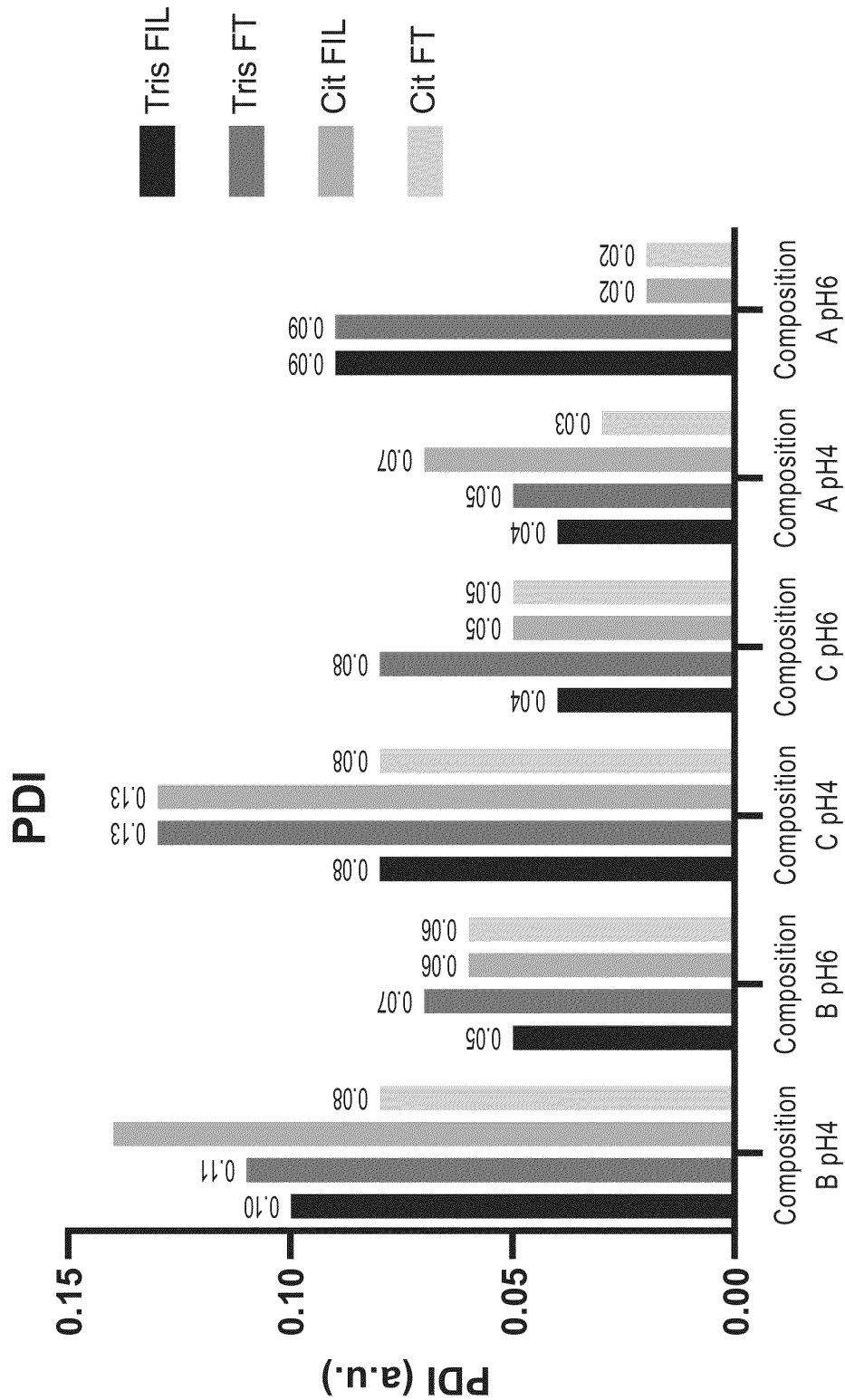


FIG. 34B

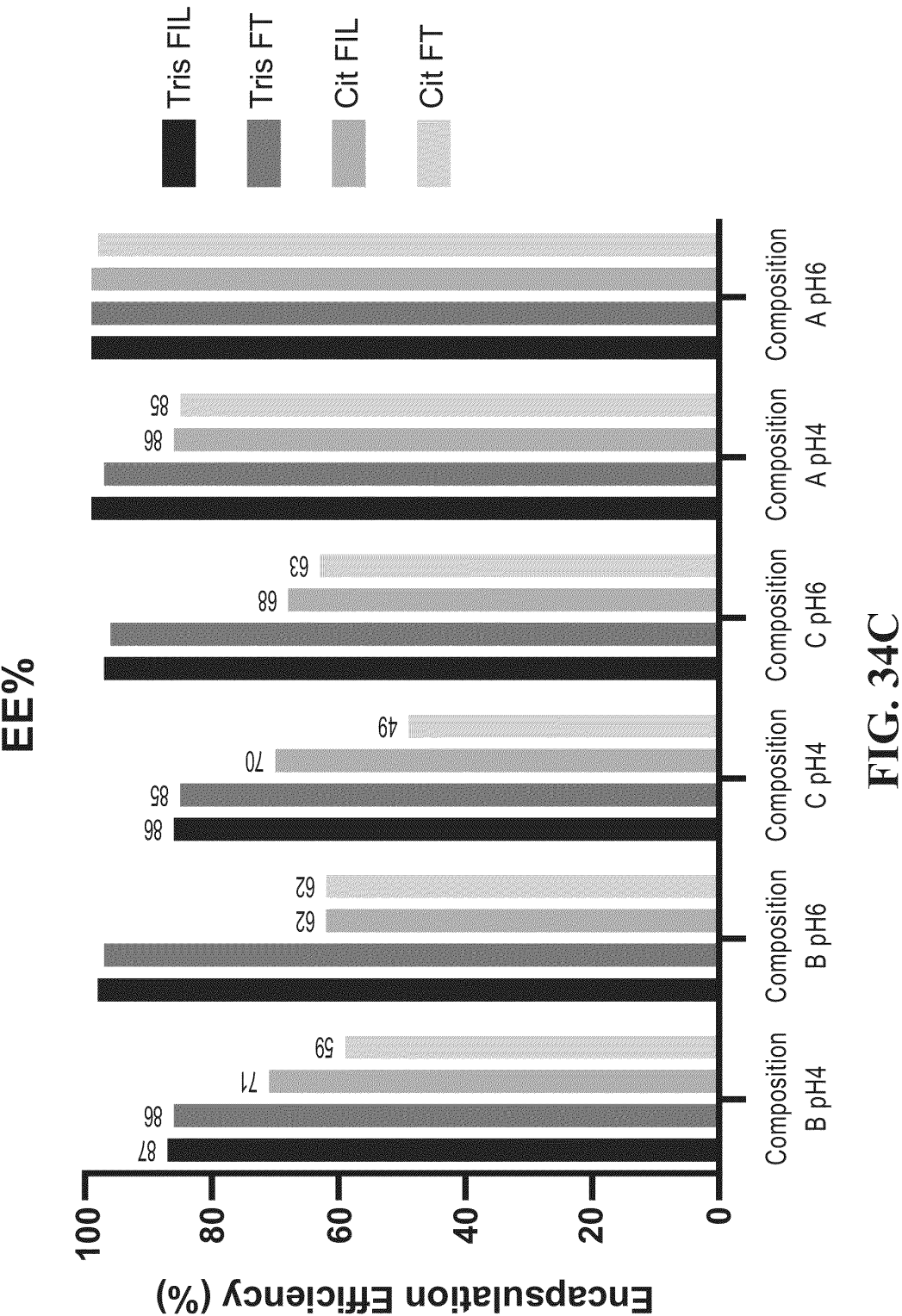


FIG. 34C

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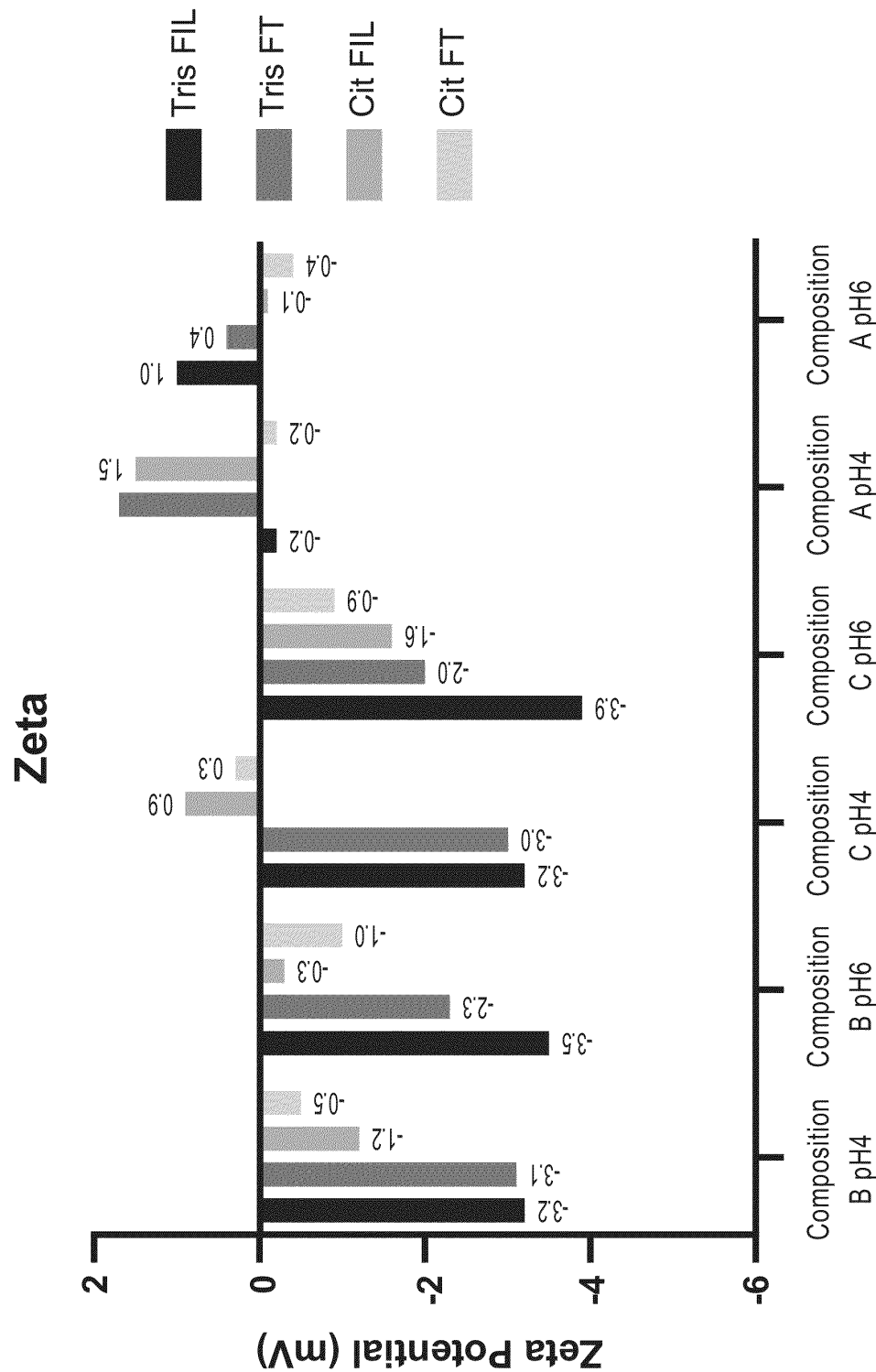


FIG. 34D

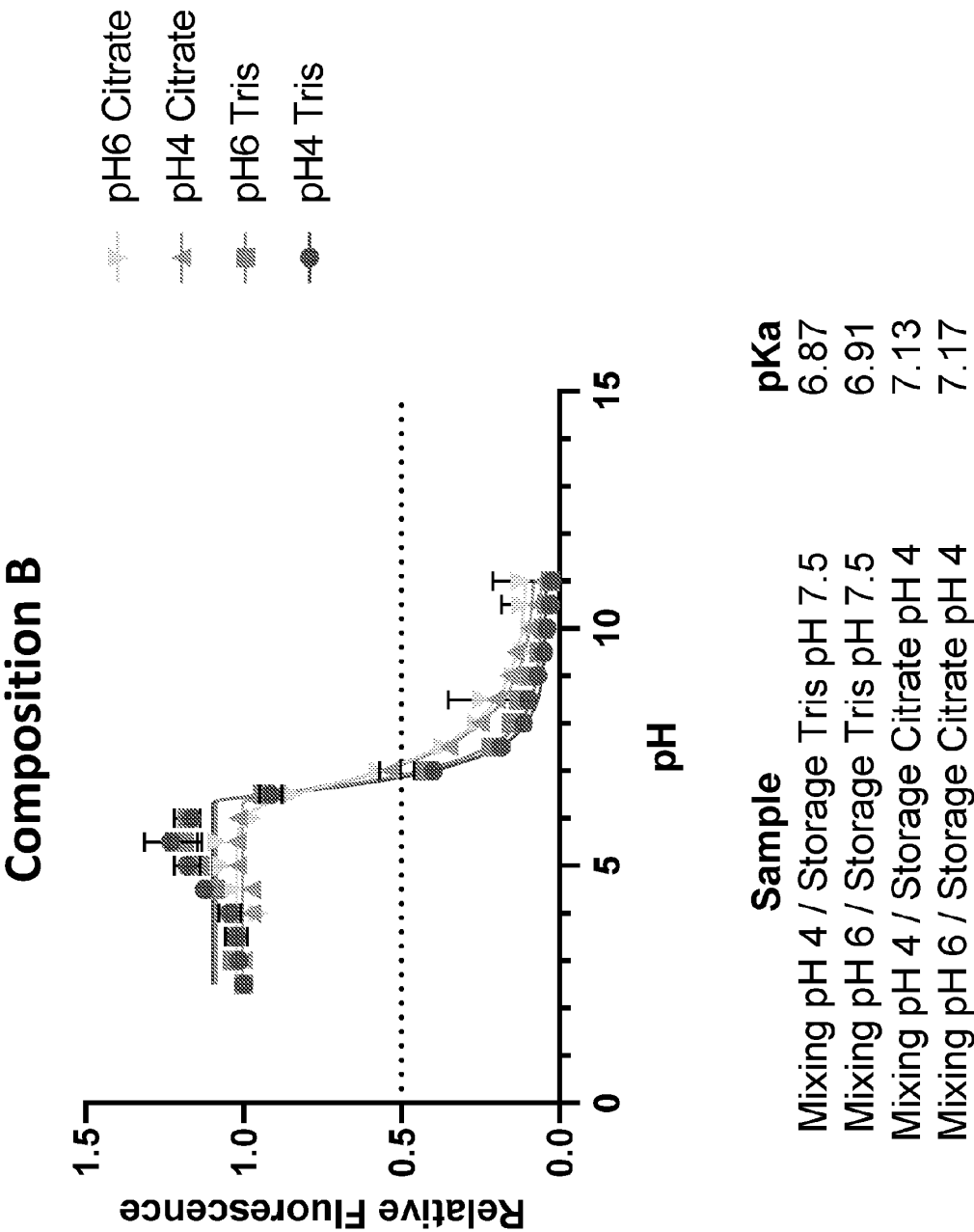


FIG. 35A

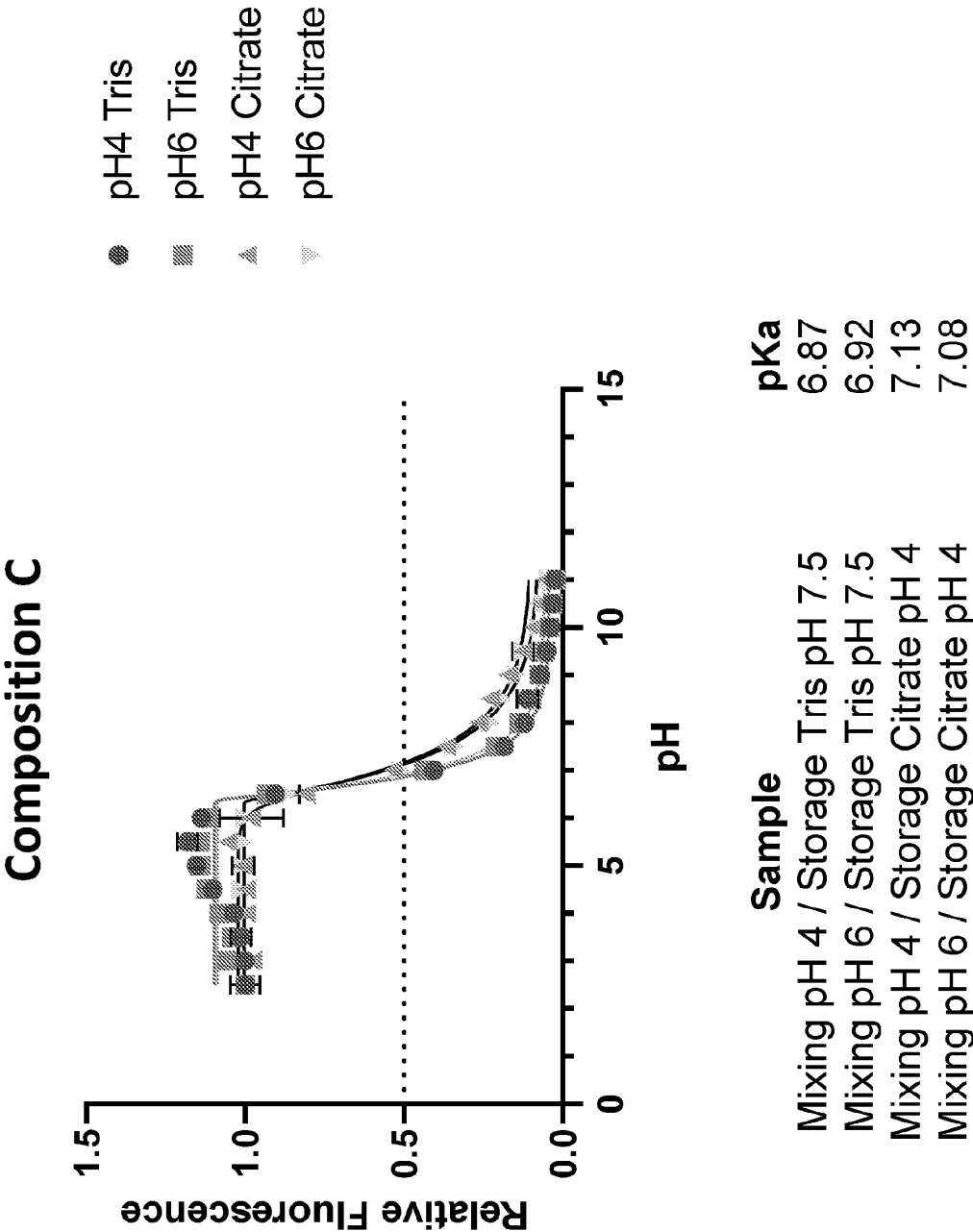
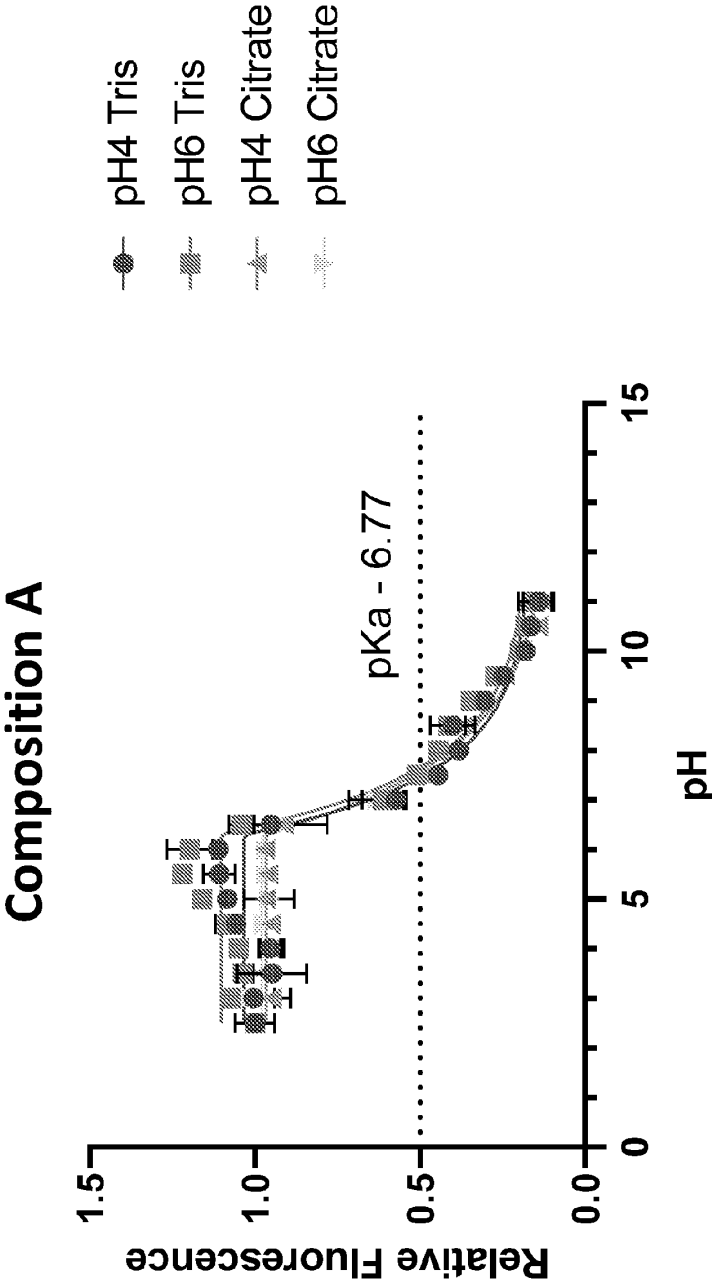


FIG. 35B



Sample	pKa
Mixing pH 4 / Storage Tris pH 7.5	7.46
Mixing pH 6 / Storage Tris pH 7.5	7.67
Mixing pH 4 / Storage Citrate pH 4	7.60
Mixing pH 6 / Storage Citrate pH 4	7.58

FIG. 35C

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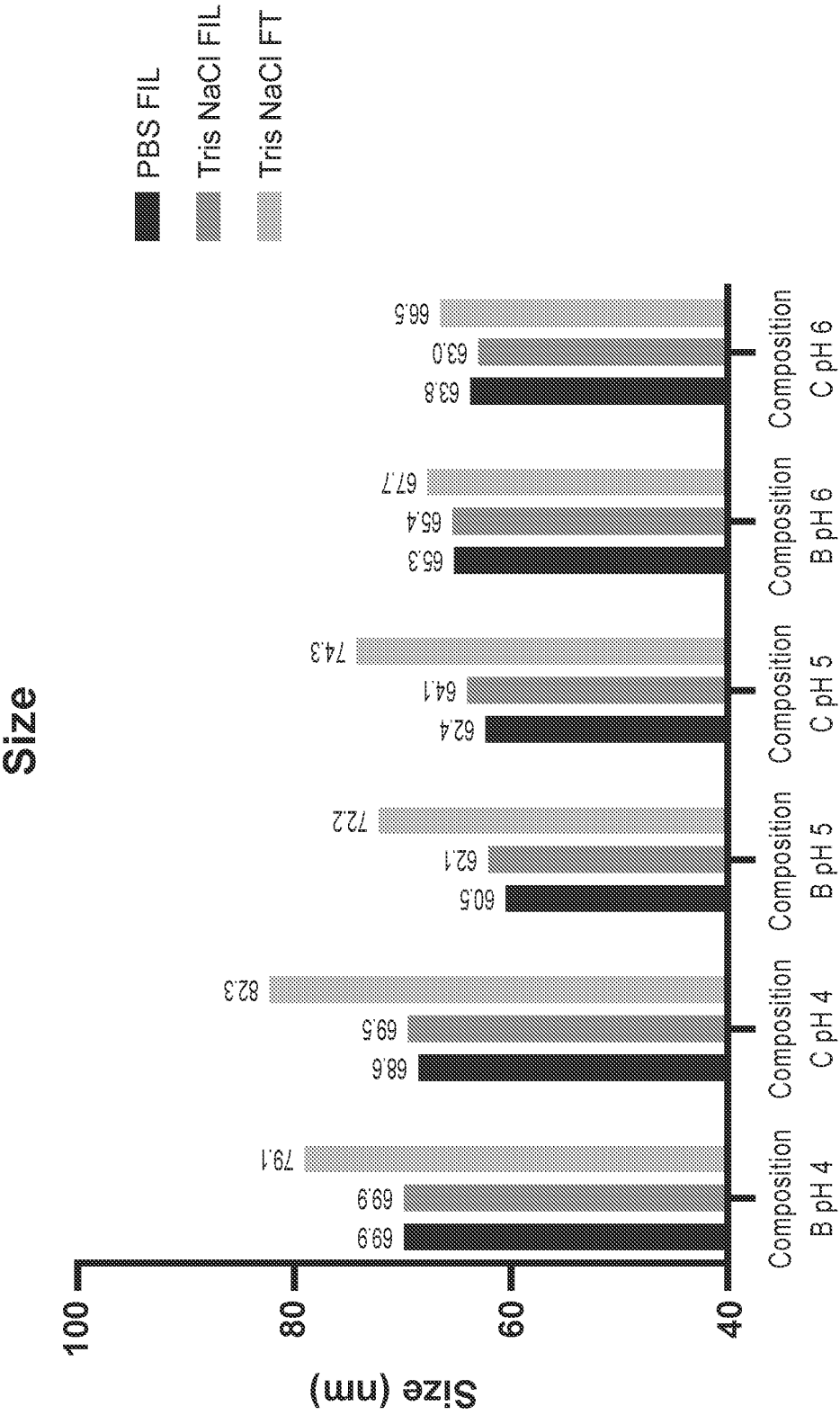


FIG. 36A

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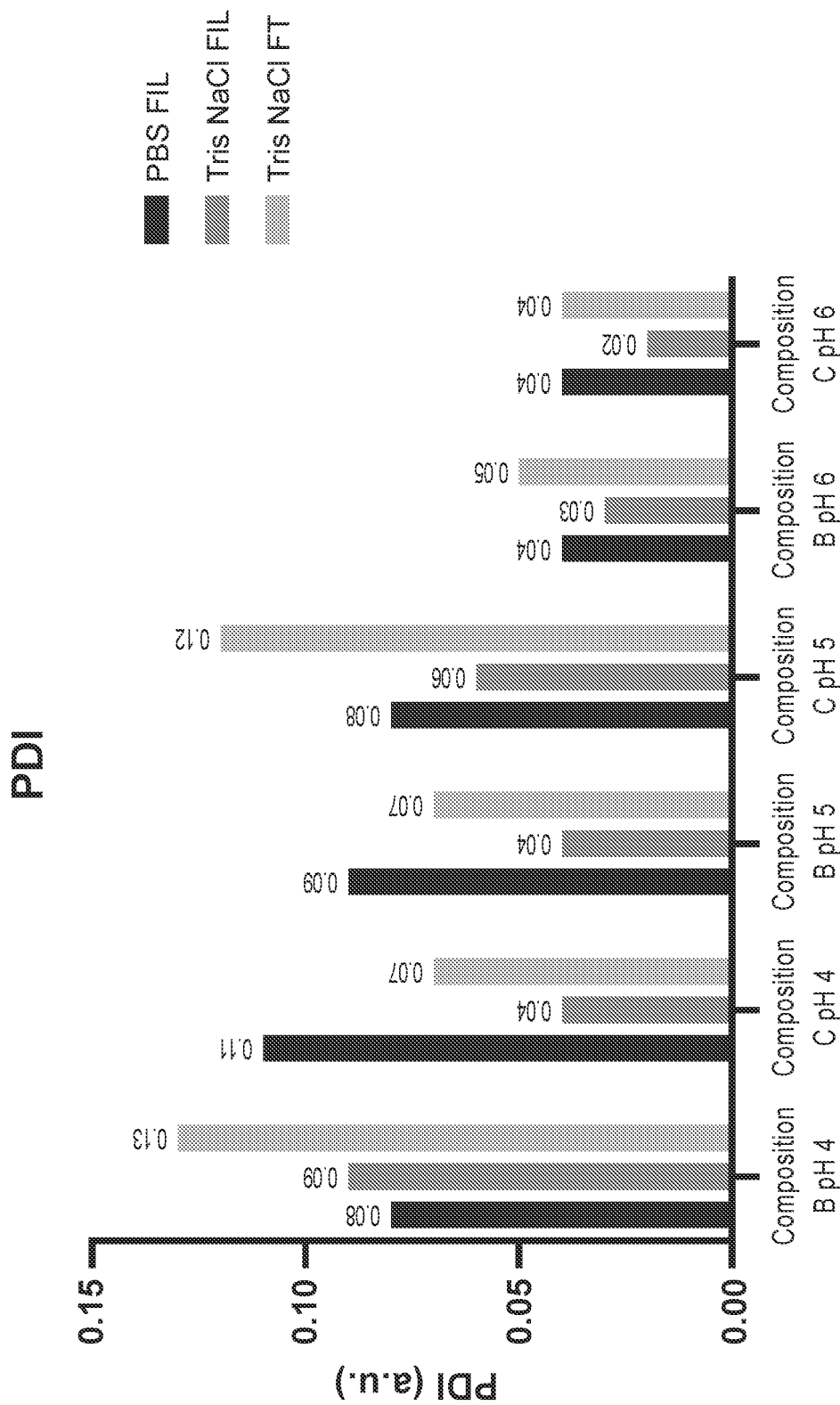


FIG. 36B

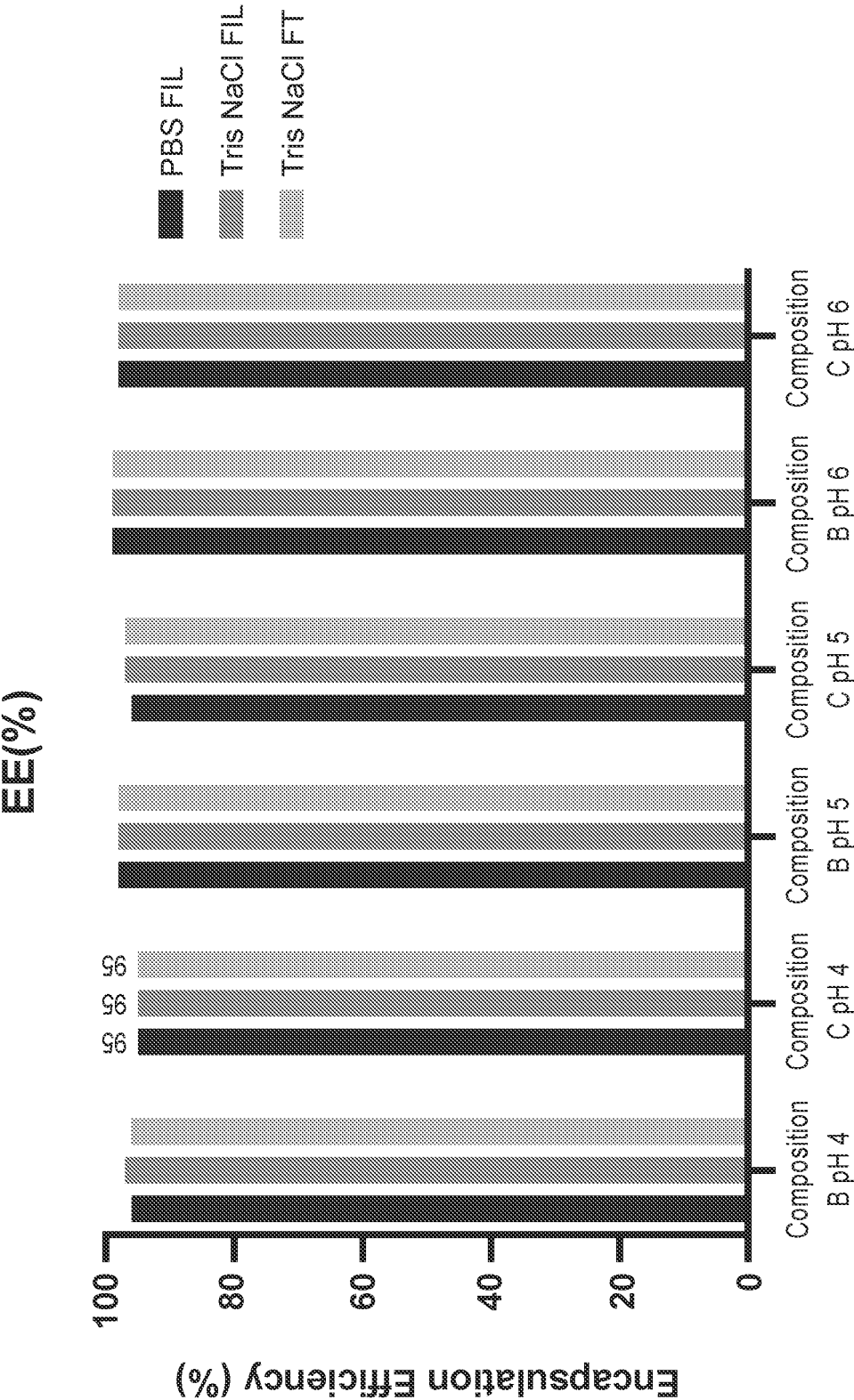


FIG. 36C

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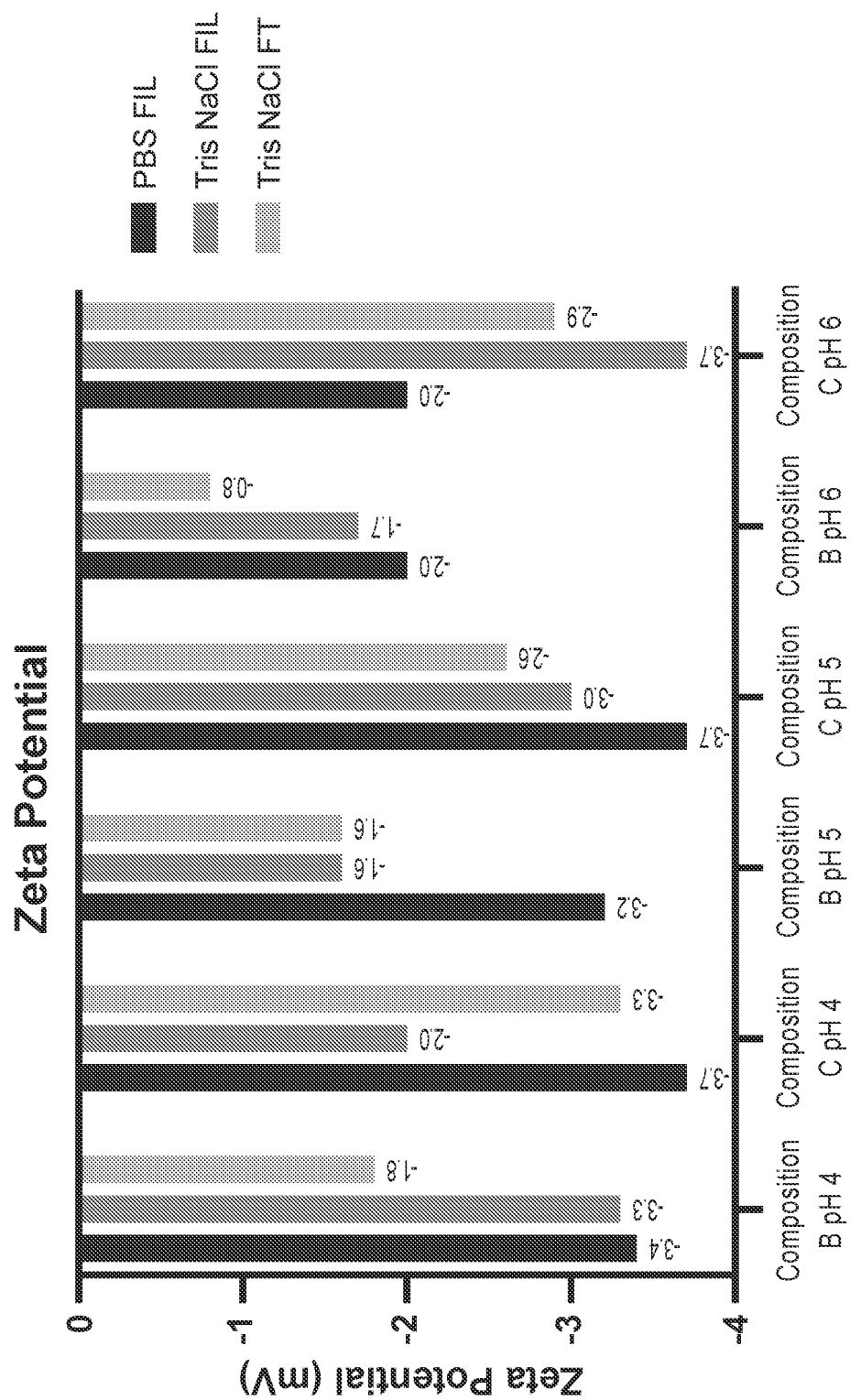


FIG. 36D

Composition B - CFTR

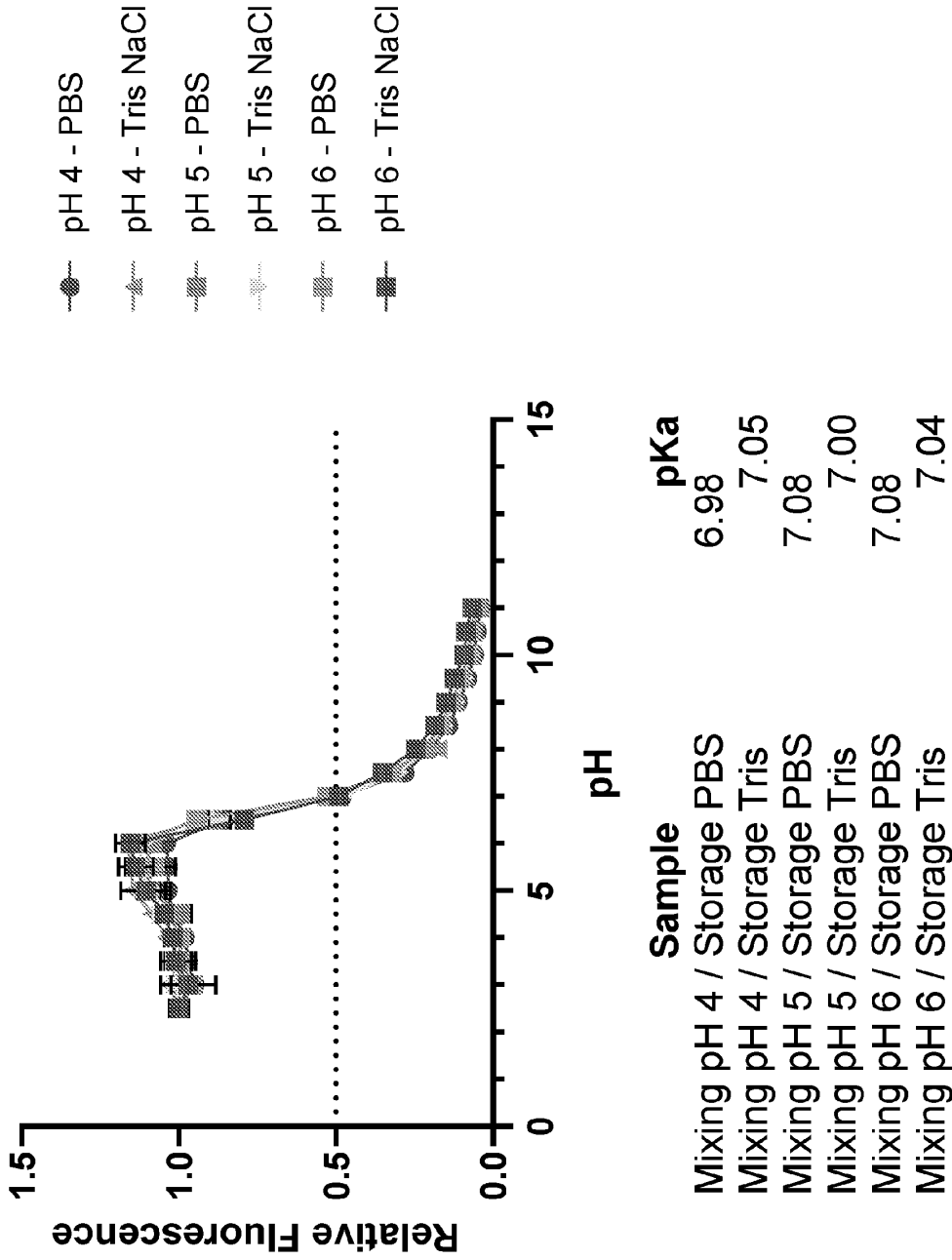


FIG. 37A

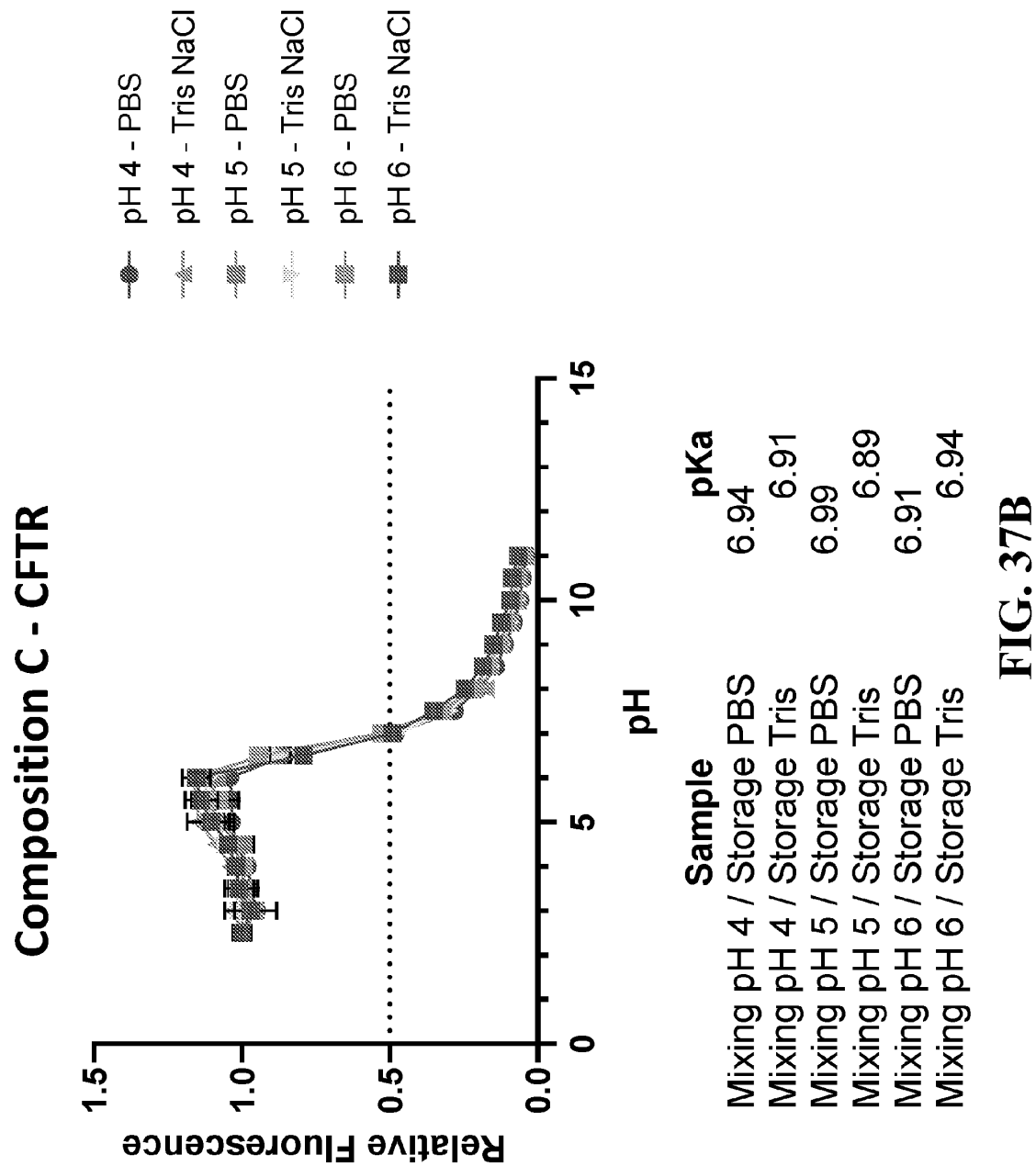


FIG. 37B

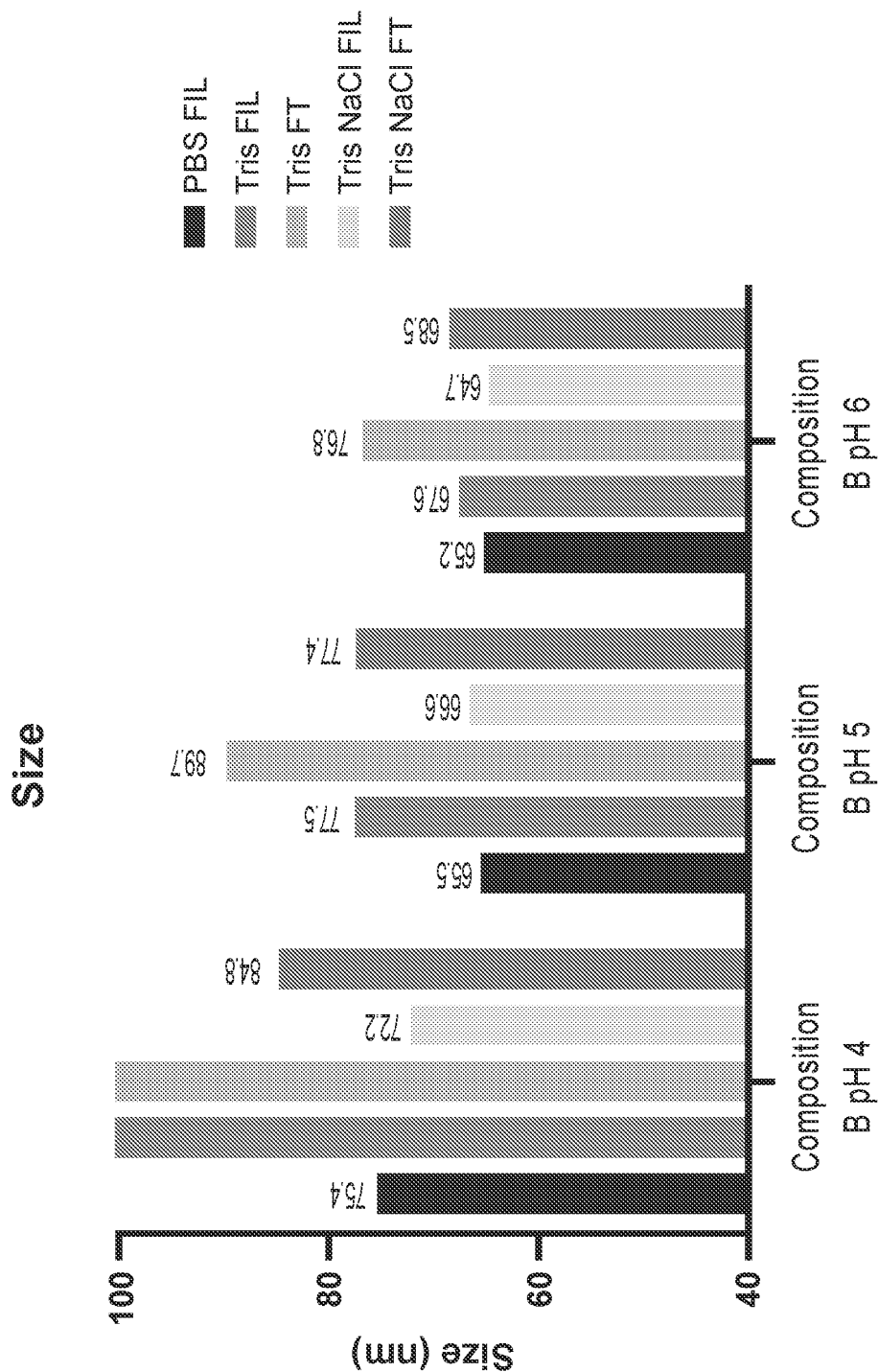


FIG. 38A

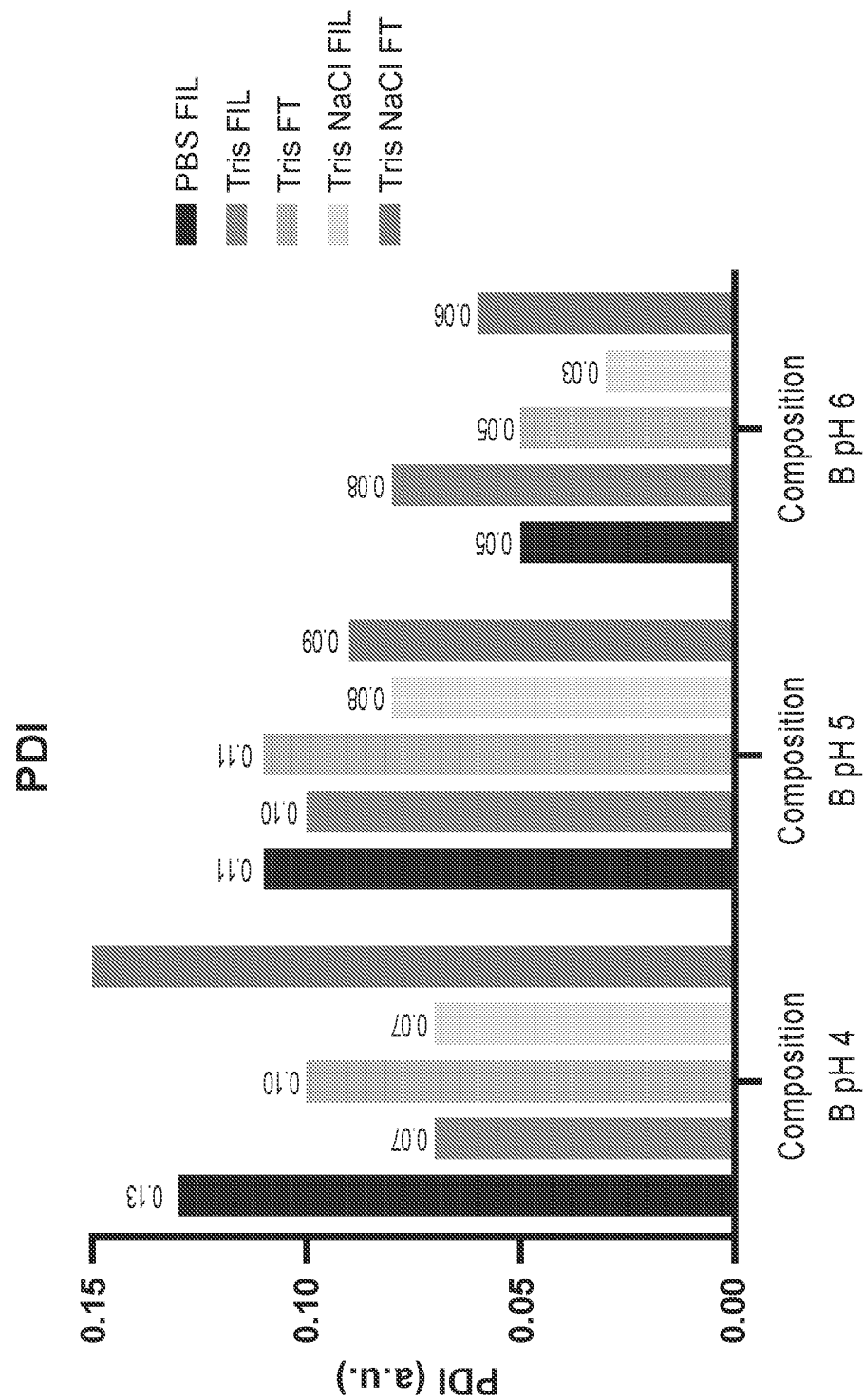


FIG. 38B

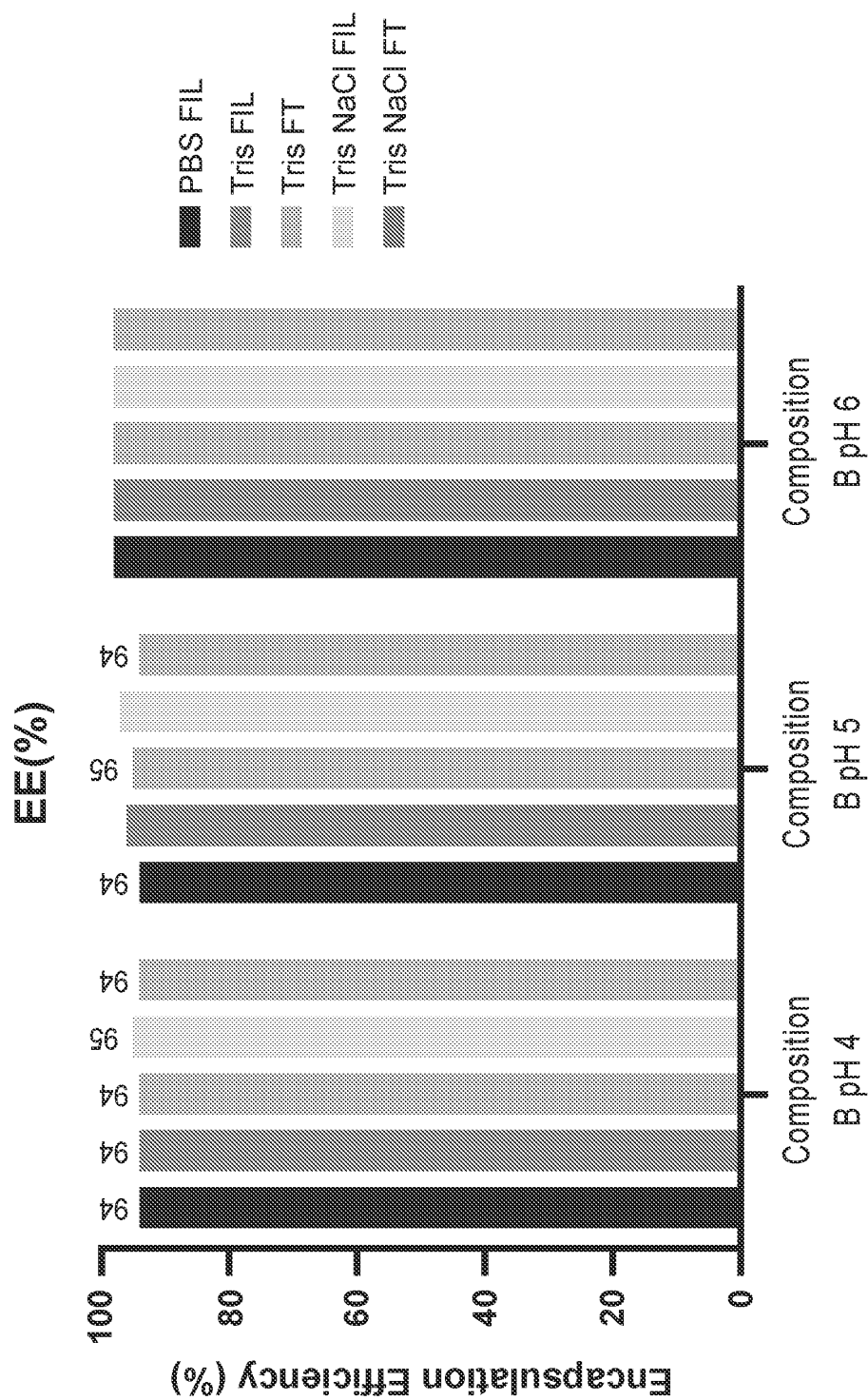


FIG. 38C

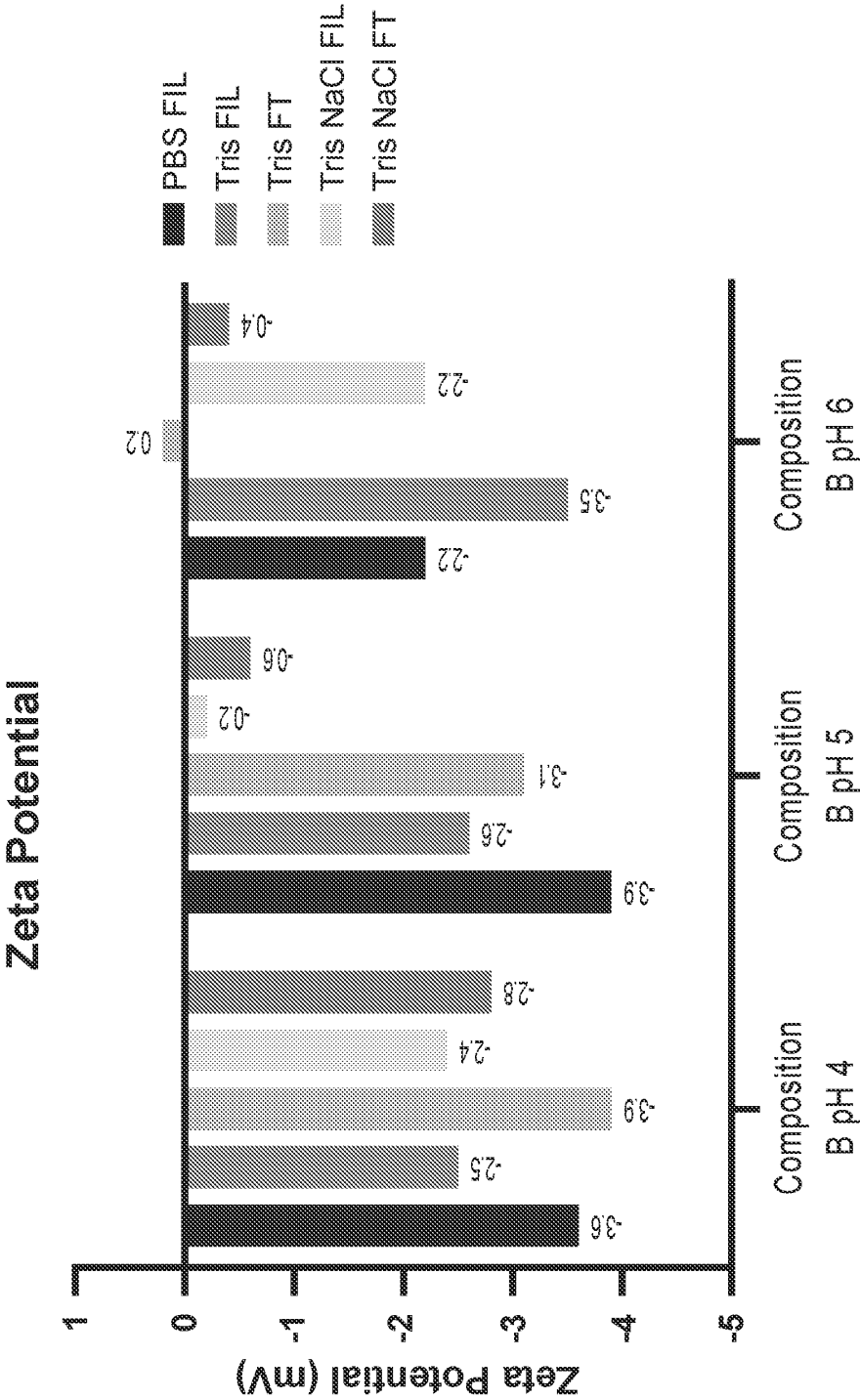


FIG. 38D

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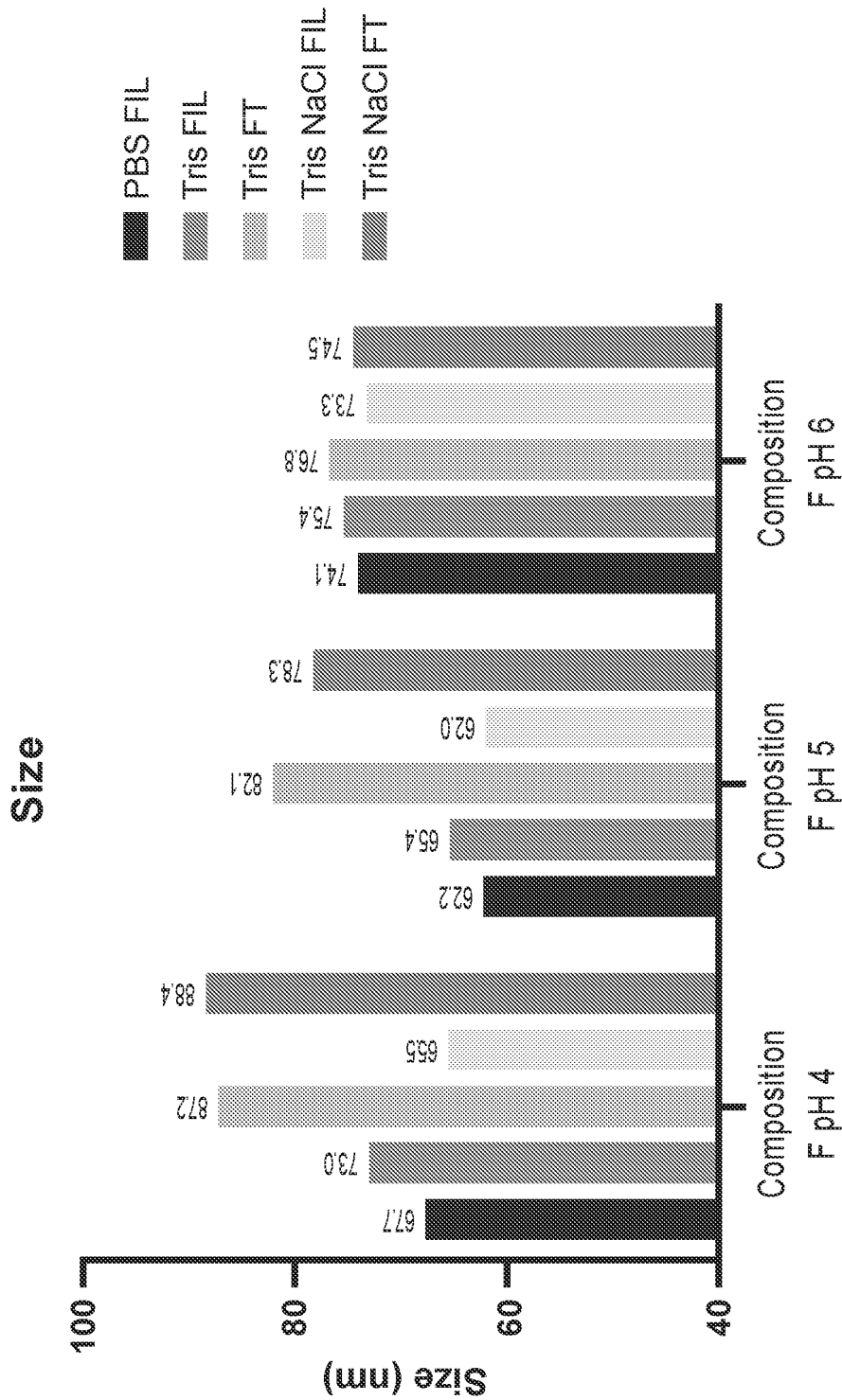


FIG. 39A

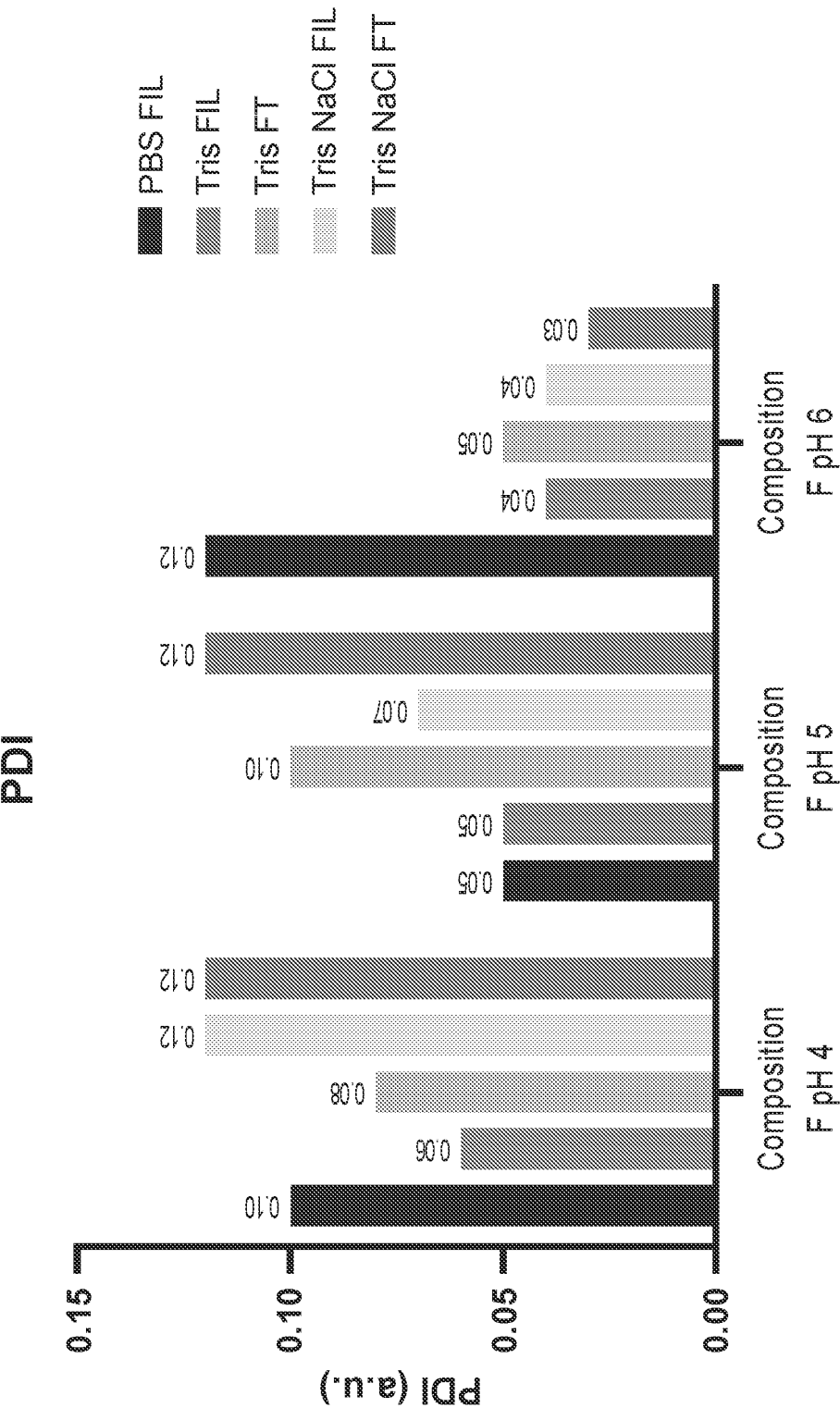


FIG. 39B

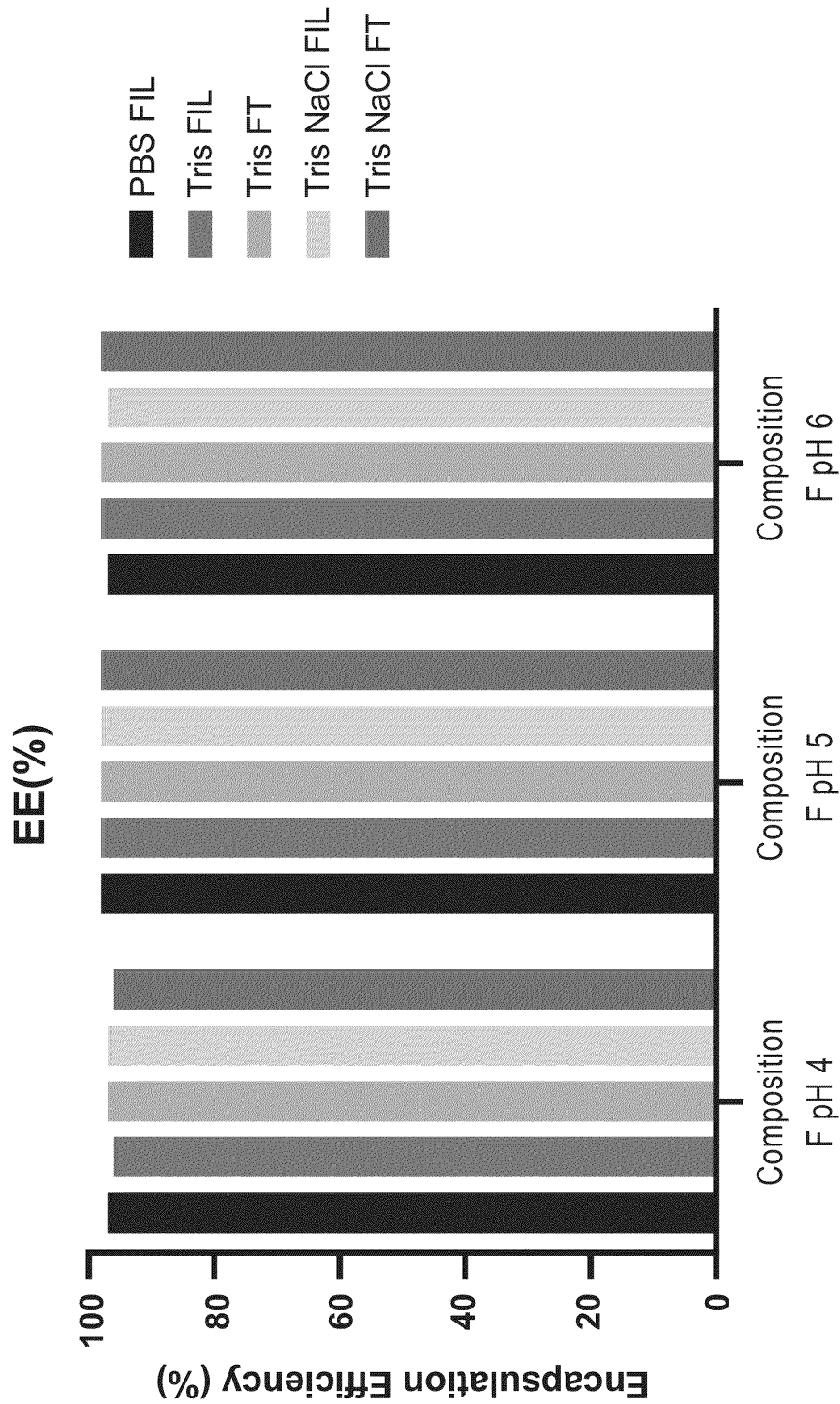


FIG. 39C

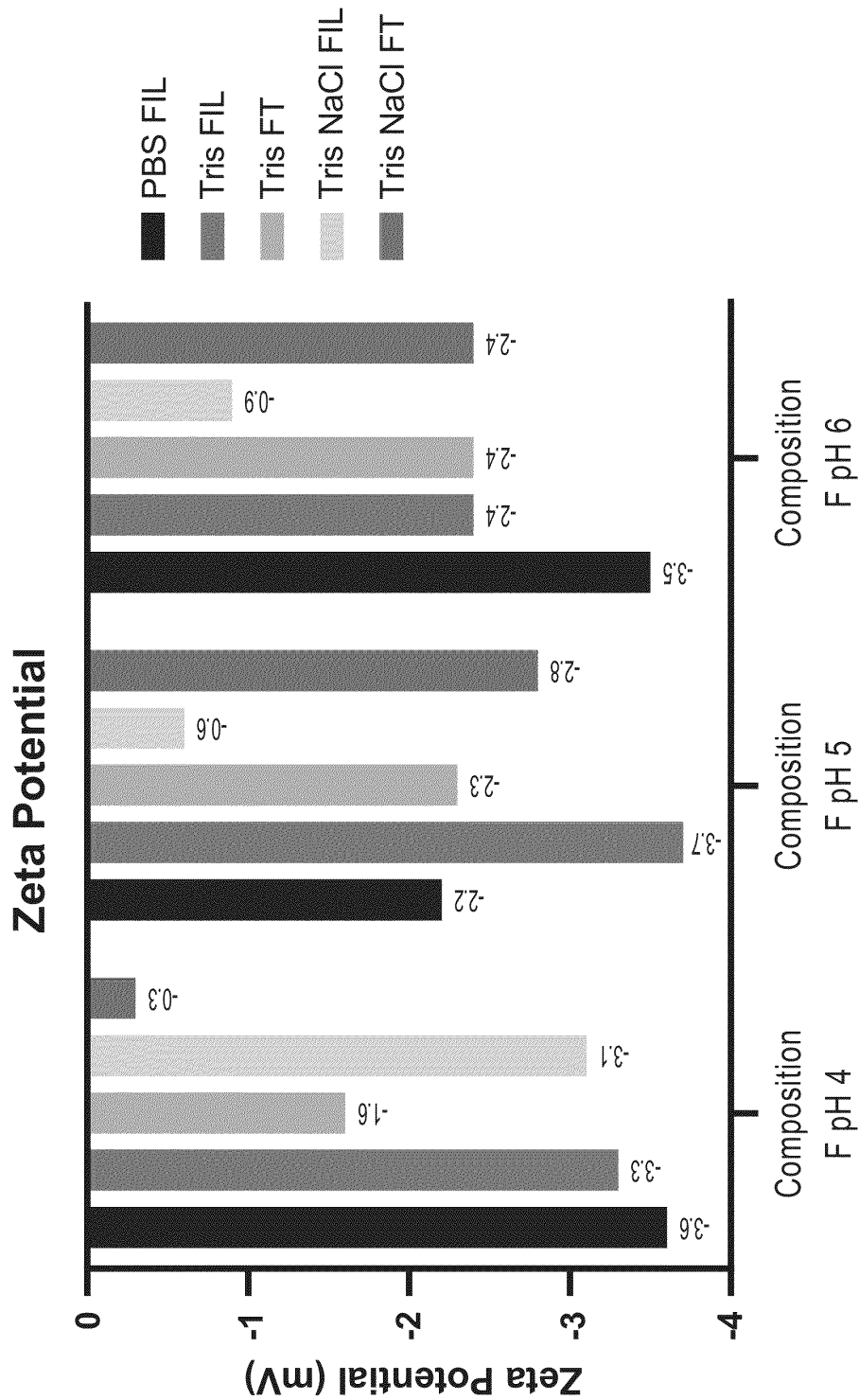


FIG. 39D

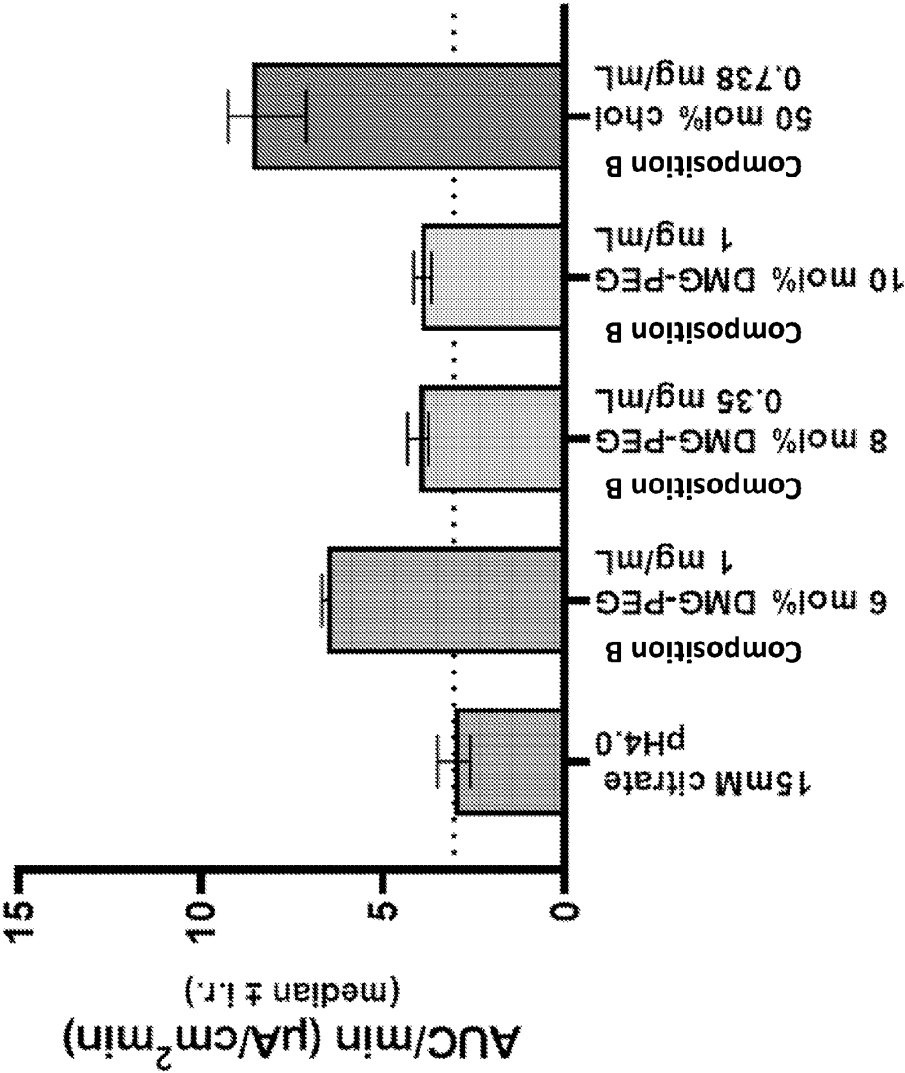


FIG. 40

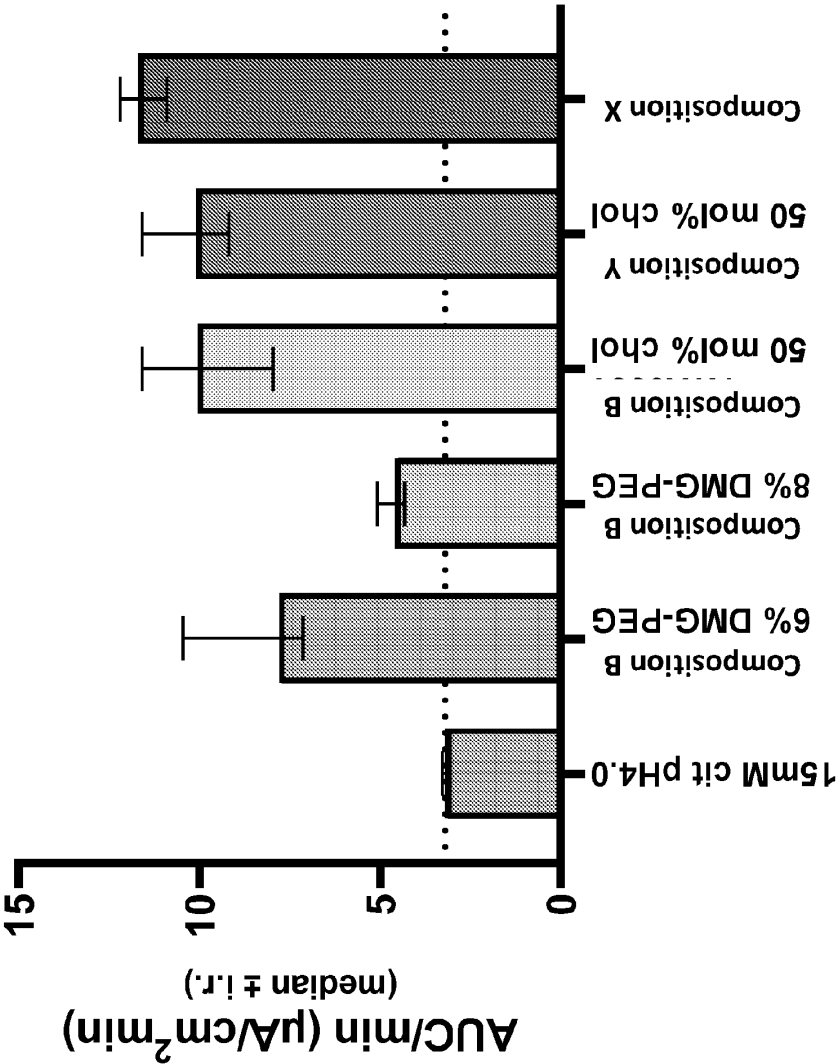


FIG. 41

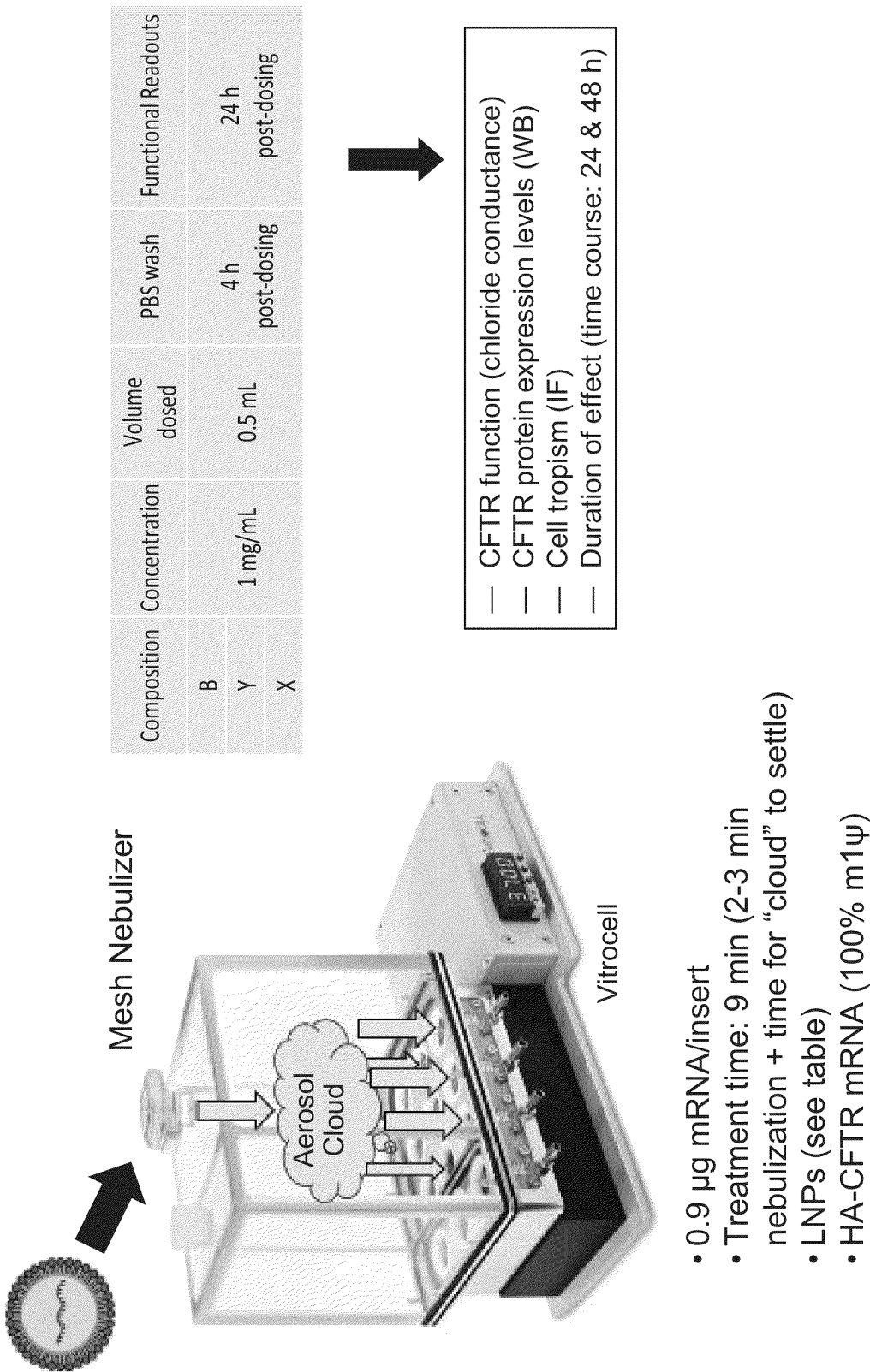


FIG. 42

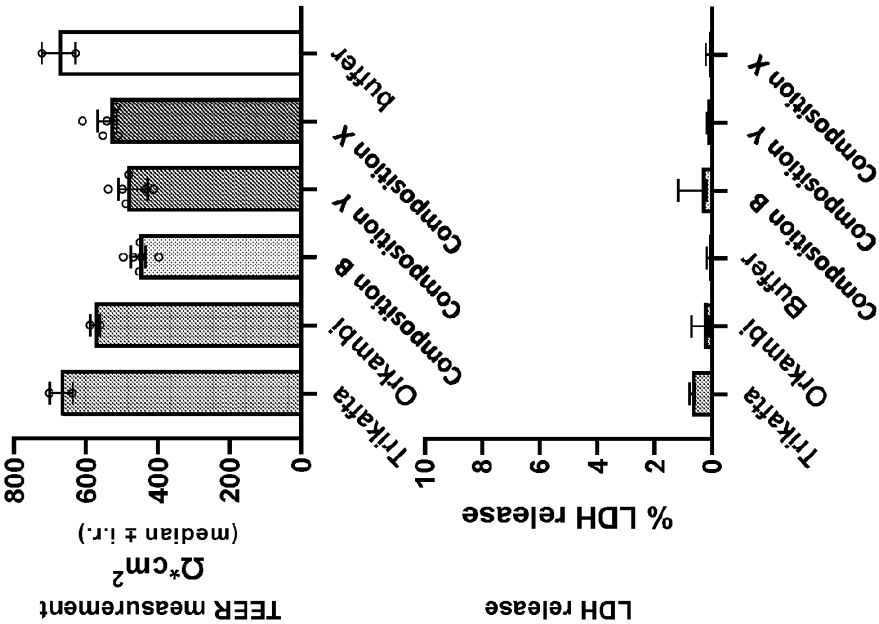


FIG. 43B

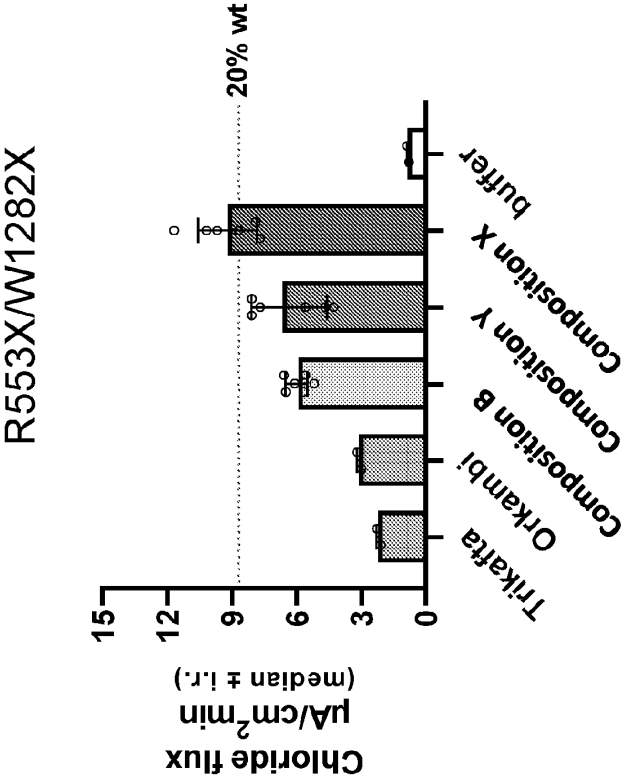


FIG. 43A

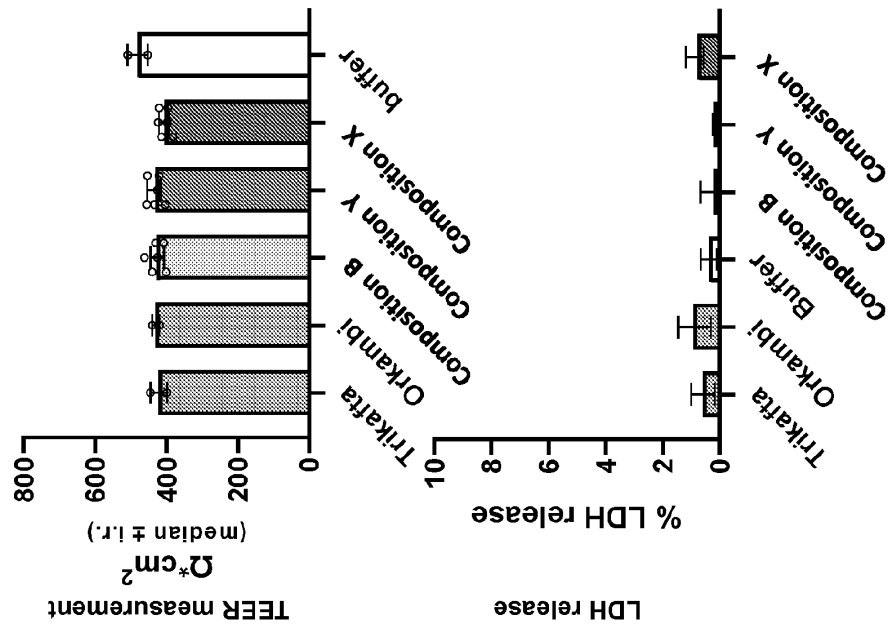


FIG. 43D

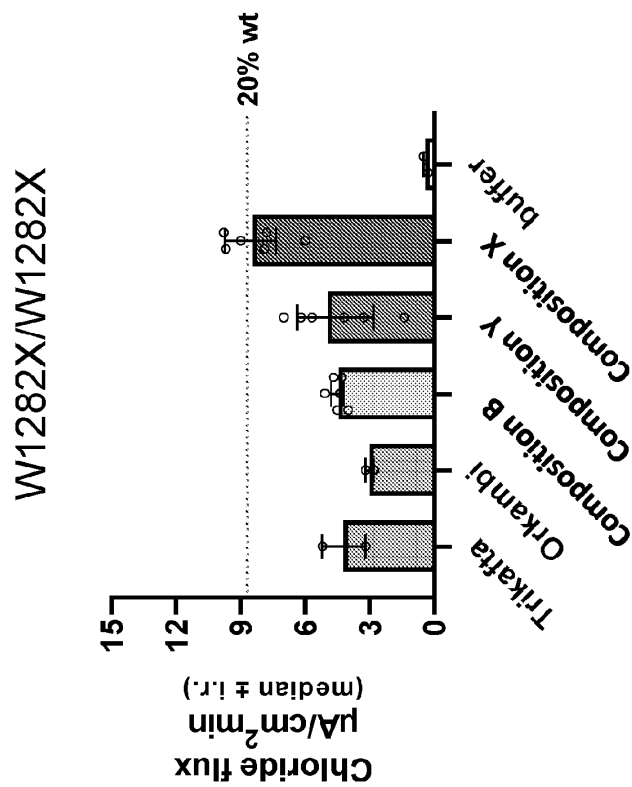


FIG. 43C

RTX vs Orkambi

* = significantly different ($p < 0.05$)

▲ = no statistical difference

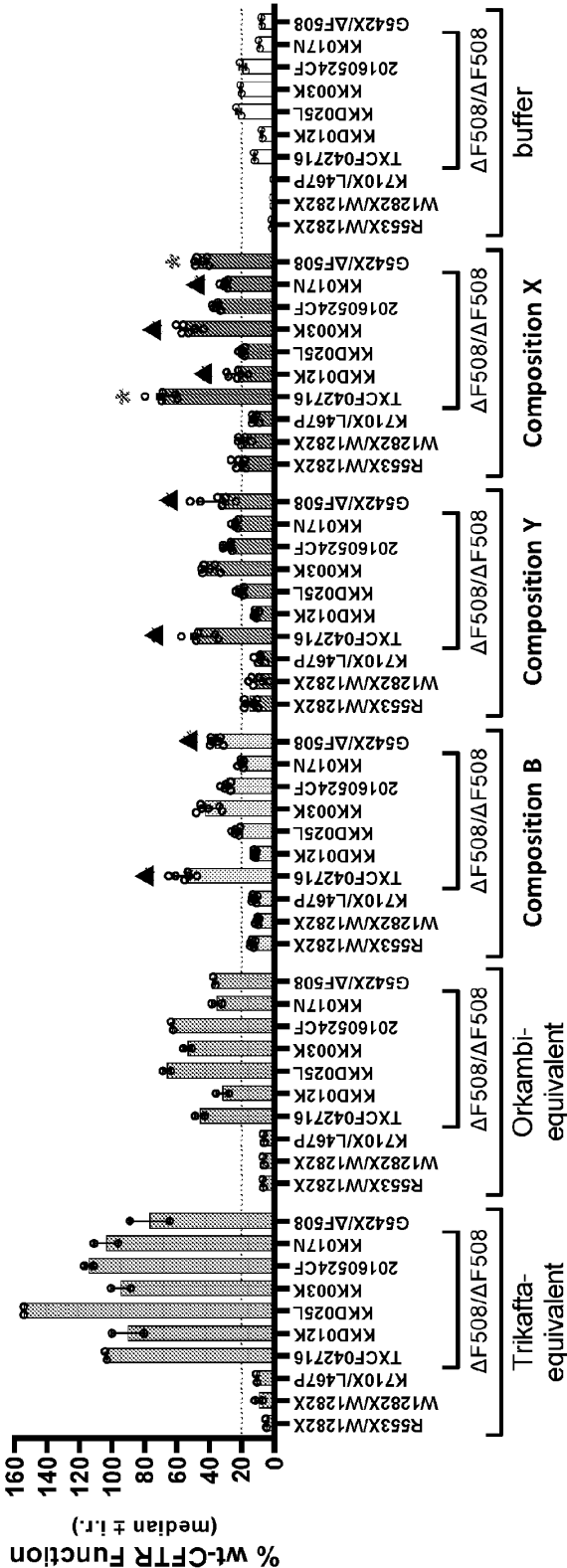


FIG. 44

donor TXCF042716

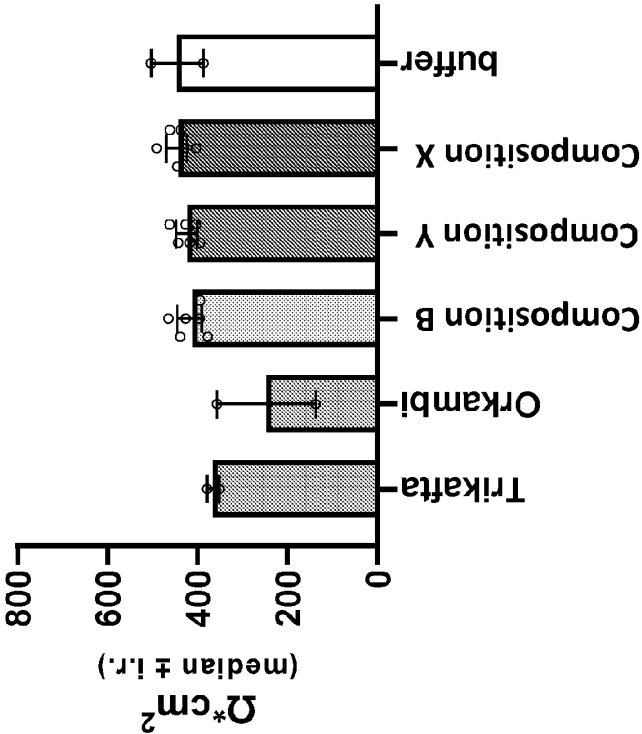


FIG. 45A

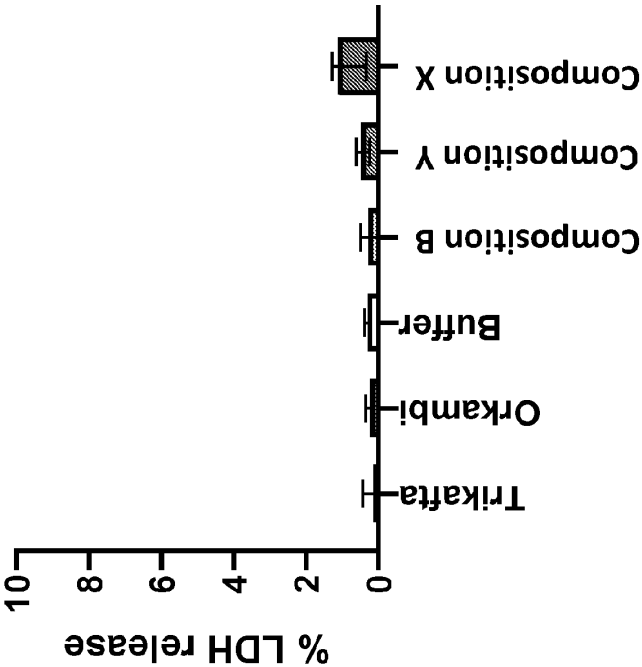


FIG. 45B

donor KKD012K

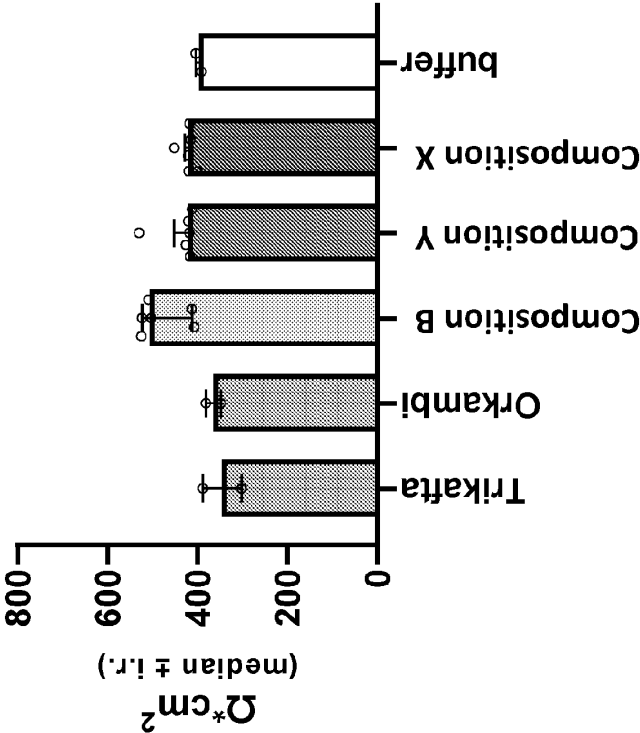


FIG. 45C

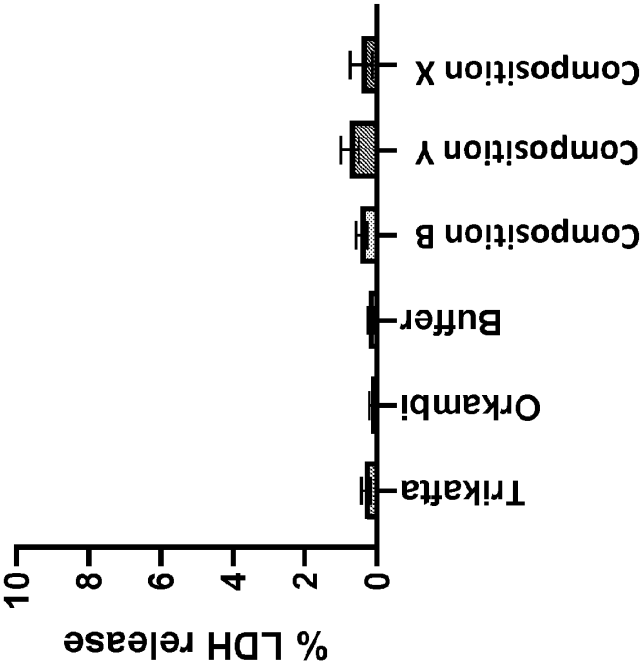


FIG. 45D

donor KKD025L

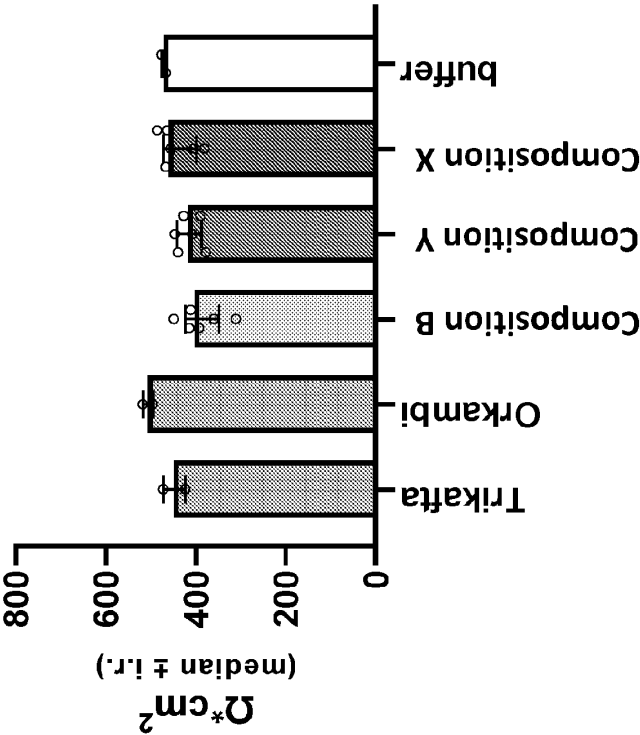


FIG. 45E

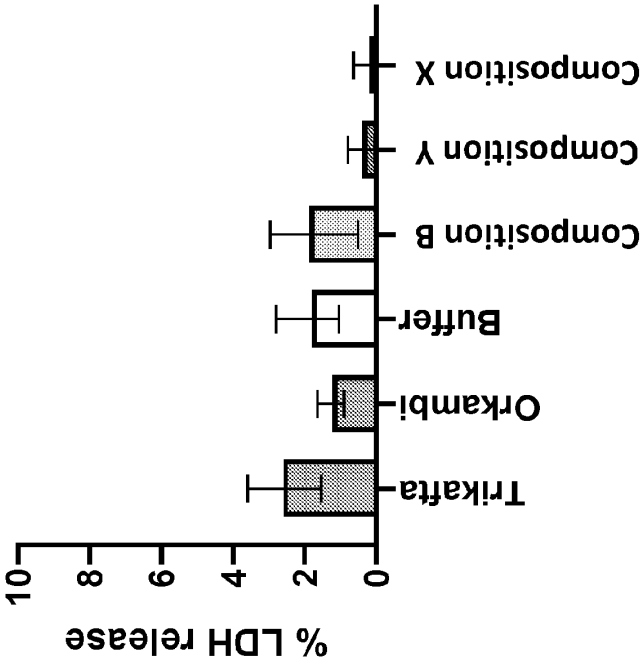


FIG. 45F

donor KKD003K

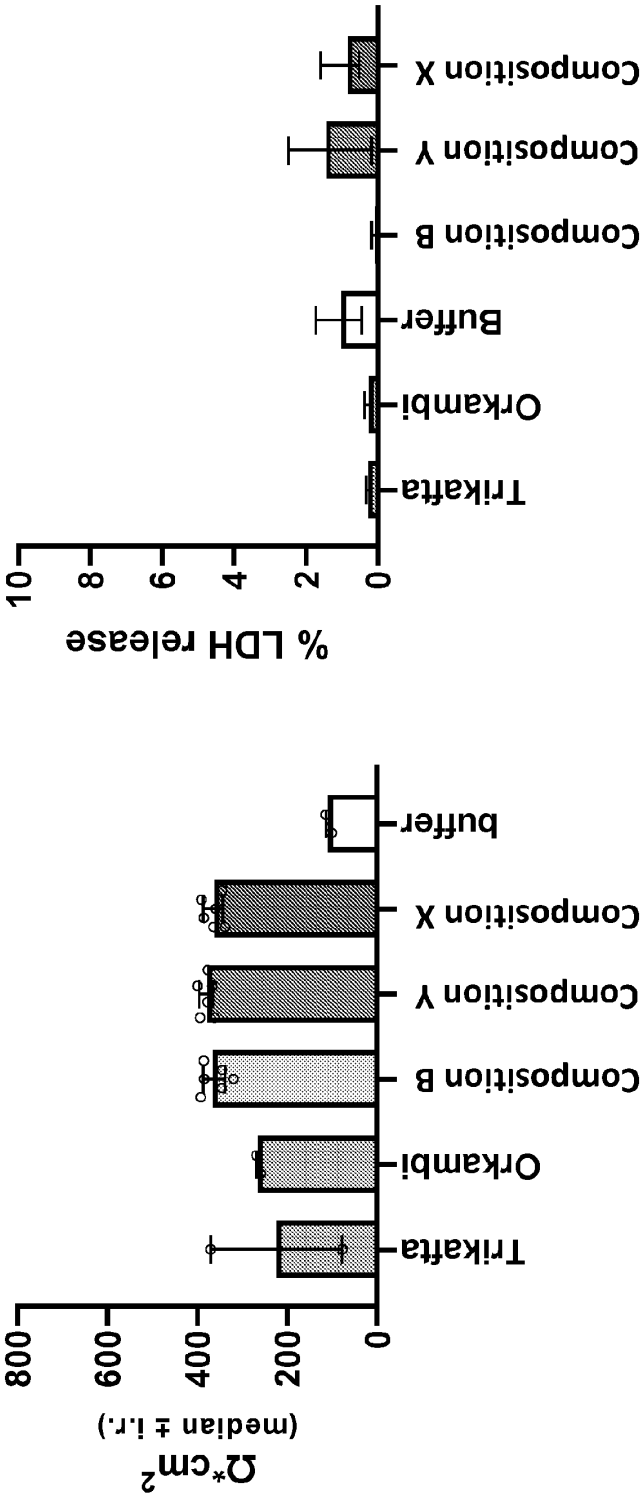


FIG. 45H

FIG. 45G

donor 20160524CF

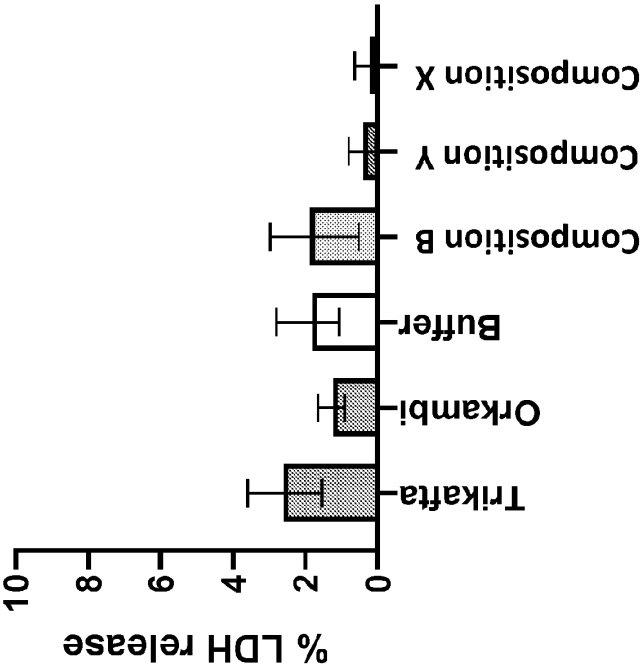


FIG. 45J

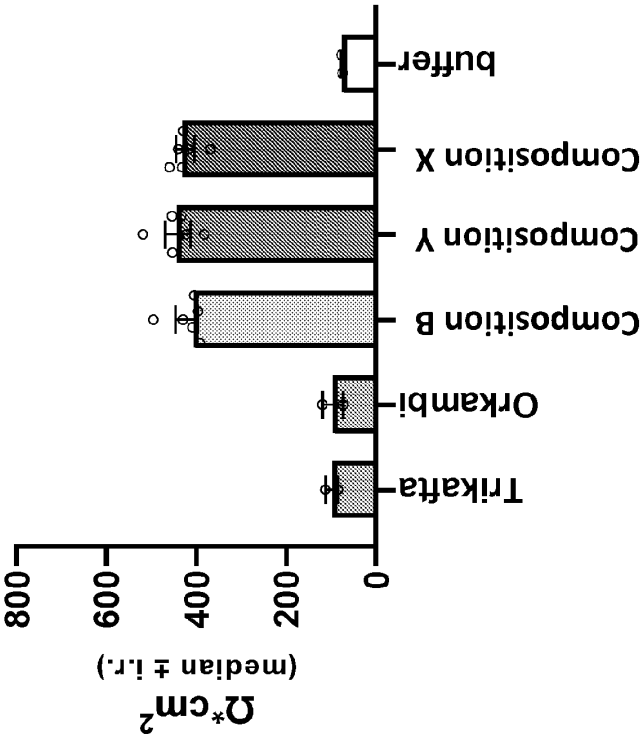


FIG. 45I

donor KK017N

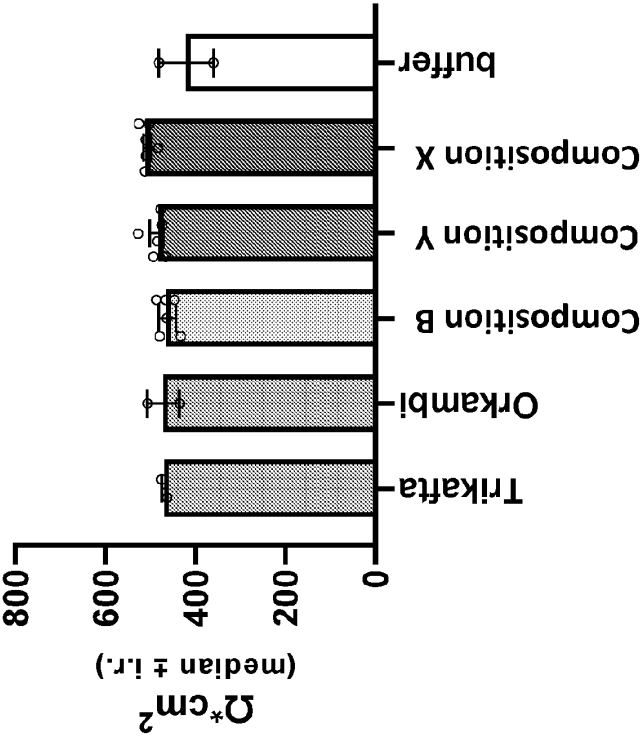


FIG. 45K

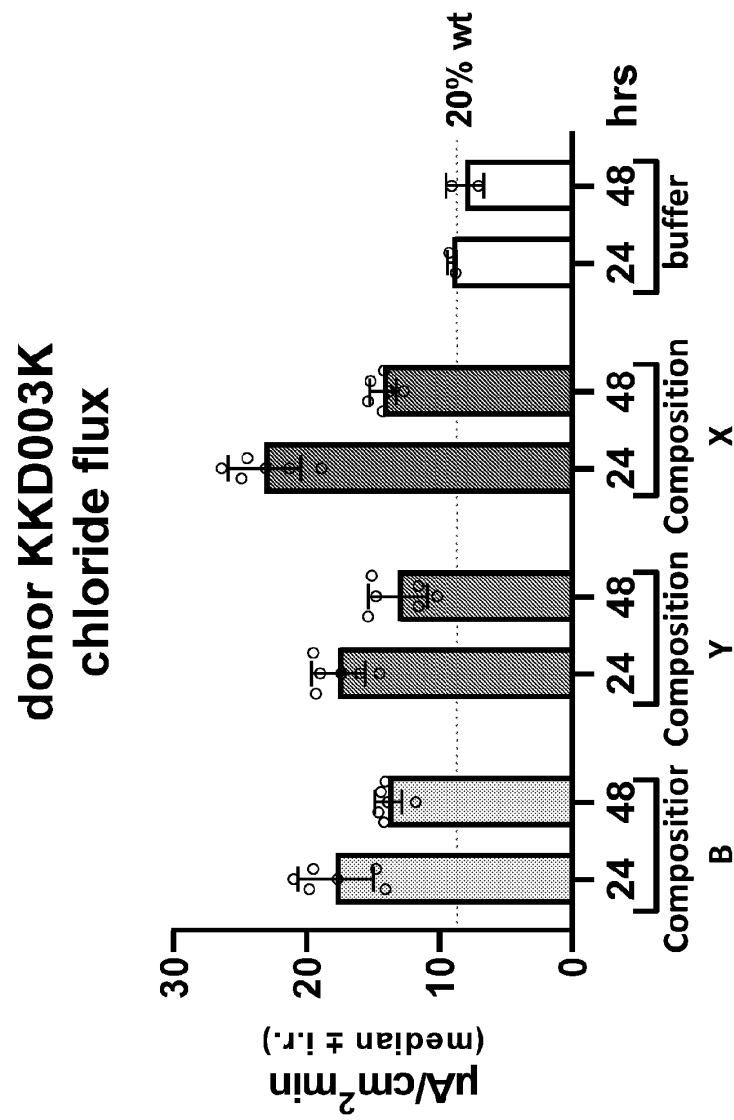


FIG. 46A

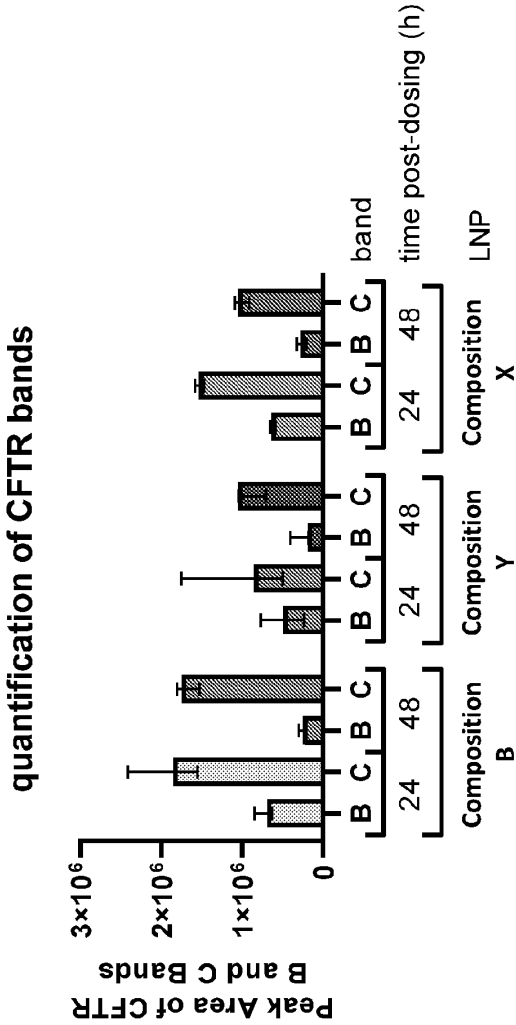


FIG. 46B

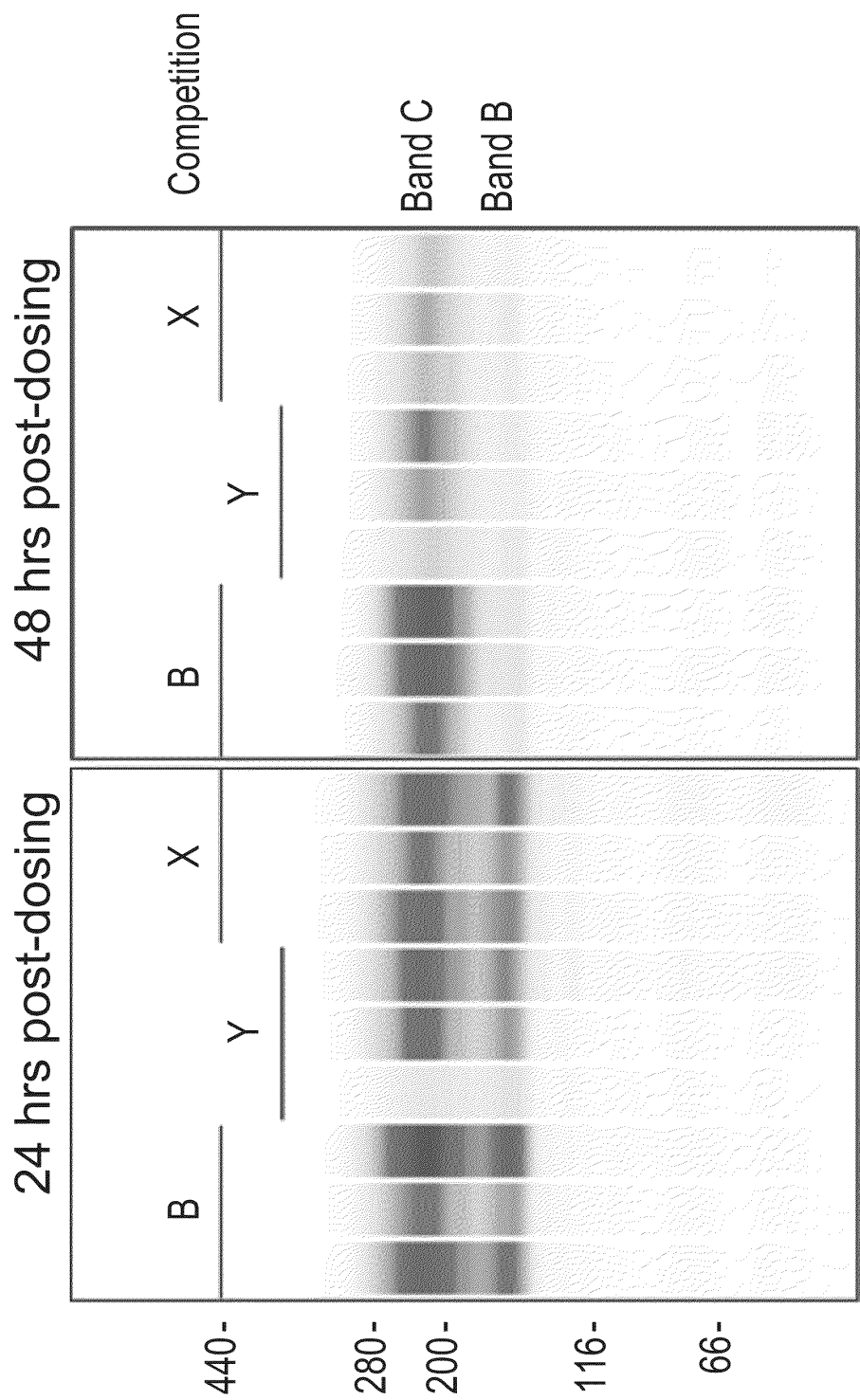


FIG. 46C

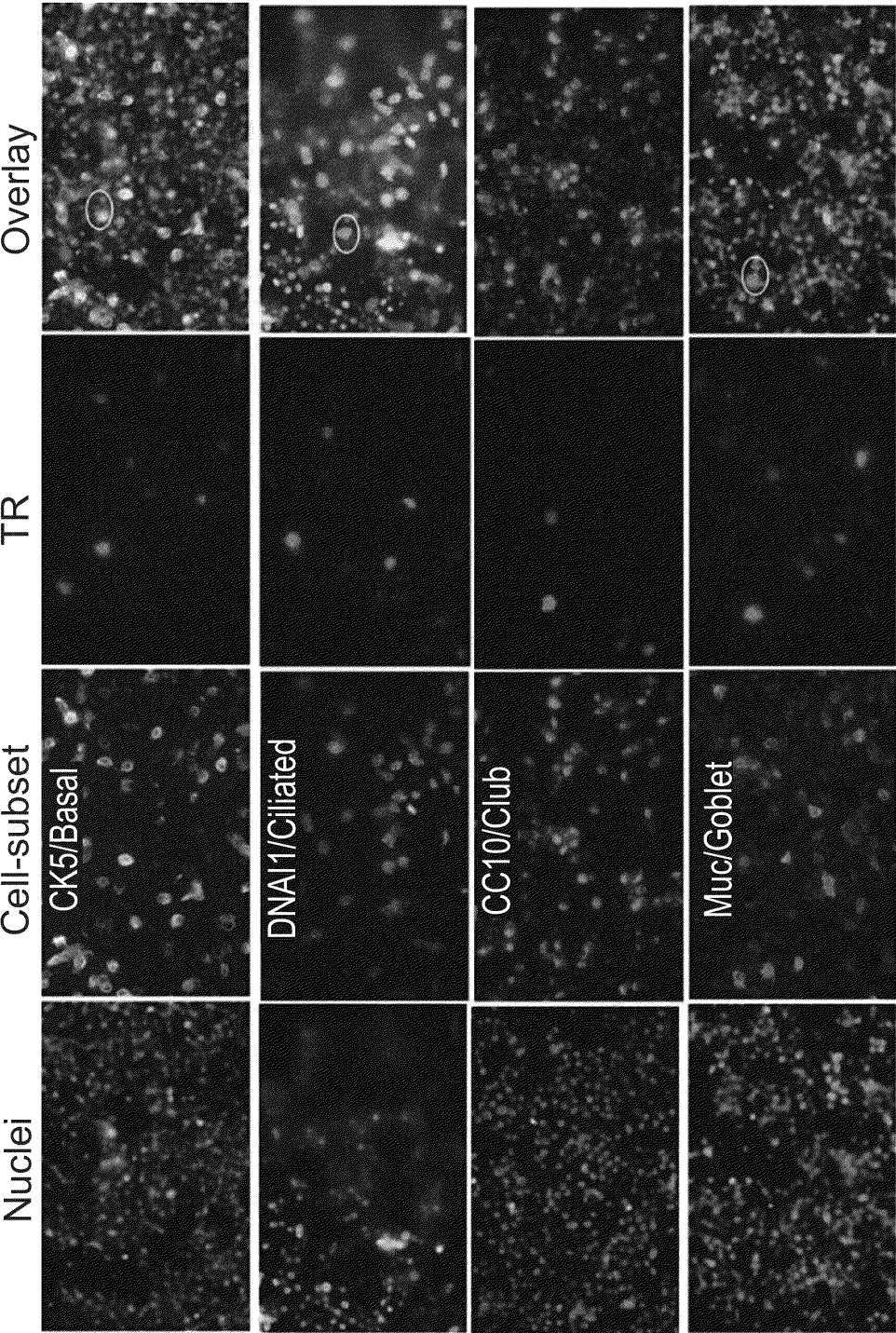


FIG. 47A

**Δ F508/ Δ F508
(donor TXCF042716)
LNP/TdTomato mRNA**

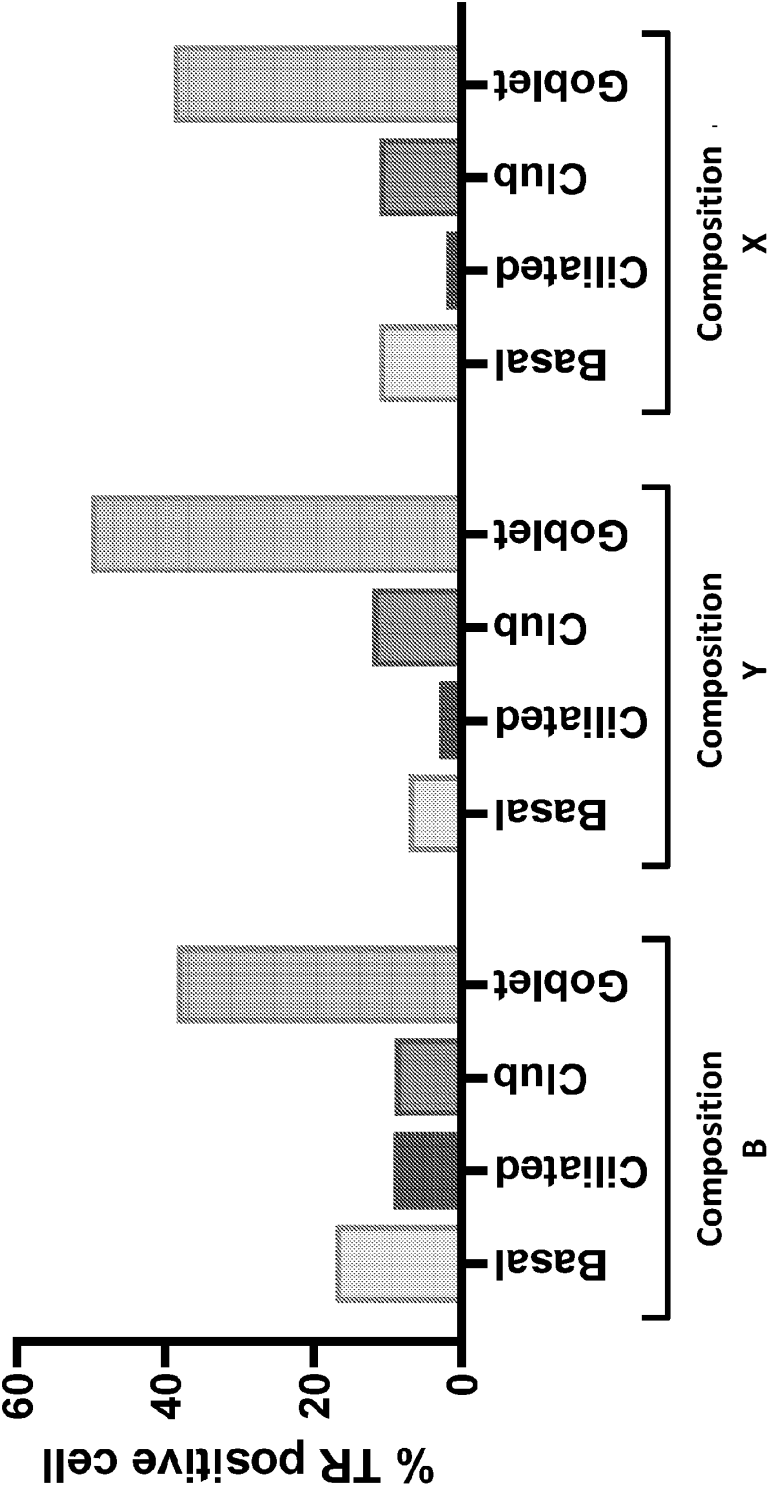


FIG. 47B

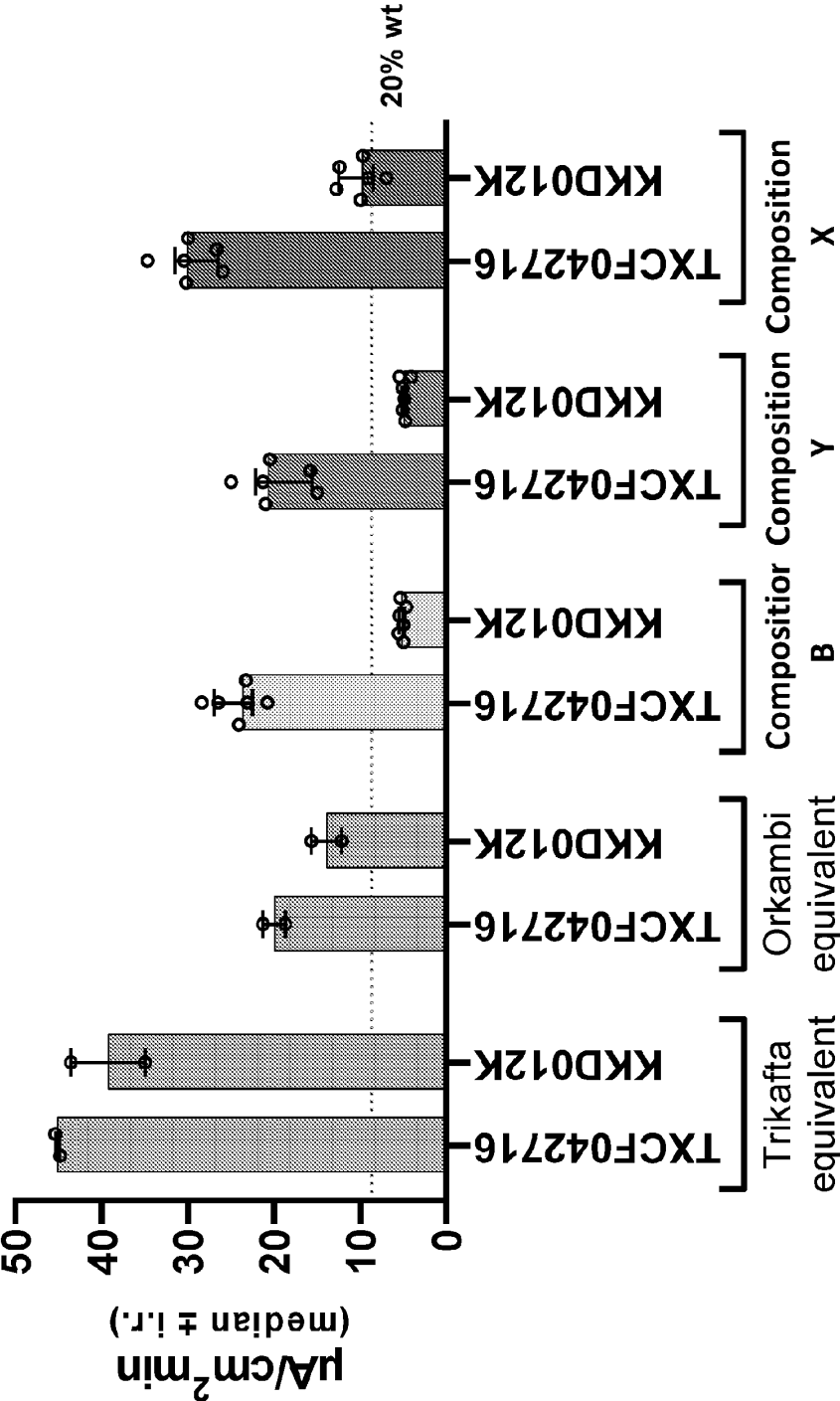


FIG. 48A

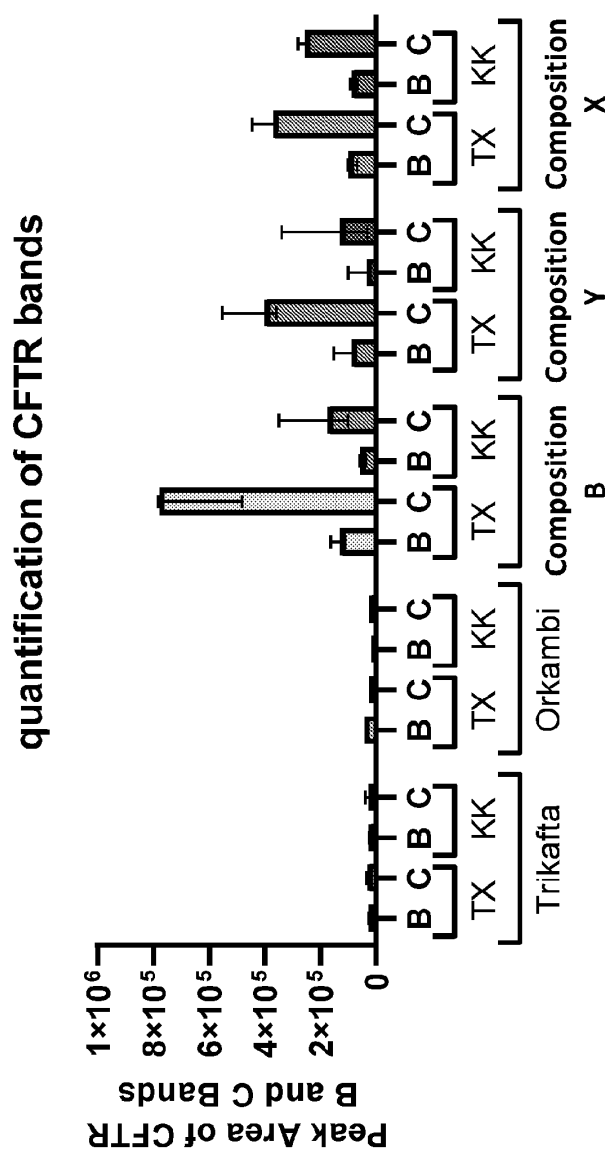
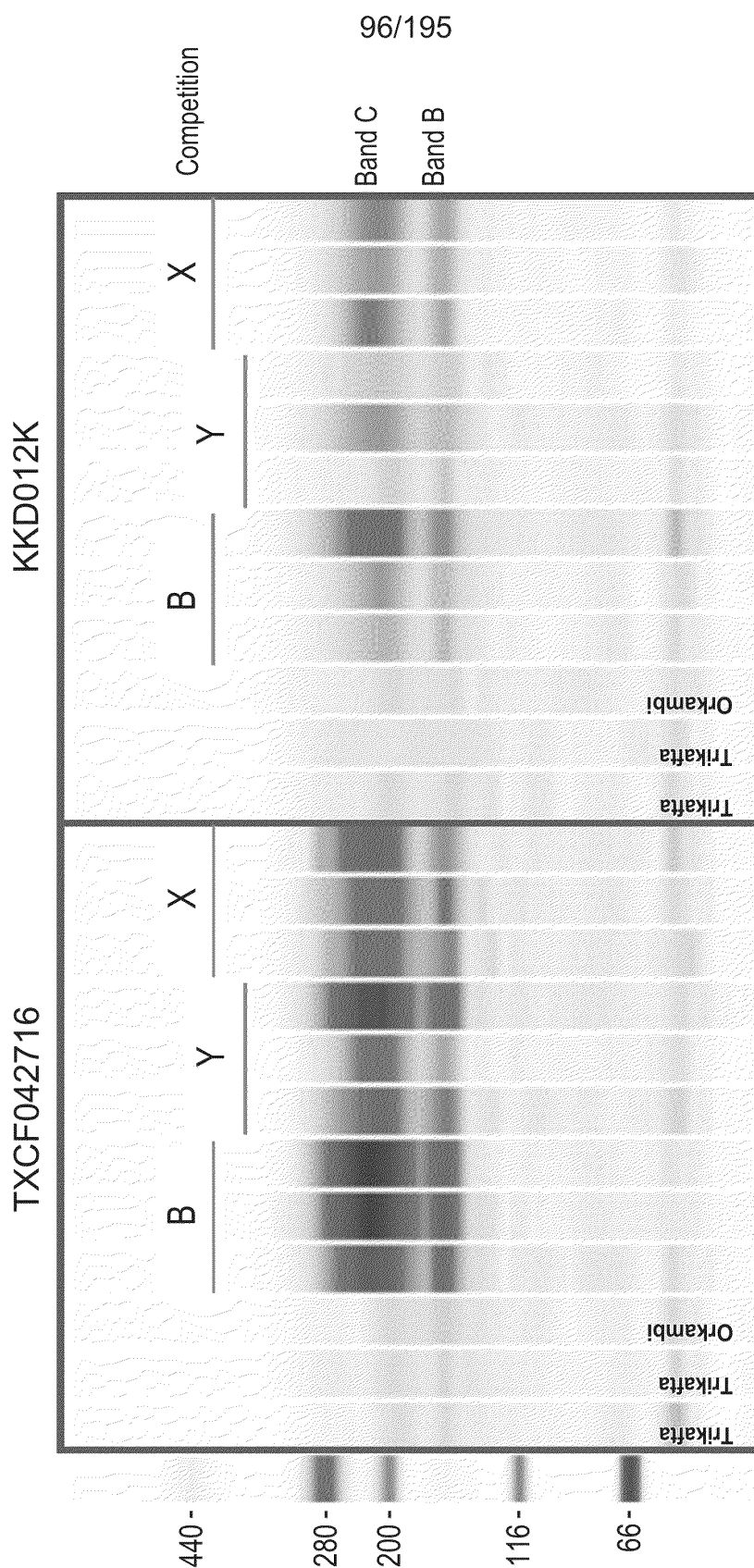
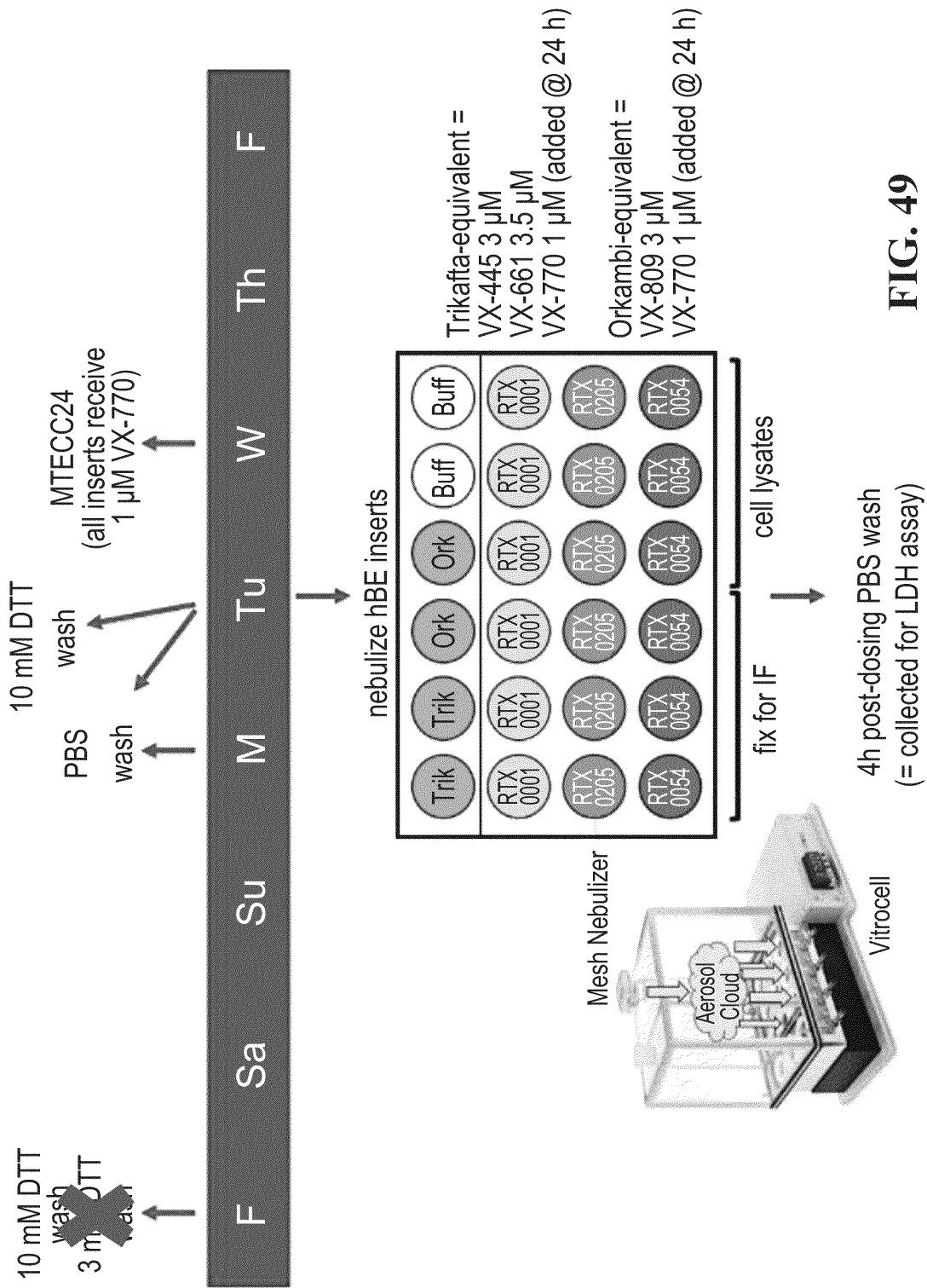


FIG. 48B





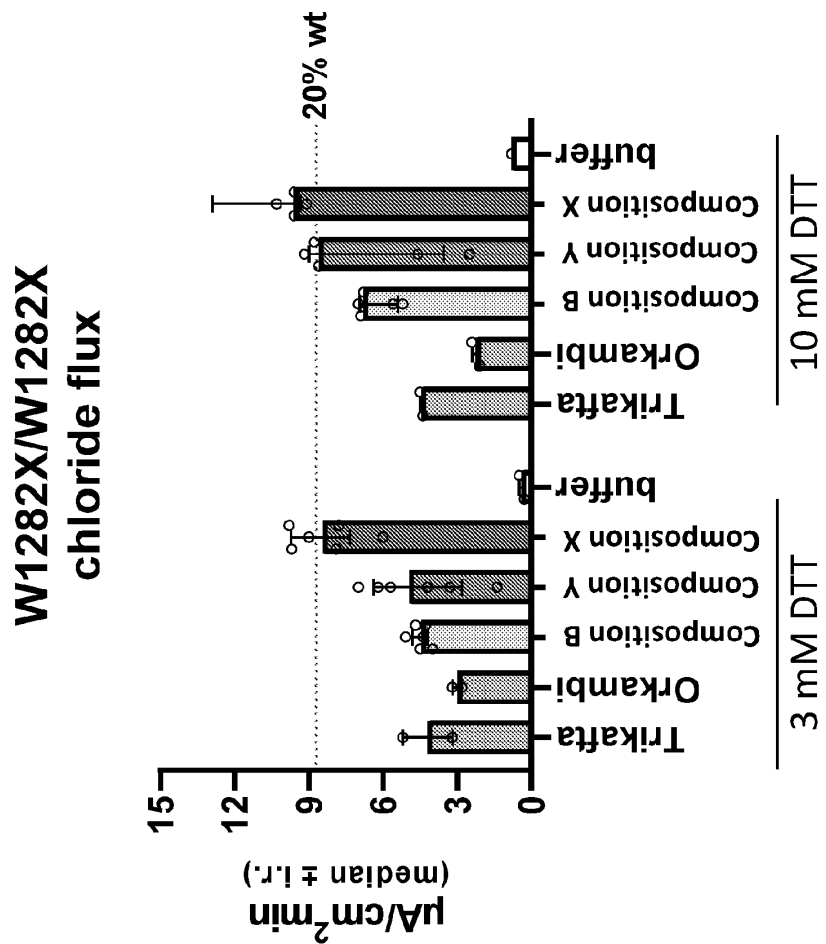


FIG. 50A

W1282X/W1282X
TEER

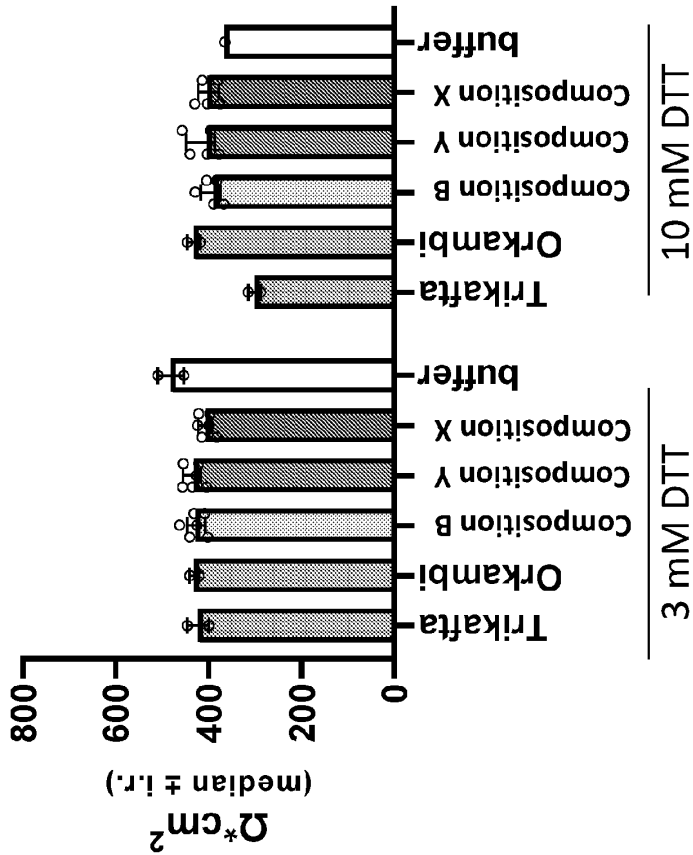


FIG. 50B

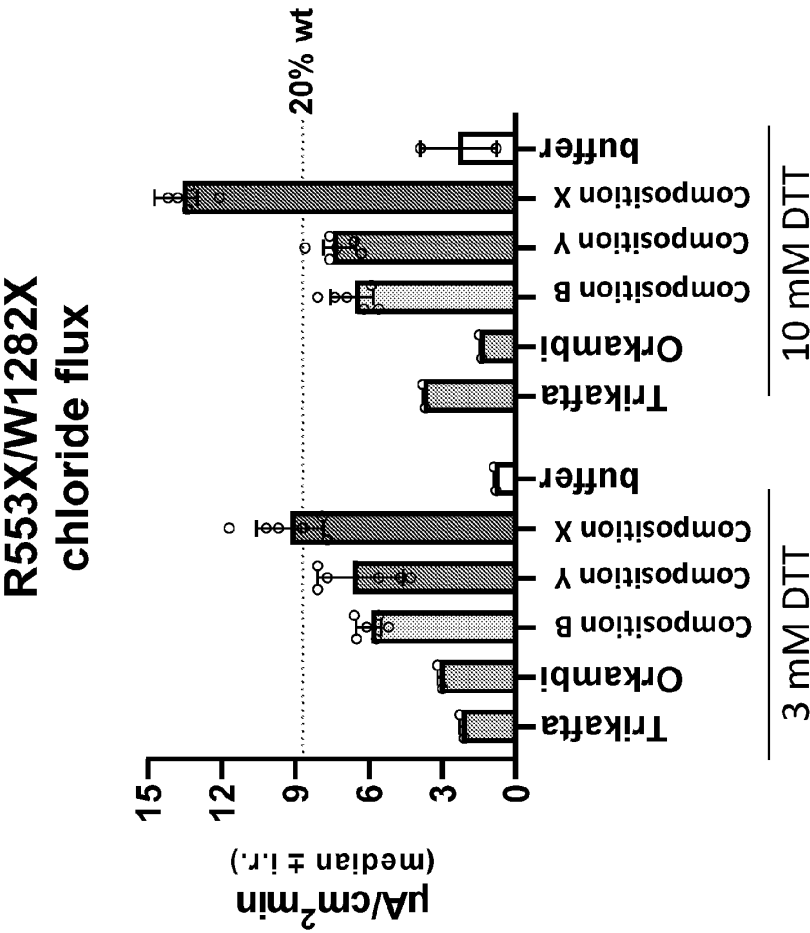


FIG. 51A

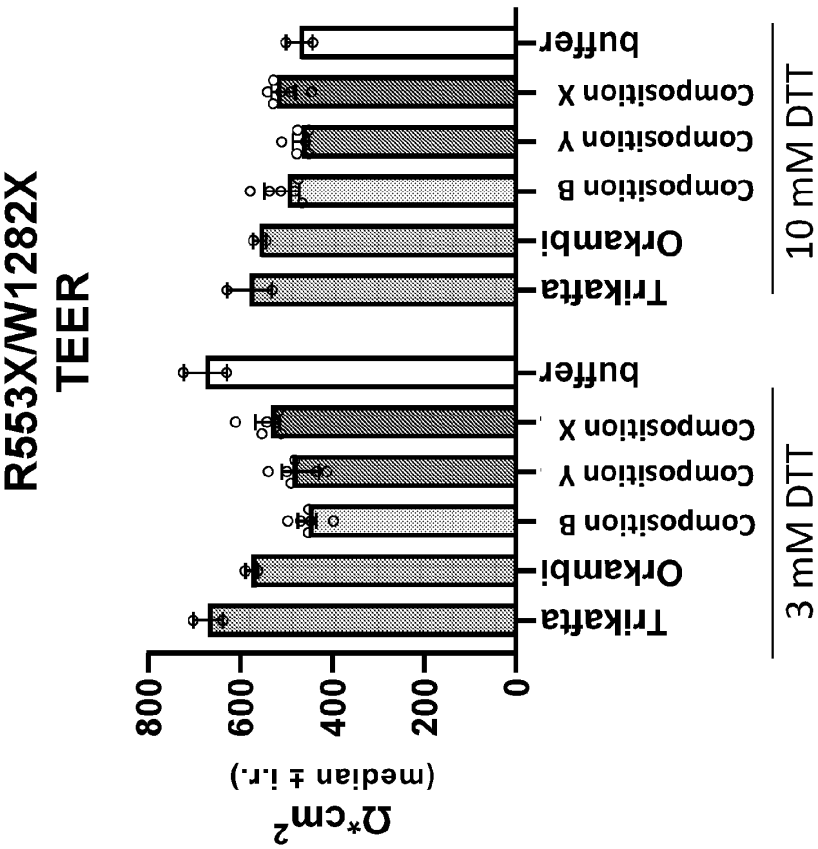


FIG. 51B

R553X/W1282X
+/- Ivacaftor (VX-770)

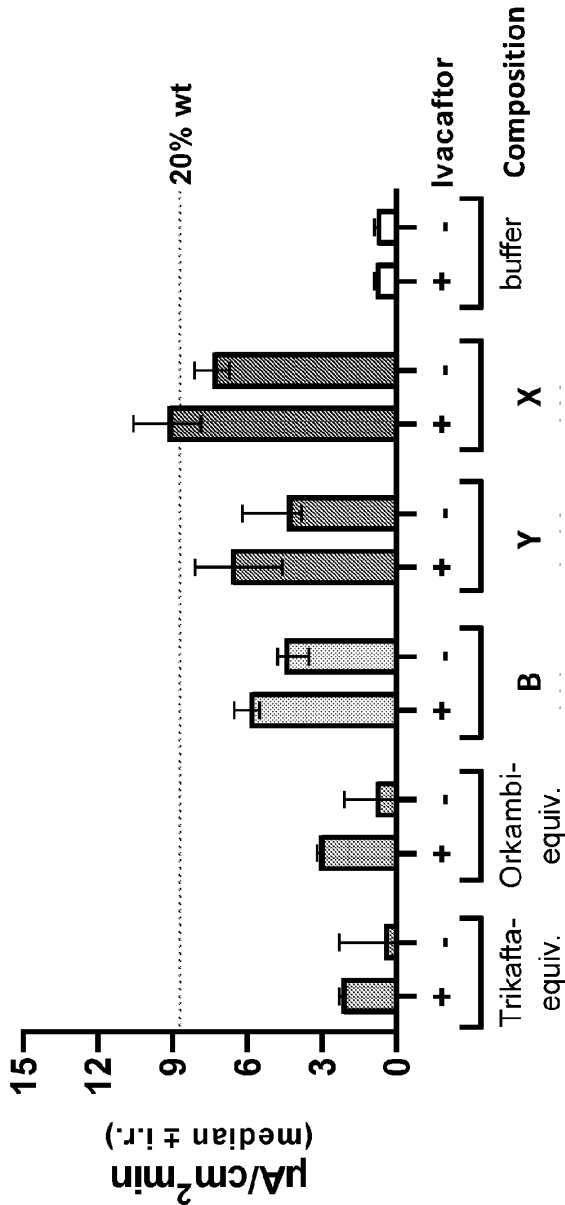


FIG. 52A

W1282X/W1282X
+/- Ivacaftor (VX-770)

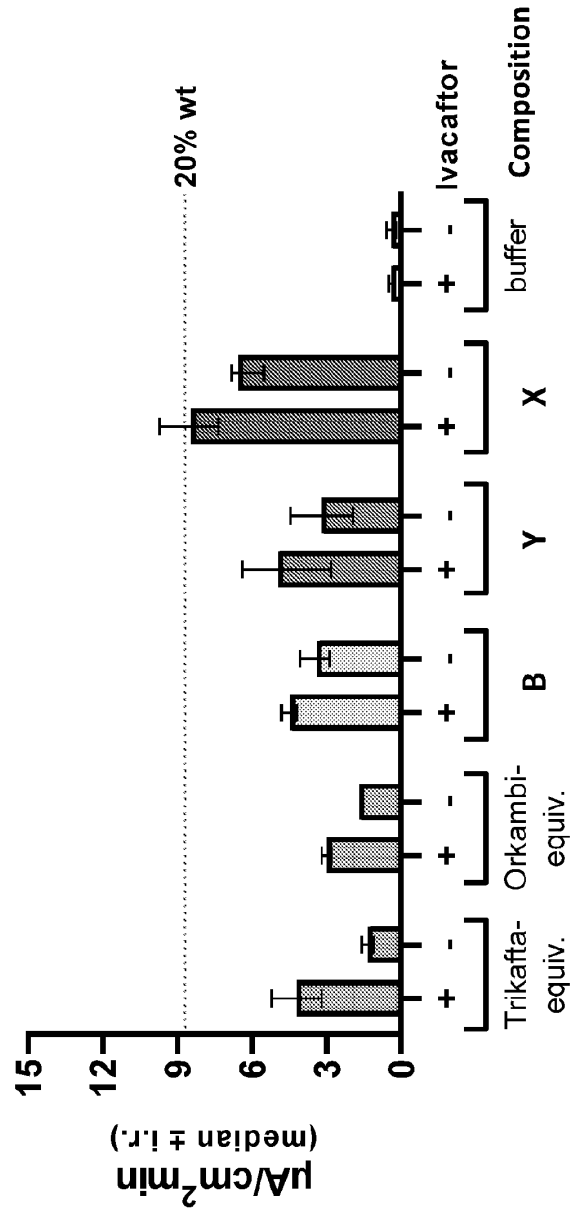


FIG. 52B

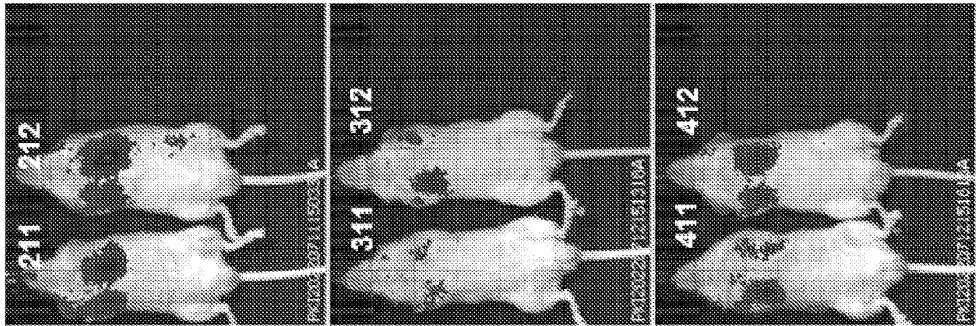


FIG. 53B

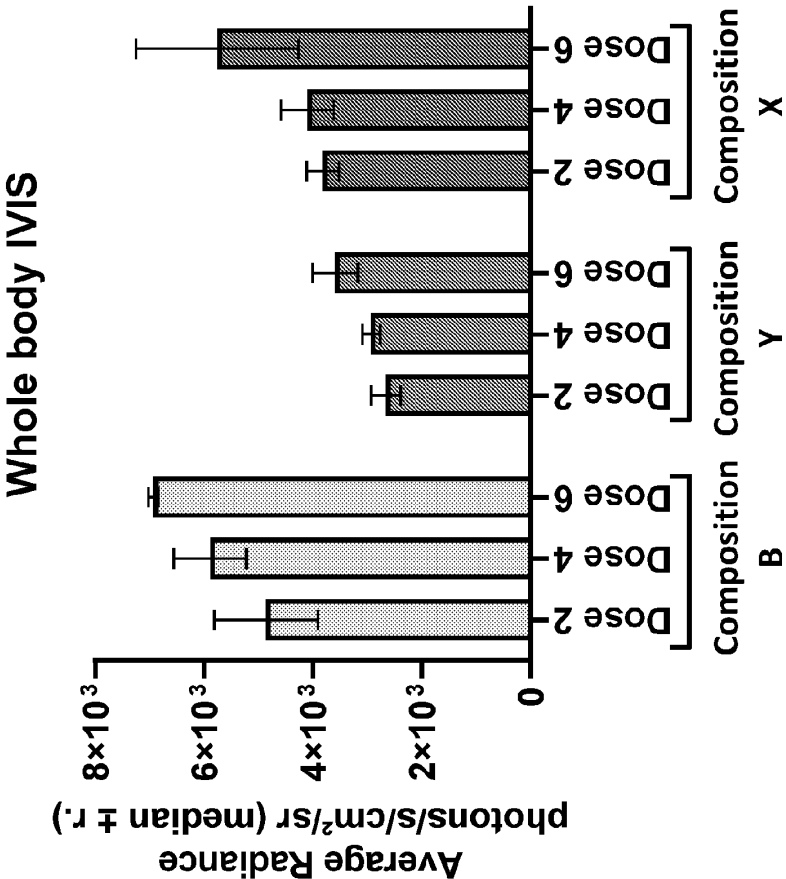


FIG. 53A

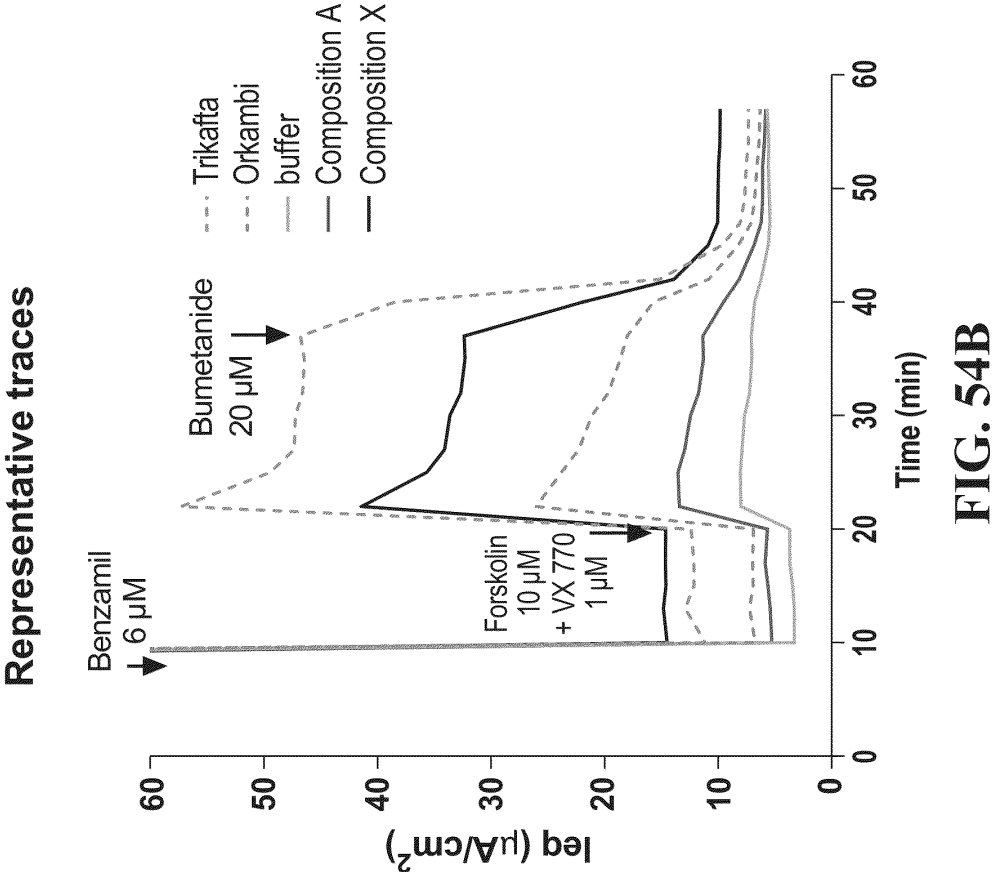


FIG. 54B

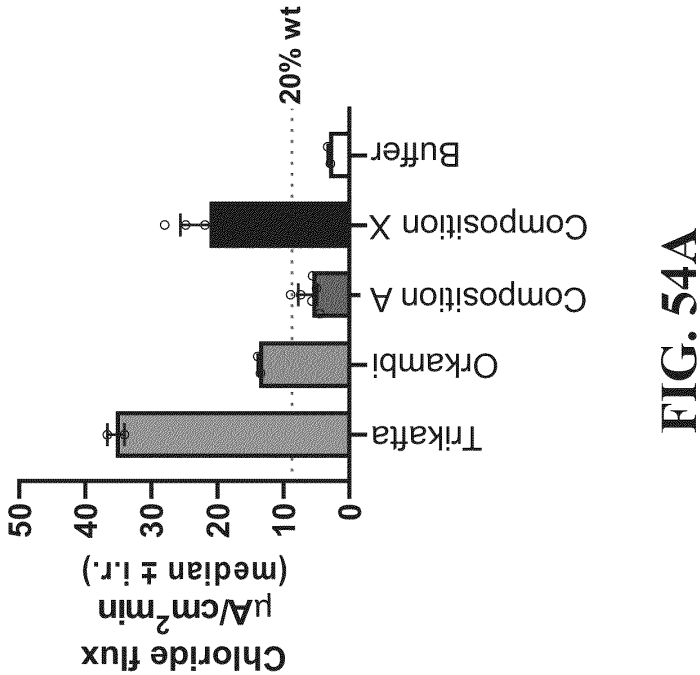


FIG. 54A

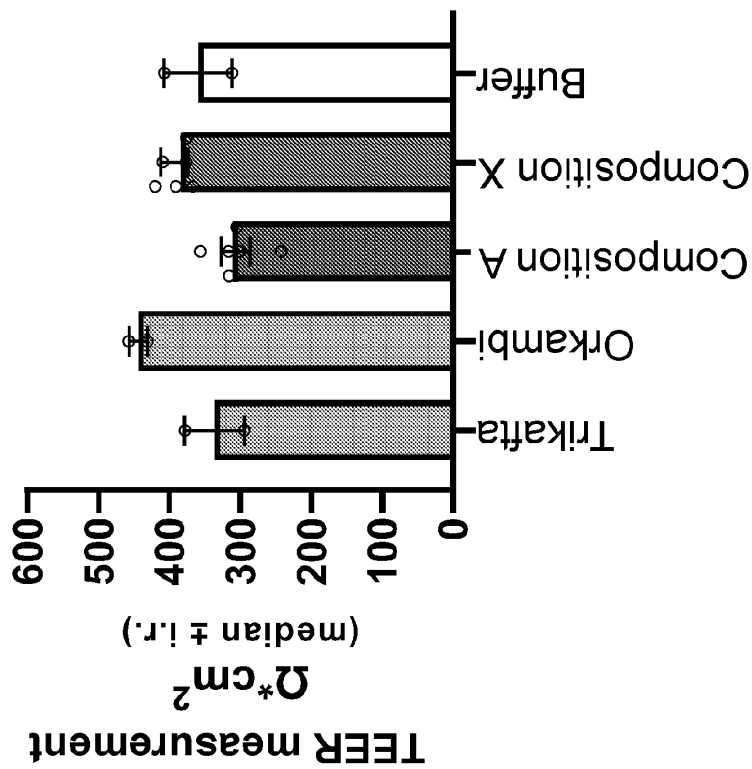


FIG. 54C

Composition B - CFTR-HA
RCT-2100-22-KP-TFF-003

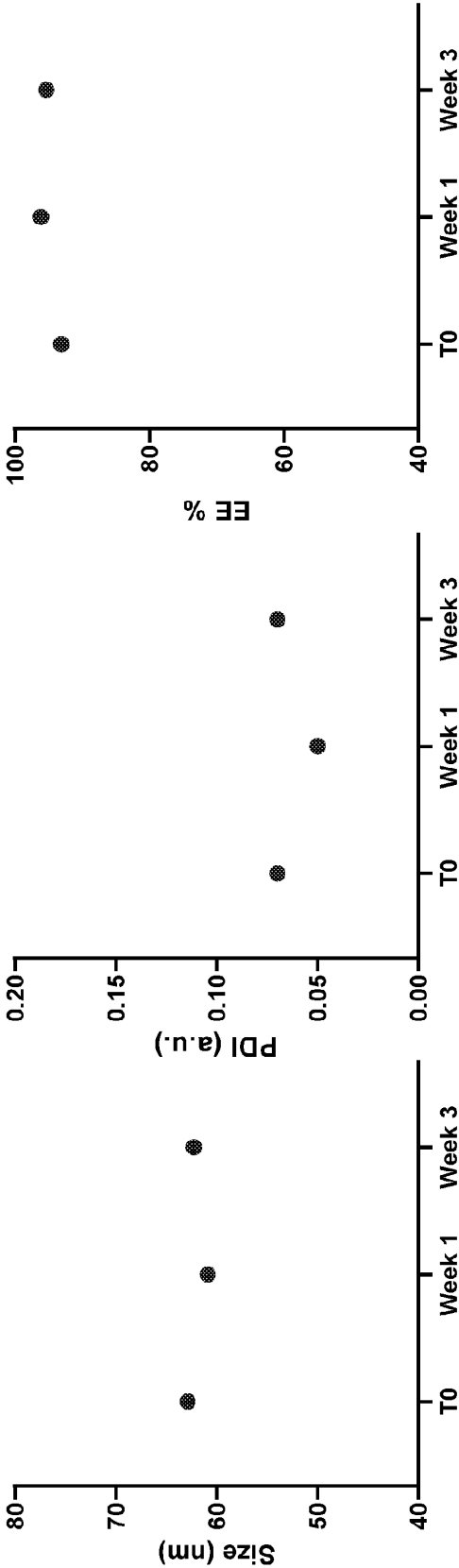


FIG. 55A

FIG. 55B

FIG. 55C

Composition X - CFTR-HA
RCT-2100-22-KP-TFF-003

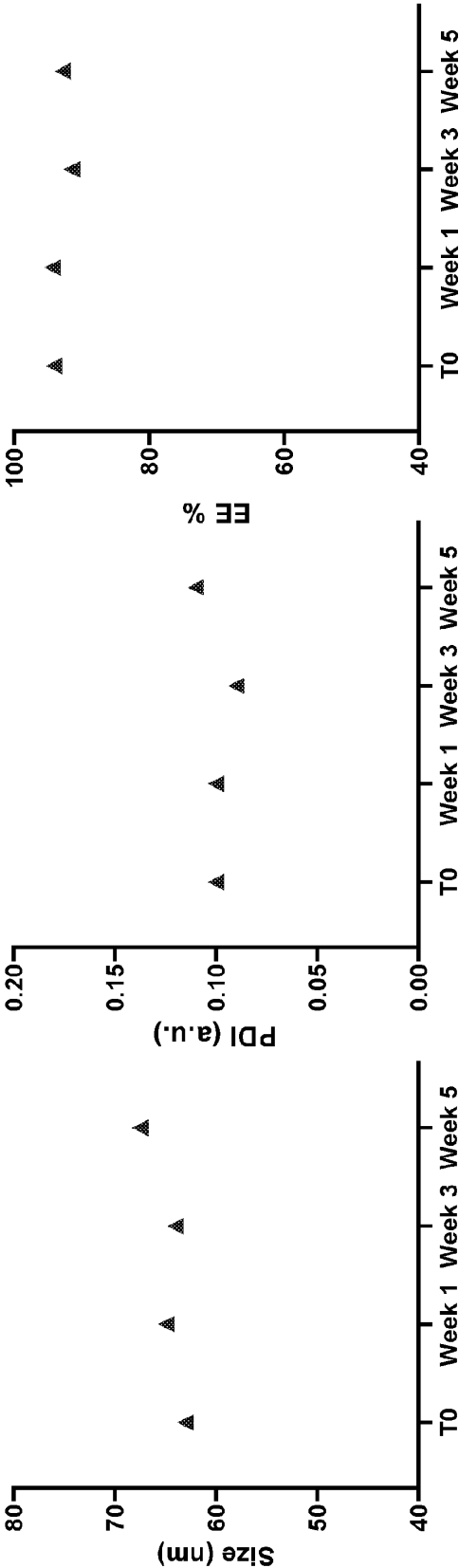


FIG. 56A

FIG. 56B

FIG. 56C

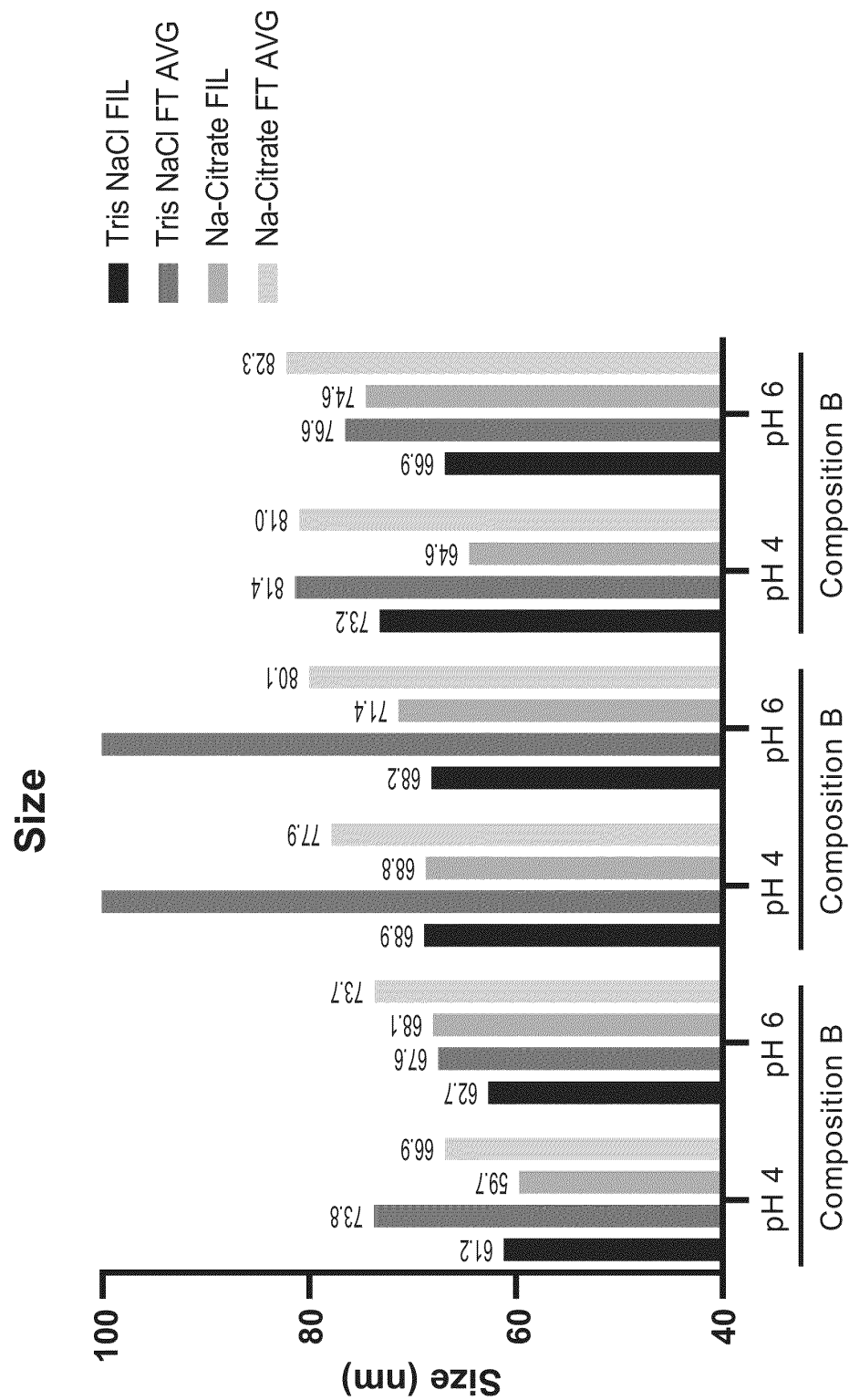


FIG. 57A

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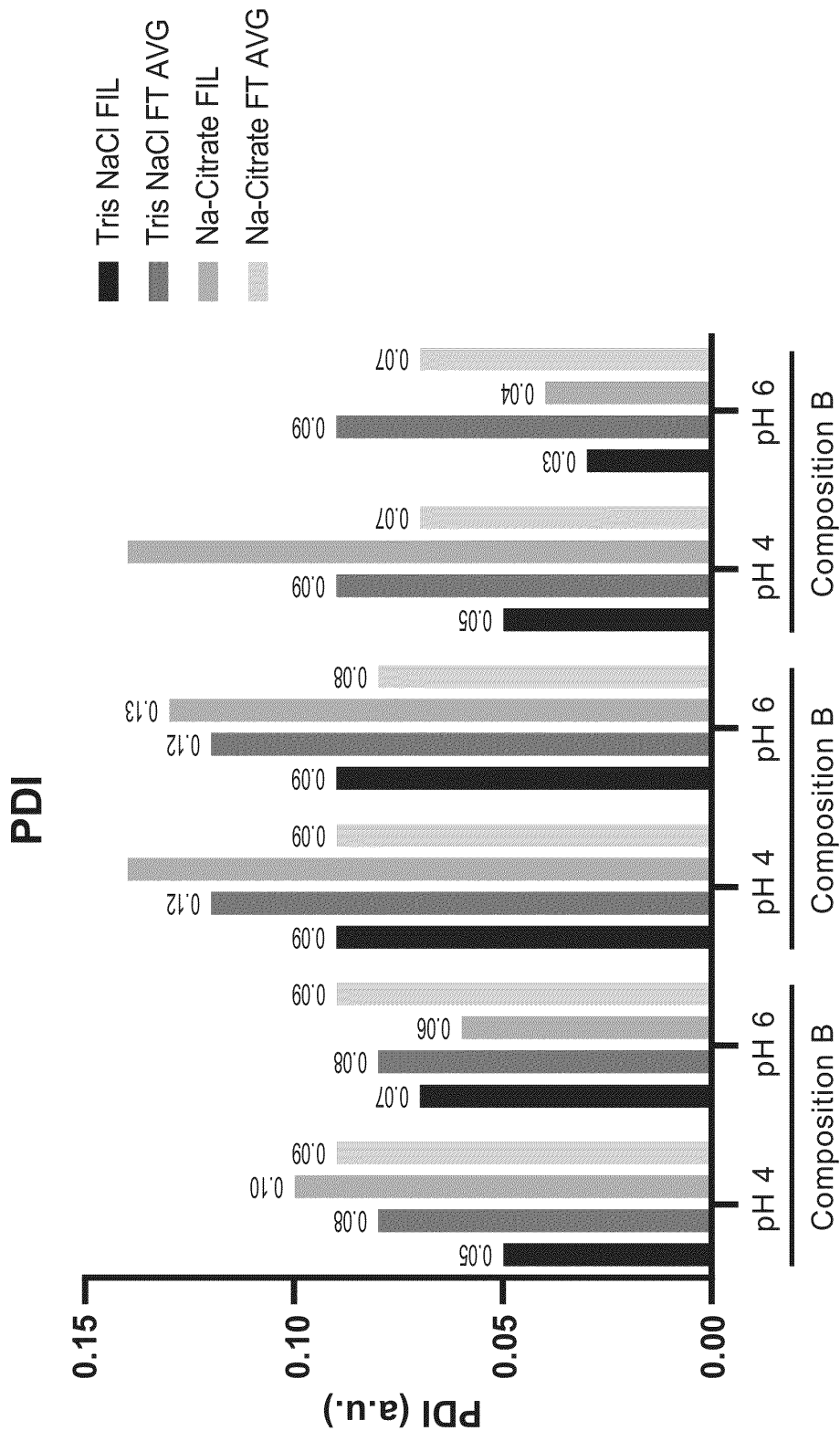


FIG. 57B

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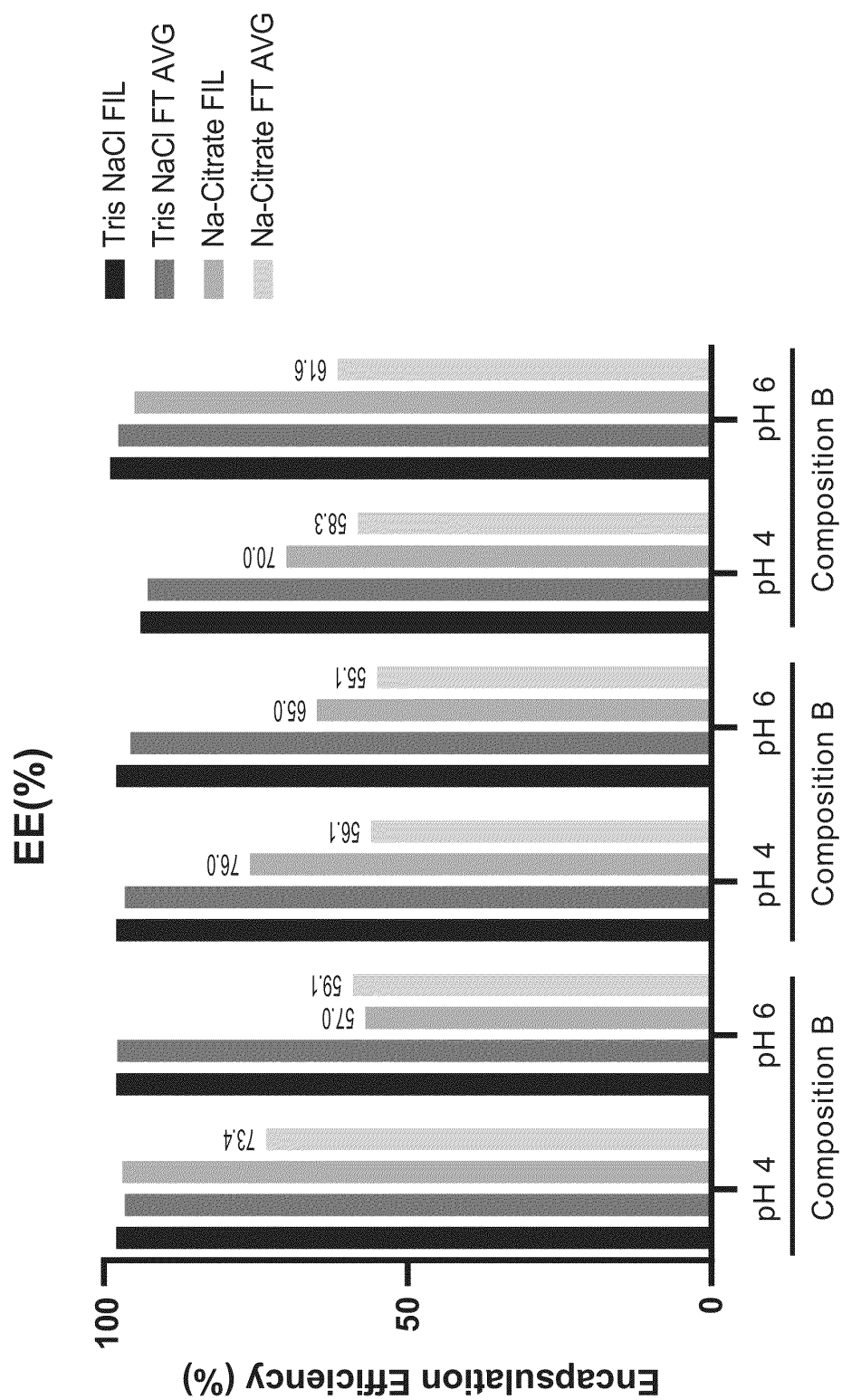


FIG. 57C

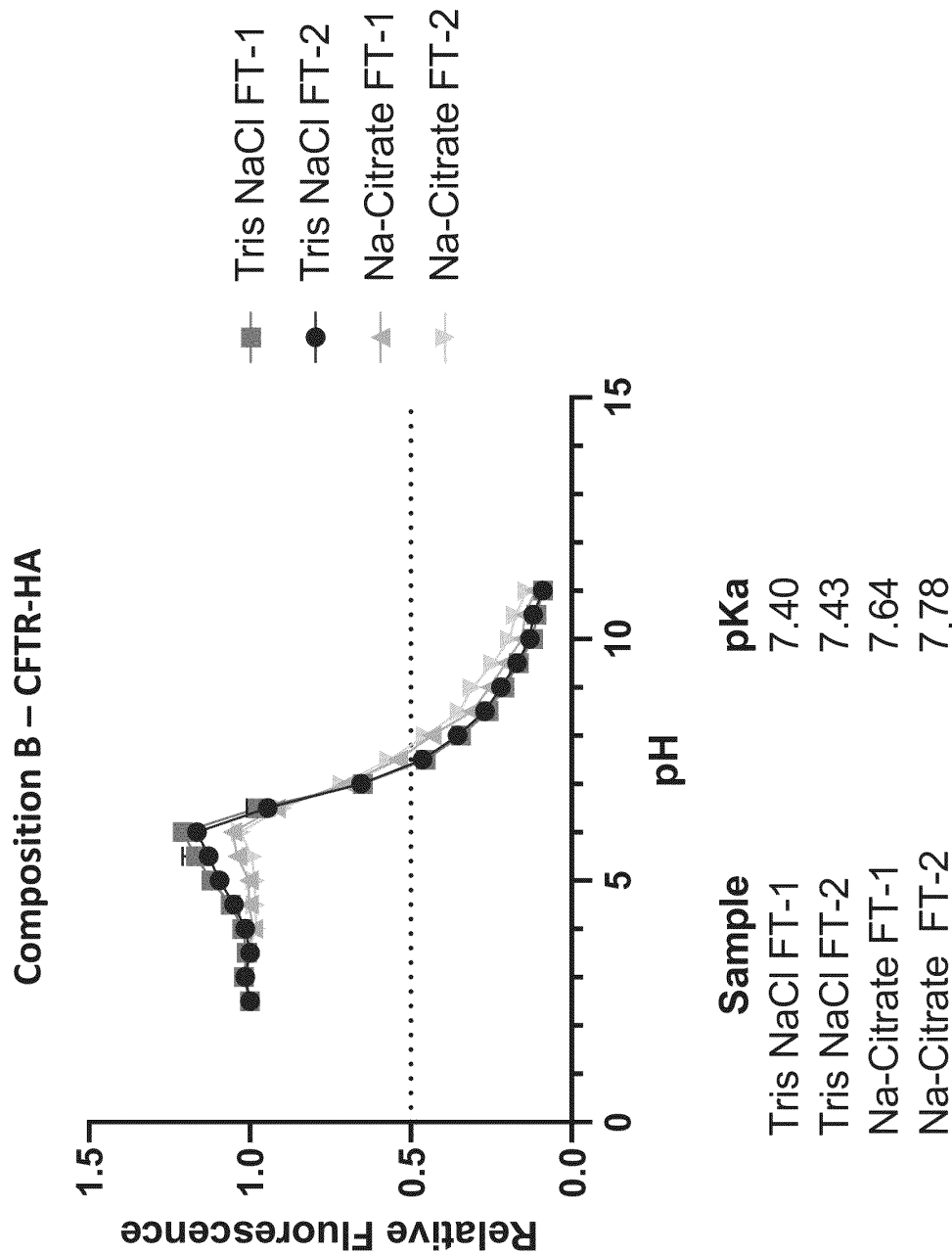


FIG. 58A

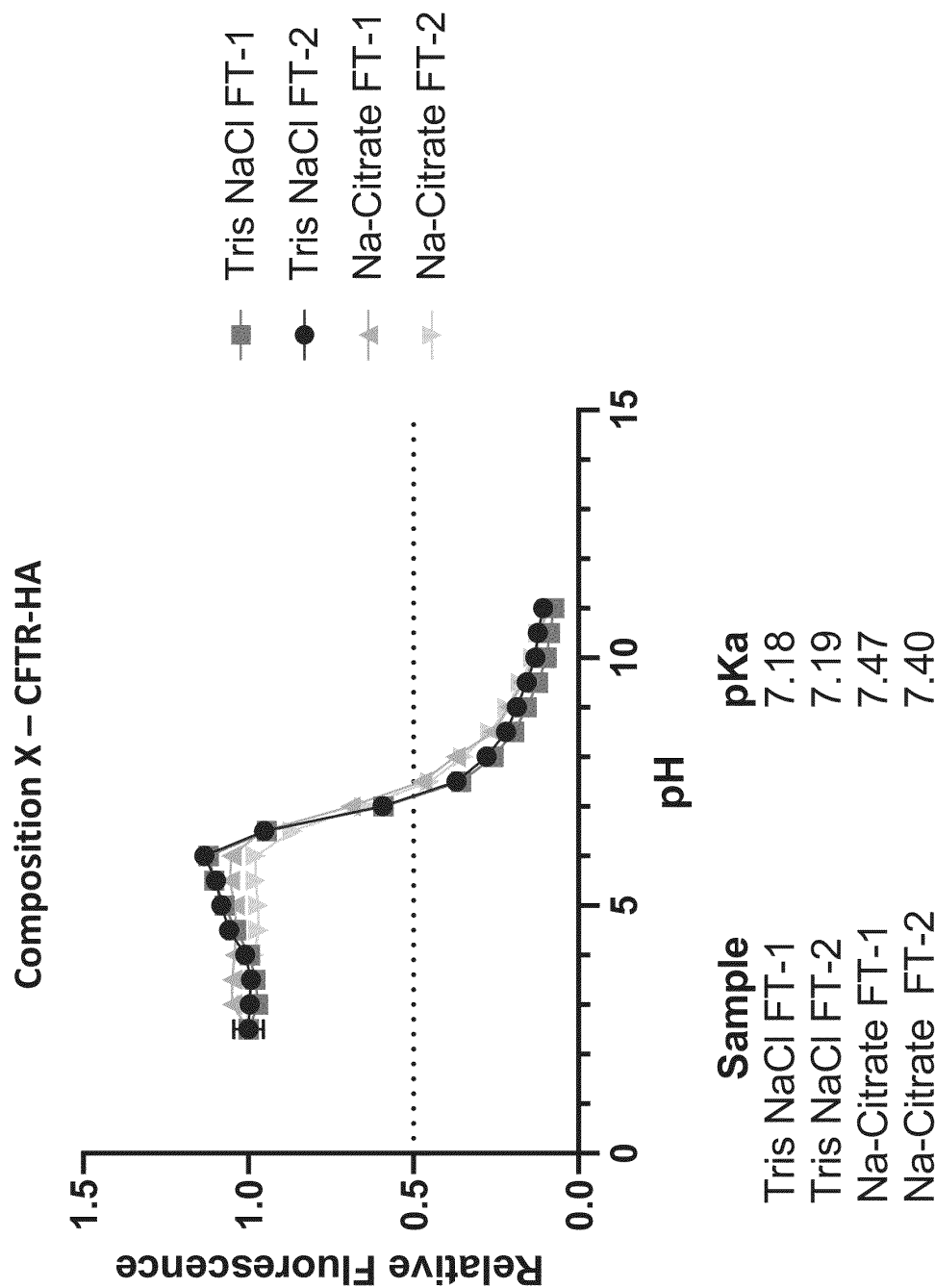


FIG. 58B

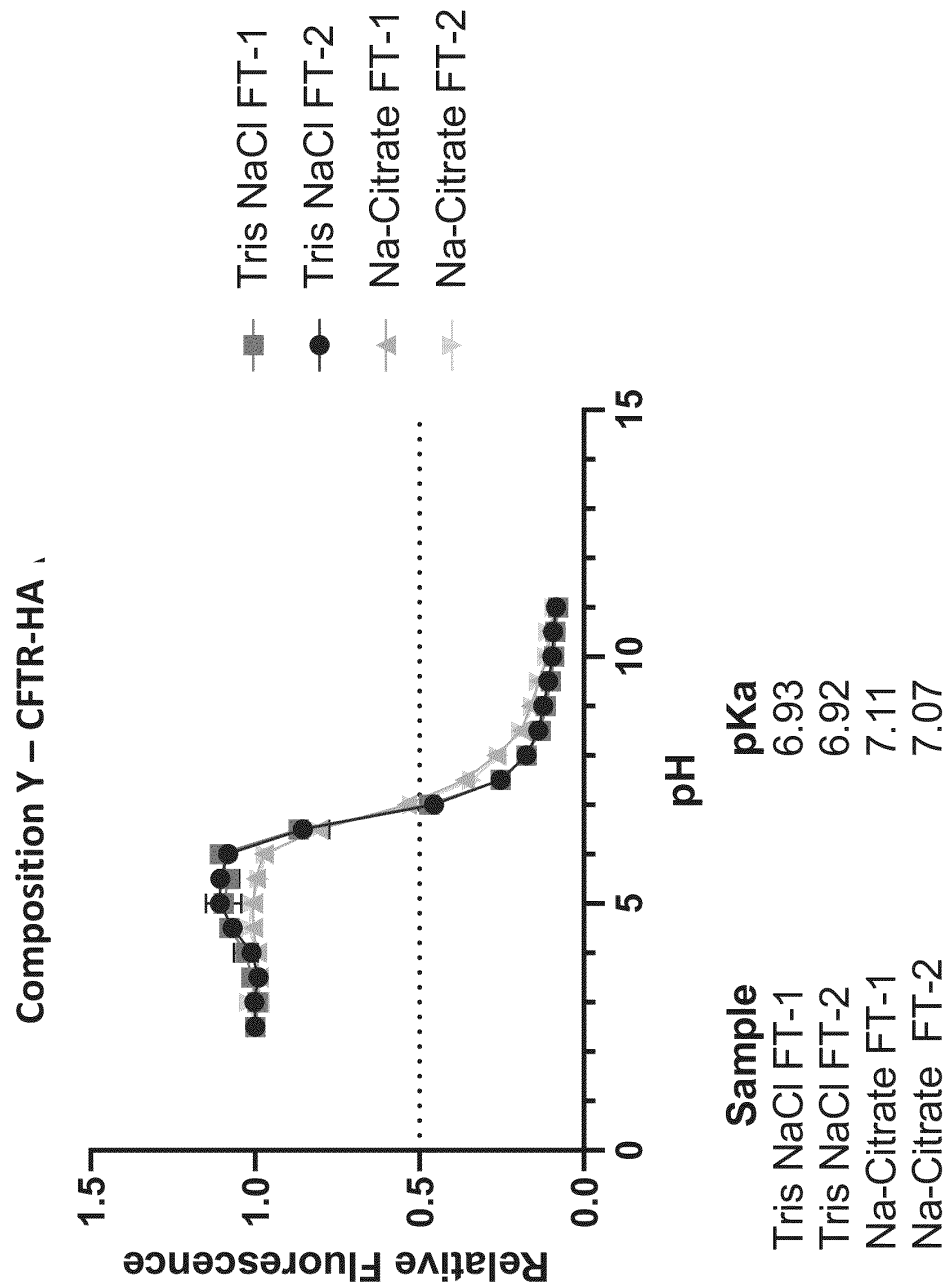


FIG. 58C

Composition B – CFTR-HA

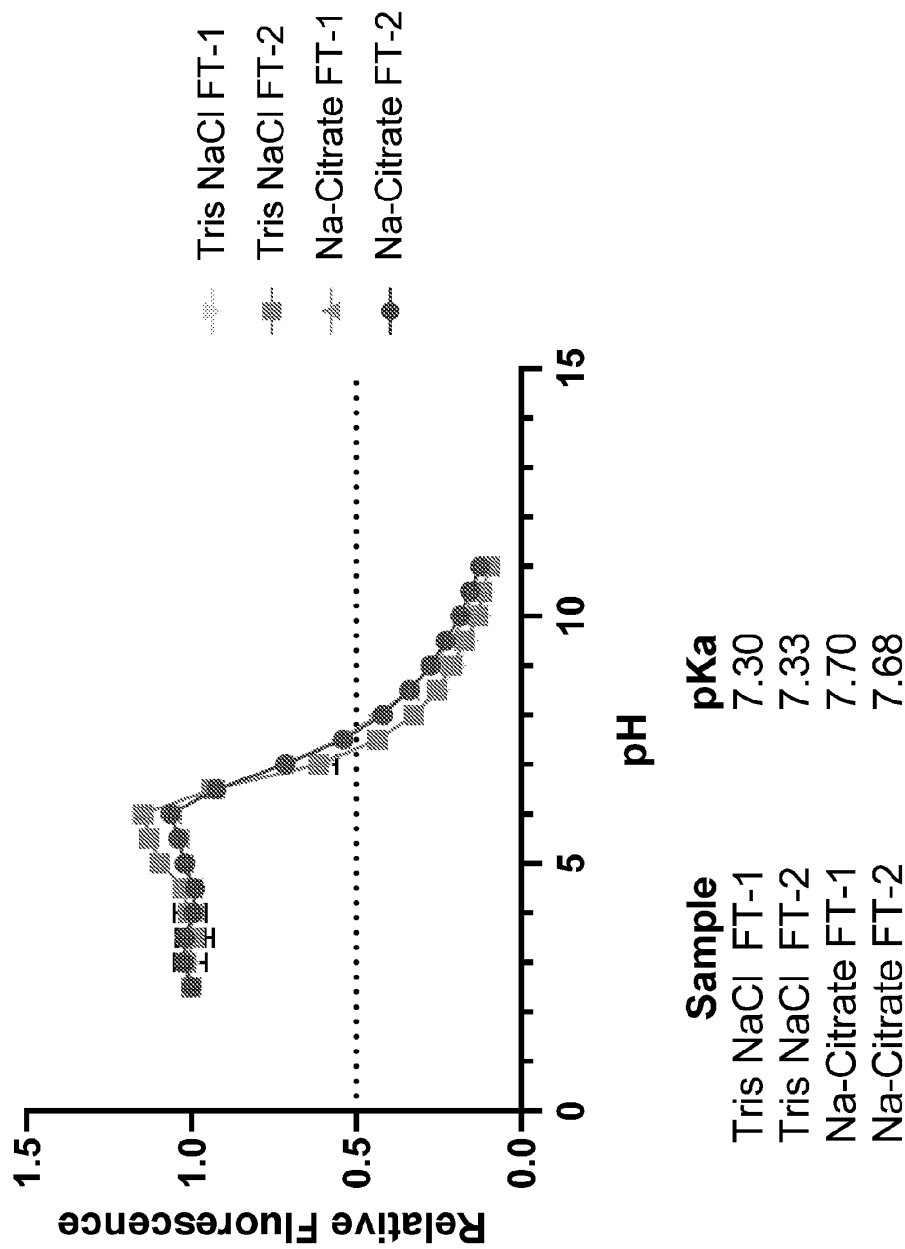


FIG. 59A

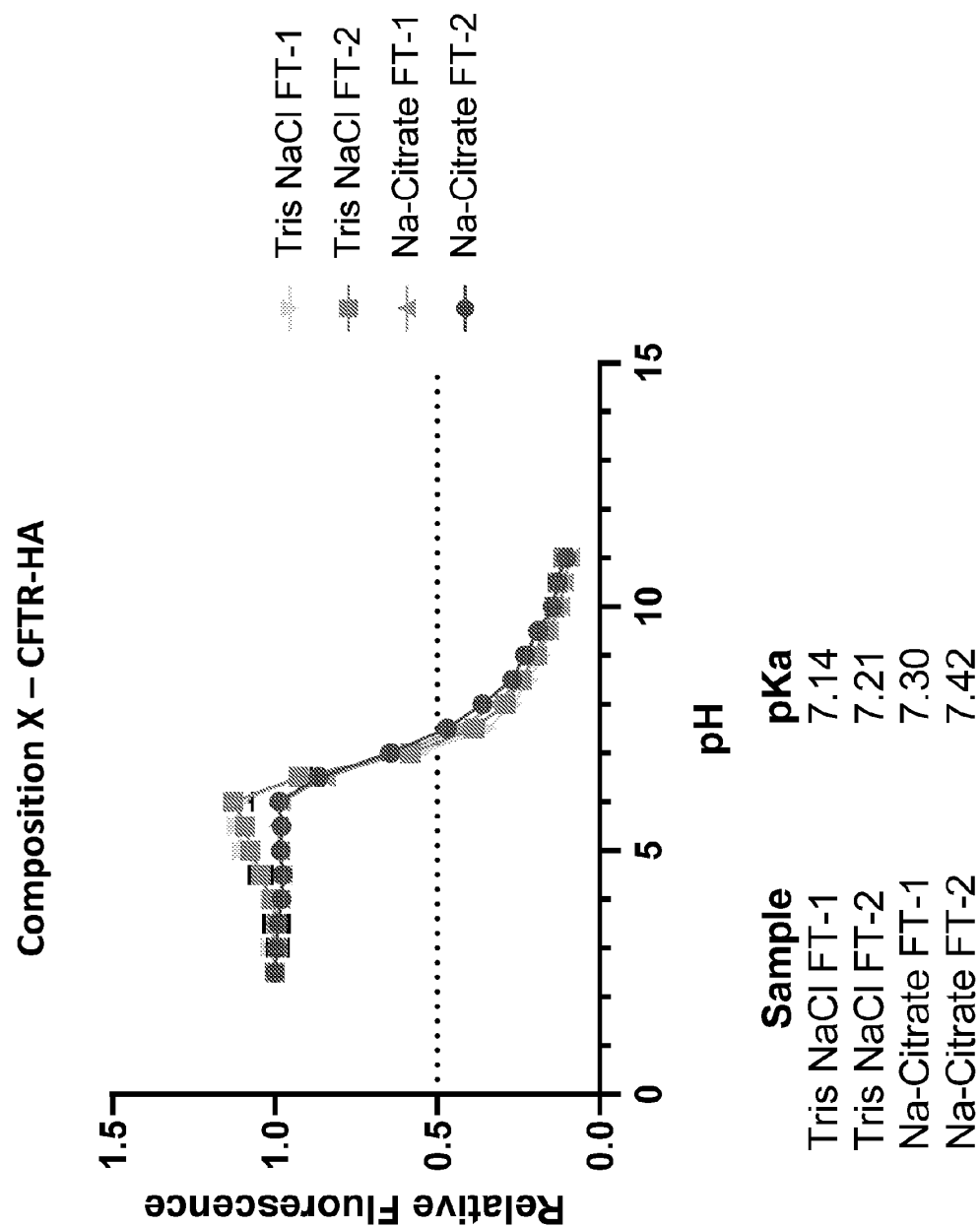


FIG. 59B

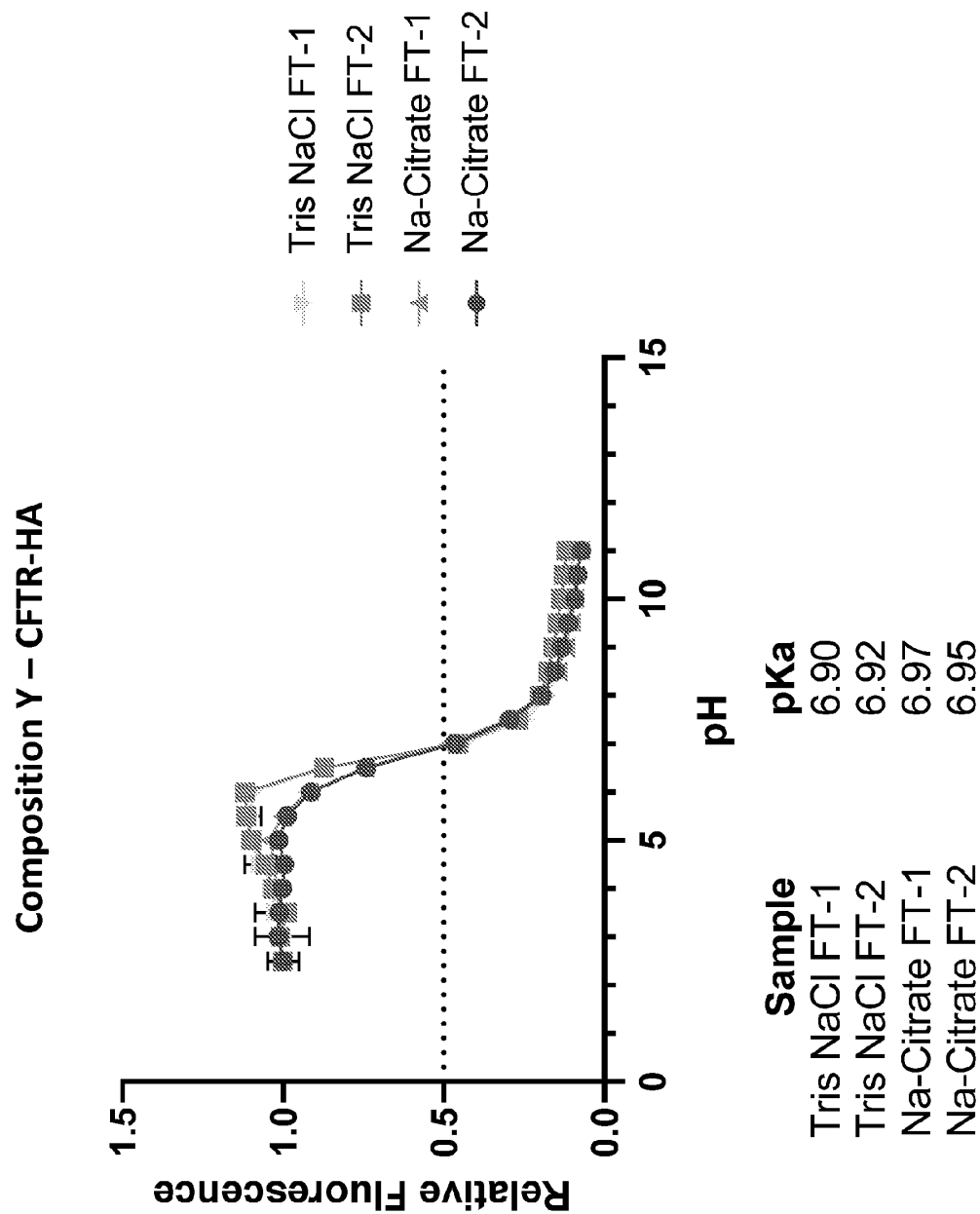


FIG. 59C

Sample #	Pre-Dialysis Details			Post Dialysis Details*		Post Nebulization			Approximate Nebulization Output	
	Manufacturing Process Details	Initial Formulation Buffer	Particle Size (nm) Pre-Dialysis	Post Dialysis Buffer	Particle Size (nm) Post Dialysis	Particle Size (nm)	Pre-neb EE%	Solo Post Neb EE%	Solo (uL/min)	PDAP (uL/min)
1	Knauer Pump + TFF	15mM Citrate pH 4.0, 10% Sucrose	68.3	15mM Tris 75mM NaCl, pH 7.5, 5% Sucrose	90.5	302	90.1	55.6	200	400
2				1X DPBS	88.3	477	92.6	3.2	200	400
3				15mM Citrate pH 4.0	72.9	273	91.1	91.1	70	N/A
4	Knauer Pump + TFF	15mM Tris 75mM NaCl, pH 7.5, 5% Sucrose	63.2	15mM Citrate pH 4.0, 10% Sucrose	76.7	174	92.8	90.1	70	N/A
5	Knauer Pump + TFF	15mM Tris 75mM NaCl, pH 7.5, 5% Sucrose	62.9	N/A	N/A	400	93.2	26.0 (Solo); 29.0 (PDAP)	200	400

Sample #	
1	Composition X-CFTR, 1mg/mL
2	Composition X-CFTR, 1mg/mL
3	Composition X-CFTR, 1mg/mL
4	Composition B-CFTR, 1mg/mL
5	Composition B-CFTR, 1mg/mL (300mg ITR Technical Batch)

FIG. 60

Sample	Scale + Process	Storage at 2-8°C				Freeze-Thaw (Storage at -80°C)			
		Z avg (nm)	PDI	EE (%)	RNA (mg/ml) Ribogreen-AL	Z avg (nm)	PDI	EE (%)	RNA (mg/ml) Ribogreen-AL
Composition X-CFTR- HA 6mL 1mg/mL RCD2100-22-KP-TFF- 001 DOM: 12SEP2022 Storage Buffer: 15mM Citrate, 10% Sucrose w/v	0.5g (Knauer Pump + TFF) Tech Trial Batch	59.8	0.10	94.1	1.11	63.0	0.10	94.5	1.01
20220824- Composition X-CFTR 15mM Citrate 10% sucrose pH 4	3mg (Syringe Pump Mixing + PD10)	56.3	0.10	93.5	1.21	64.7	0.08	92.2	1.11
20220830- Composition X-CFTR	6mg (Syringe Pump Mixing + PD10)	56.6	0.11	94.0	1.08	74.7	0.08	93.4	1.06

FIG. 61

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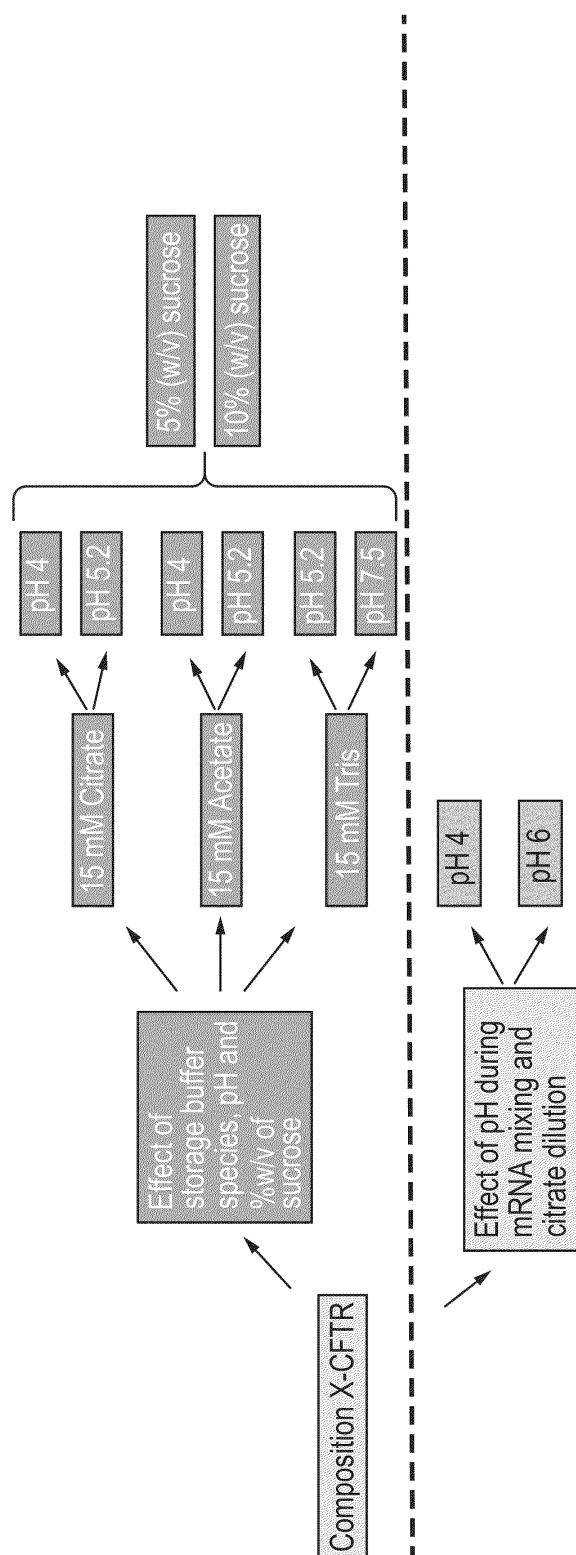


FIG. 62A

Sample#	Starting mRNA Buffer/ Citrate Inline Dilution	Formulation Buffer	Sucrose % (w/v)
1	10mM Citrate, pH4.0	15mM Citrate pH 4.0	5
2		15mM Citrate pH 5.2	
3		15mM Sodium Acetate pH 4.0	
4		15mM Sodium Acetate pH 5.2	
5		15mM Tris pH 5.2	
6		15mM Tris pH 7.5	
7		15mM Citrate pH 4.0	10
8		15mM Citrate pH 5.2	
9		15mM Sodium Acetate pH 4.0	
10		15mM Sodium Acetate pH 5.2	
11		15mM Tris pH 5.2	
12		15mM Tris pH 7.5	
13	10mM Citrate, pH6.0	15mM Citrate pH 4.0	
14		15mM Citrate pH 5.2	
15		15mM Sodium Acetate pH 4.0	
16		15mM Sodium Acetate pH 5.2	
17		15mM Tris pH 7.5	

FIG. 62B

Sample#	F/T cycle 1			F/T cycle 2			F/T cycle 3		
	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency
1	72	0.153	91	81	0.098	91	90	0.138	90
2	78	0.095	93	97	0.124	88	111	0.124	83
3	75	0.061	94	82	0.083	91	99	0.154	91
4	98	0.157	86	134	0.181	80	200	0.214	69
5	212	0.088	92	120	0.118	83	133	0.093	80
6	109	0.107	84	140	0.178	79	175	0.165	67
7	64	0.145	91	67	0.125	91	97	0.255	90
8	72	0.094	92	87	0.122	86	94	0.110	73
9	61	0.082	91	64	0.069	91	67	0.084	89
10	75	0.133	92	85	0.128	83	96	0.185	83
11	198	0.074	94	97	0.124	91	106	0.124	86
13	67	0.120	94	69	0.109	95	71	0.103	93
14	84	0.088	93	89	0.117	88	99	0.153	84
15	73	0.067	93	82	0.121	80	84	0.110	85
16	87	0.119	87	102	0.189	77	103	0.180	77
17	125	0.184	91	126	0.211	90	130	0.169	87

FIG. 62C

Sample#	Week 1			Week 2			Week 3			Week 4			Week 7		
	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency
1	85	0.137	91	78	0.128	91	x	x	x	x	x	x	x	x	x
2	87	0.082	92	117	0.139	91	x	x	x	x	x	x	x	x	x
3	79	0.065	92	78	0.058	91	x	x	x	x	x	x	x	x	x
4	102	0.192	87	91	0.158	87	x	x	x	x	x	x	x	x	x
5	108	0.097	90	103	0.152	90	x	x	x	x	x	x	x	x	x
6	124	0.160	84	114	0.132	85	x	x	x	x	x	x	x	x	x
7	69	0.169	91	64	0.130	91	69	0.209	91	66	0.126	88	66	0.159	90
8	85	0.124	86	122	0.121	90	129	0.113	90	x	x	x	x	x	x
9	62	0.099	92	61	0.080	91	63	0.132	91	70	0.189	89	62	0.079	91
10	82	0.175	91	75	0.112	90	93	0.243	91	78	0.138	88	83	0.163	90
11	91	0.187	92	93	0.159	92	102	0.186	91	94	0.178	89	94	0.136	91
13	67	0.126	93	67	0.101	94	67	0.133	93	78	0.192	91	69	0.099	93
14	86	0.126	92	112	0.055	92	130	0.057	92	114	0.096	90	159	0.081	91
15	74	0.136	92	73	0.087	92	74	0.117	92	75	0.110	92	76	0.056	92
16	87	0.129	88	86	0.134	89	88	0.111	87	89	0.164	86	98	0.133	81
17	122	0.205	91	117	0.168	91	111	0.185	90	108	0.191	88	133	0.213	92

FIG. 62D

Sample#	Starting mRNA Buffer/ Citrate Inline dilution	Formulation Buffer	Sucrose % (w/v)	P188 %(w/v)
1	10mM Citrate, pH4.0	15mM Citrate pH 4.0	0	0
2		15mM Sodium Acetate pH 4.0		
3		15mM Sodium Acetate pH 4.9		
4		15mM Histidine, pH 6.0		
5		15mM Citrate pH 4.0		
6		15mM Sodium Acetate pH 4.0	10	0.005
7		15mM Sodium Acetate pH 4.9		
8		15mM Histidine, pH 6.0		
9		15mM Citrate pH 4.0		
10		15mM Citrate pH 4.0		
	10mM Citrate, pH6.0			

FIG. 62E

Sample#	F/T cycle 1			F/T cycle 2			F/T cycle 3		
	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency
1	62	0.058	92	68	0.048	92	72	0.090	91
2	64	0.042	91	68	0.068	91	71	0.030	90
3	61	0.107	92	63	0.128	92	64	0.119	92
4	82	0.155	91	87	0.149	91	91	0.169	91
5	63	0.080	93	68	0.065	93	72	0.061	92
6	61	0.089	93	64	0.072	93	65	0.054	92
7	60	0.097	93	62	0.102	93	64	0.107	92
8	89	0.141	92	94	0.173	90	99	0.144	89
9	72	0.122	93	76	0.099	92	79	0.117	91
10	75	0.130	94	78	0.140	93	81	0.129	93

FIG. 62F

Sample#	Week 1			Week 3			Week 4			Week 6		
	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency	Particle Size (nm)	Polydispersity Index	% Encapsulation efficiency
1	61	0.076	93	62	0.062	91	63	0.070	91	62	0.070	90
2	65	0.058	92	64	0.072	91	67	0.069	91	64	0.062	89
3	61	0.117	93	65	0.135	91	62	0.127	92	63	0.118	91
4	79	0.146	92	85	0.153	91	87	0.163	91	86	0.142	91
5	61	0.076	93	61	0.069	92	65	0.054	93	65	0.068	91
6	60	0.066	93	60	0.066	92	63	0.085	93	61	0.070	92
7	57	0.113	93	63	0.142	92	63	0.099	92	64	0.145	92
8	83	0.141	92	85	0.152	91	87	0.148	91	89	0.140	90
9	72	0.159	93	74	0.114	92	75	0.143	92	75	0.122	91
10	73	0.147	94	76	*	93	78	0.135	93	78	0.142	92

* Missing datapoint

FIG. 62G

							Analyst 01		Analyst 02	
Formulation	Buffer Strength & Species	pH	P-188 (%w/v)	Sucrose (%w/v)	Solo Output Rate (uL/min)		%EE Pre-Neb	%EE Post Neb	%EE Pre-Neb	%EE Post Neb
Composition X-HA-CFTR	15mM Citrate	4.0	0	10	50-90*		-	-	93.0	87.8
	15mM Acetate	5.0	0	10	85.1		93.24	87.12	93.79	86.45
	15mM Citrate	5.5	0	10	94.5		92.78	88.13	92.89	88.2
	15mM Citrate	6.0	0	10	113.5		92.81	78.6	93.06	82.59
	15mM Tris	7.0	0	10	114		92.64	53.7	91.47	54.79
	15mM Tris	7.5	0.005	10	148.5		92.4	22.06	92.17	21.44

FIG. 63

Sample #	Formulation	Formulation Buffer	mRNA	pH	NaCl (mM)	% Sucrose (w/v)	Solo Output Rate (uL/min)	%EE Pre-Neb		Solo %EE Post-Neb	
								Analyst 01	Analyst 02	Analyst t 01	Analyst t 02
1	Composite X	15mM Citrate	CFTR	6.0	0	10	94	90.92	92.58	76.54	80.33
2			CFTR	6.5	0	10	127	89.00	89.93	70.32	71.36
3			CFTR	6.0	50	10	122	90.48	91.34	71.66	70.58
4			CFTR	6.5	50	10	134	92.76	93.21	70.52	70.17

FIG. 64

G542X/F508del

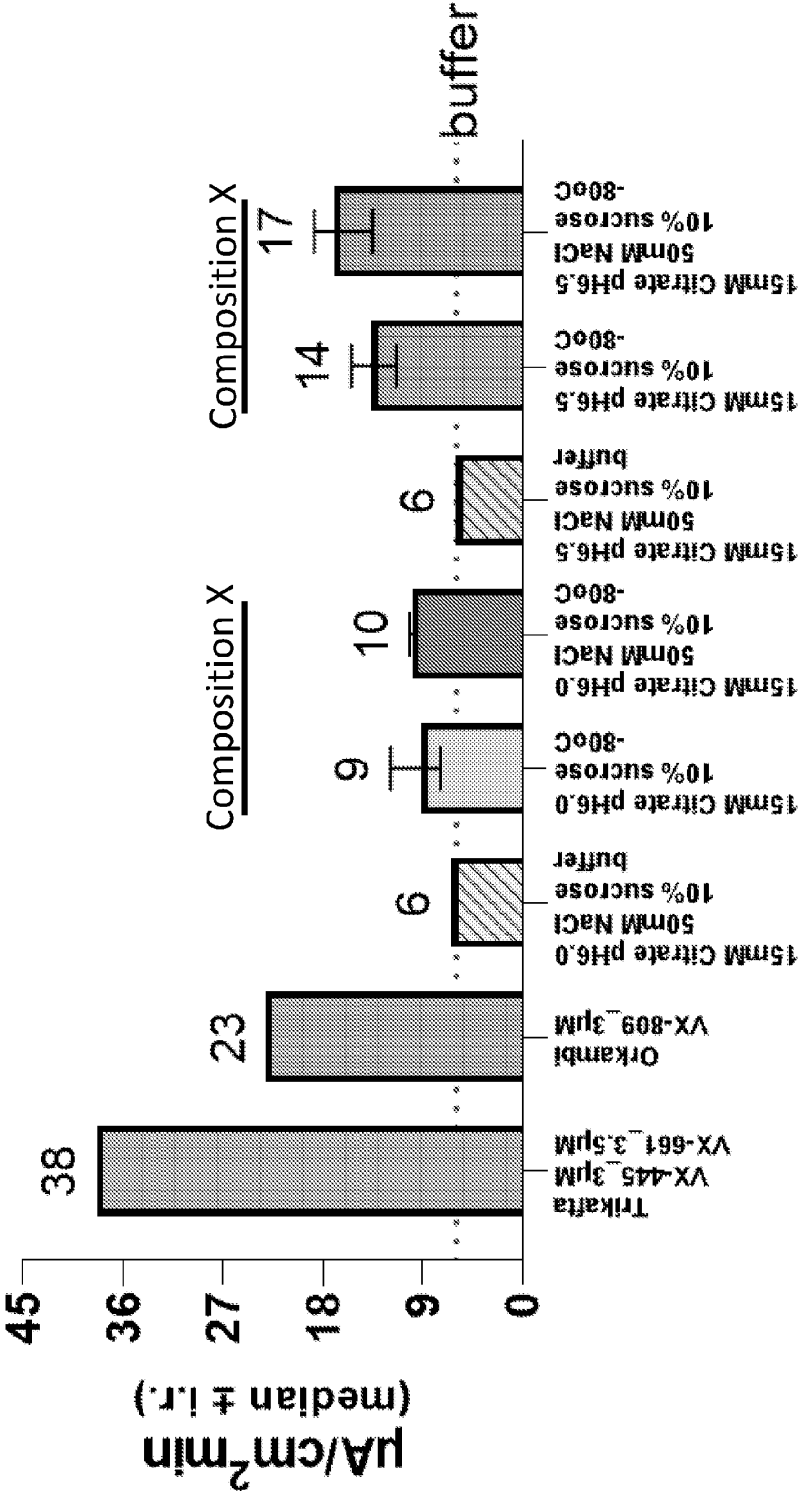
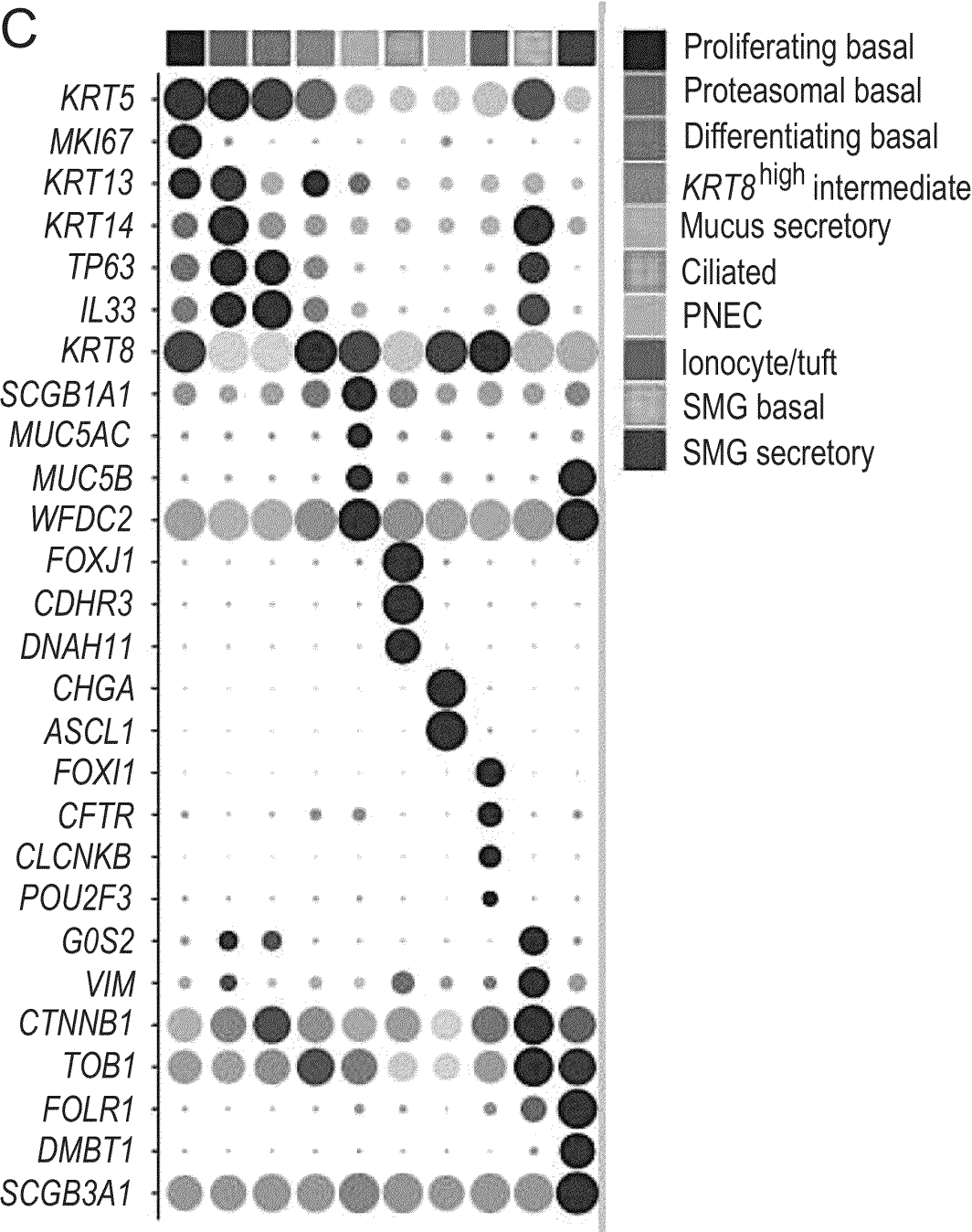


FIG. 65



Extracted from Goldfarbmuren *et al.* (2020) Nat Commun. 11: 2485.

FIG. 66

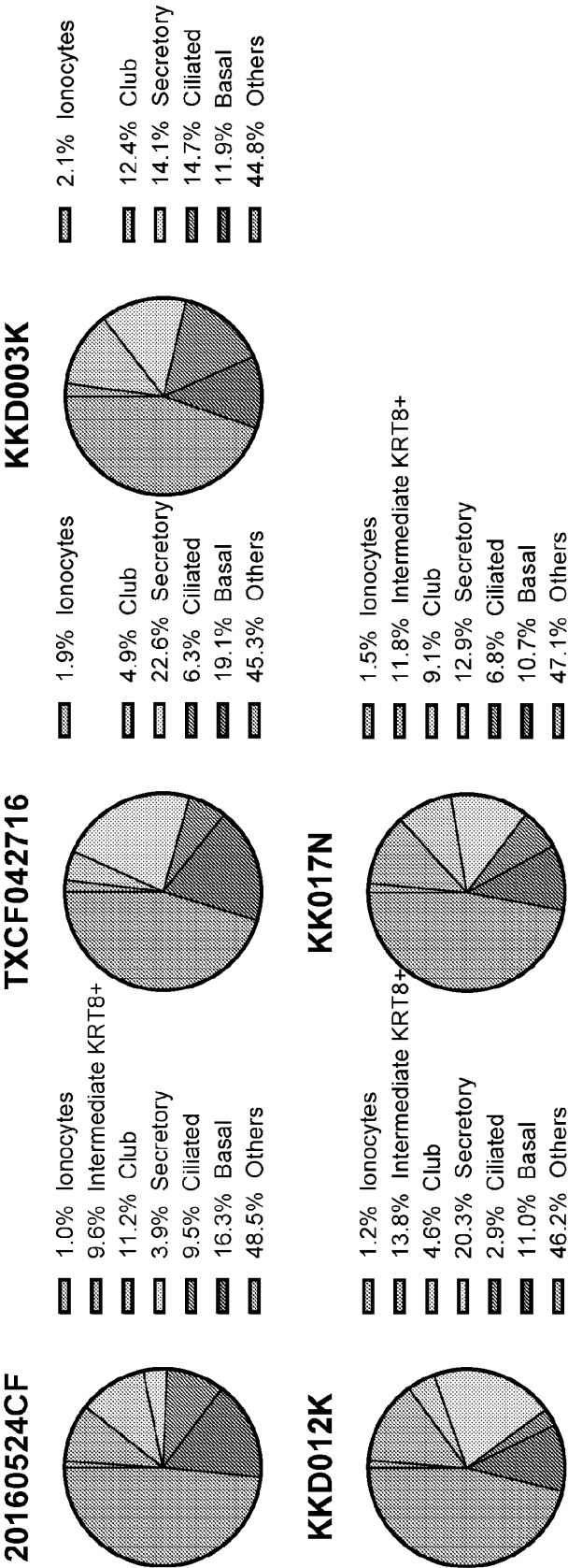


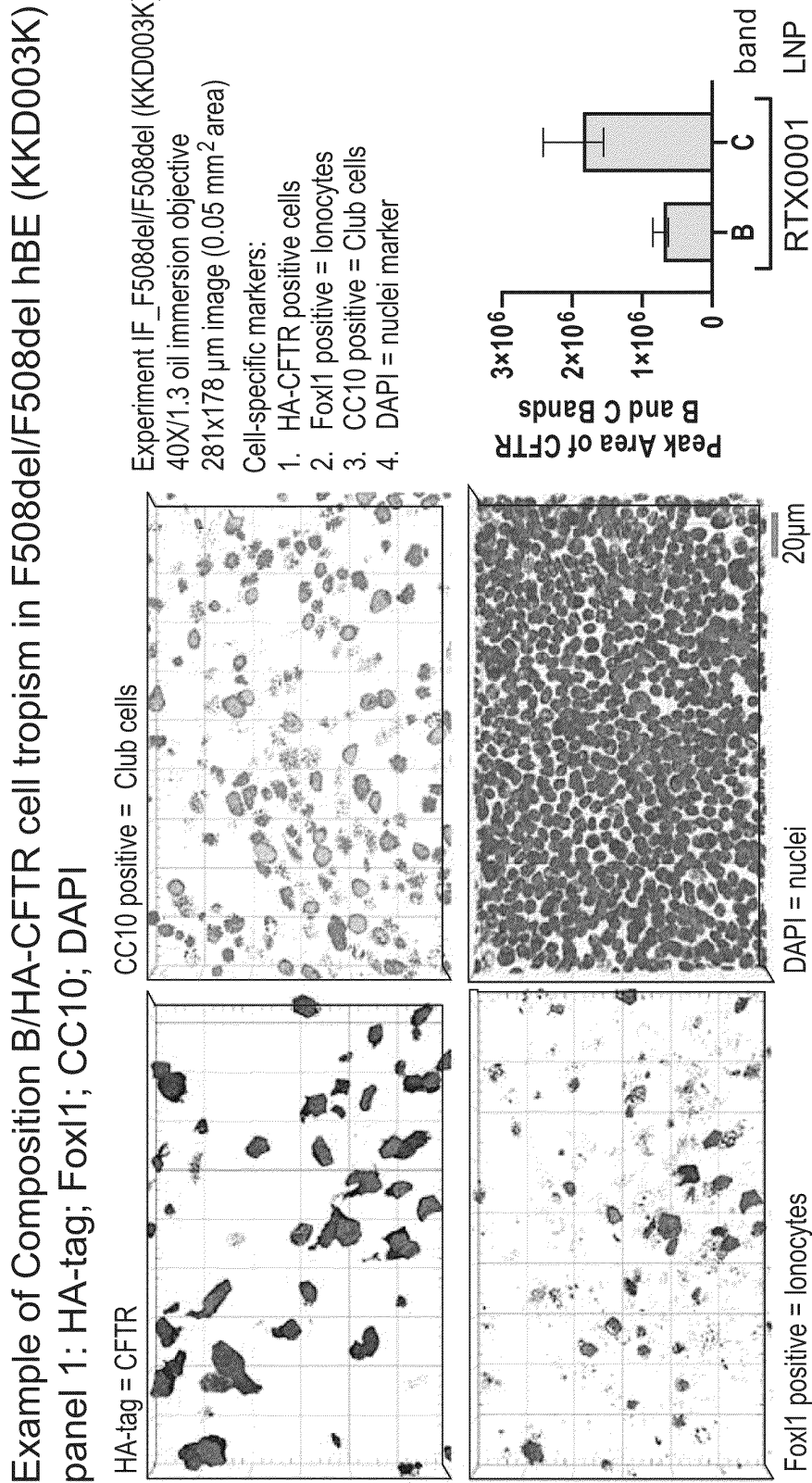
FIG. 67A

Genotype	Donor Codes
ΔF508/ΔF508	TXCF042716 KKD012K KKD025L KKD003K
	20160524CF KKD017N
	UI0014
	UI0009
	ND13816
K710X/L467P	
G542X/ΔF508	KKCFFT0051

FIG. 67B

Cell type	Antibody
Ionocytes	FoxI1
Proliferating basal, secretory, ionocyte, and SMG basal	KRT8
Basal cells	KRT5
Club cells	CC10
Secretory cells	Mucin
Ciliated cells	Tubulin

FIG. 67C



Example of Composition B/HA-CFTR cell tropism in F508del/F508del hBE (KKD003K)
panel 2: HA-tag; Mucin; Tubulin; DAPI

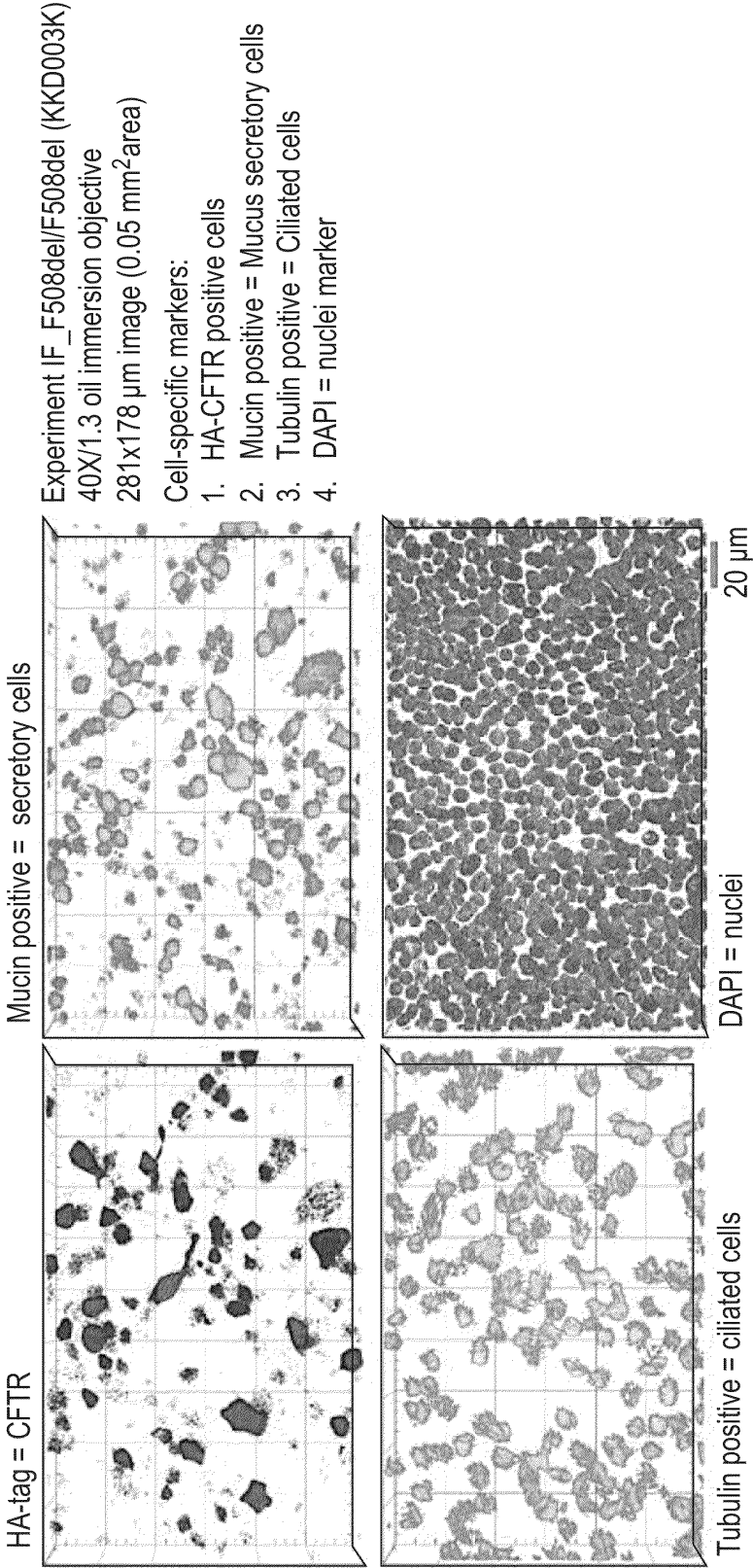


FIG. 69

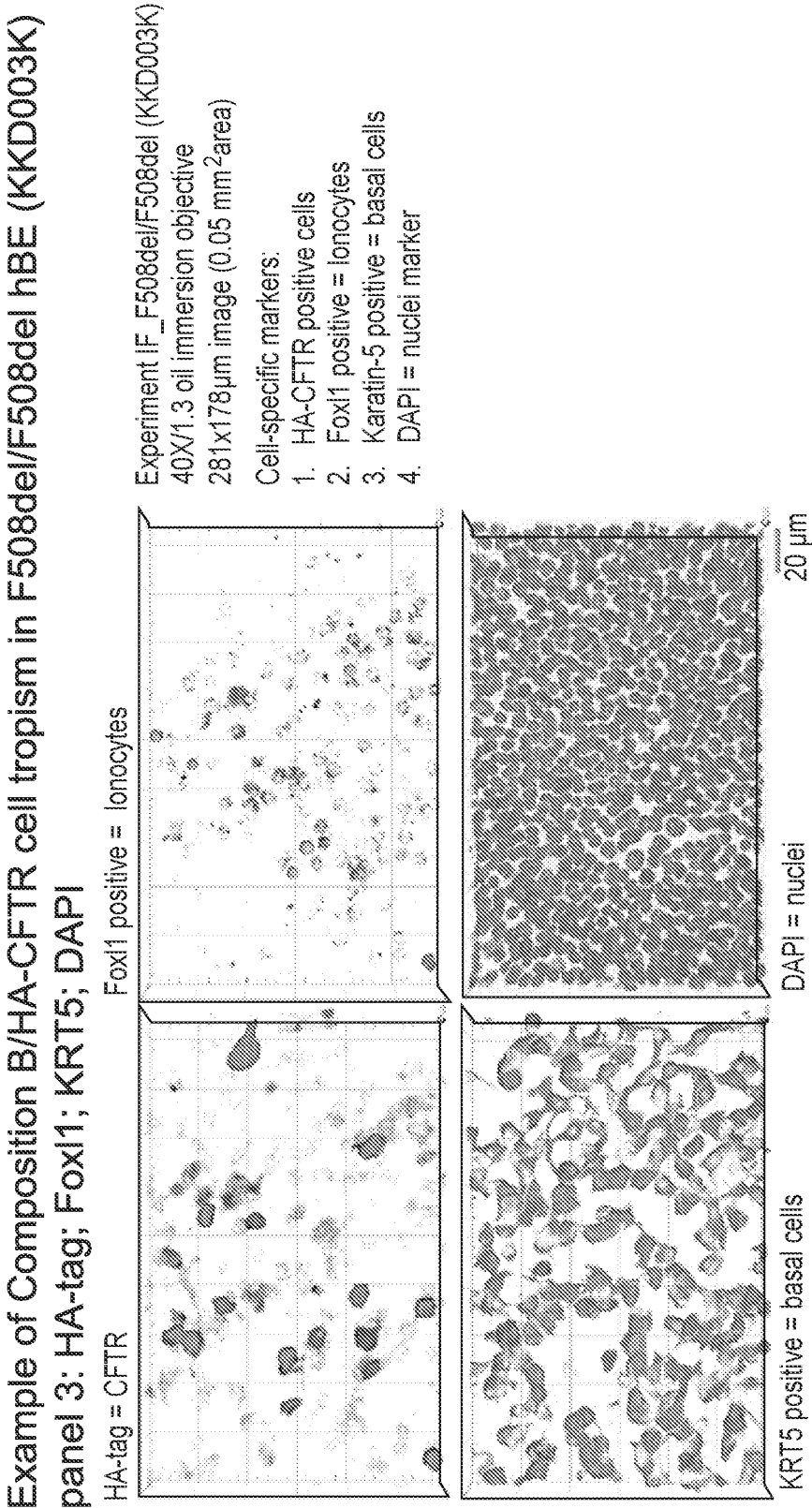


FIG. 70

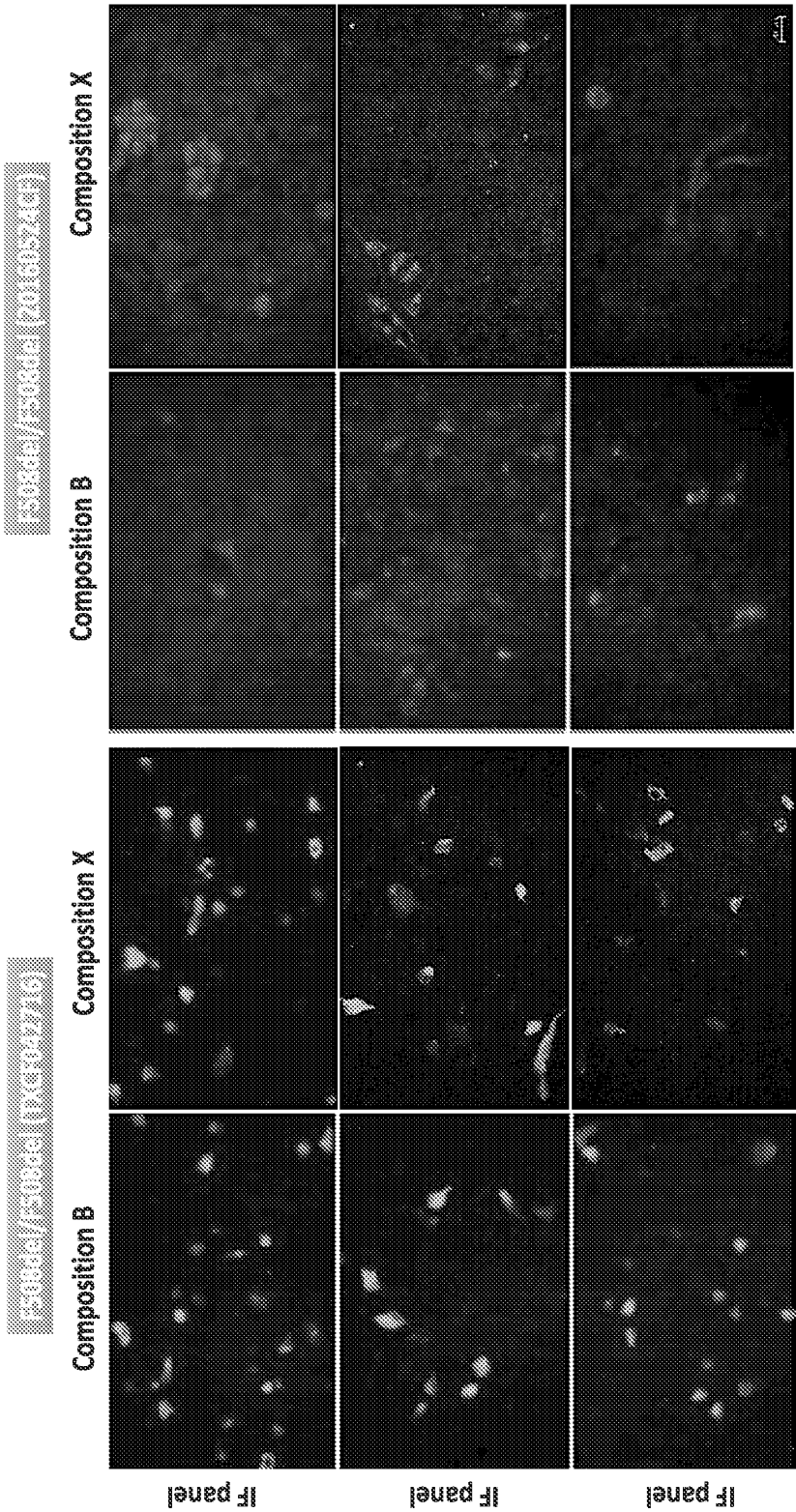
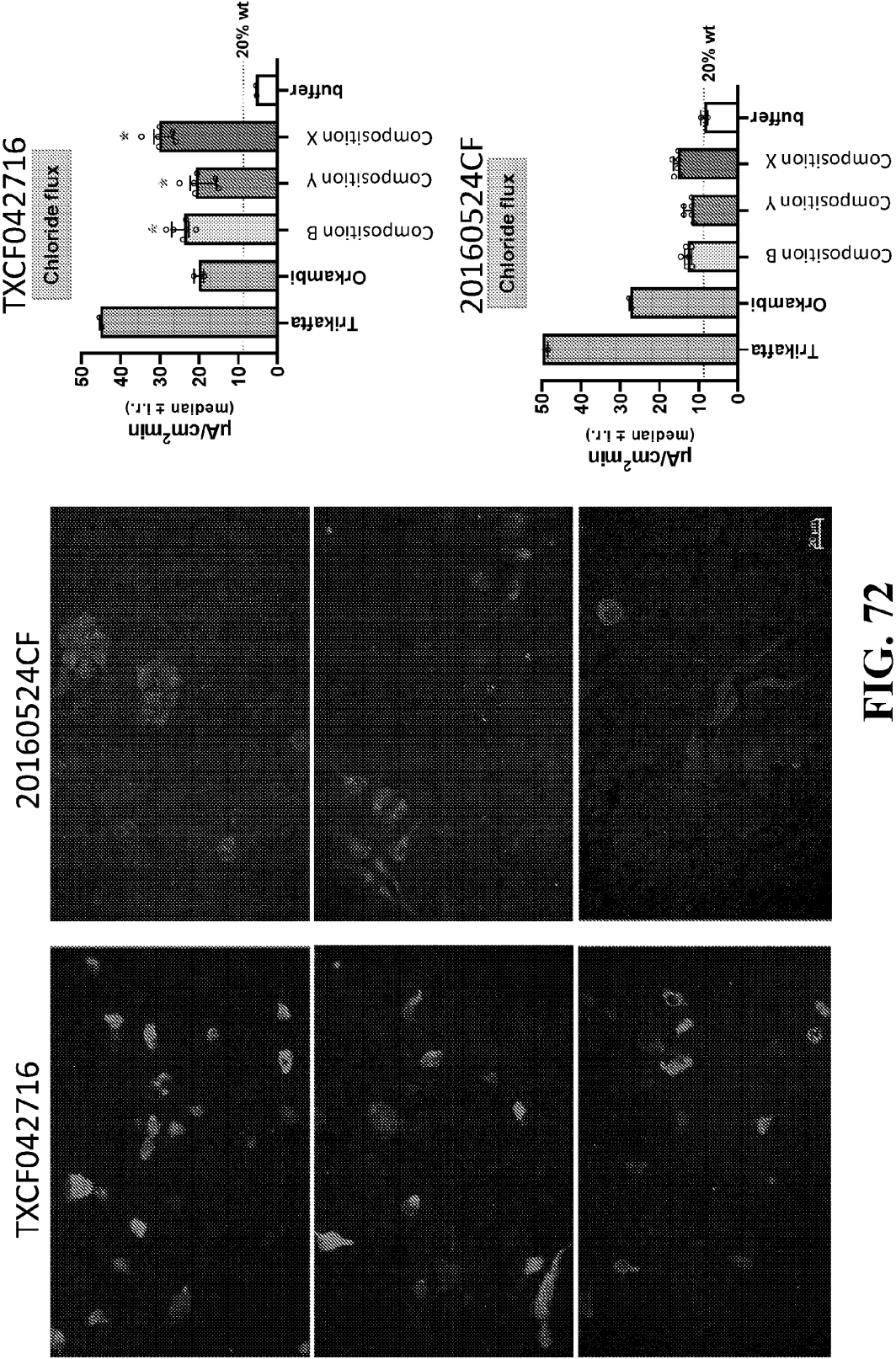


FIG. 71B

FIG. 71A



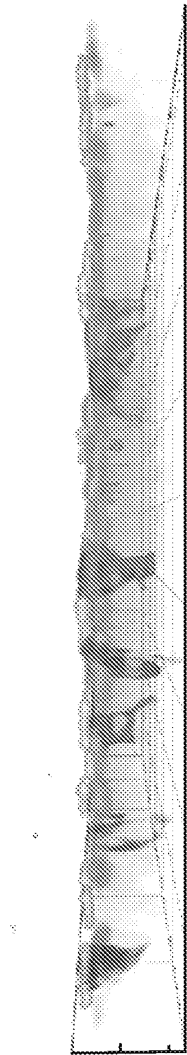
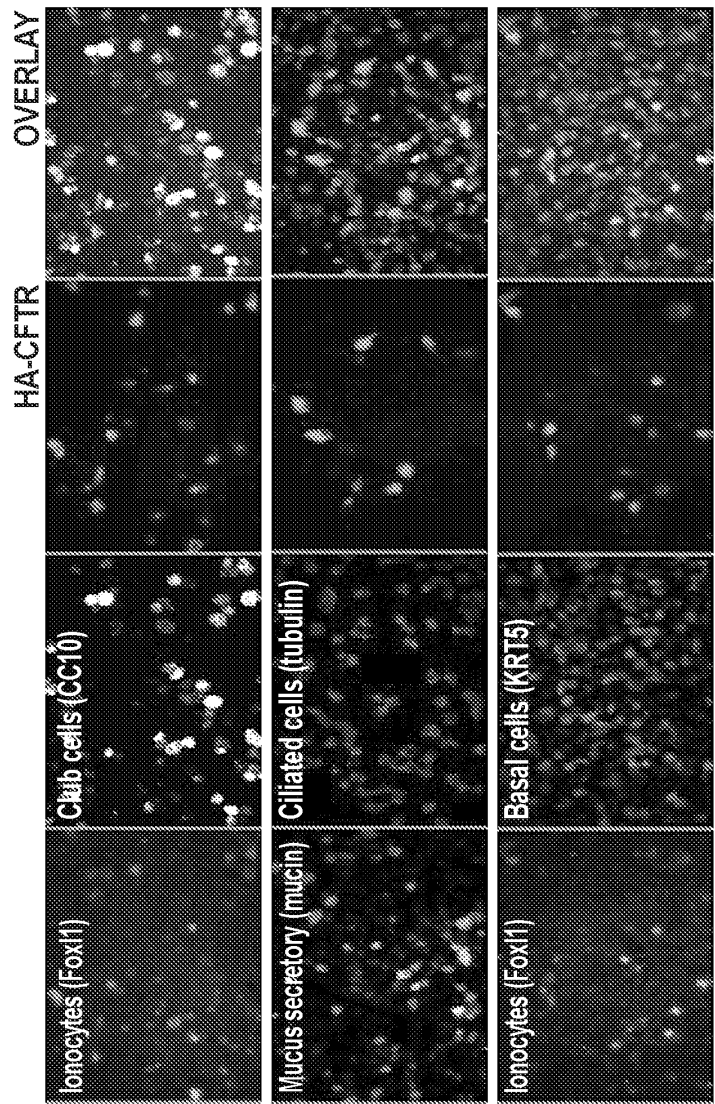


FIG. 73A

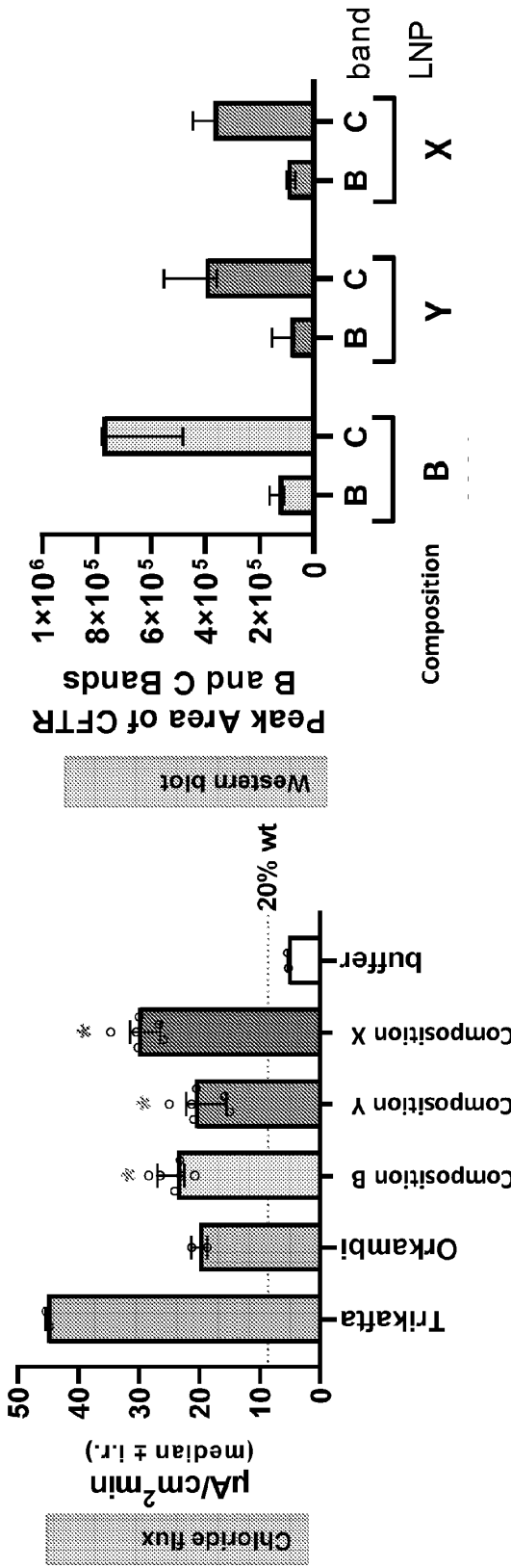


FIG. 73B

FIG. 73C

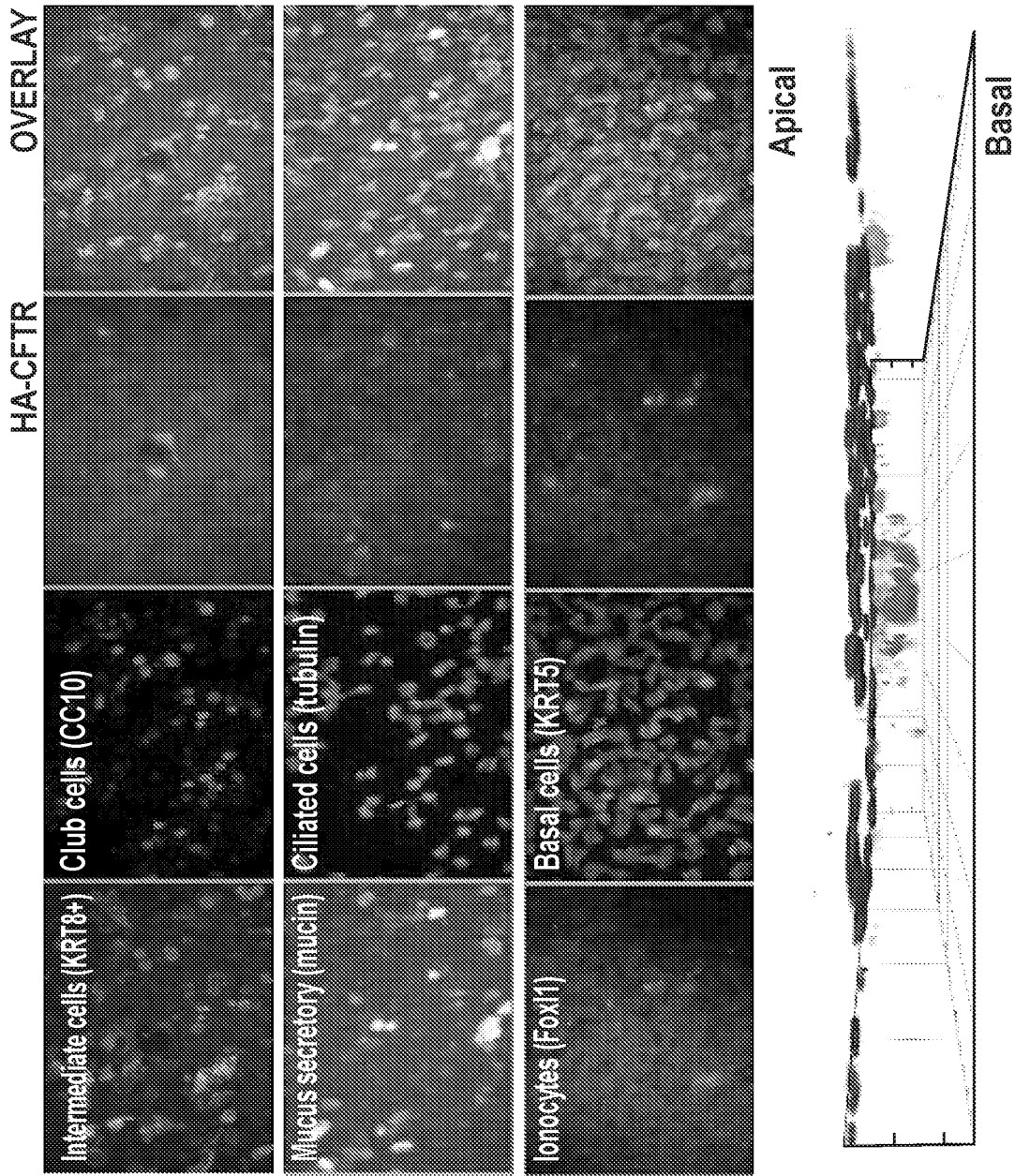


FIG. 74A

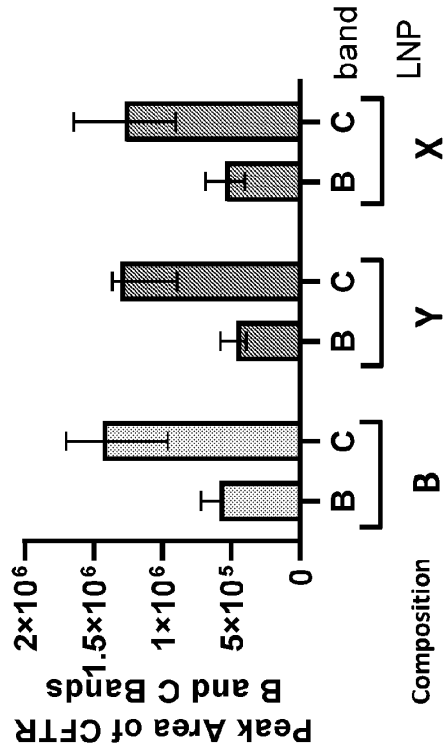


FIG. 74C

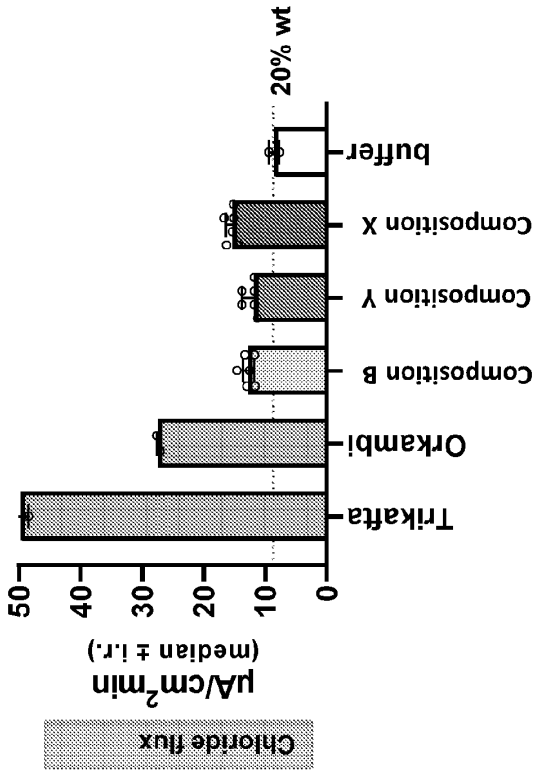


FIG. 74B

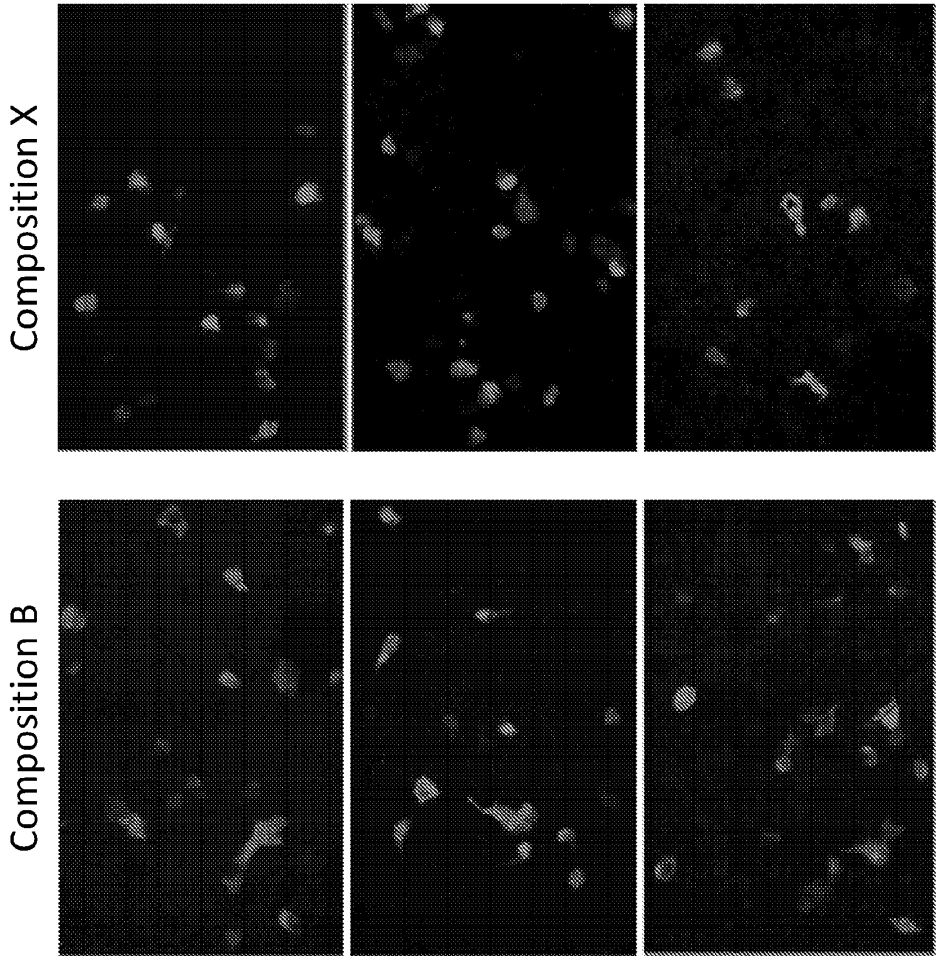
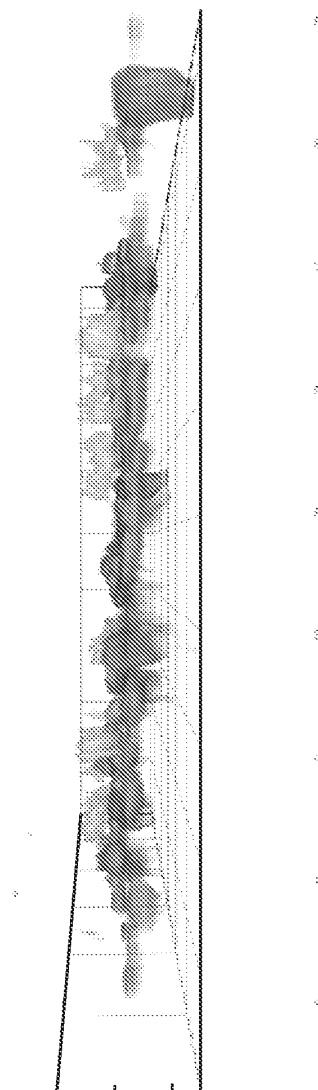


FIG. 75



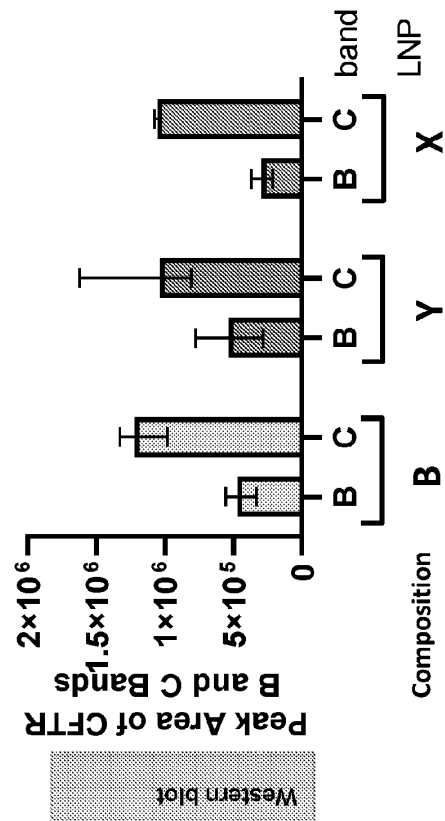


FIG. 76C

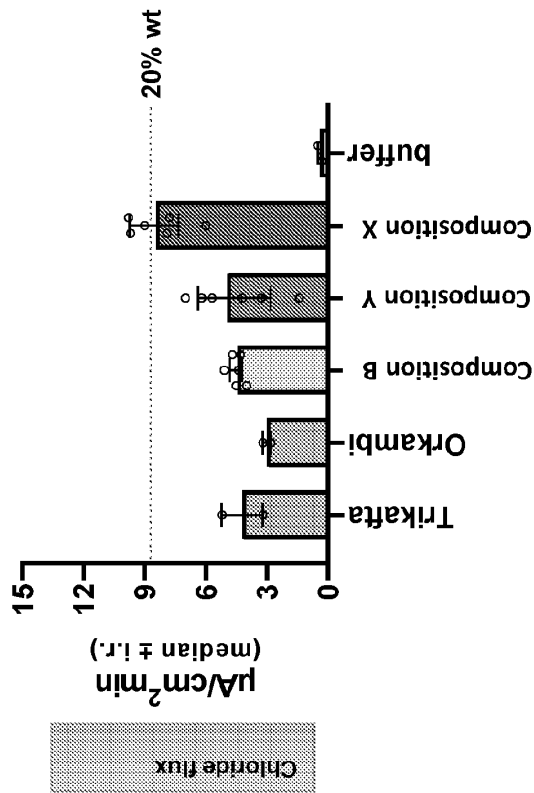


FIG. 76B

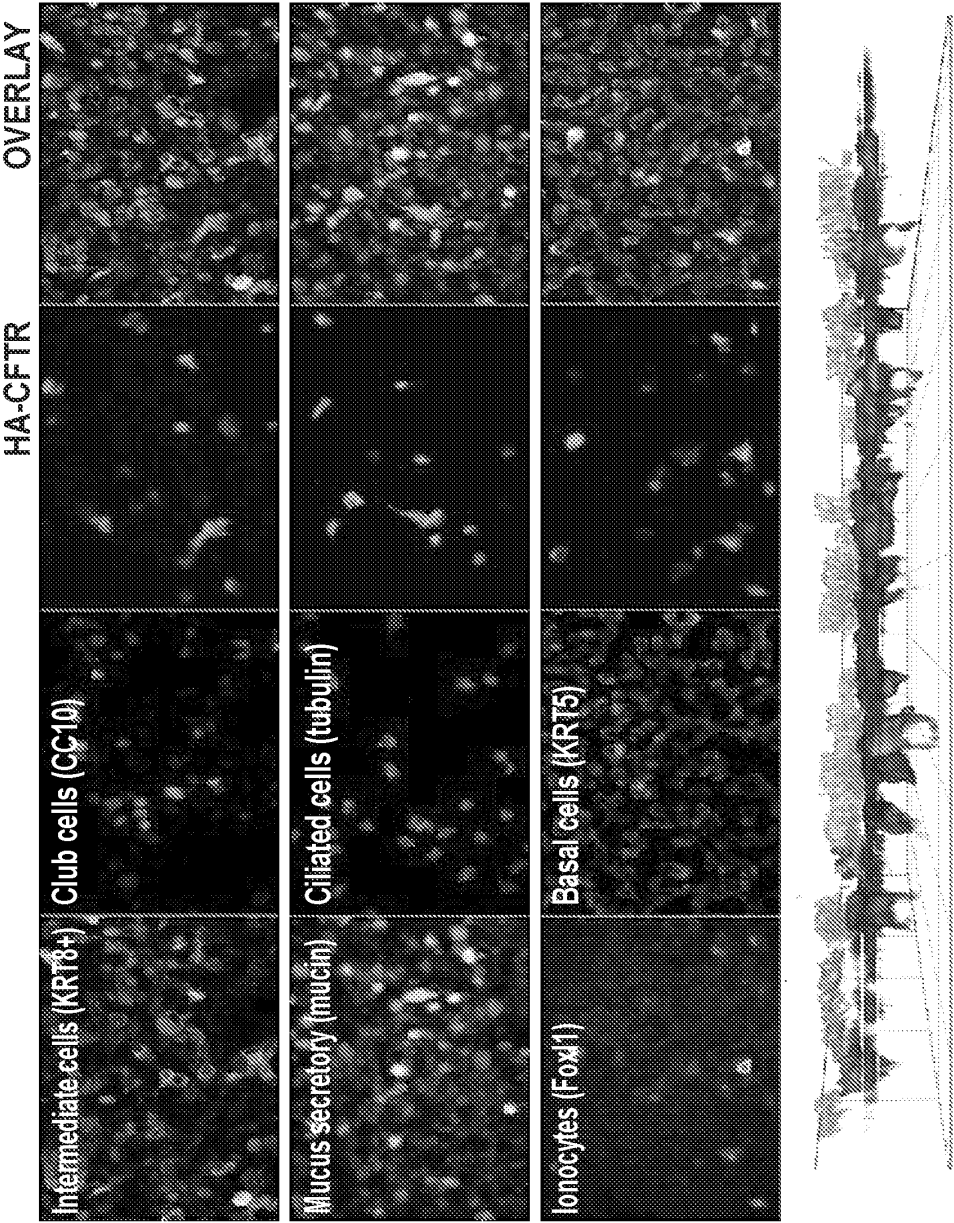


FIG. 77A

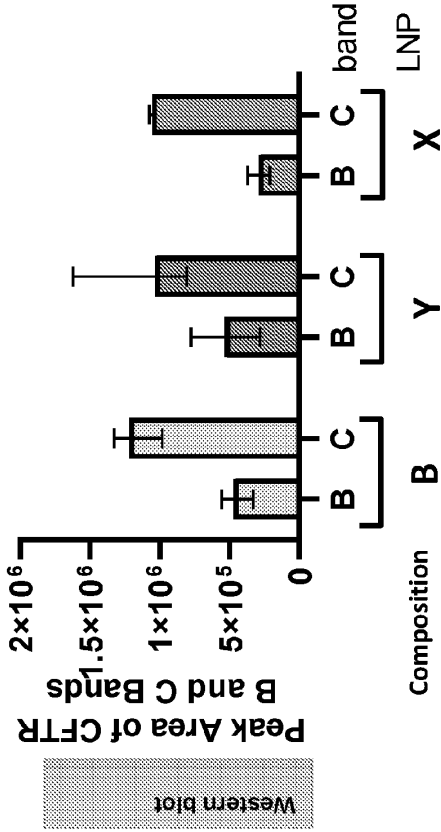


FIG. 77C

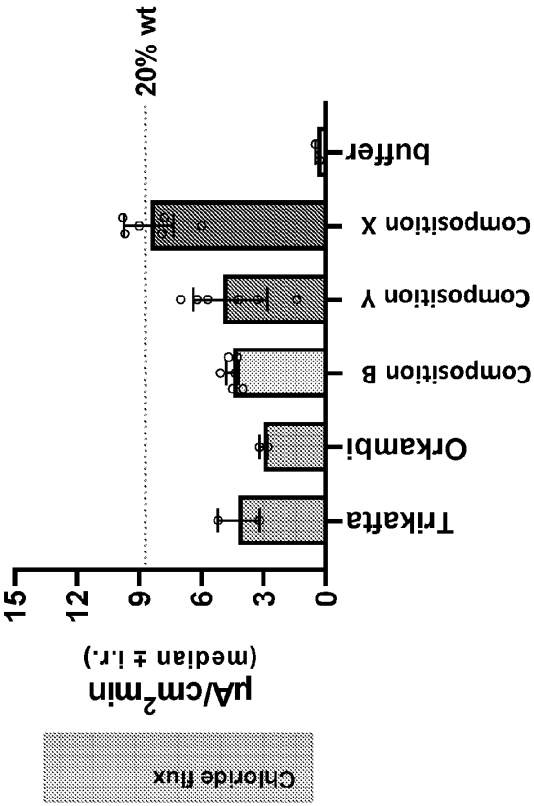


FIG. 77B

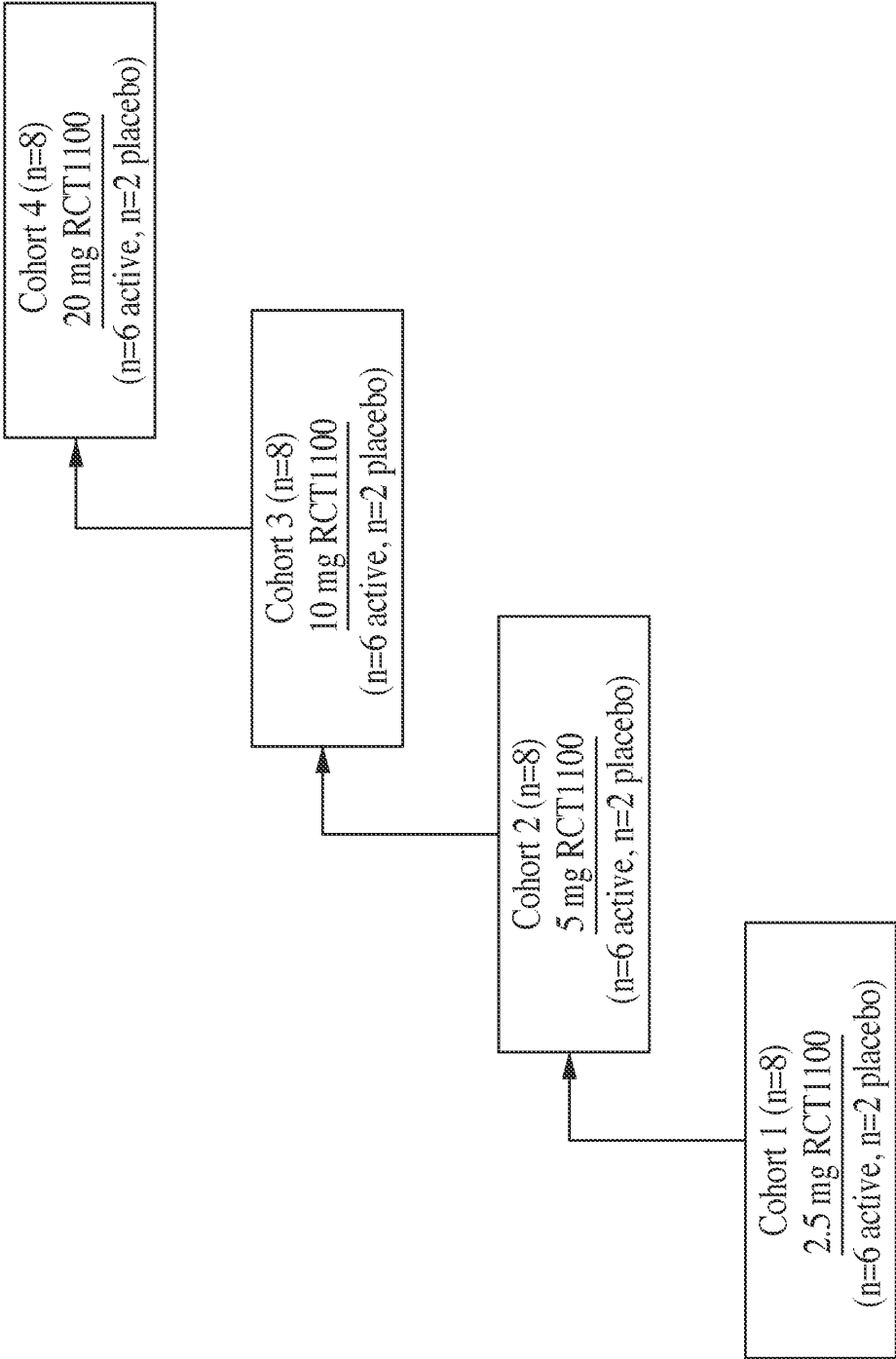


FIG. 78

Cohort	Planned Dose	Number of Participants
Cohort 1	2.5 mg	8 (6 active, 2 placebo)
Cohort 2	5.0 mg	8 (6 active, 2 placebo)
Cohort 3	10.0 mg	8 (6 active, 2 placebo)
Cohort 4	20.0 mg	8 (6 active, 2 placebo)

Abbreviation: SRC, safety review committee.

Notes:

Dose units refer to the nominal dose of the study drug that will be loaded into the nebulizer. Doses for Cohorts 1 to 4 are planned. As new safety and/or laboratory data become available, the planned dose escalation scheme may change following a review of the data by the SRC. If needed based on the recommendation of the SRC, dose levels may be adjusted and/or additional cohorts added or expanded as necessary to adequately characterize the safety of the study drug. The maximum dose strength administered is planned to be 20.0 mg and the maximum increase between dose strengths is planned to be approximately 2x.

FIG. 79

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Procedure ^(a)	Phase	Screening	Check-in
	Day	-28 to -2	-1
	Hours Postdose		
	Time Window		
Admission to clinic			X
Discharge from clinic ^(b)			
Outpatient visit		X	
Informed consent		X	
Demographics		X	
Serology ^(c)		X	
Serum FSH ^(d)		X	
Inclusion/exclusion criteria		X	X
Medical history		X	X
Height, weight, and BMI ^(e)		X	X
Physical examination ^(f)		X	X
Vital sign measurements ^(g)		X	X
12-lead ECG ^(h)		X	X
Clinical laboratory testing ⁽ⁱ⁾		X	X
Cytokines ⁽ⁱ⁾			X
Urinalysis ⁽ⁱ⁾		X	X
Spirometry ⁽ⁱ⁾		X	
Alcohol breath/urine drug and cotinine screen ^(k)		X	X
SARS-CoV-2 screening ^(l)		X	
Salbutamol HFA administration ^(m)			
Study drug administration ⁽ⁿ⁾			
Anti <i>DNAII</i> binding antibodies, antiPEG antibodies			X
<i>DNAII</i> mRNA			X
LNP SORT components ^(o)			X
AEs ^(p)			
Prior/concomitant medications		◀	

FIG. 80

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Treatment Period						
1					2	3
Predose	0	0.5	1	4	24	48
		±5 min	±10 min	±10 min	±60 min	±60 min
						X
					X	X
X		X	X	X	X	X
				X	X	X
					X	X
			X	X	X	X
					X	X
X(j)			X	X	X	X
X						
	X					
		X	X	X	X	X
		X	X	X	X	X
X					X	
X						

FIG. 80 (cont.)

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Follow-up		
8	15	29 EOS / ET
±1 day	±1 day	±1 day
X	X	X
		X
X	X	X
		X
X	X	X
		X
		X
X	X	X
	X	X
X	X	
X	X	

FIG. 80 (cont.)

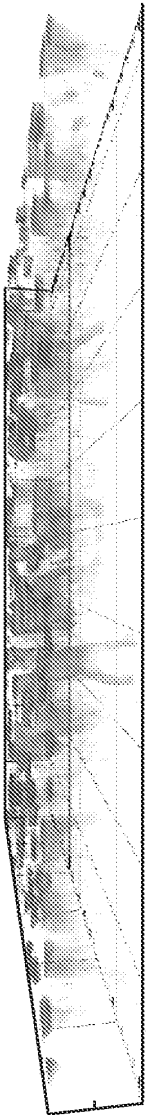
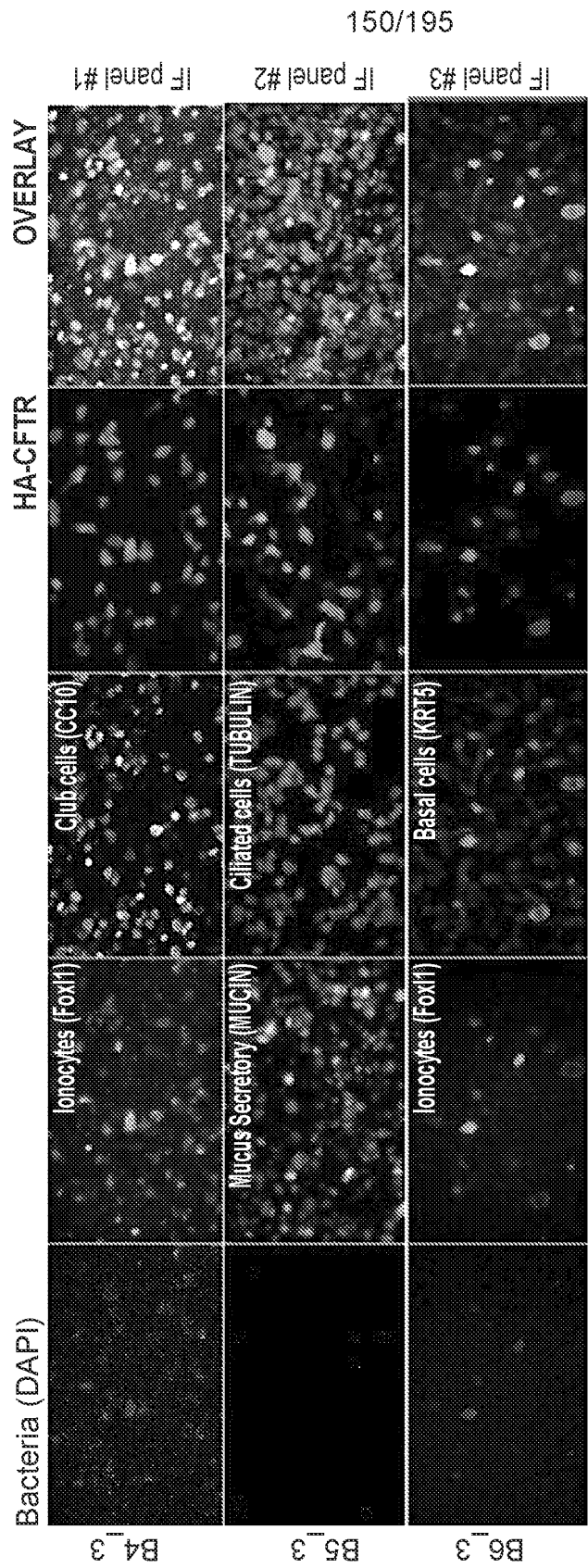


FIG. 81

IF panel #1 DAPI/Foxl1/CC10/HA-CFTR

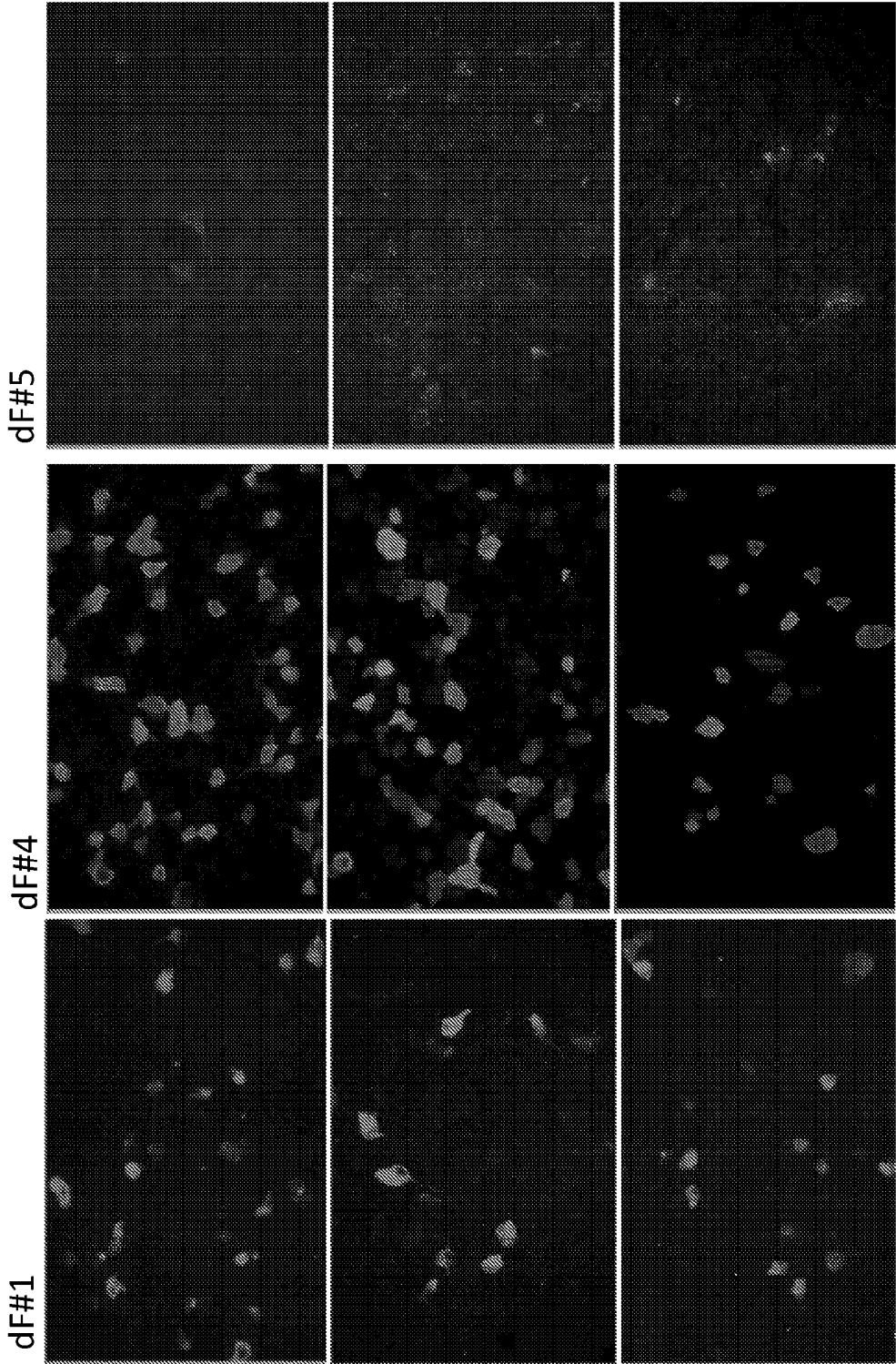
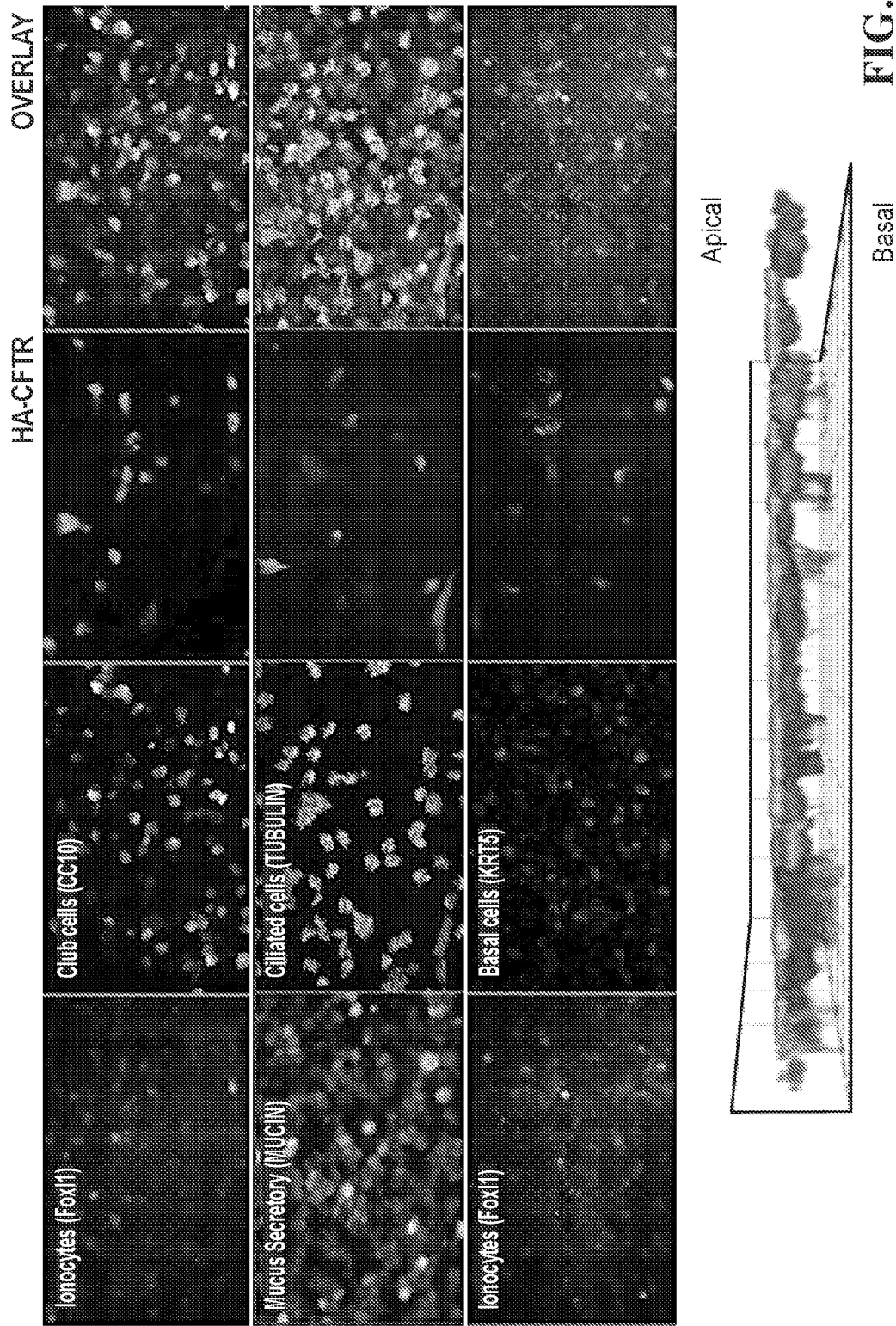


FIG. 82



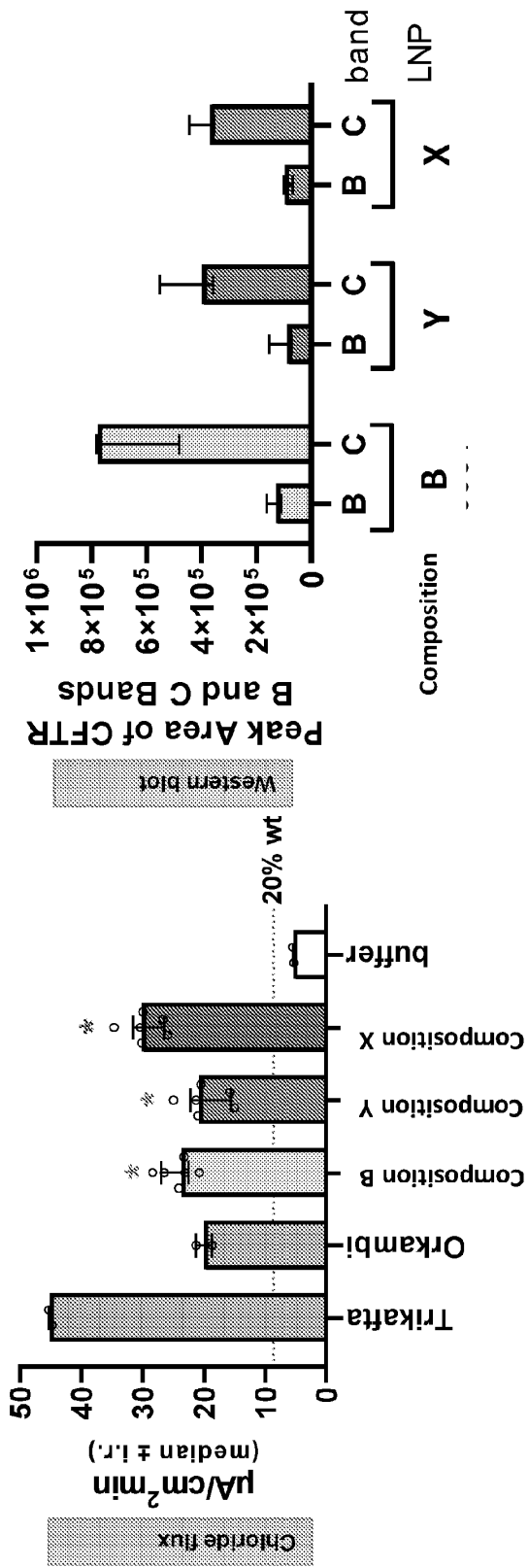


FIG. 83B

FIG. 83C

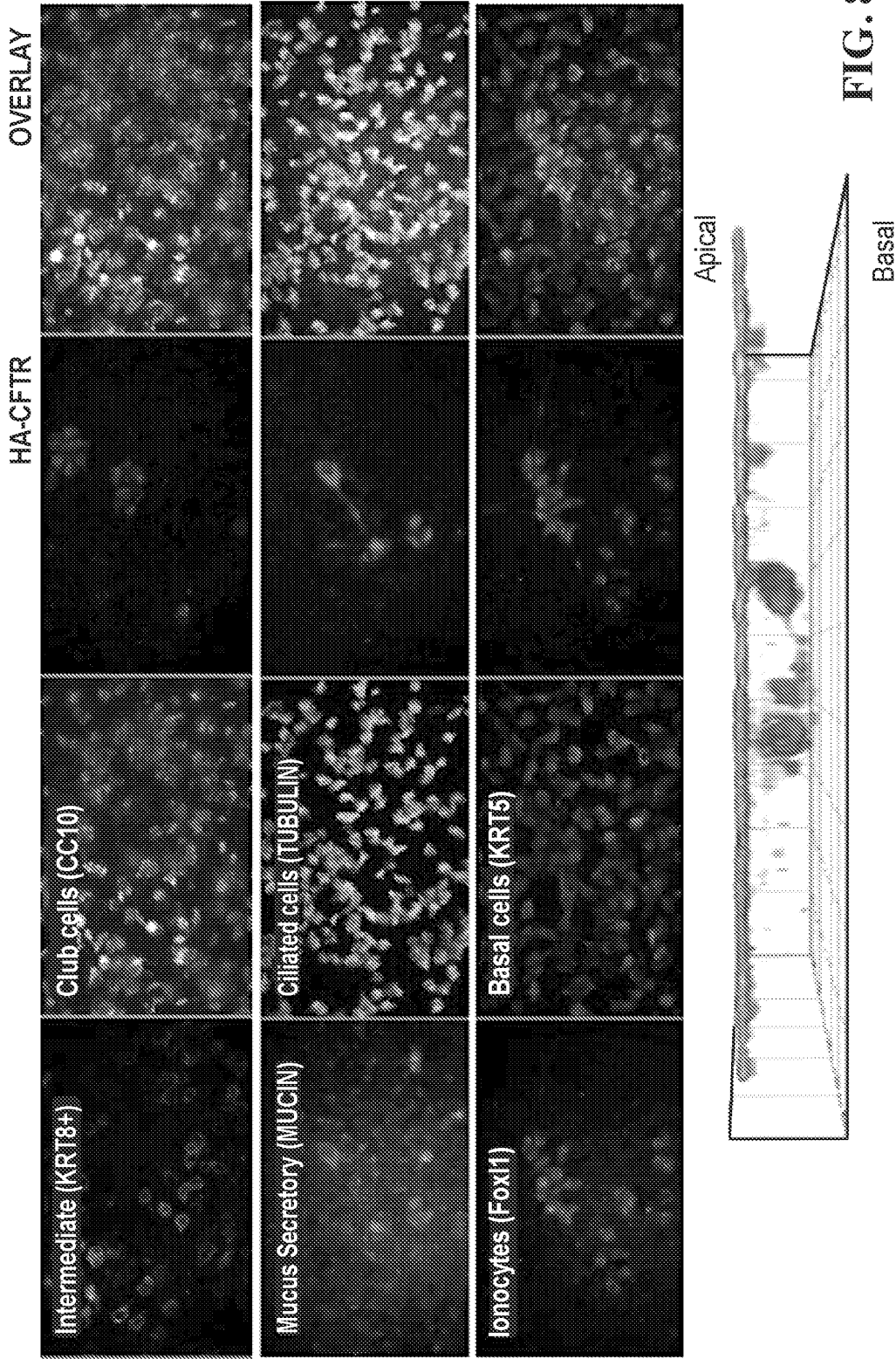


FIG. 84A

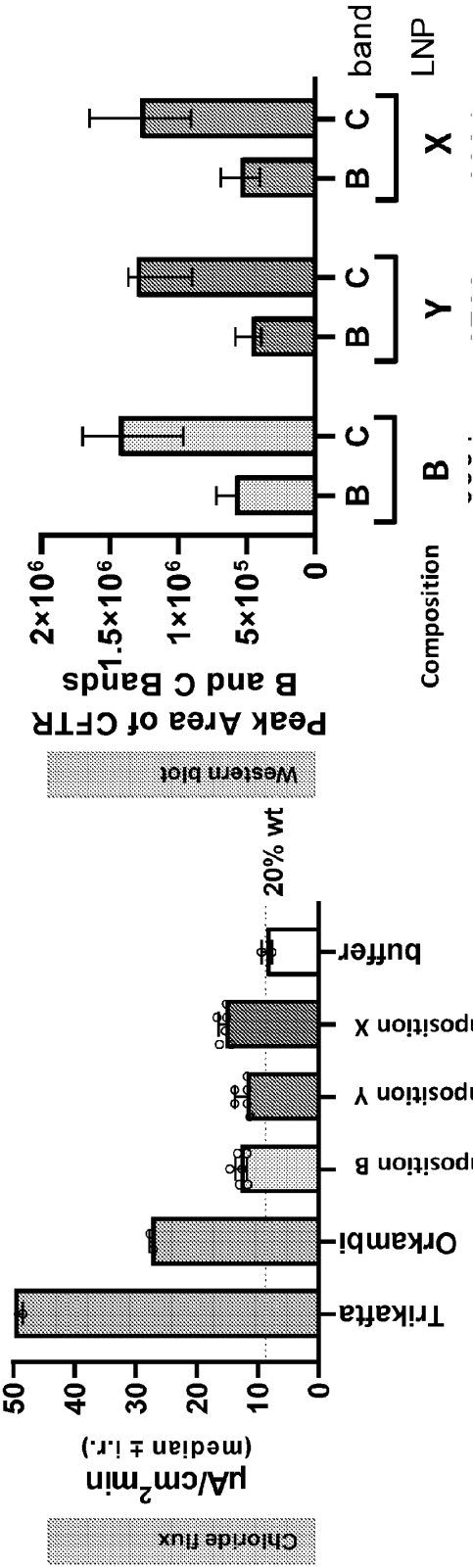
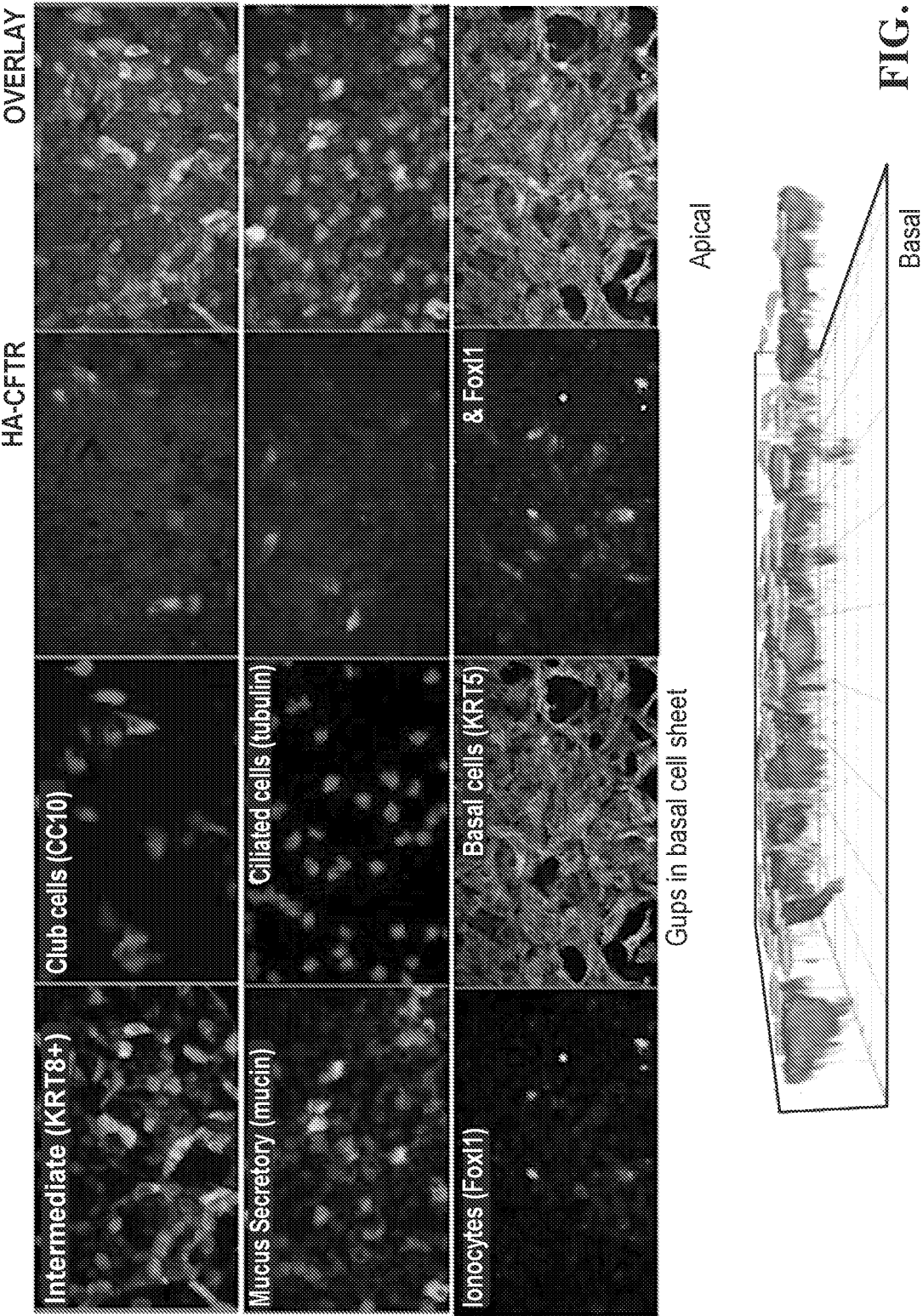


FIG. 84C

FIG. 84B



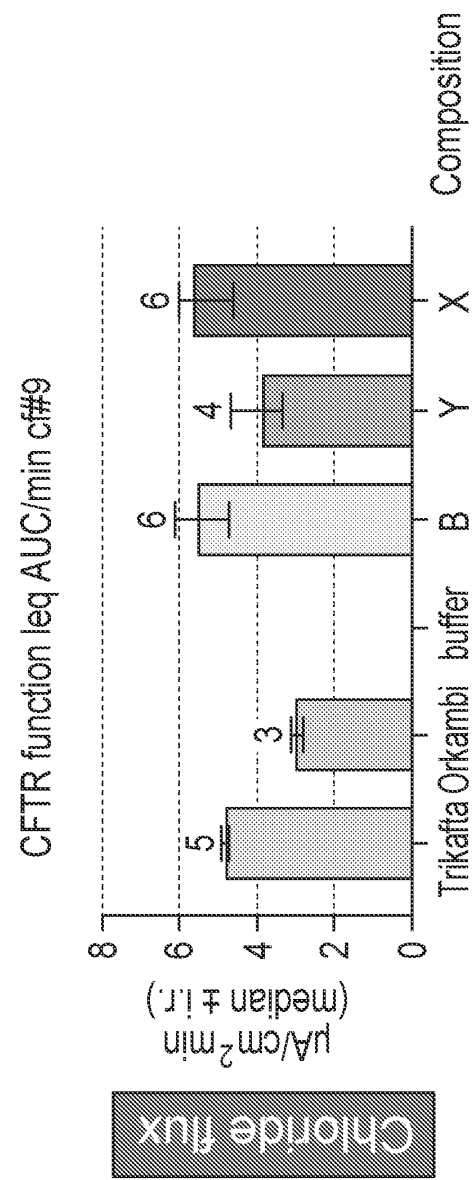


FIG. 85B

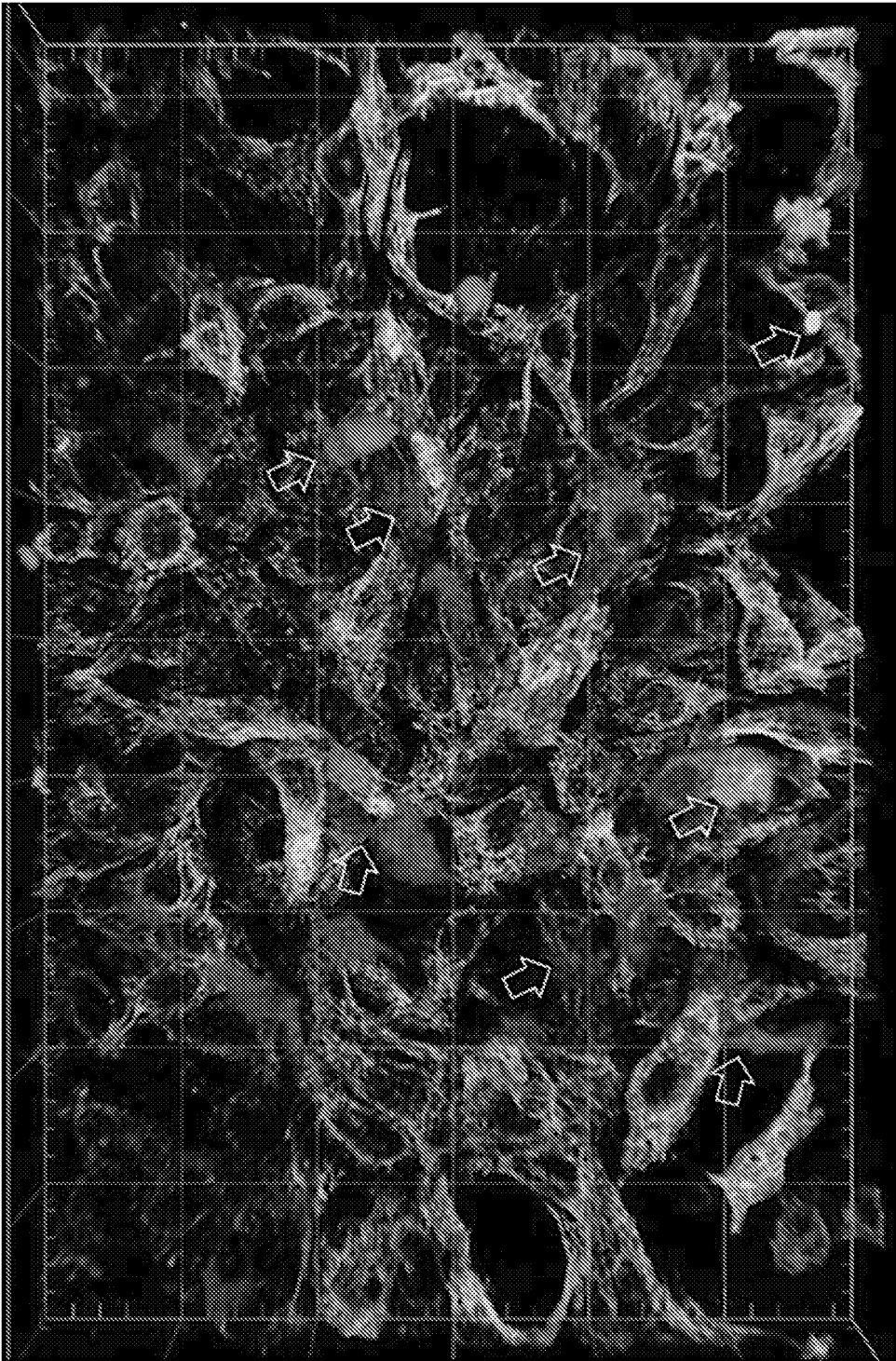


FIG. 86

Foxl1
KRT5
HA-tag

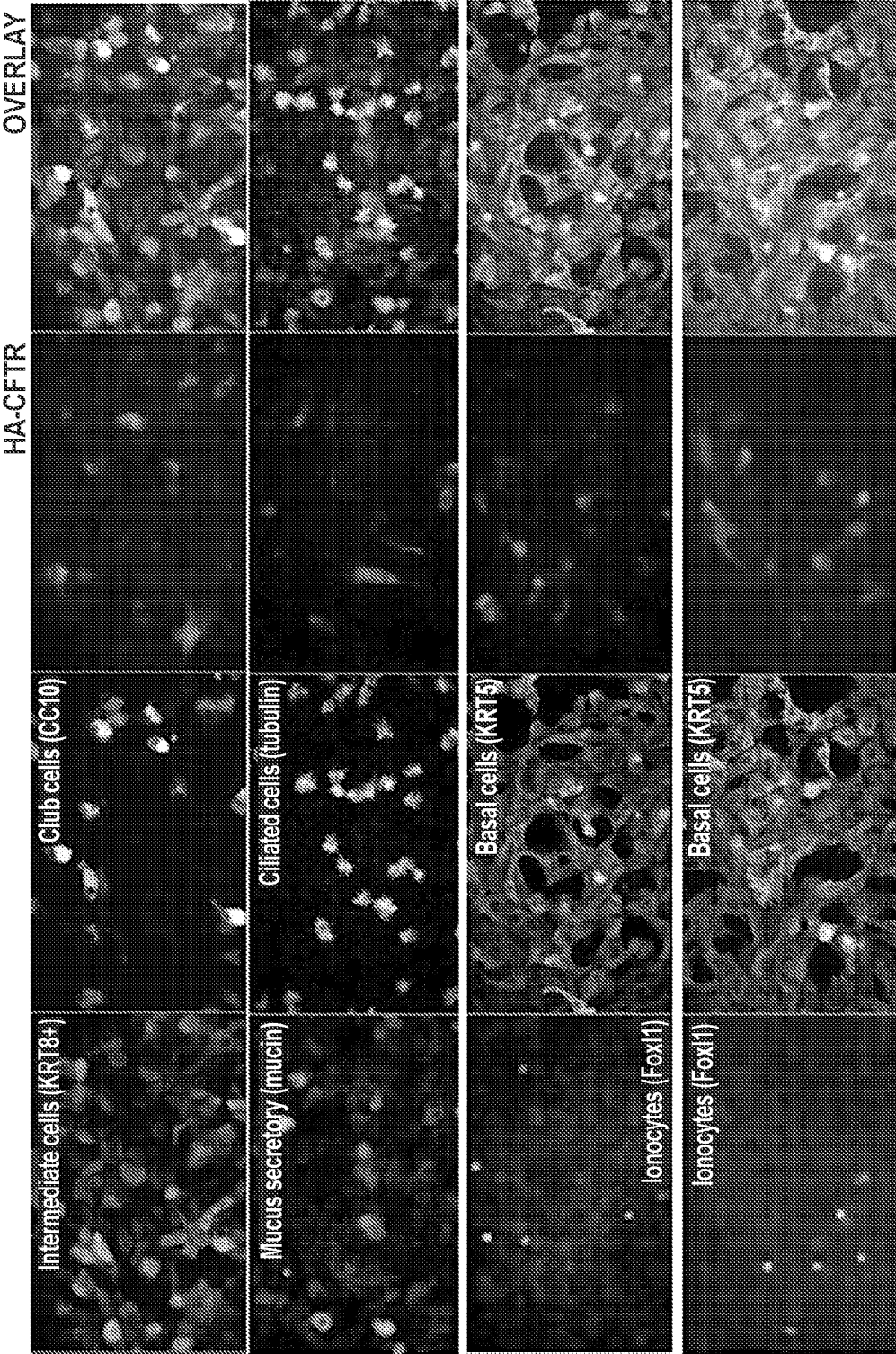
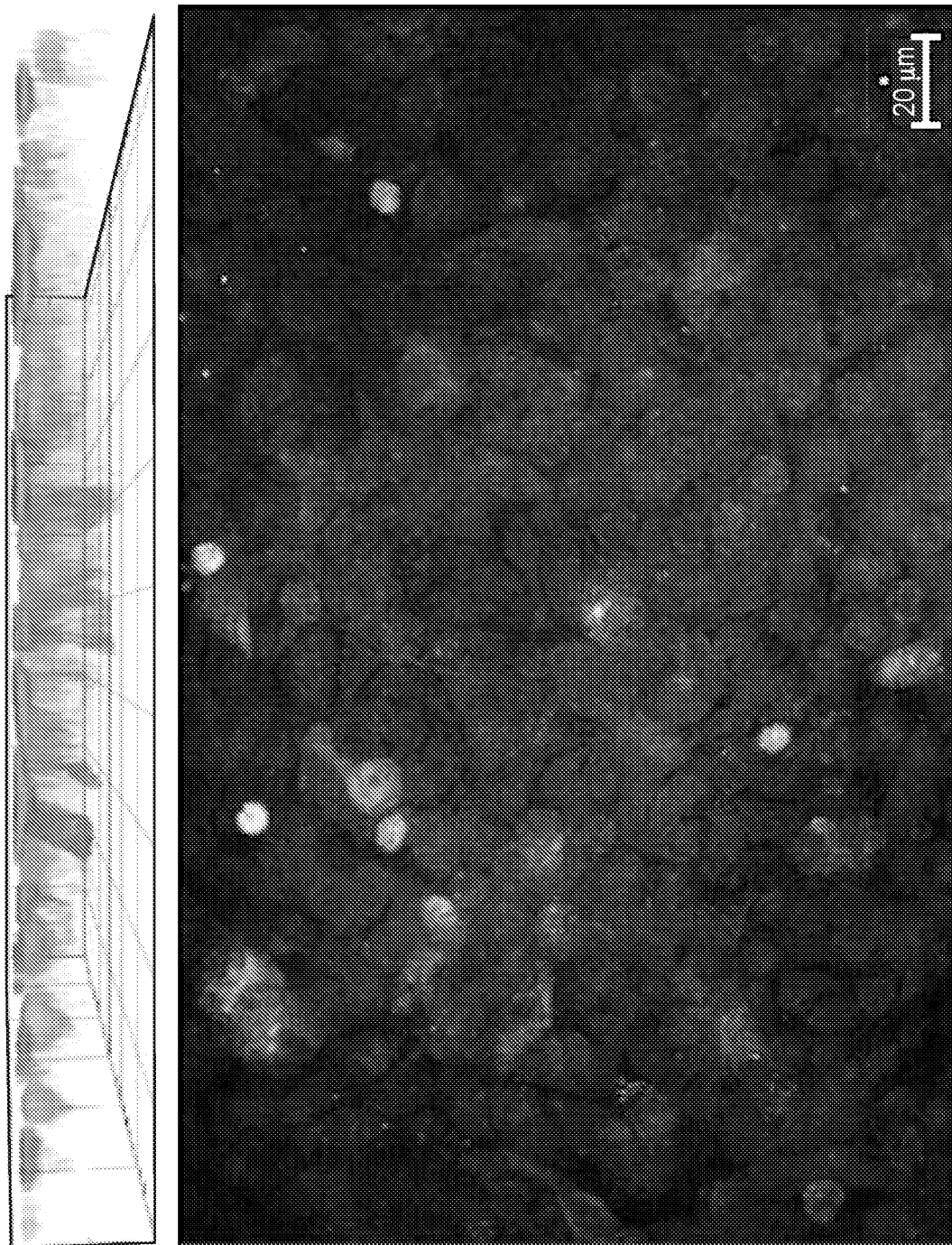


FIG. 87A

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FIG. 87B



SUBSTITUTE SHEET (RULE 26)

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FIG. 88

Foxl1
KRT5
HA-tag

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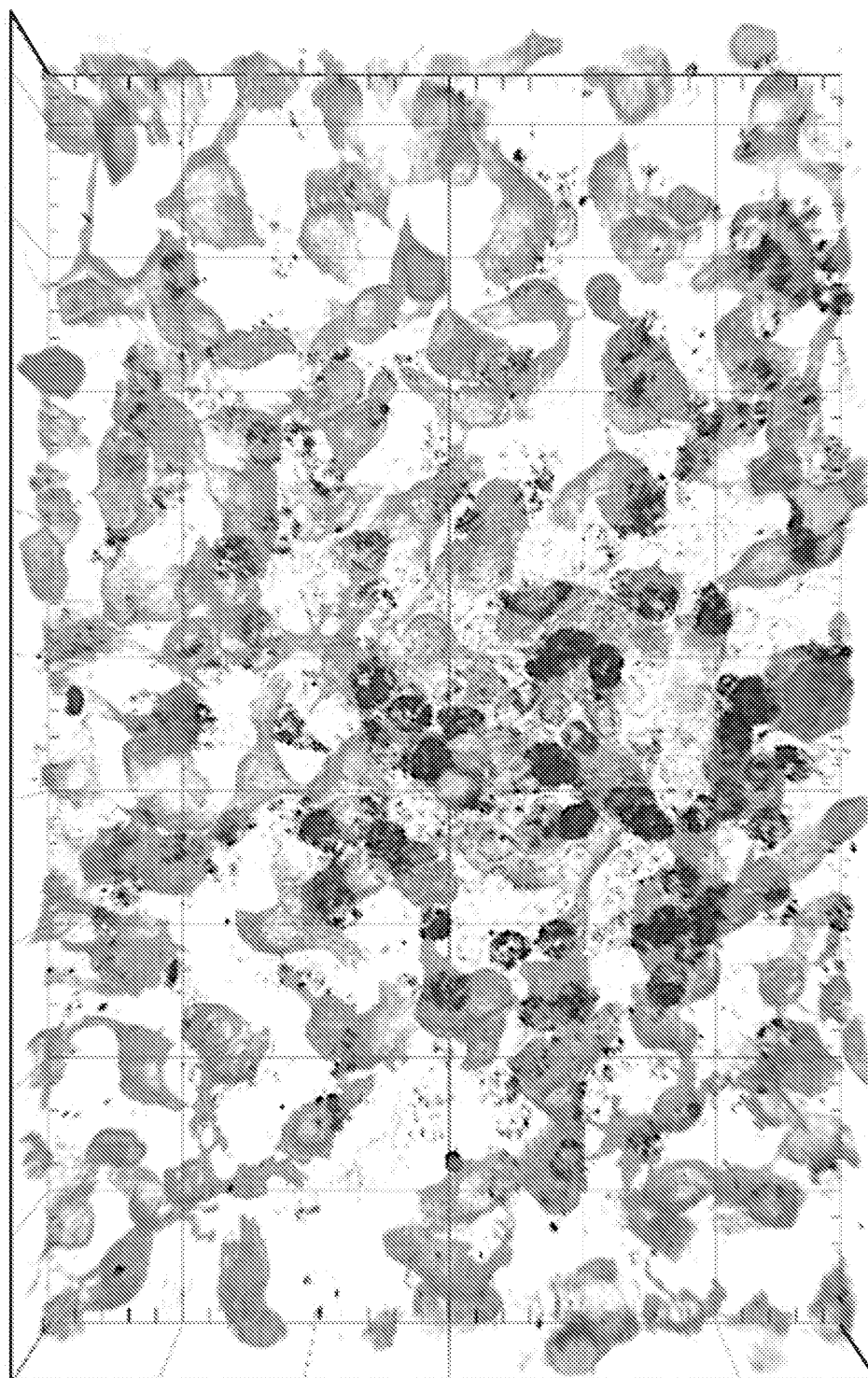


FIG. 89

Foxl1
KRT5
HA-tag

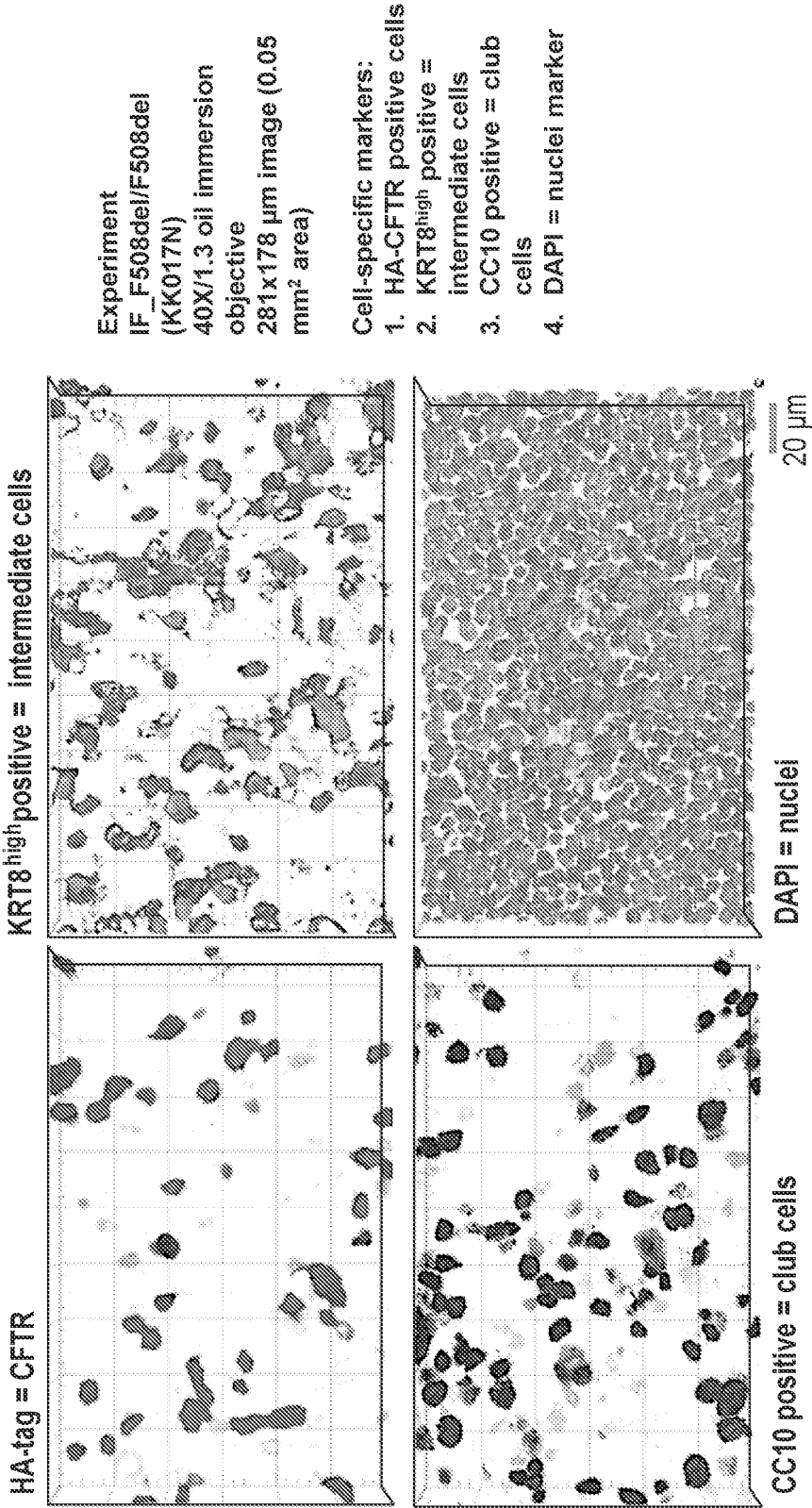


FIG. 90

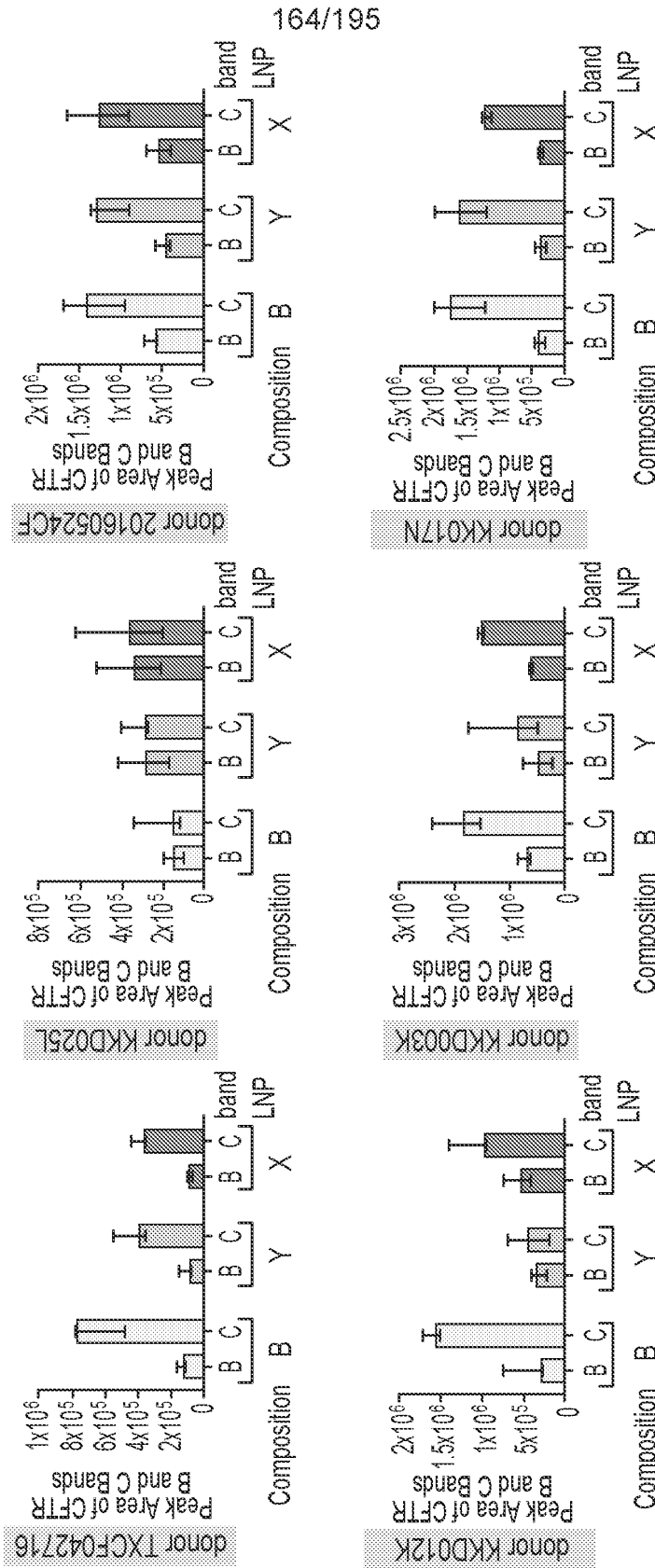


FIG. 91

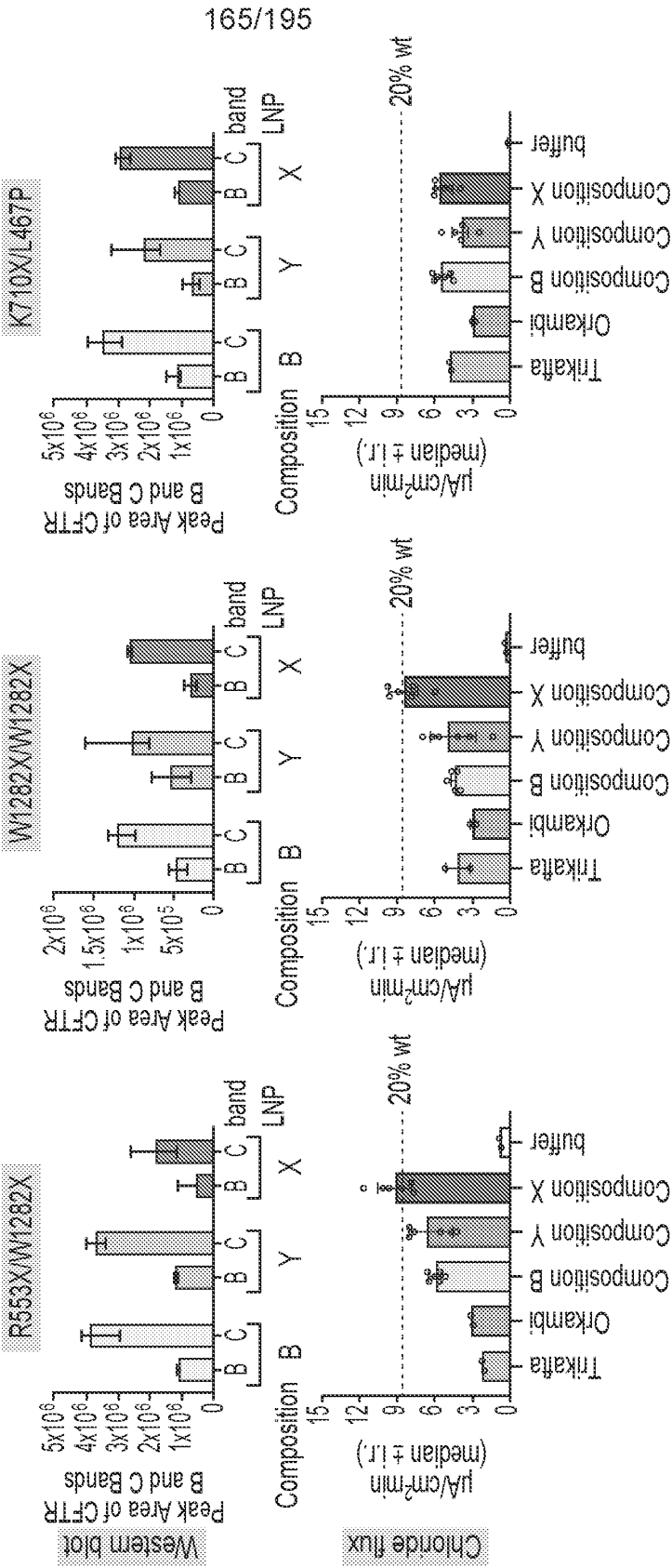


FIG. 92

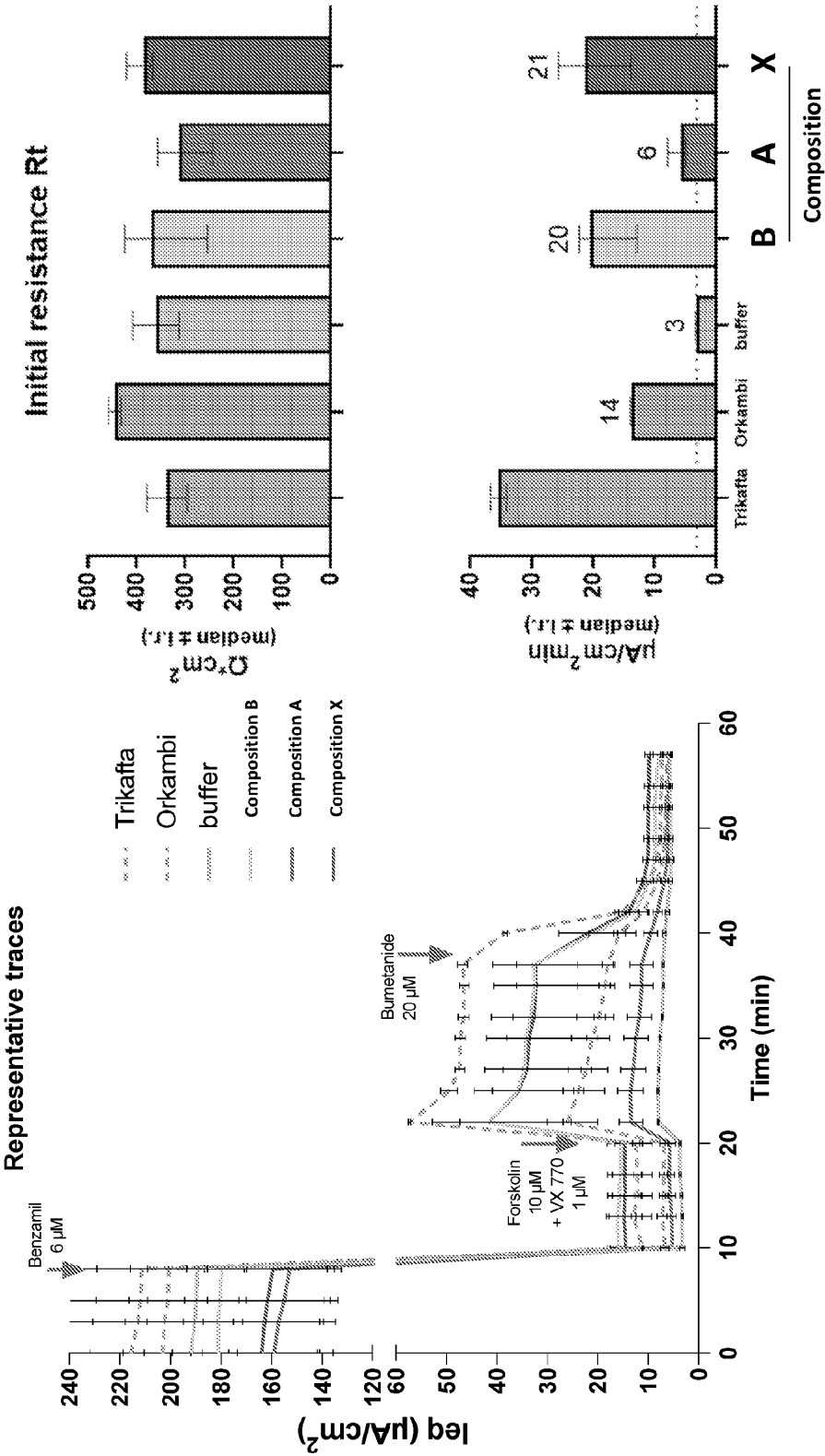


FIG. 93A

FIG. 93B

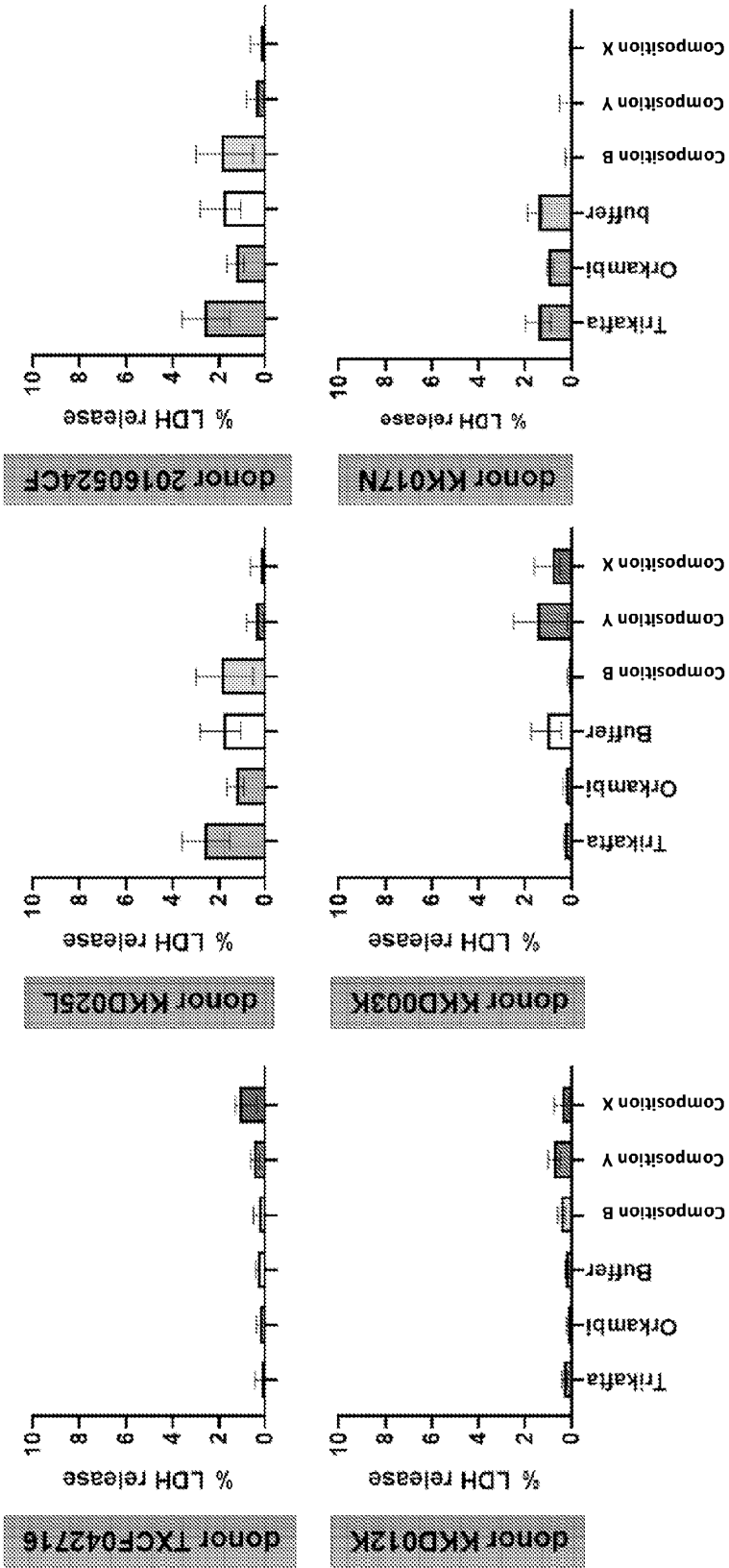


FIG. 94

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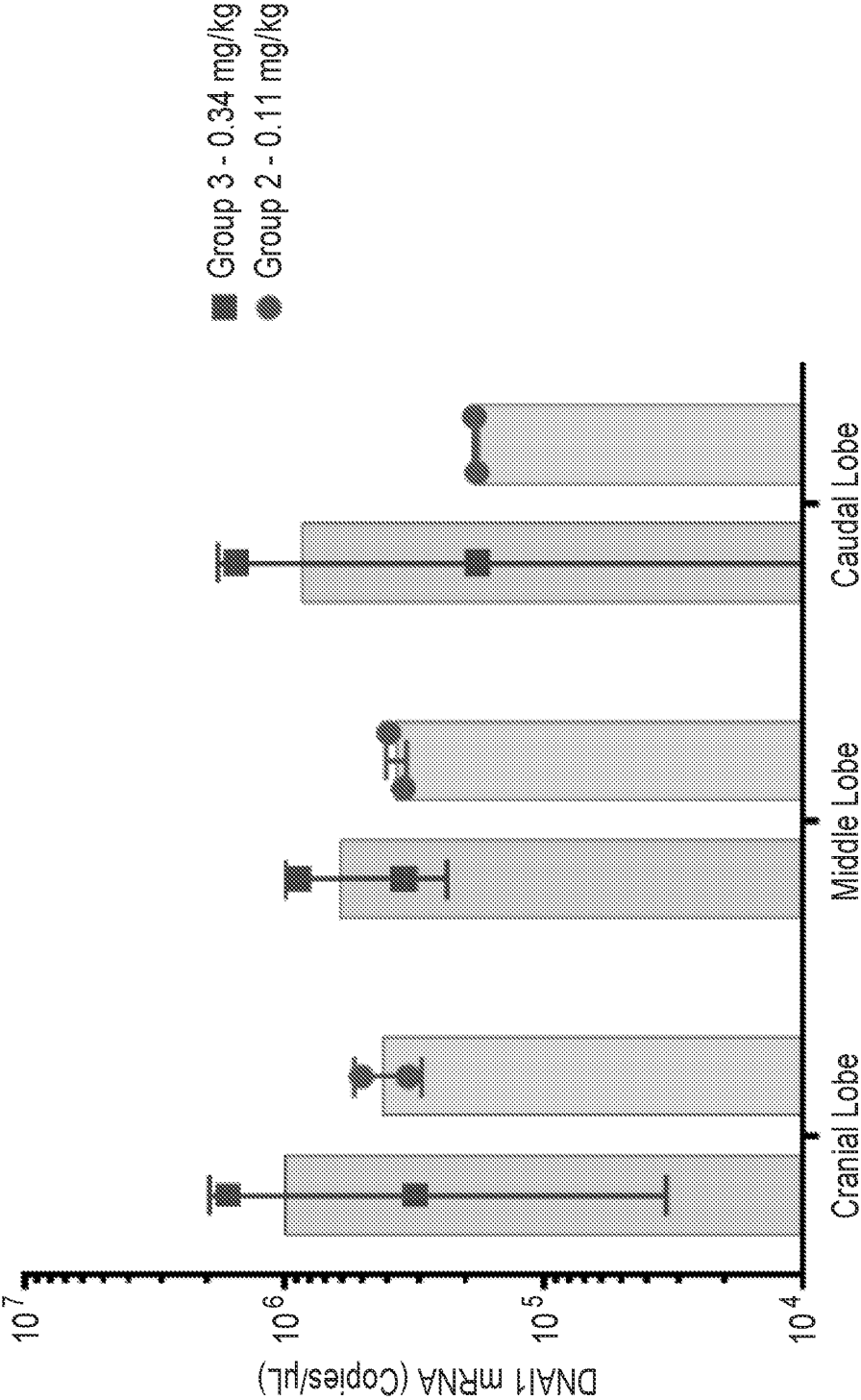


FIG. 95

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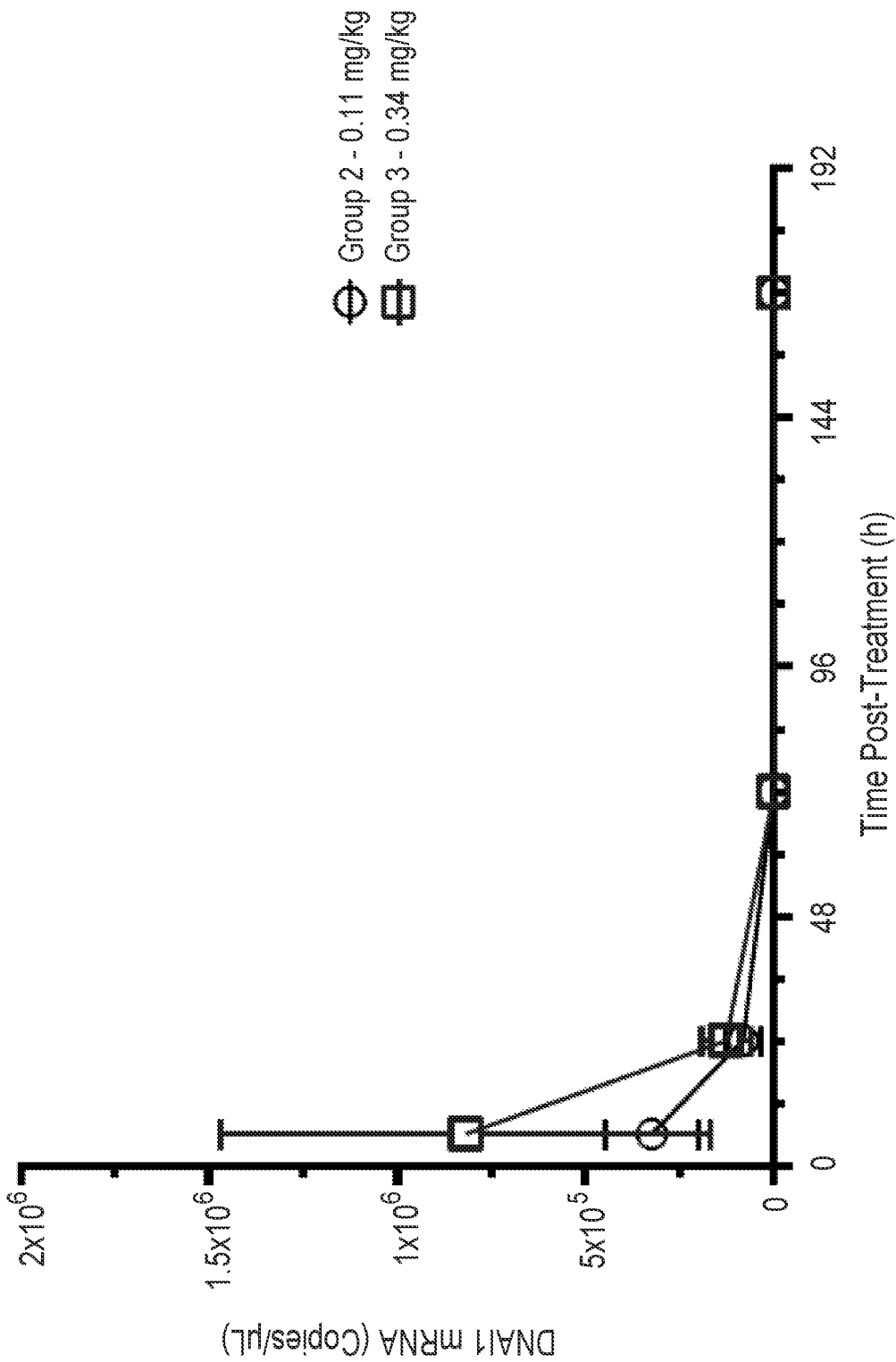


FIG. 96

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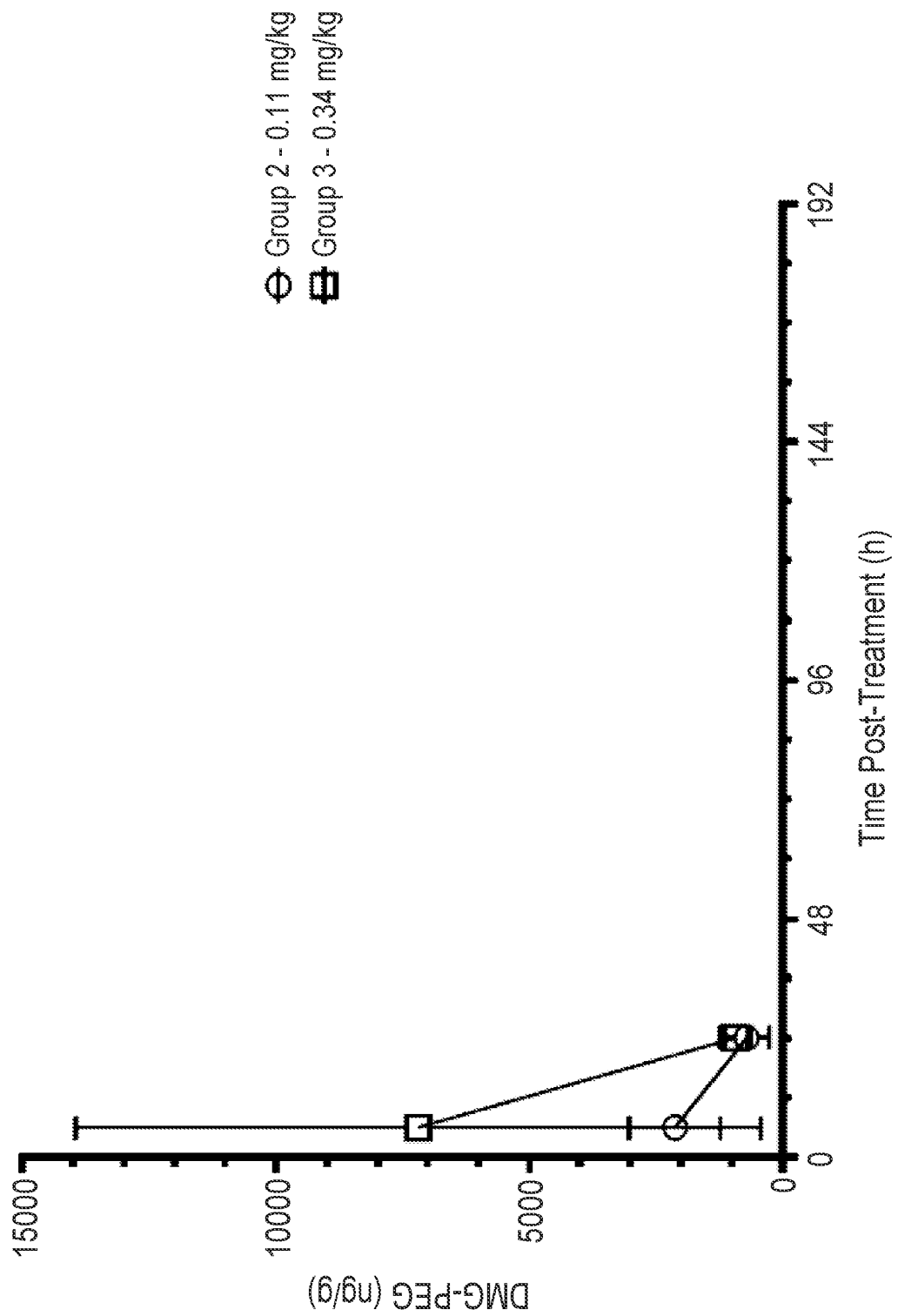


FIG. 97

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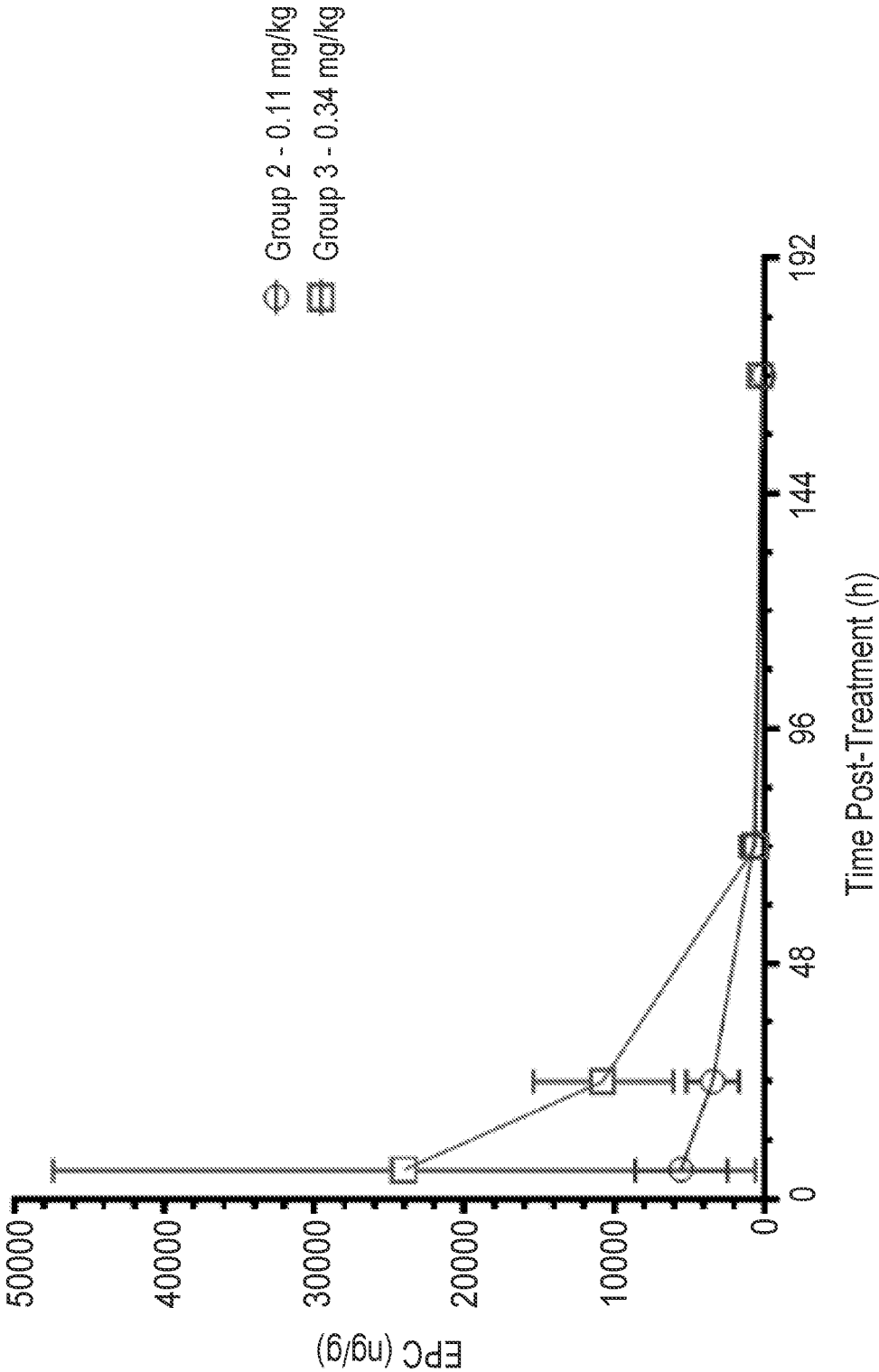


FIG. 98

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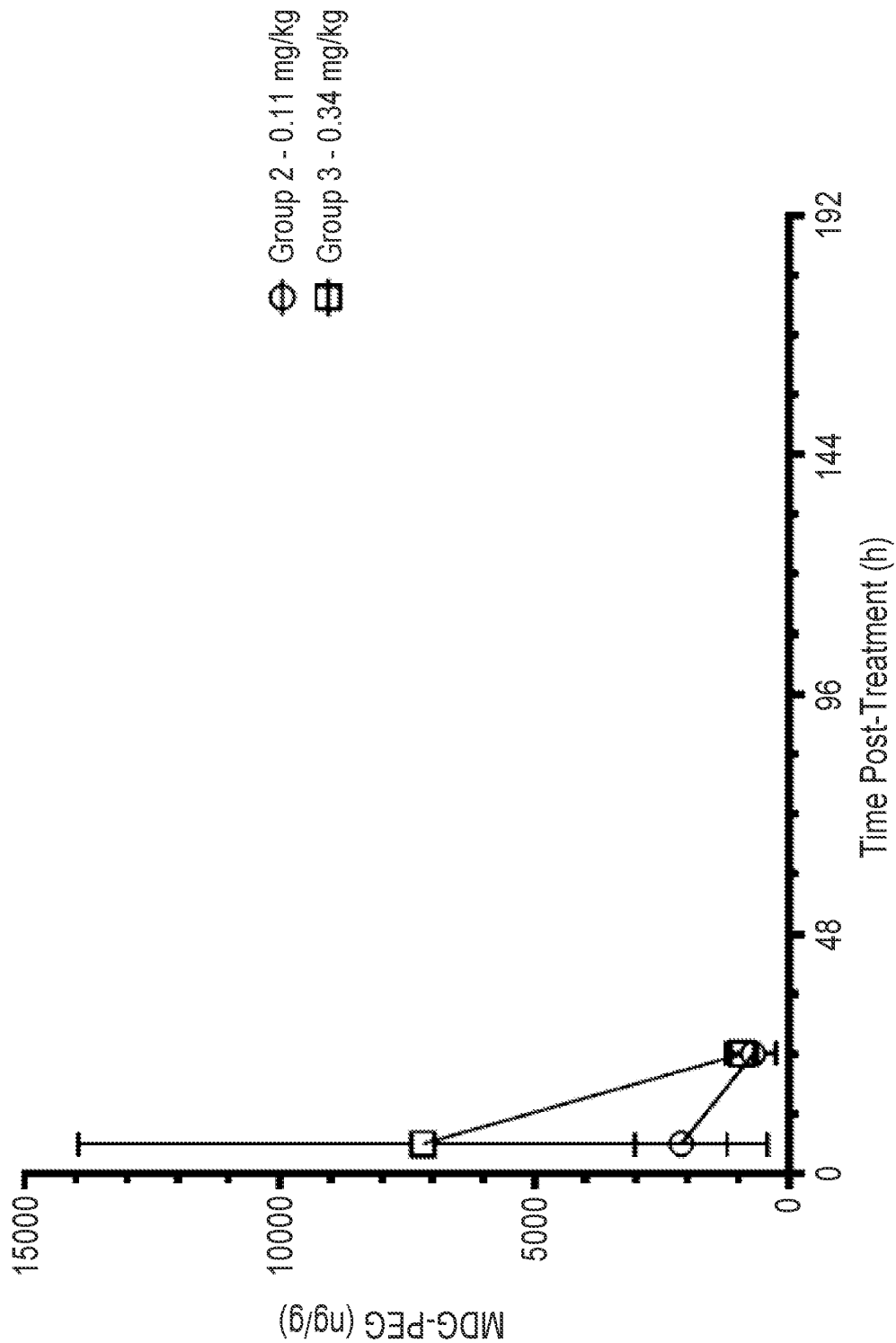


FIG. 99

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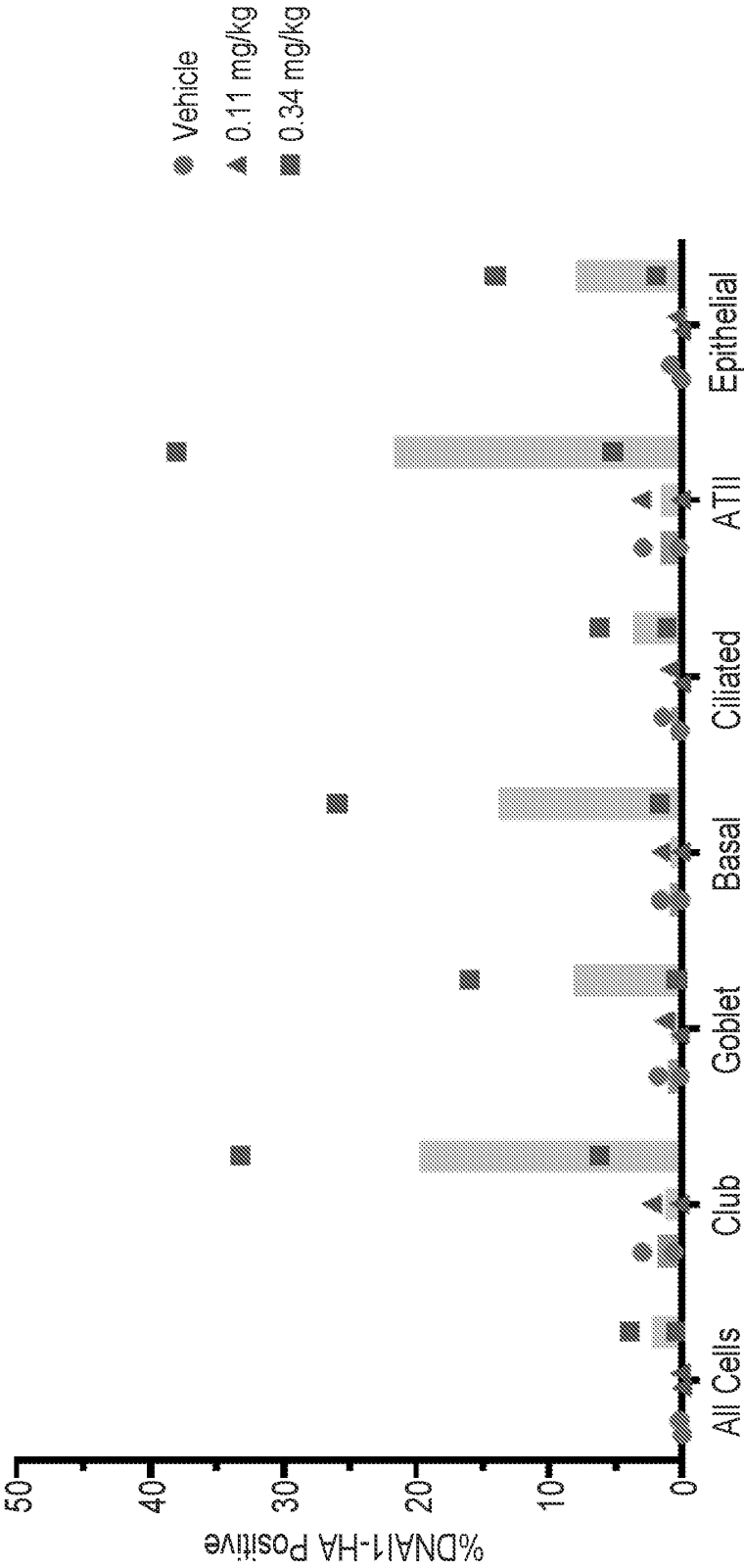


FIG. 100

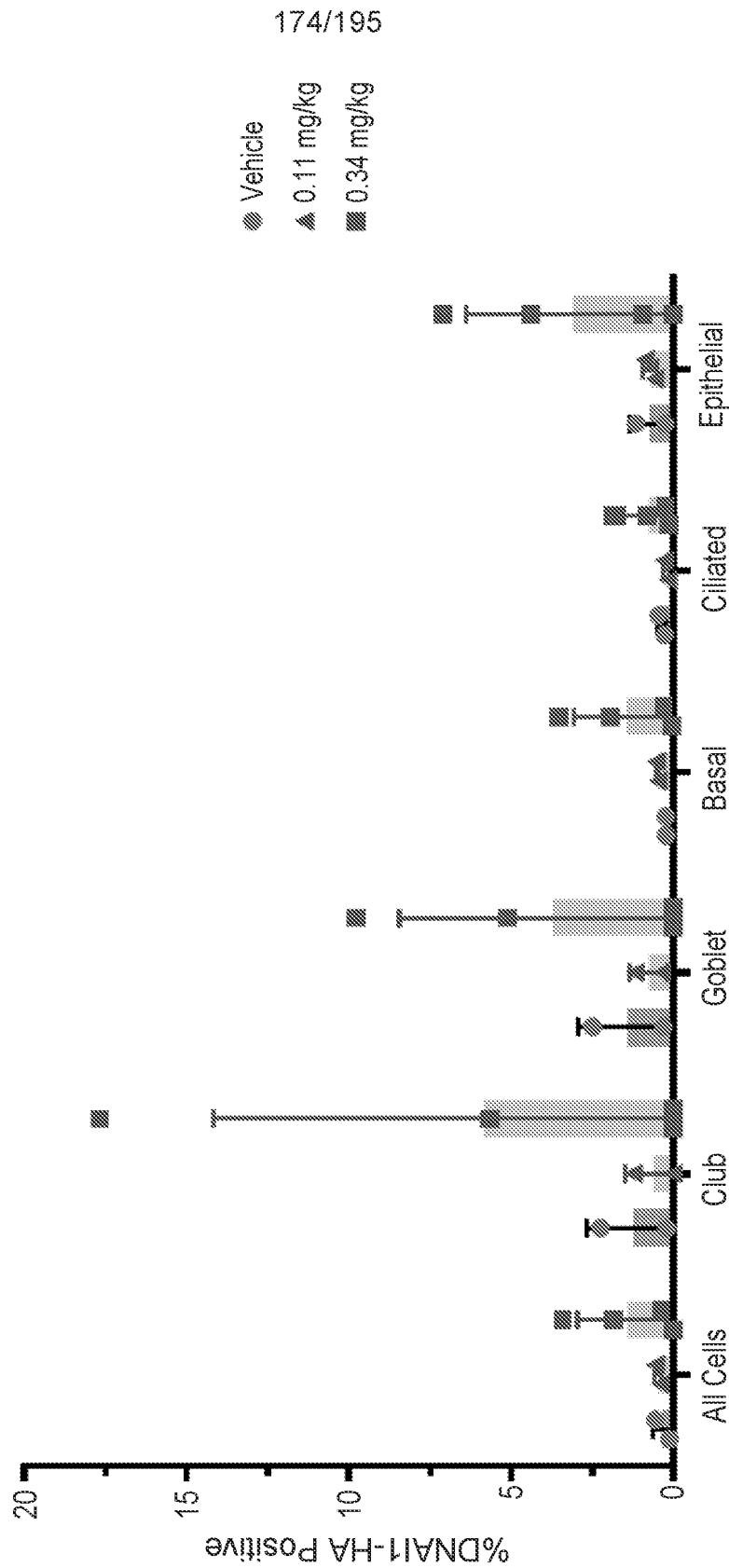


FIG. 101

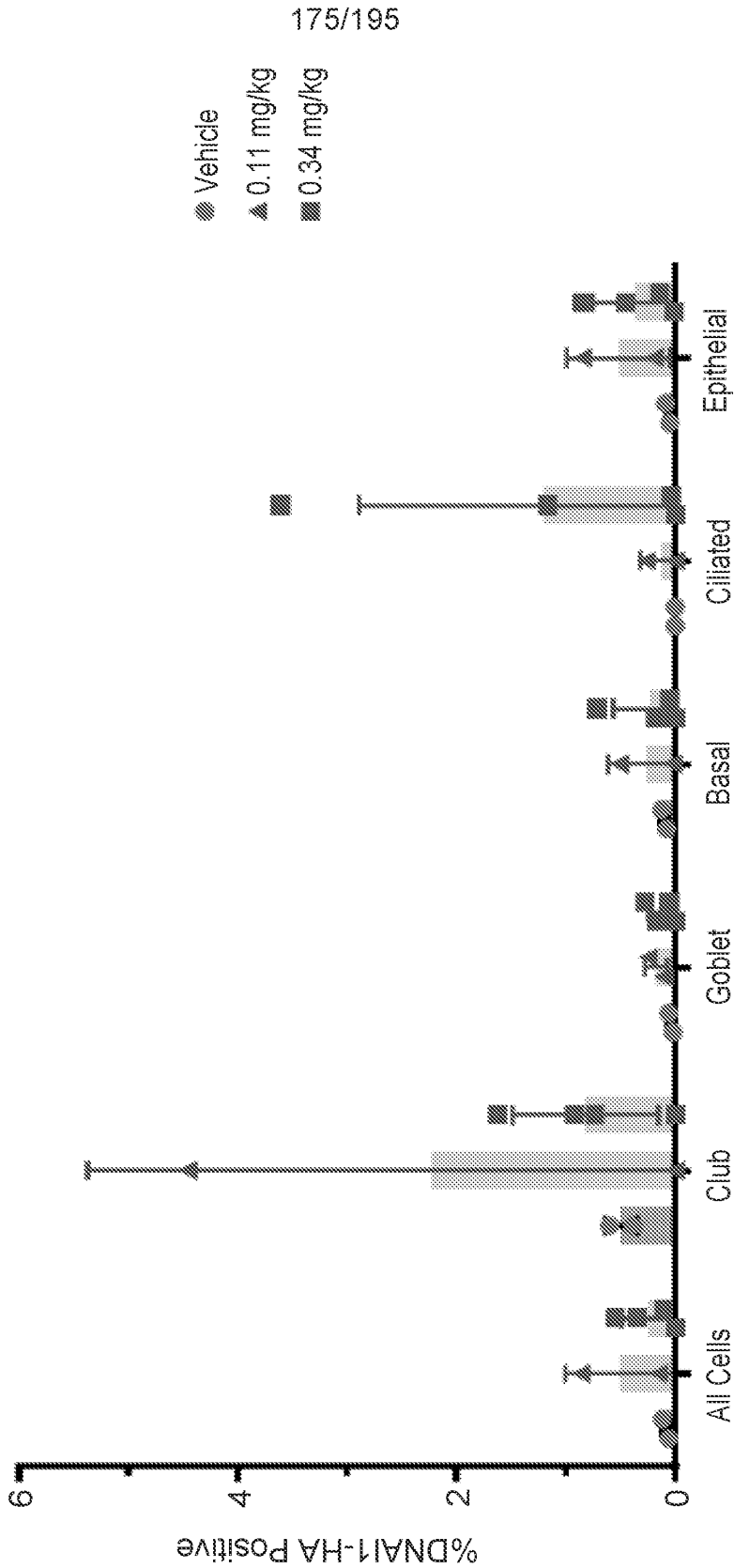
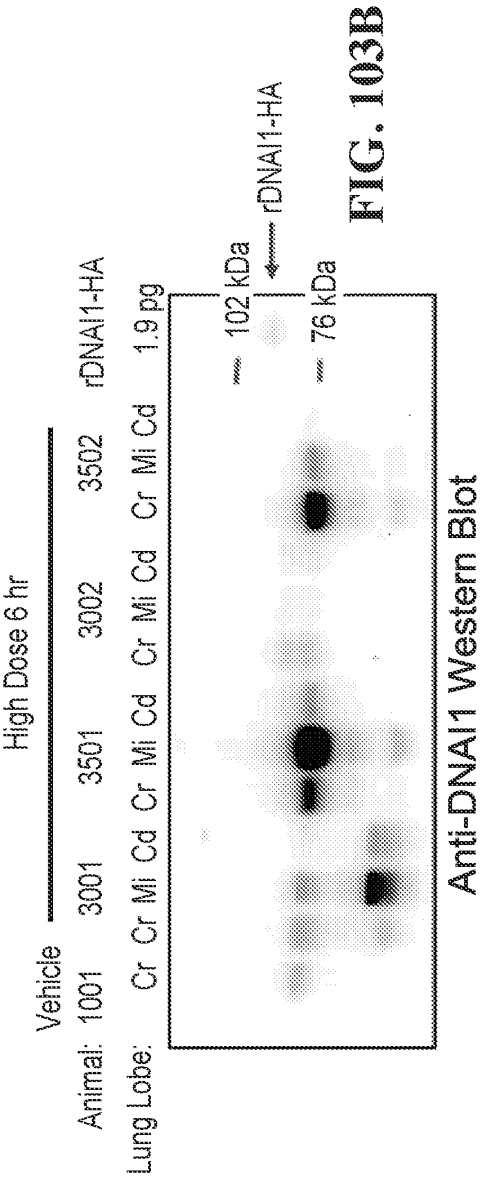
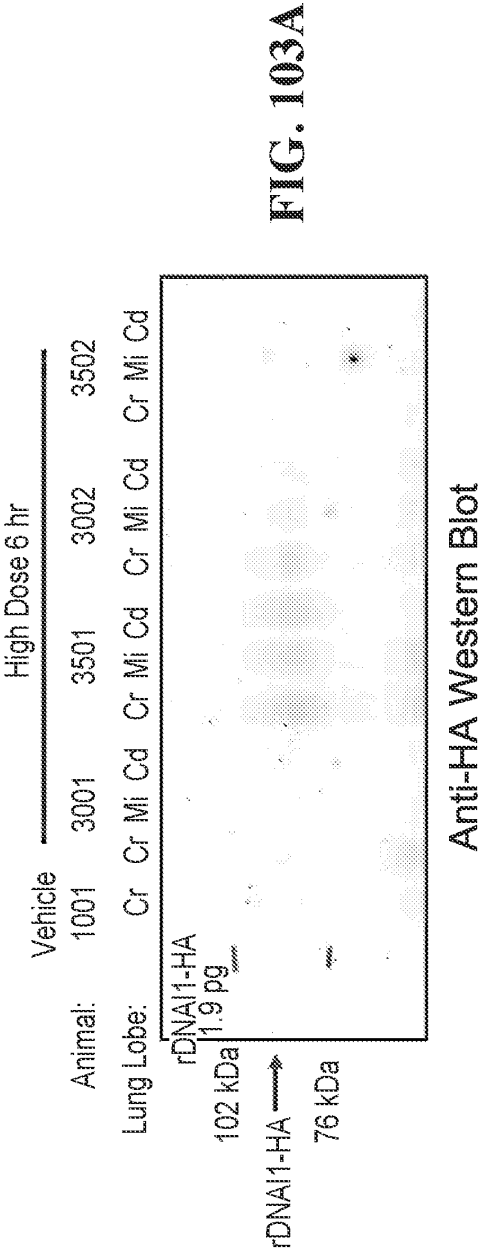


FIG. 102



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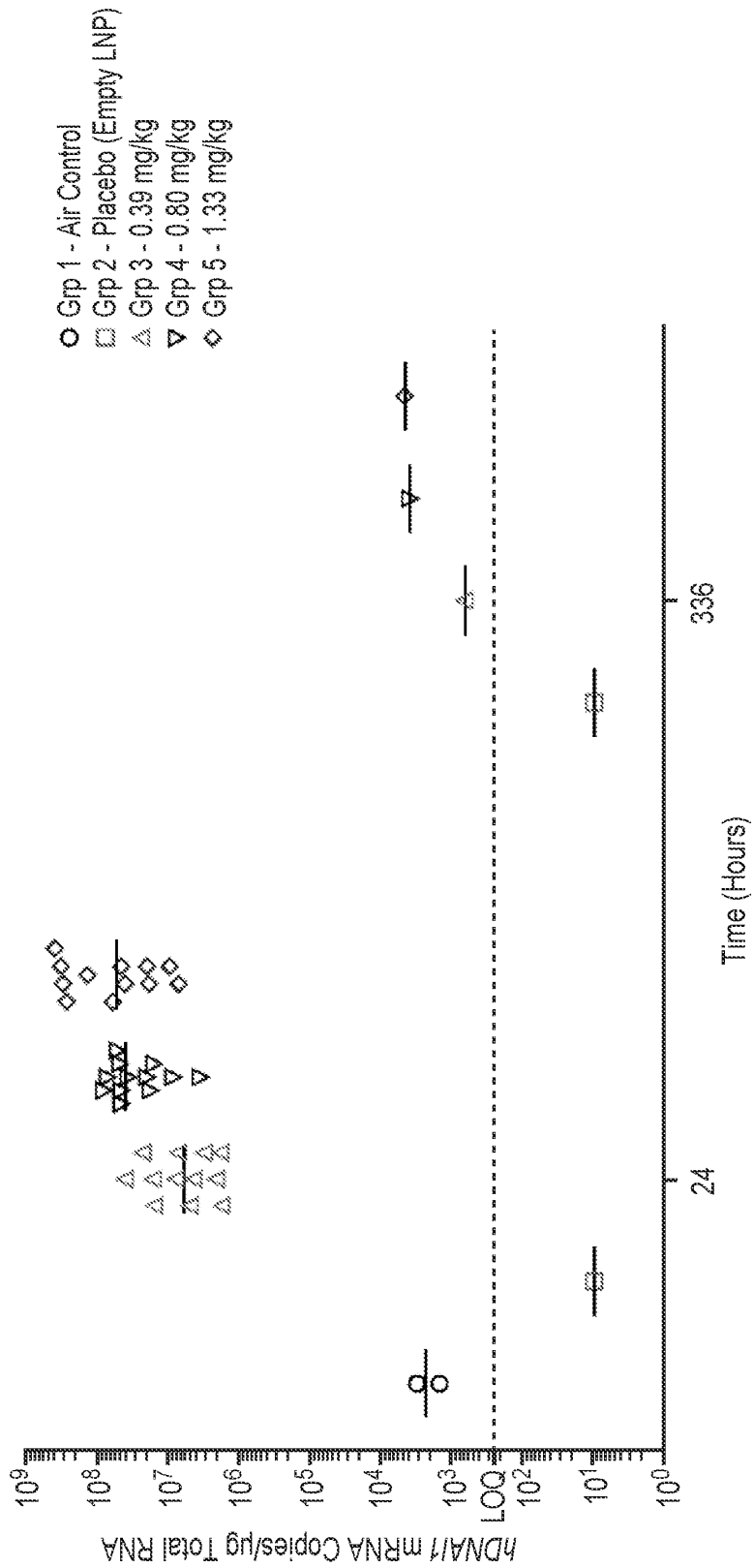


FIG. 104

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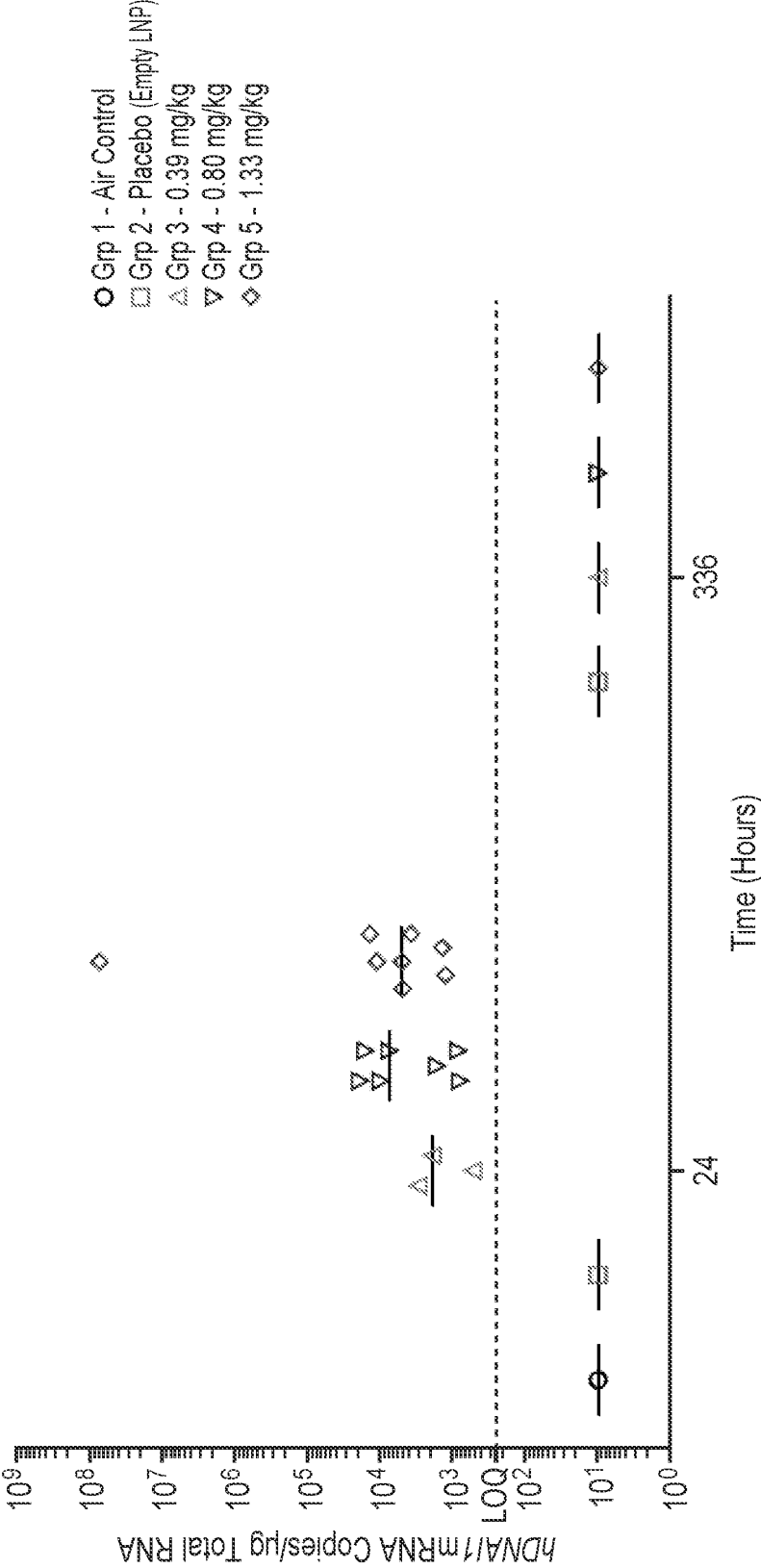


FIG. 105

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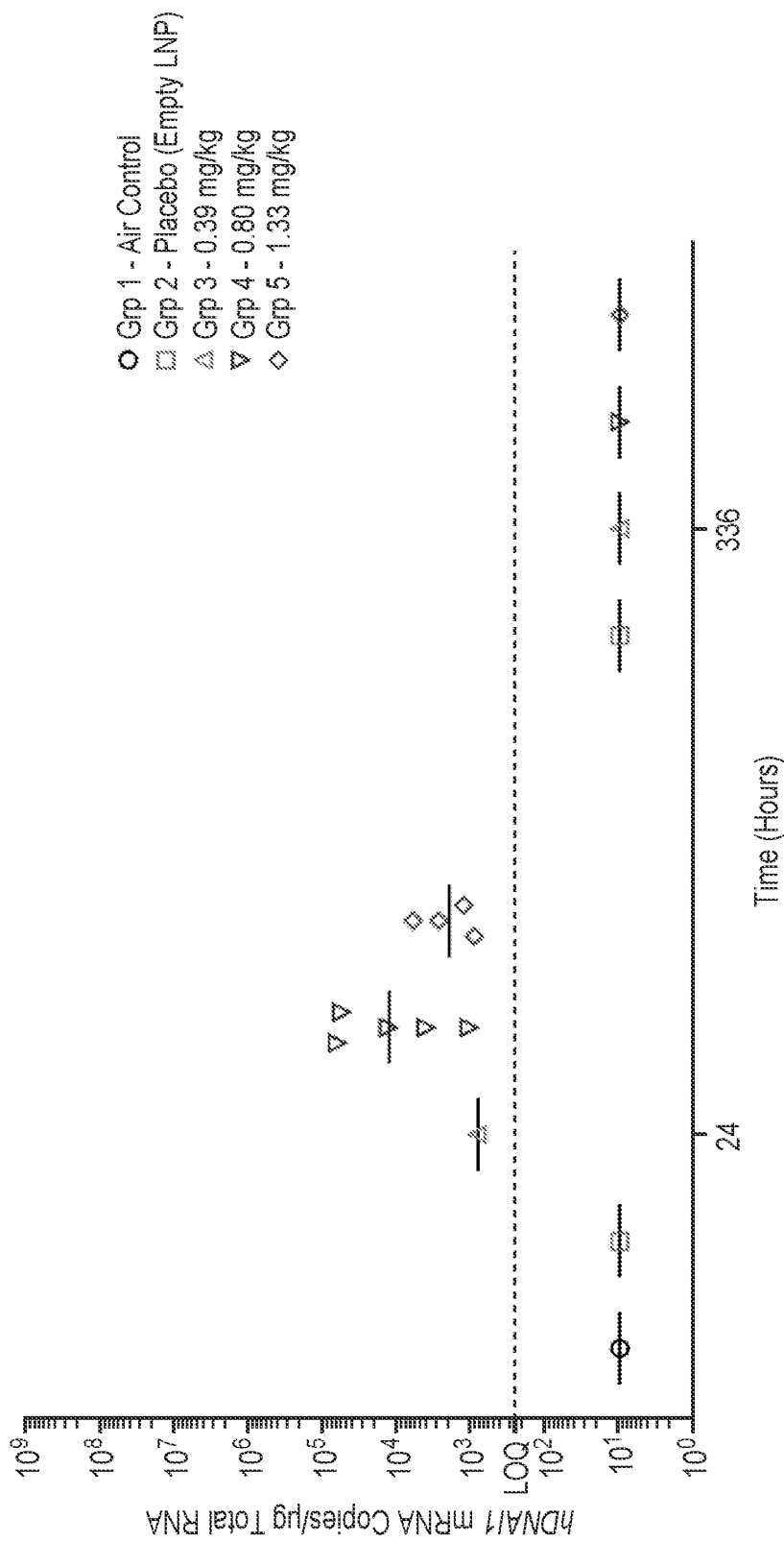


FIG. 106

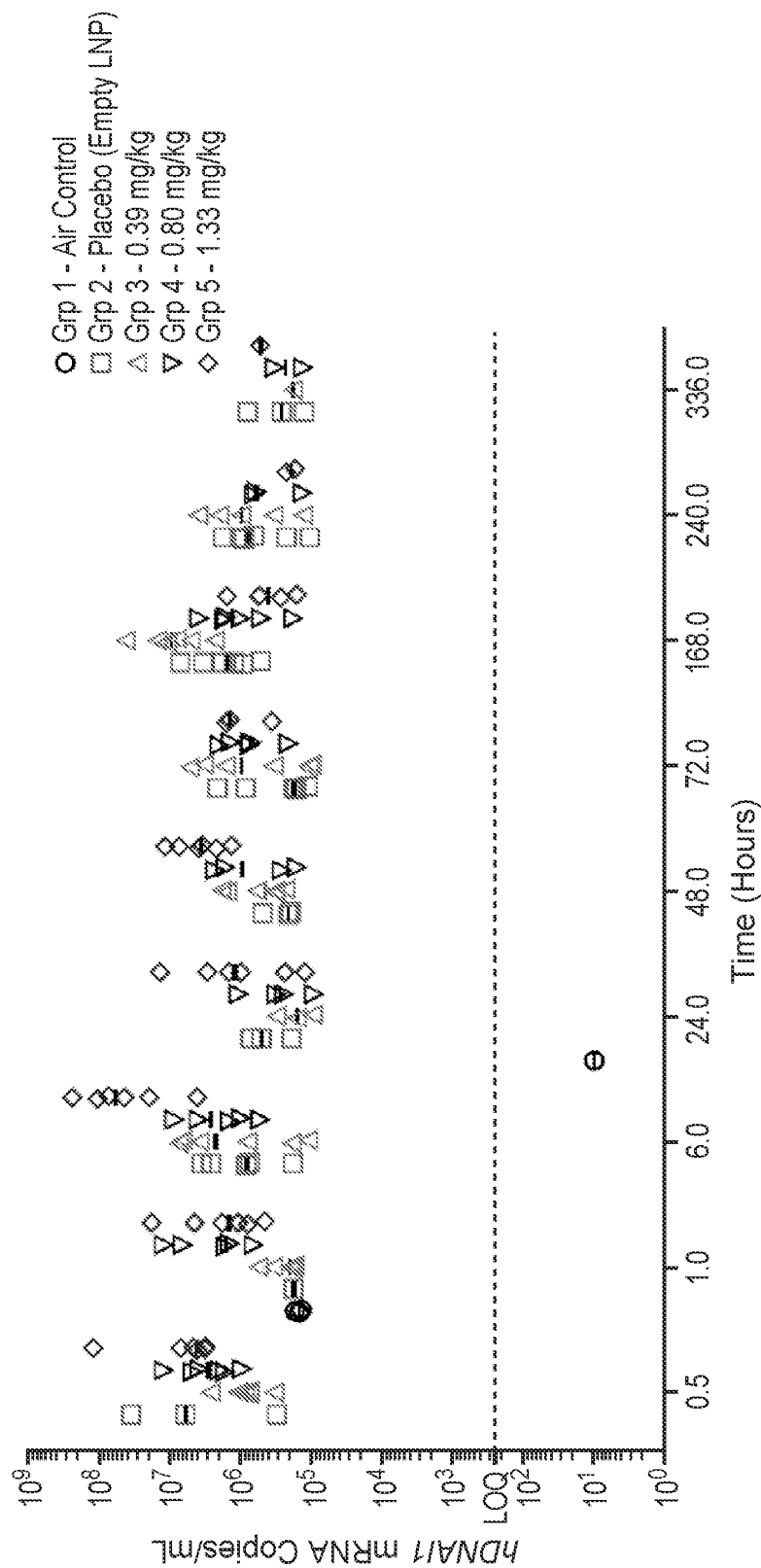


FIG. 107

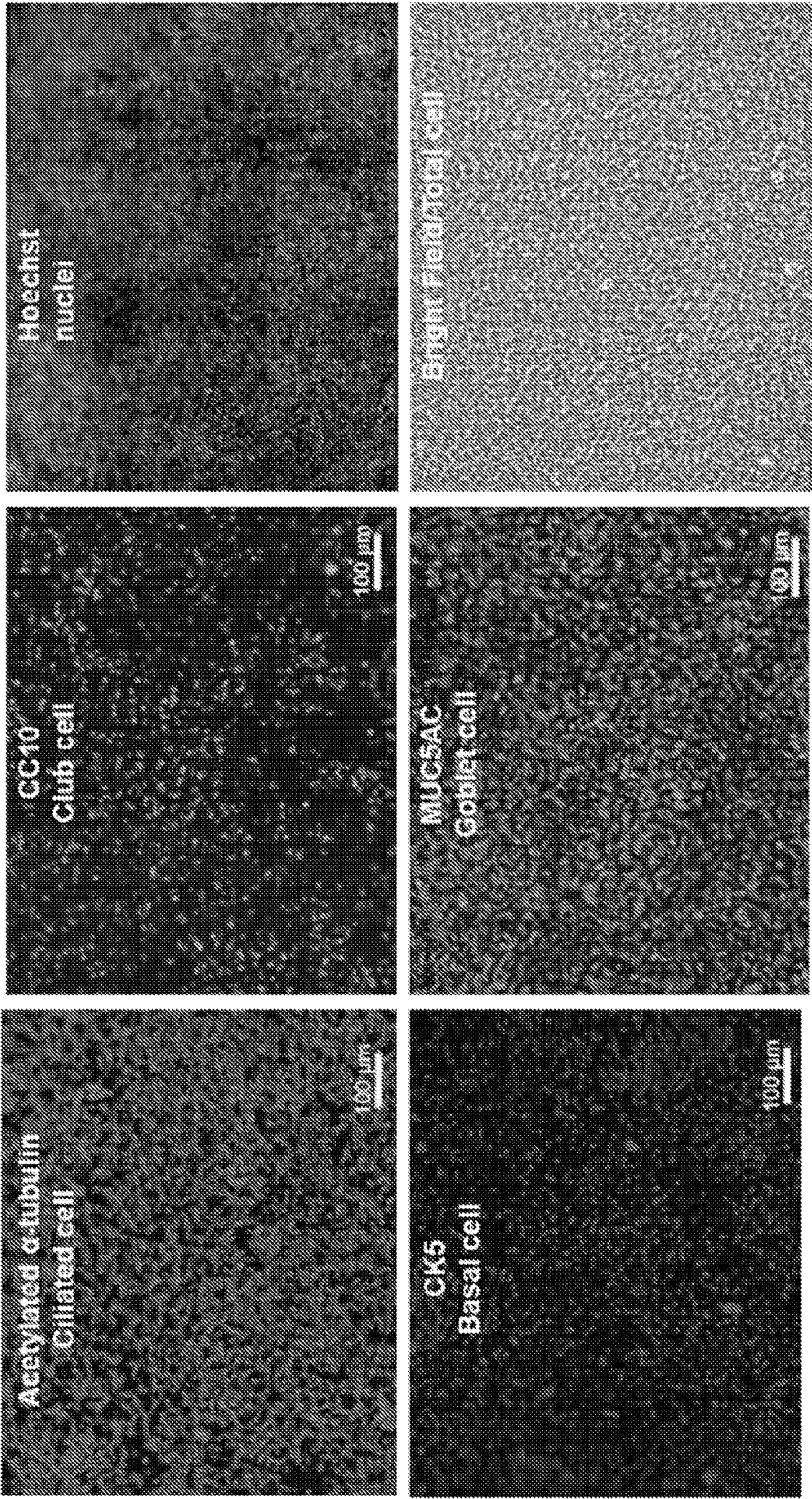


FIG. 108

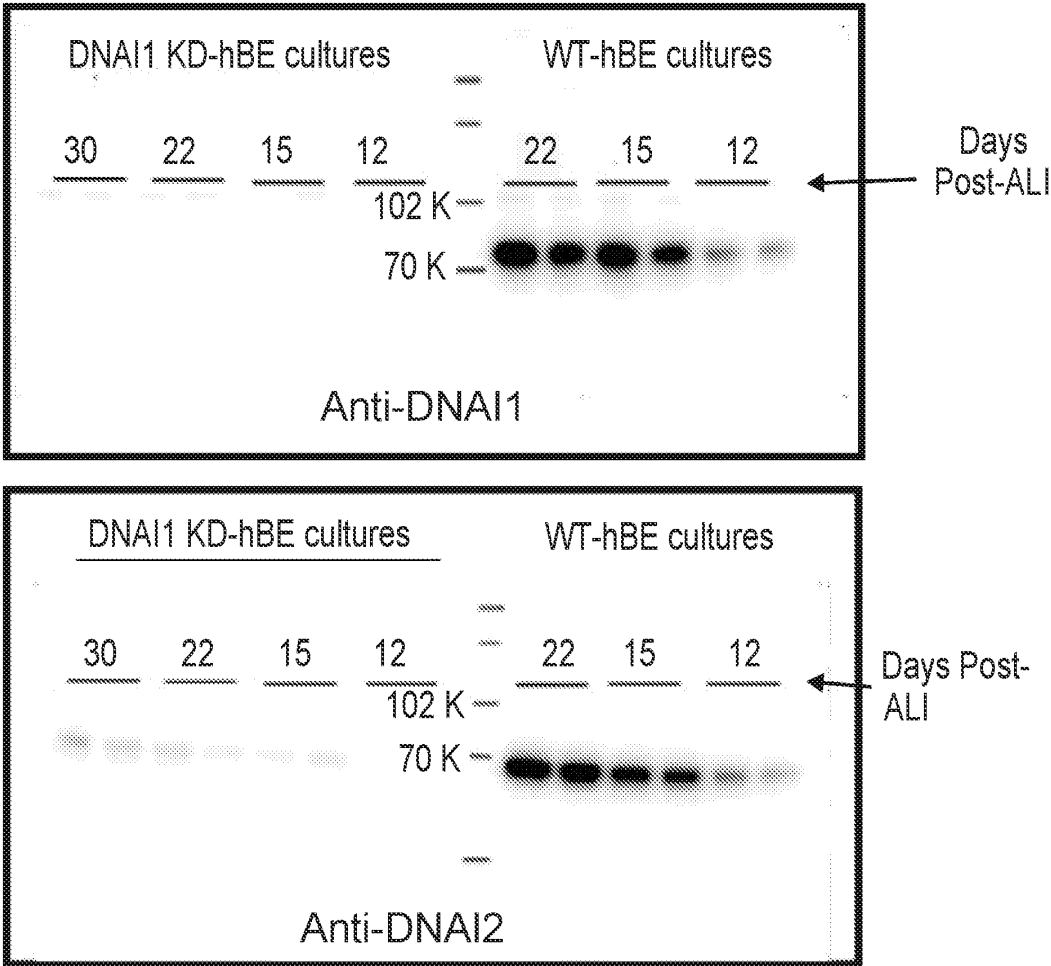


FIG. 109

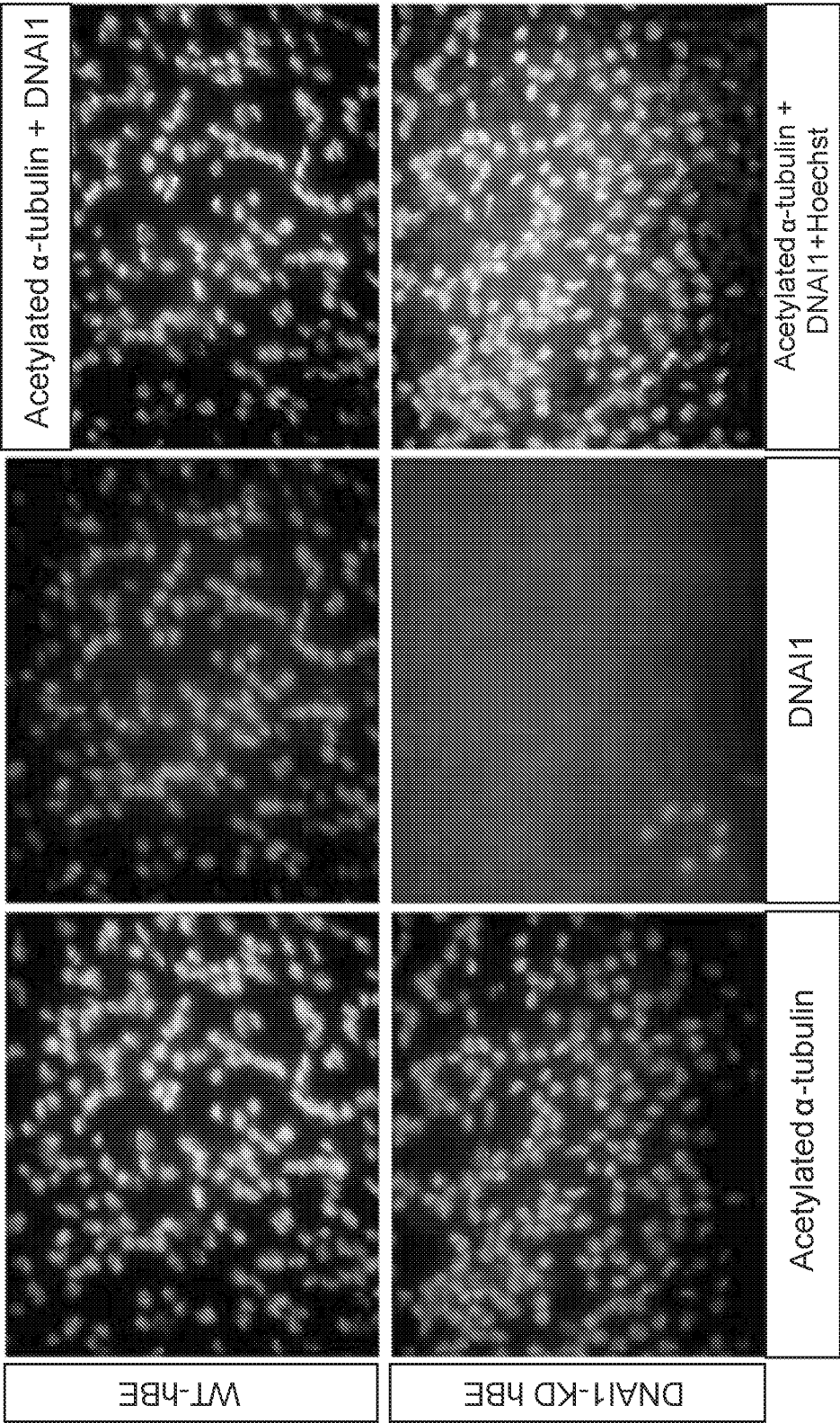


FIG. 110

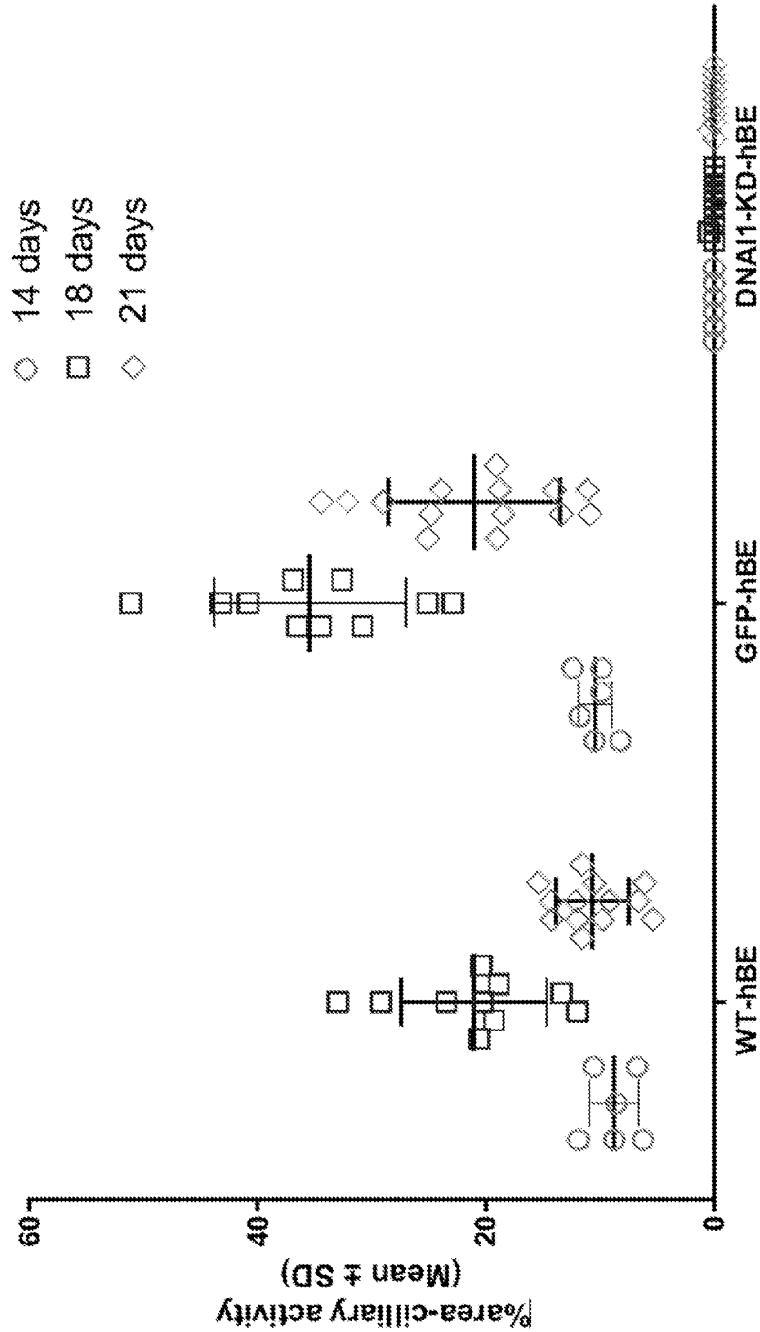


FIG. 111

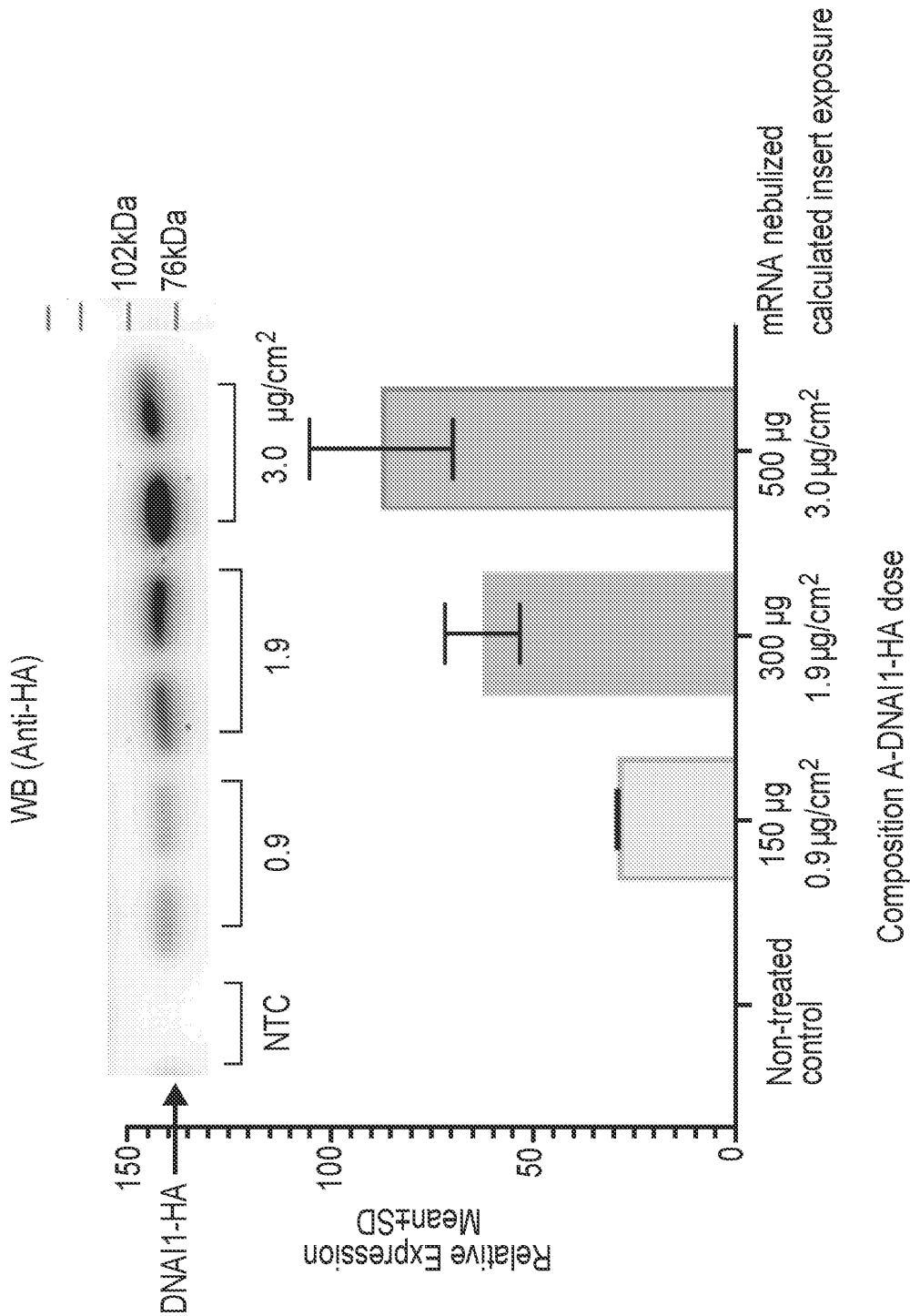


FIG. 112

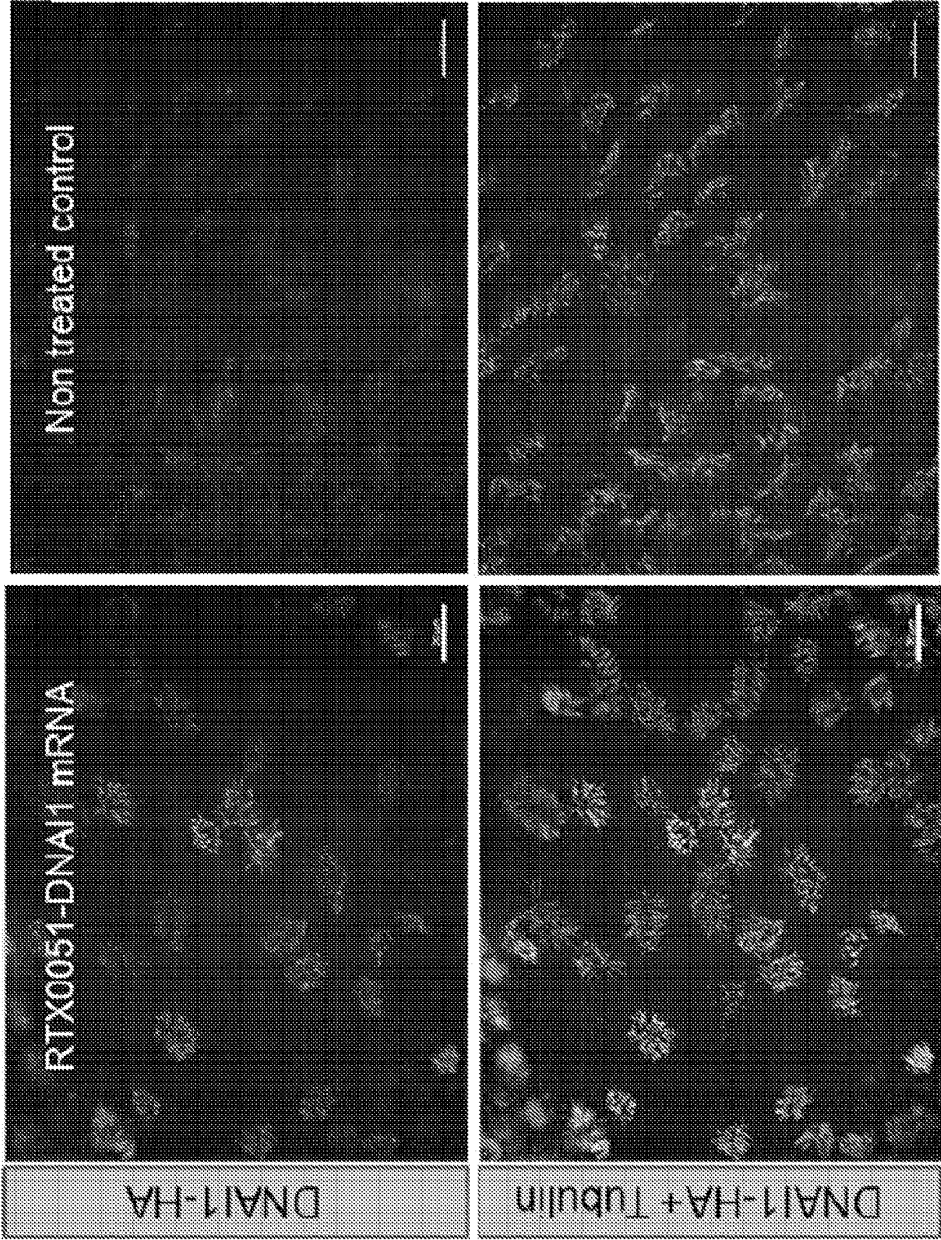
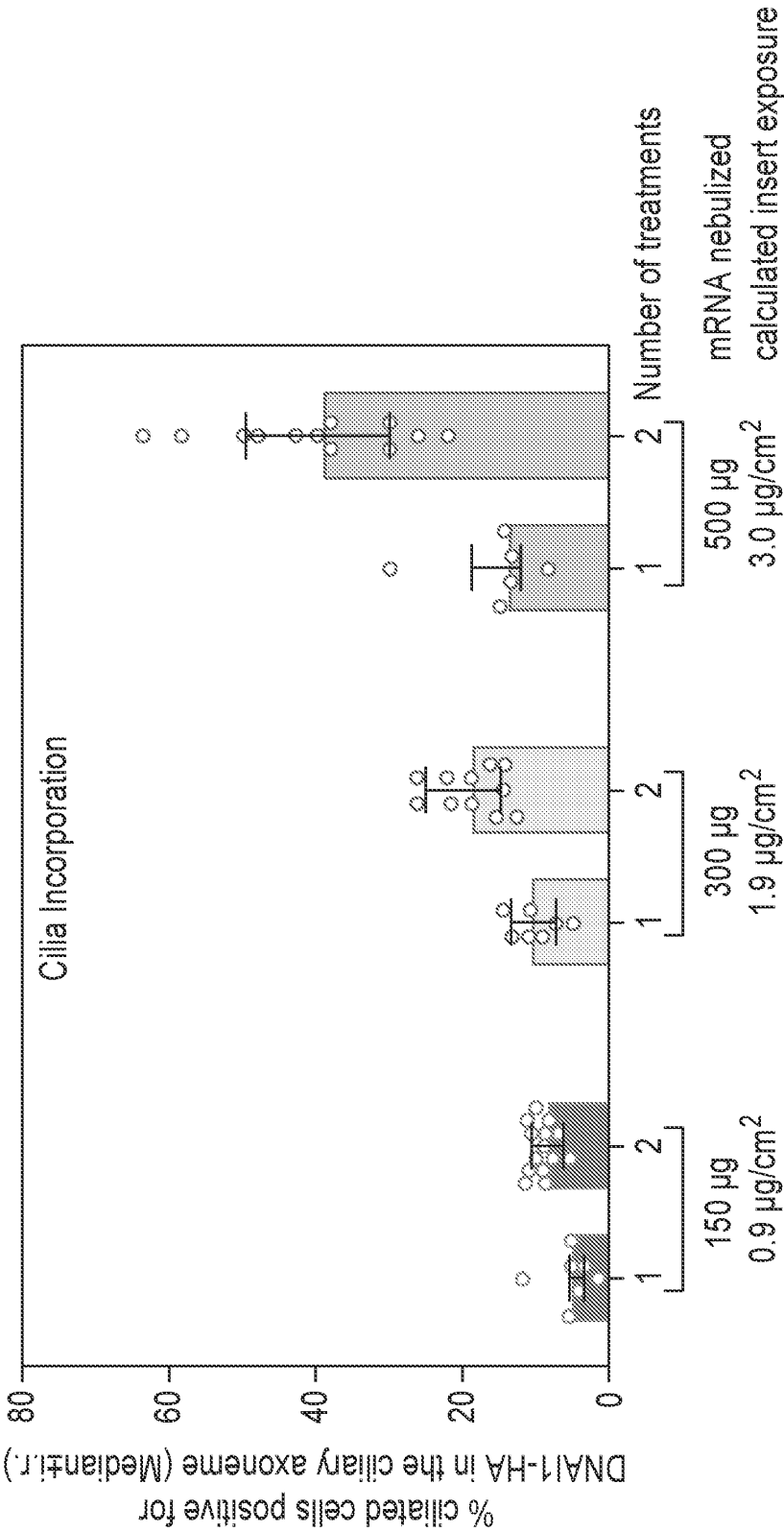


FIG. 113



Composition A-DNAI1-HA dose

FIG. 114

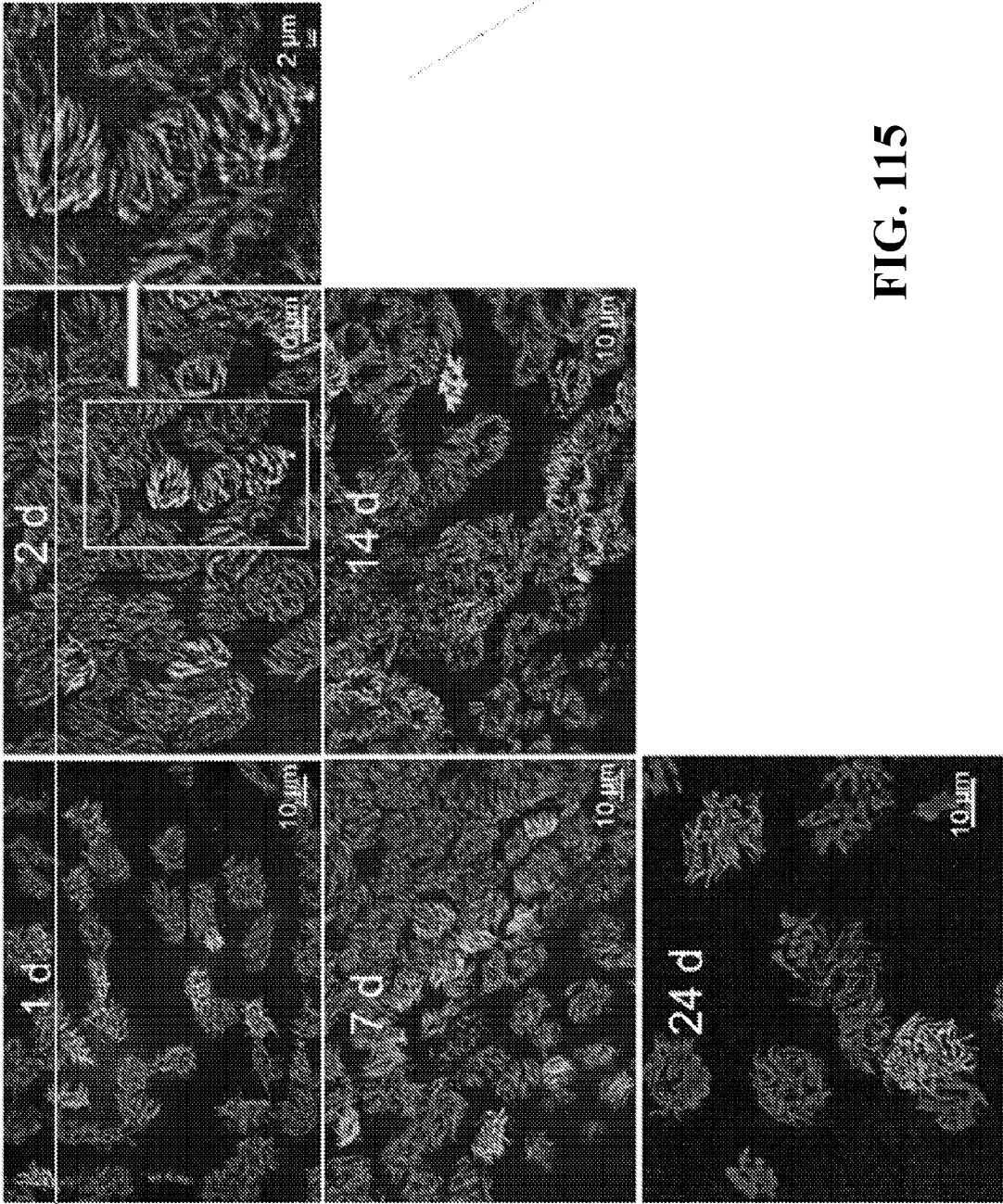
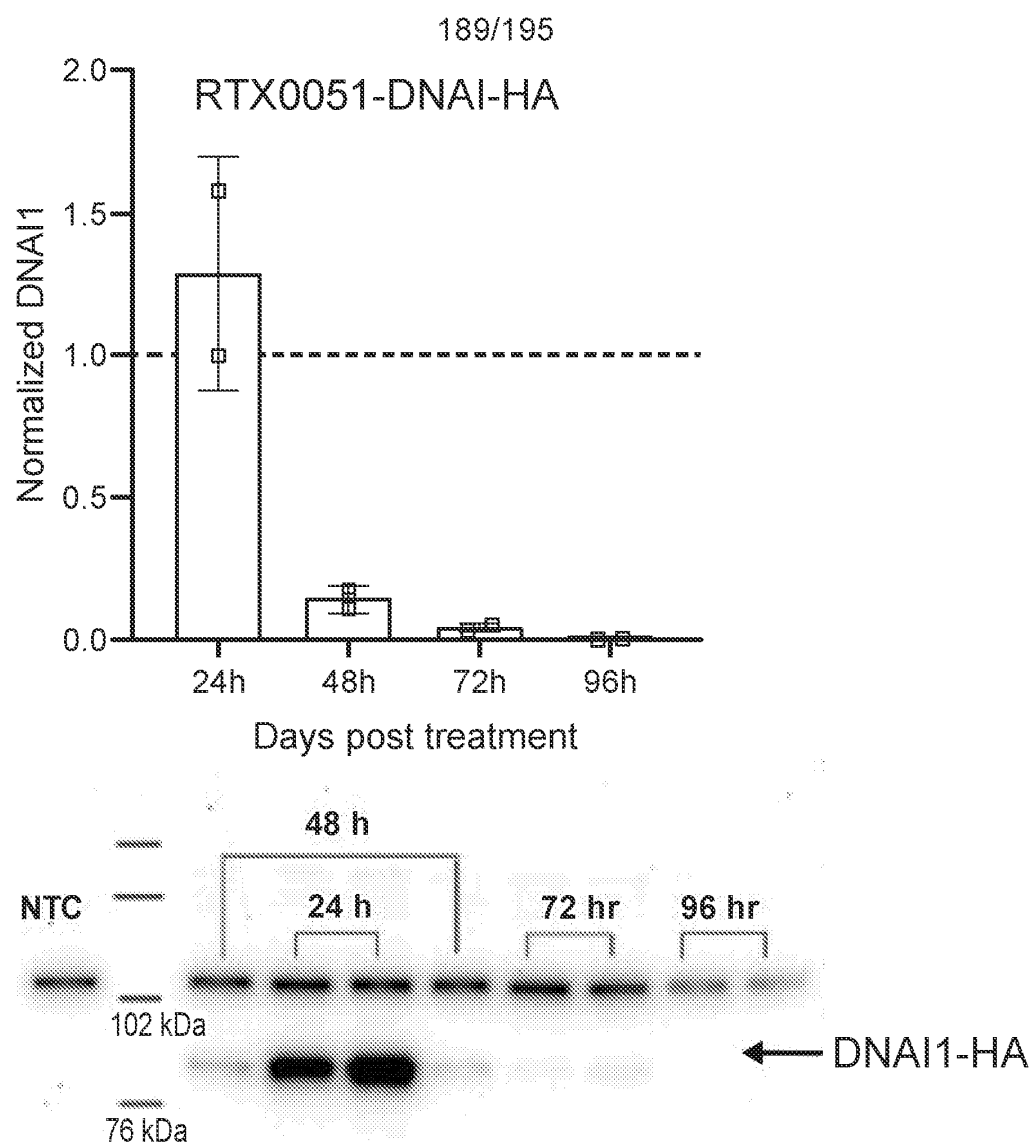


FIG. 115

**FIG. 116**

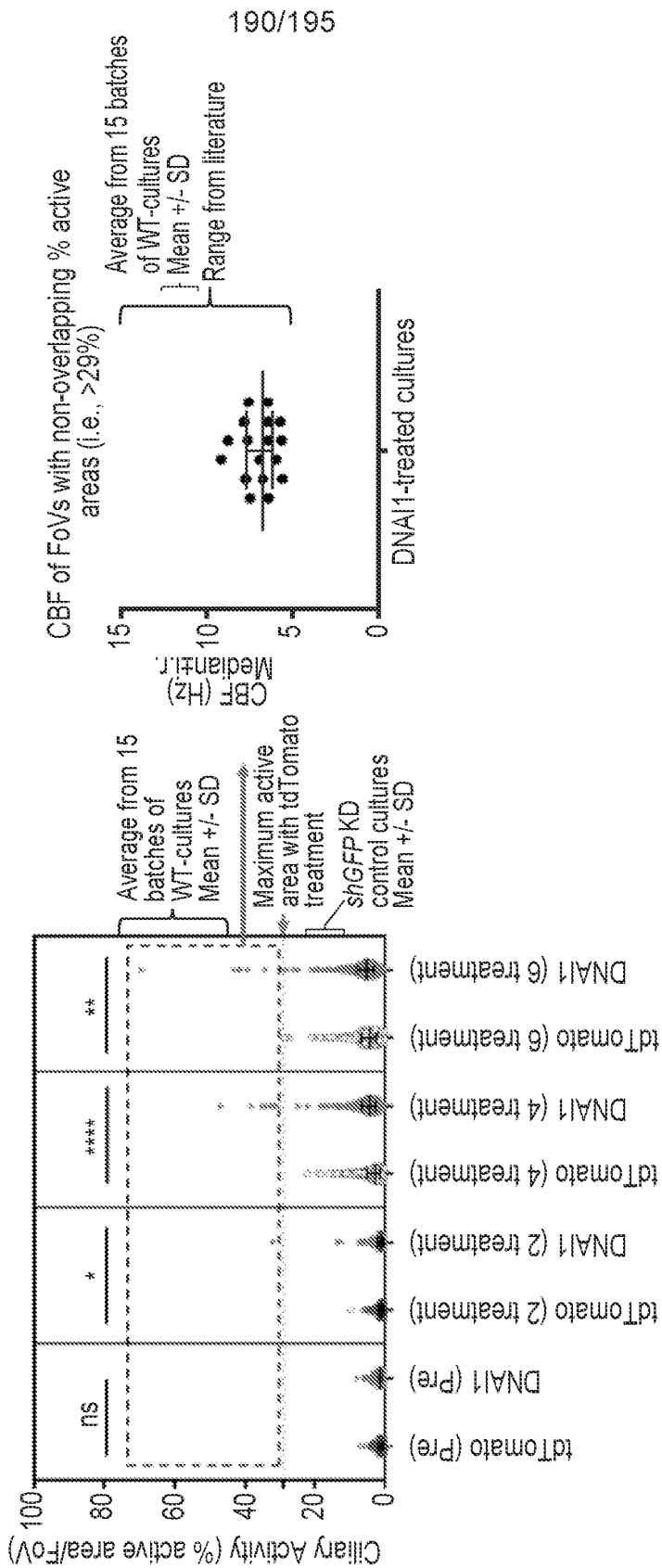


FIG. 117

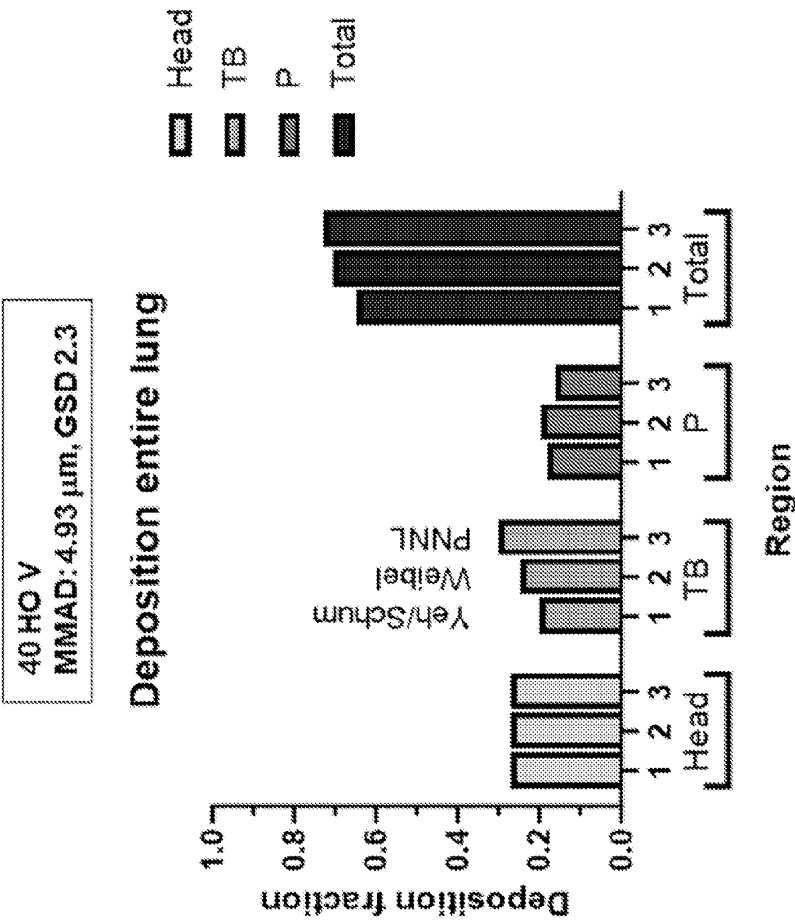


FIG. 118

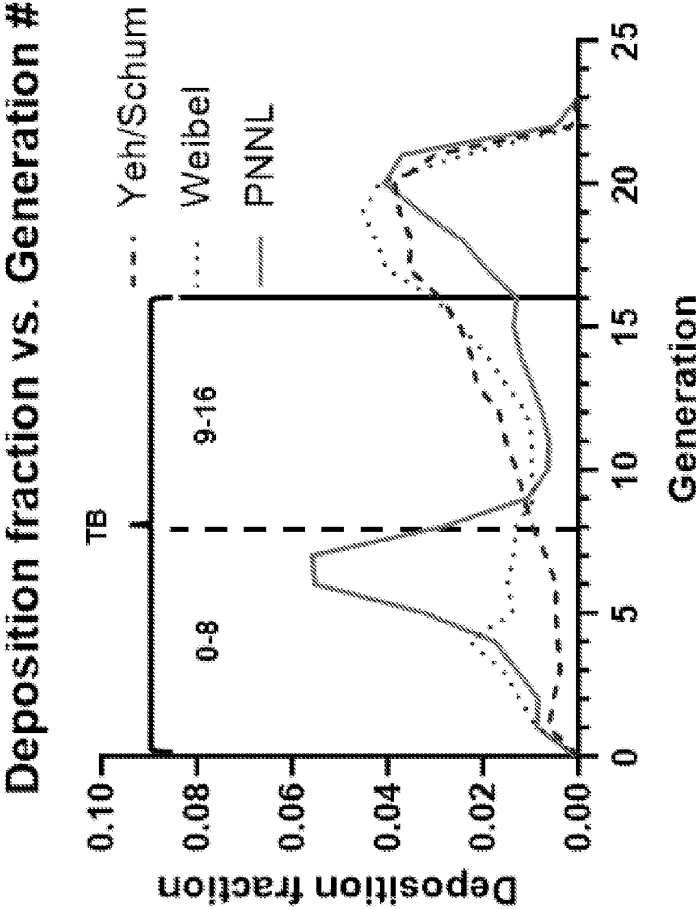


FIG. 119

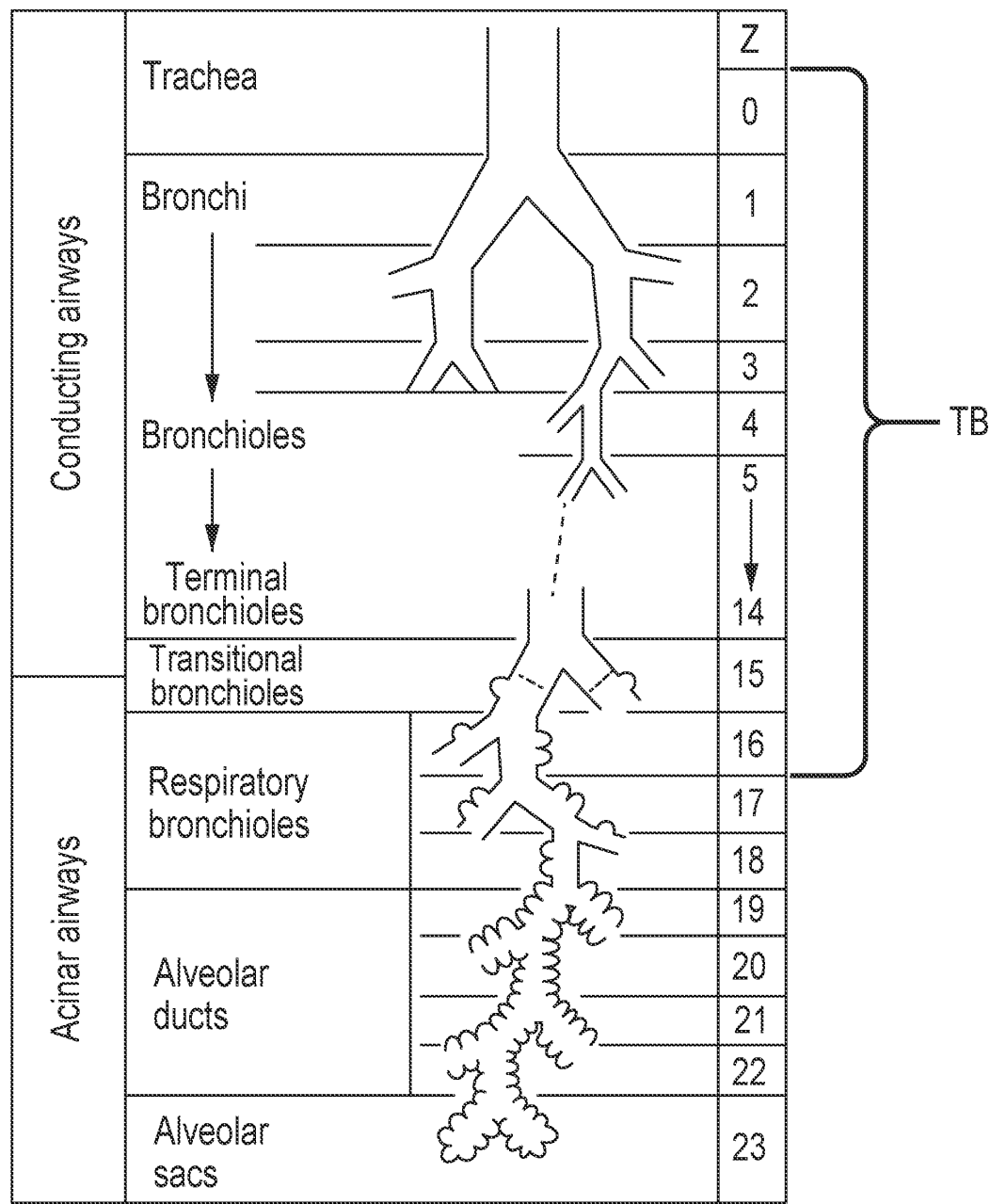


FIG. 120

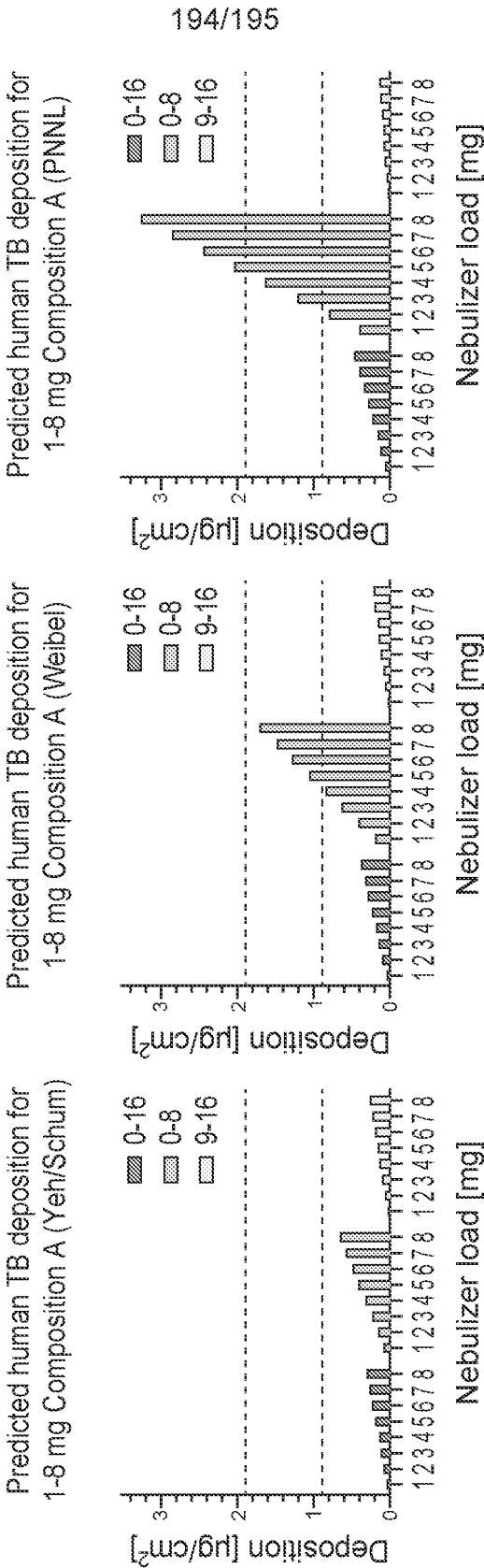


FIG. 121

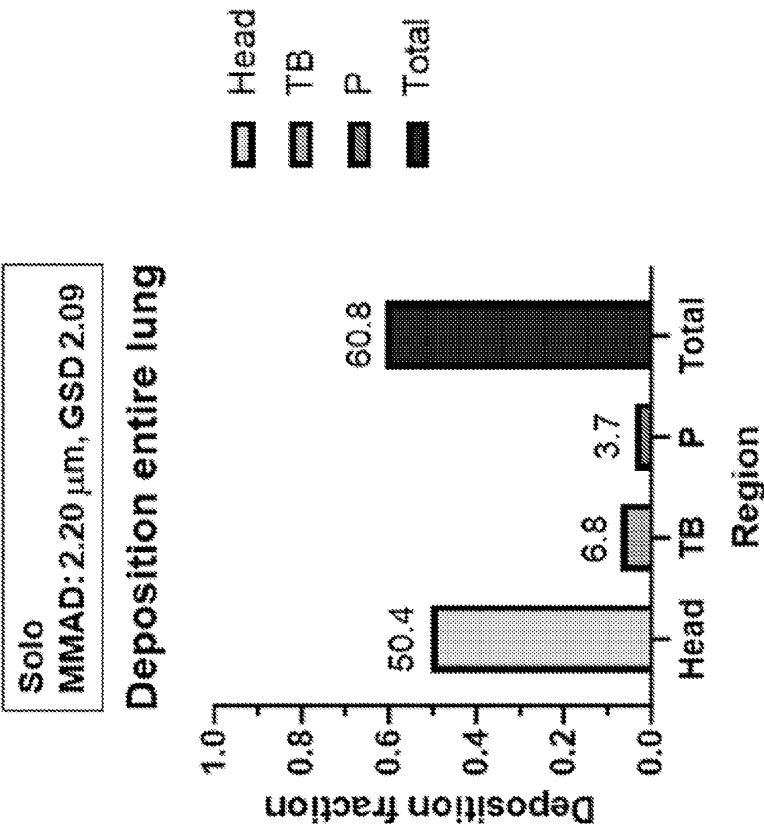


FIG. 122