

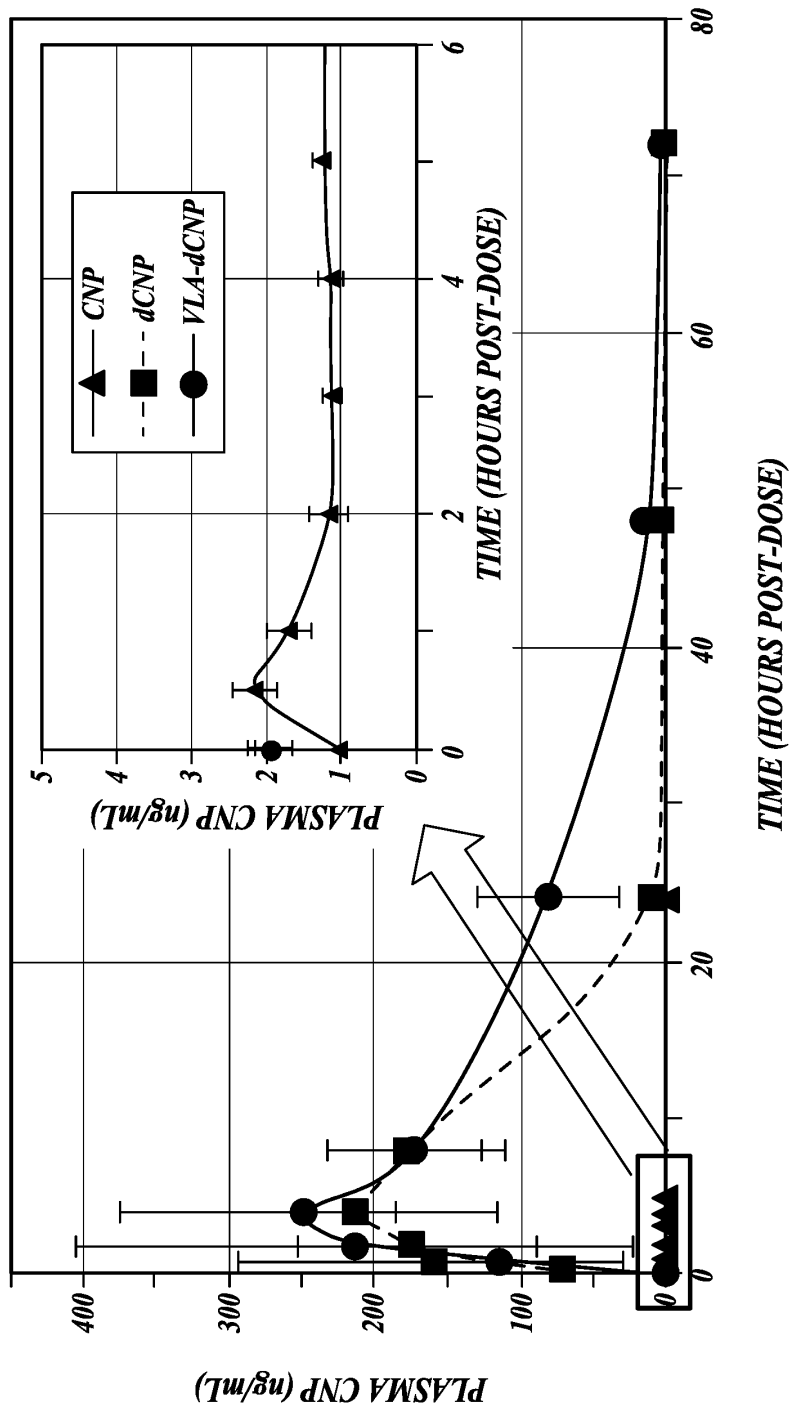


FIG. 1A

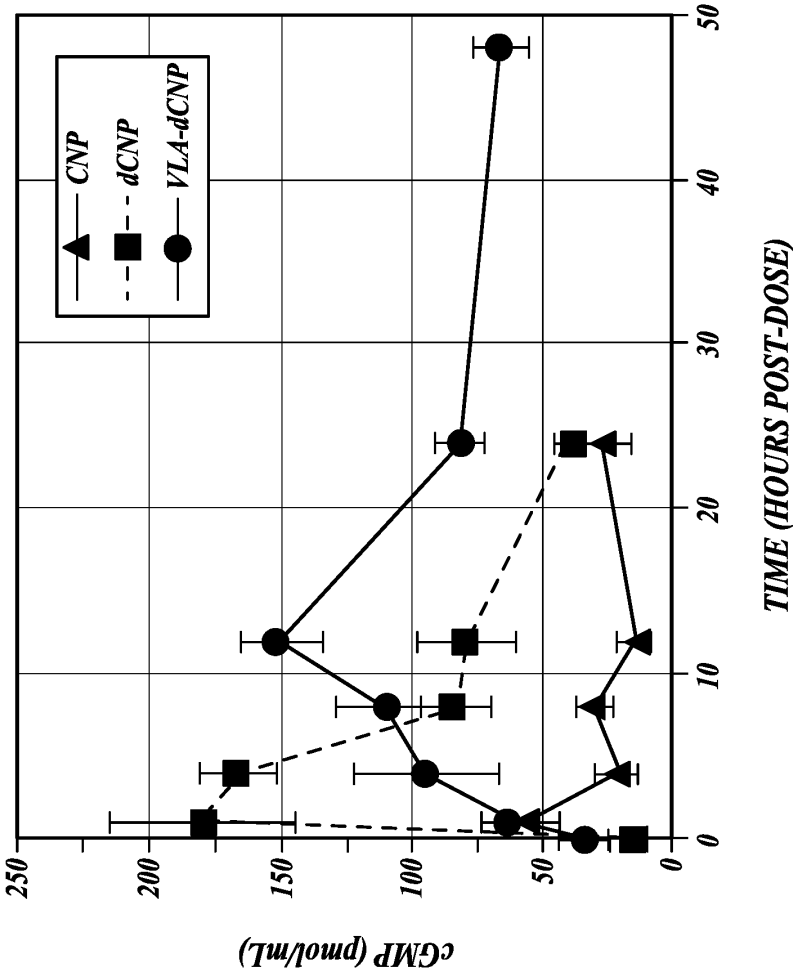


FIG. 1B

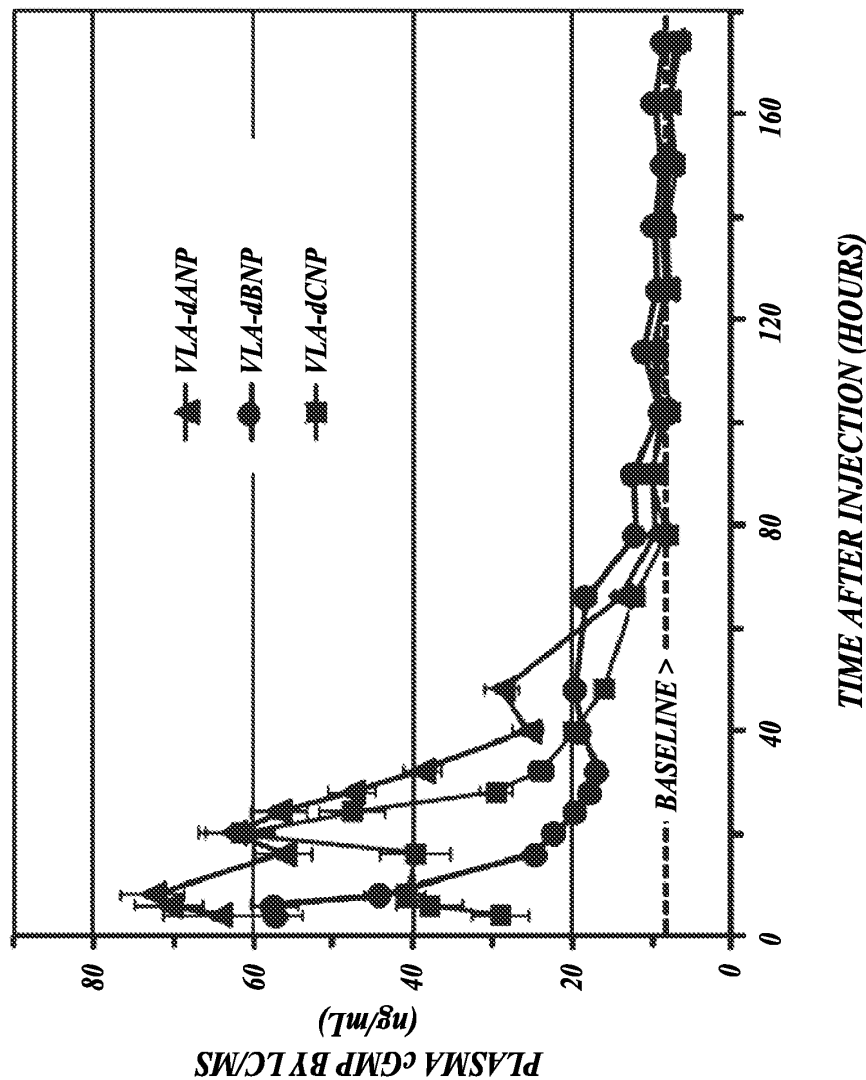


FIG. 2A

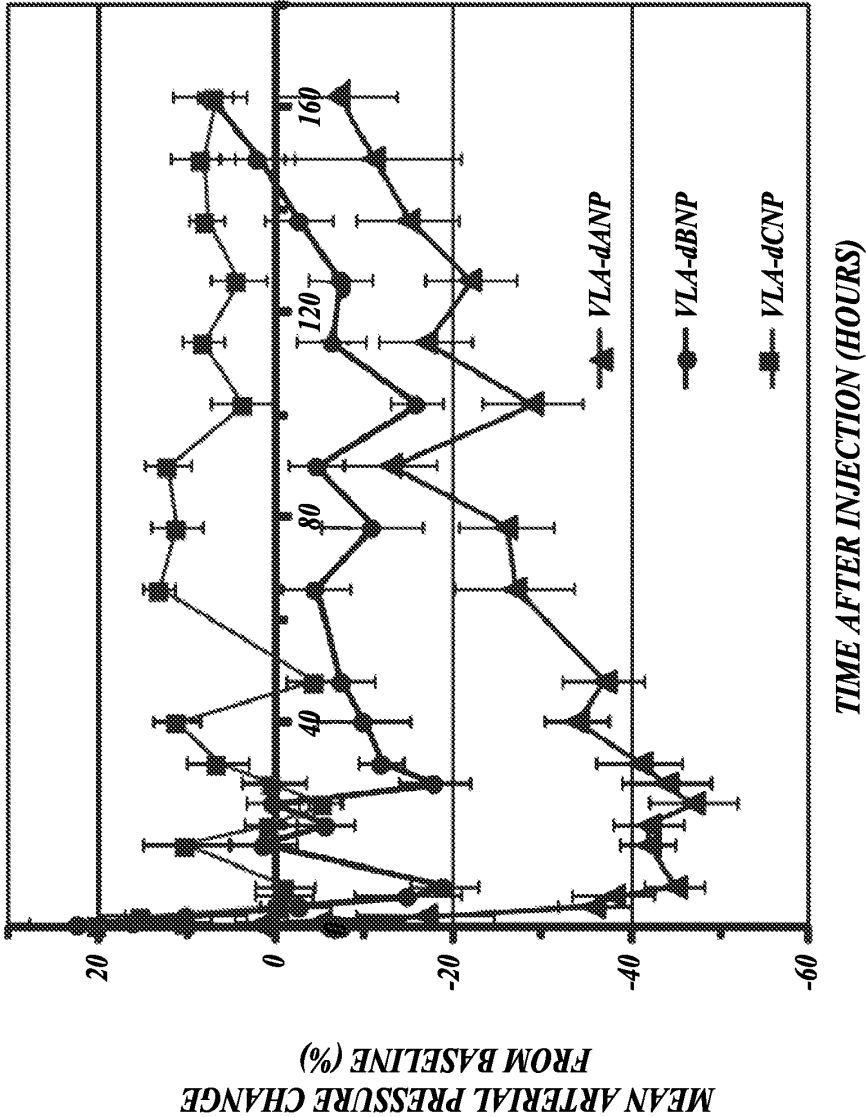
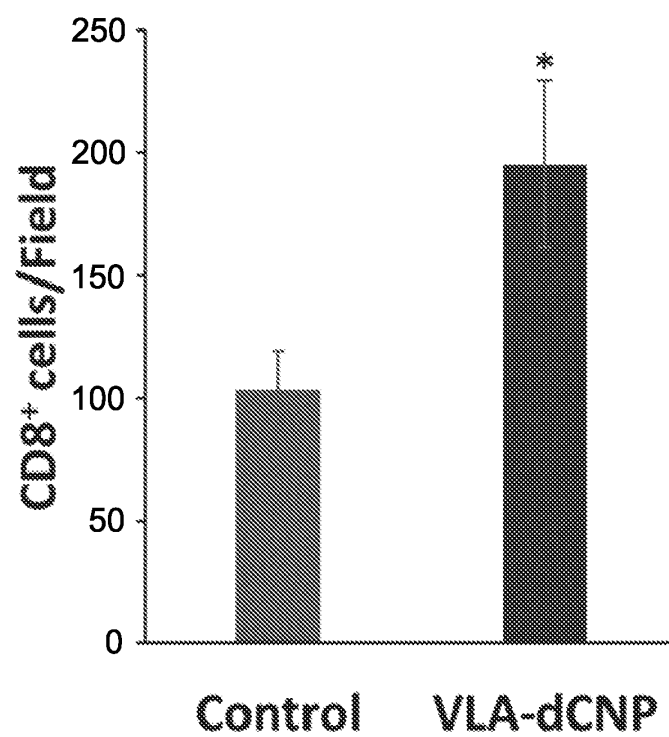
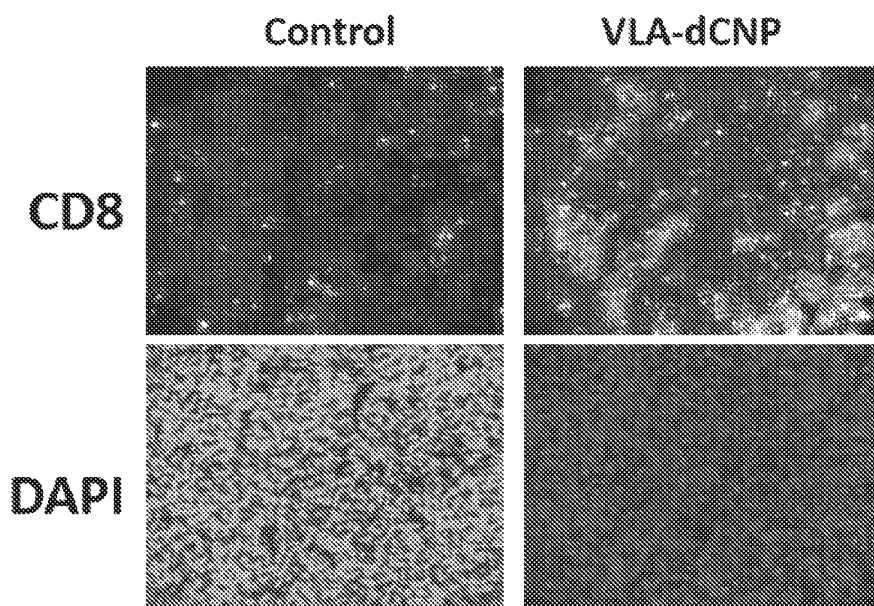


FIG. 2B

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**FIG. 3A****FIG. 3B**

CD8
(CD3+/CD8+)

Activated CD8
(CD3+/CD8+/IFN γ +) (NK1.1+/Perforin+)

Activated NK

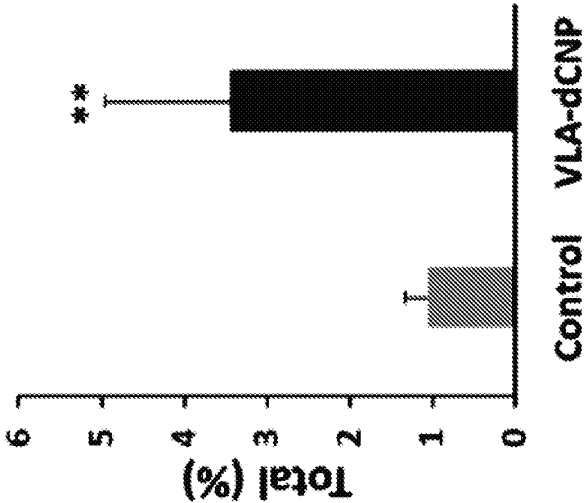


FIG. 4A

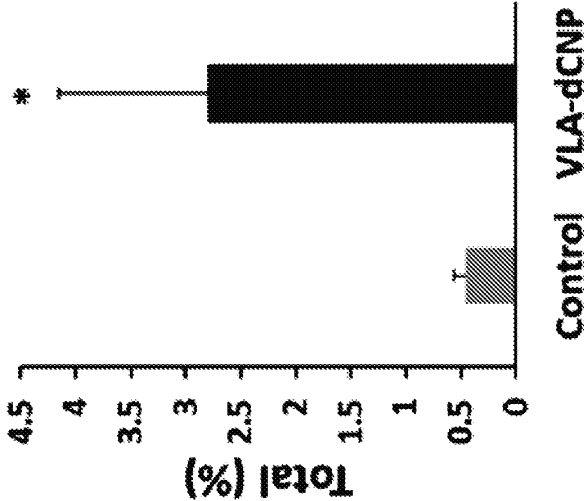


FIG. 4B

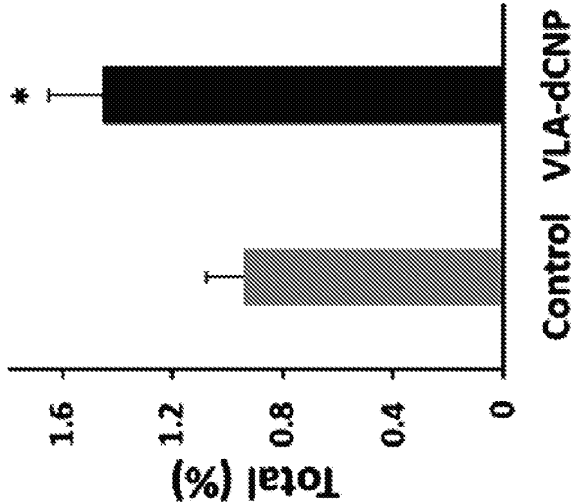


FIG. 4C

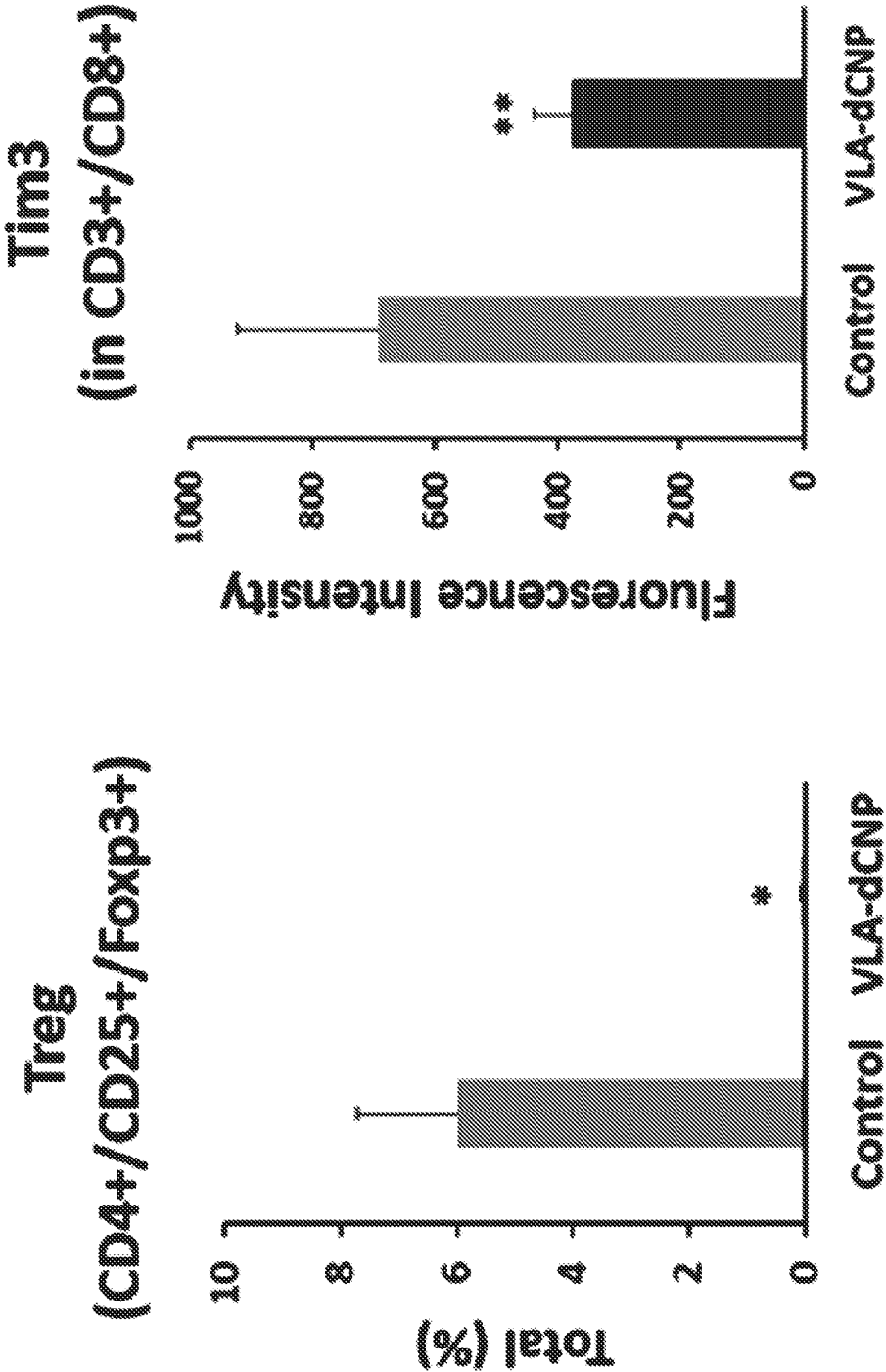


FIG. 5A

FIG. 5B

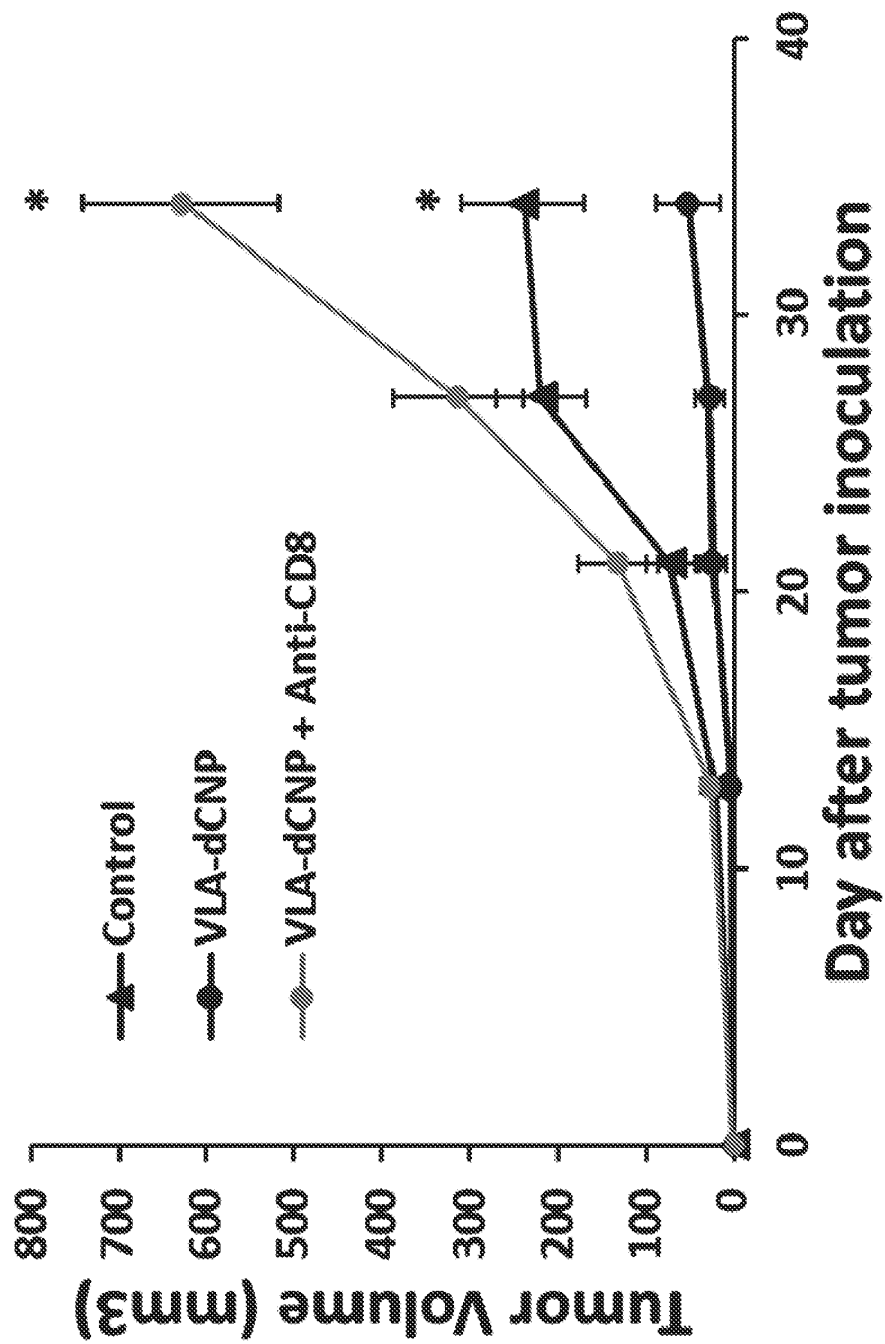


FIG. 6

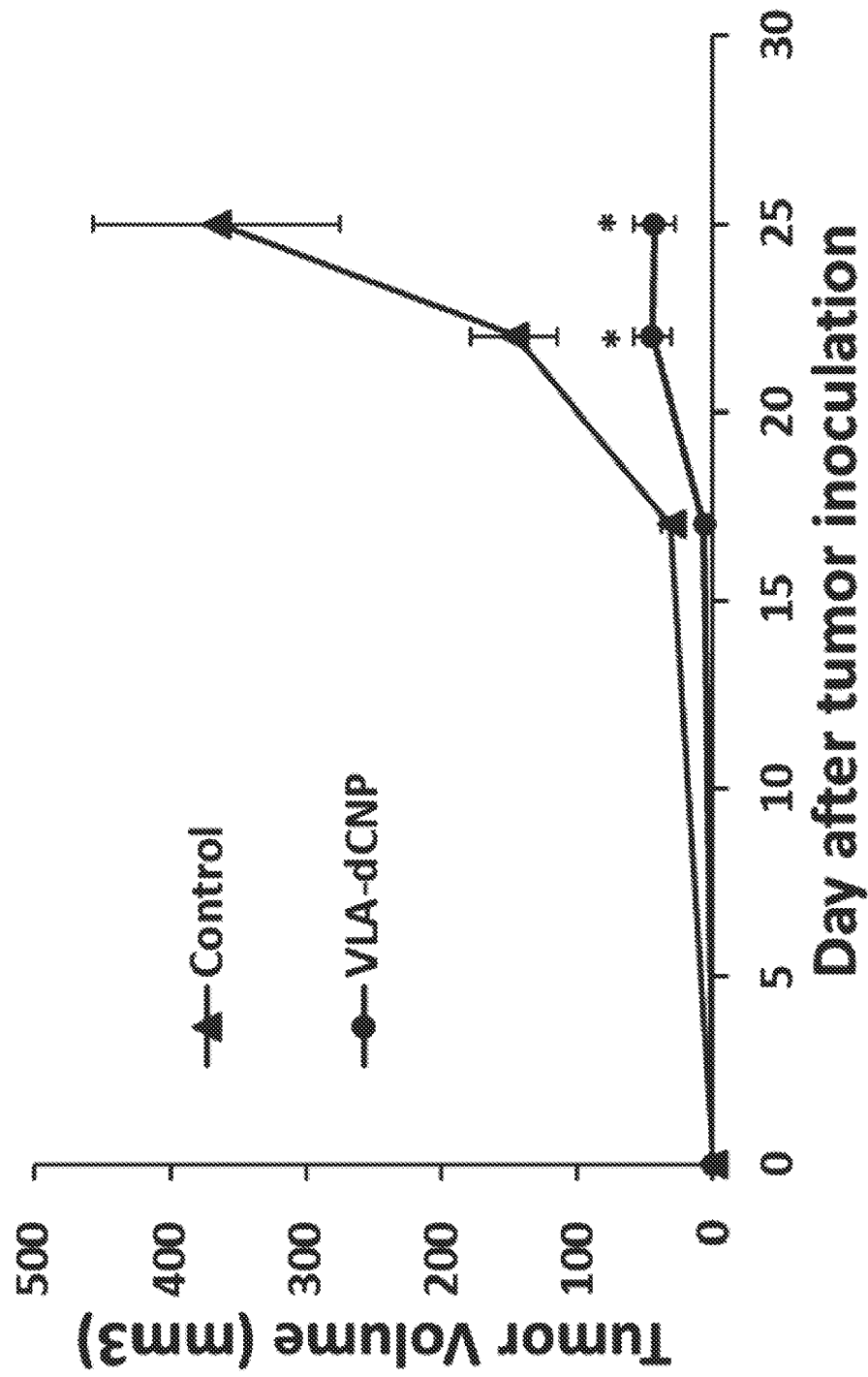


FIG. 7

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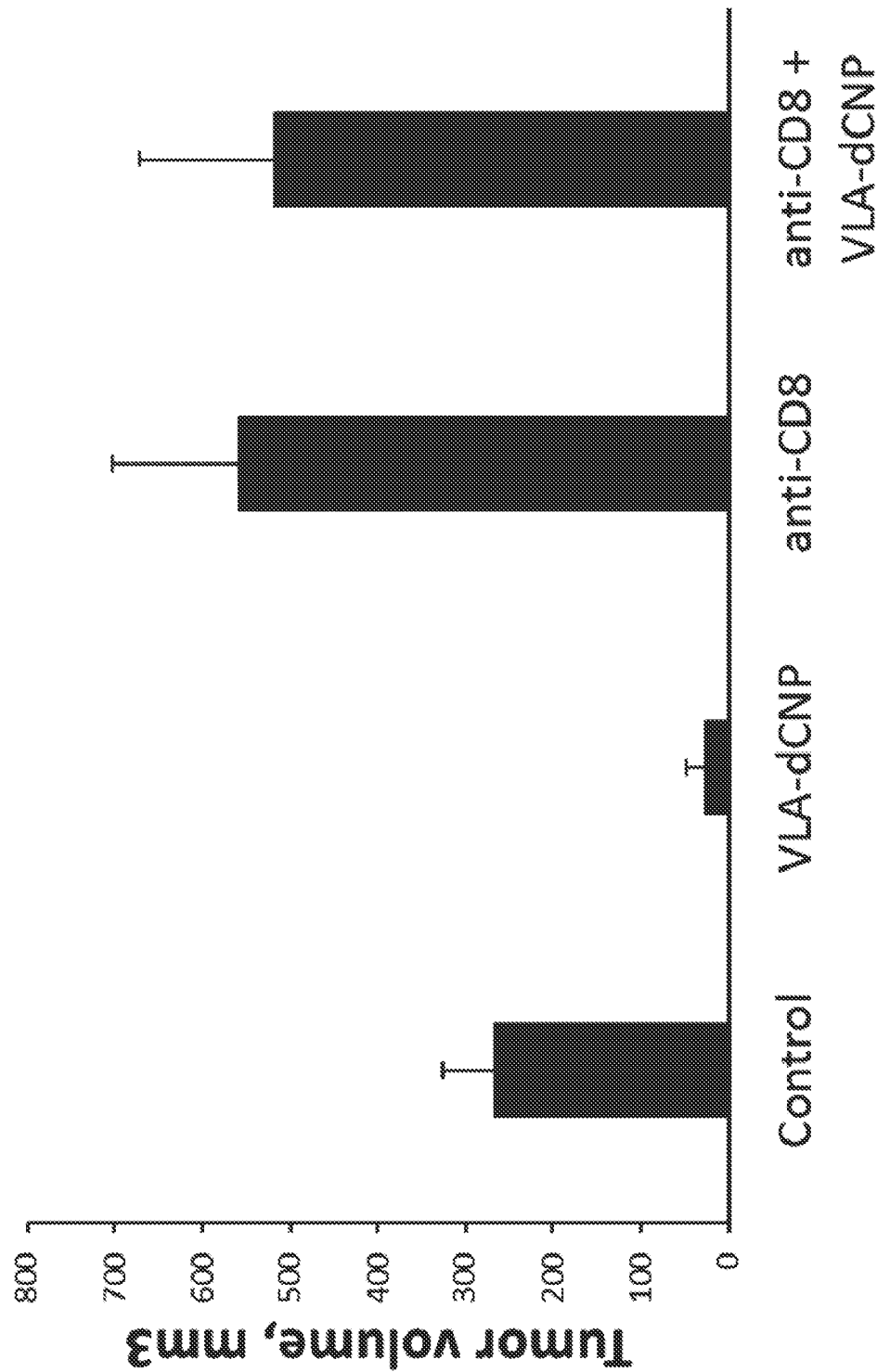
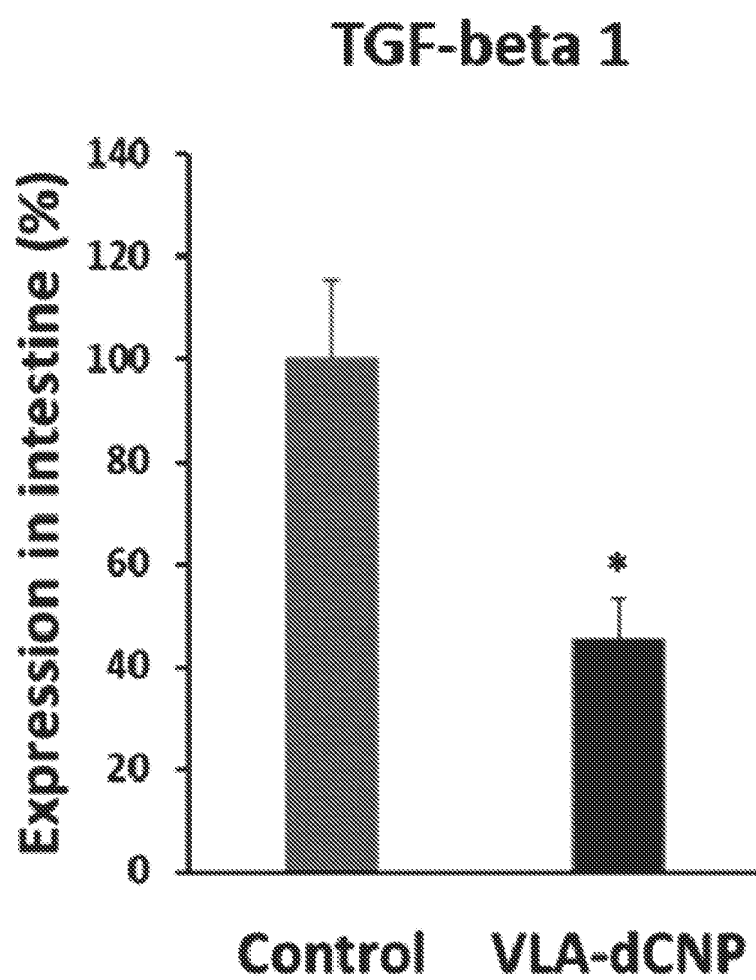
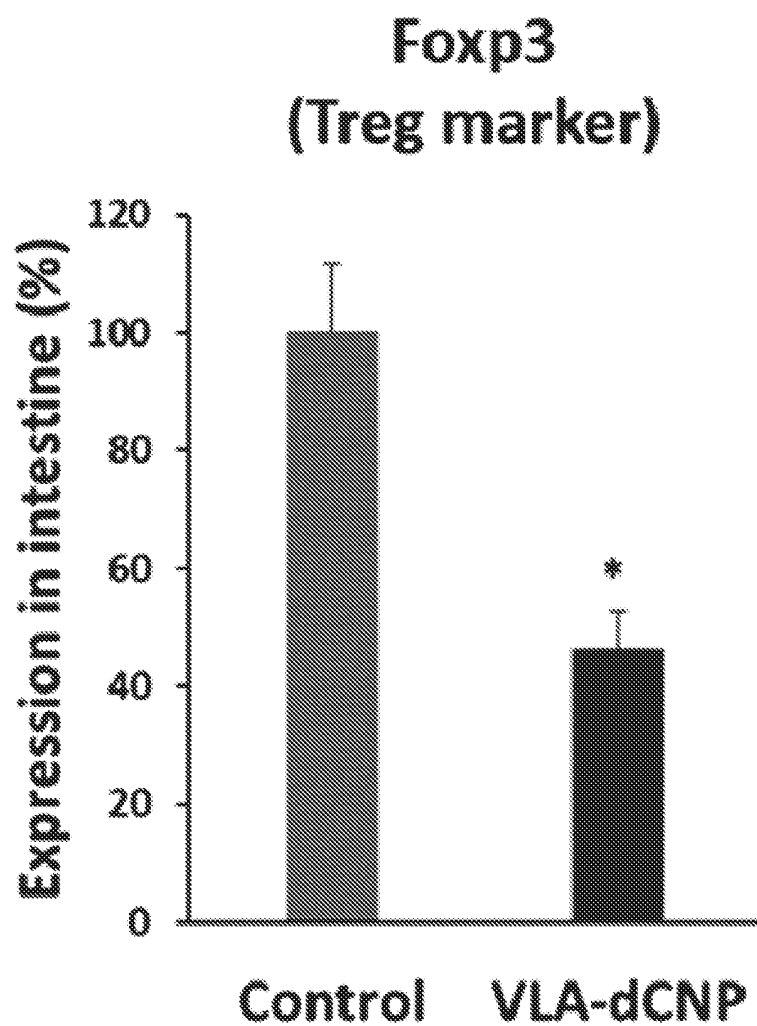


FIG. 8A

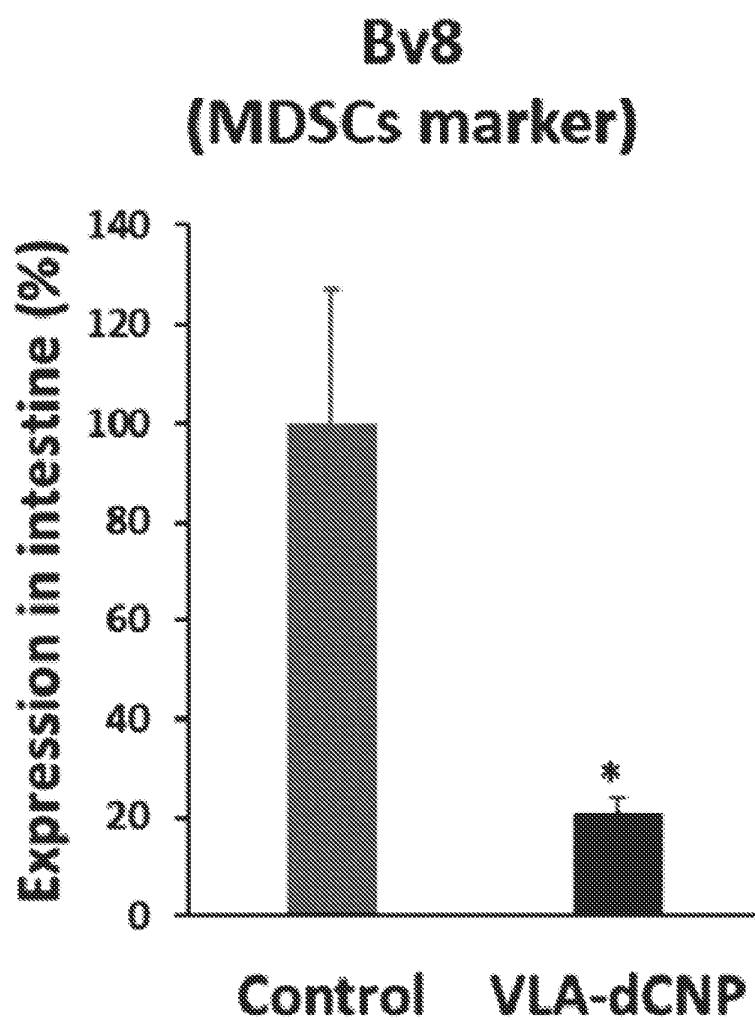
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***FIG. 8B***

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***FIG. 8C***

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***FIG. 8D***

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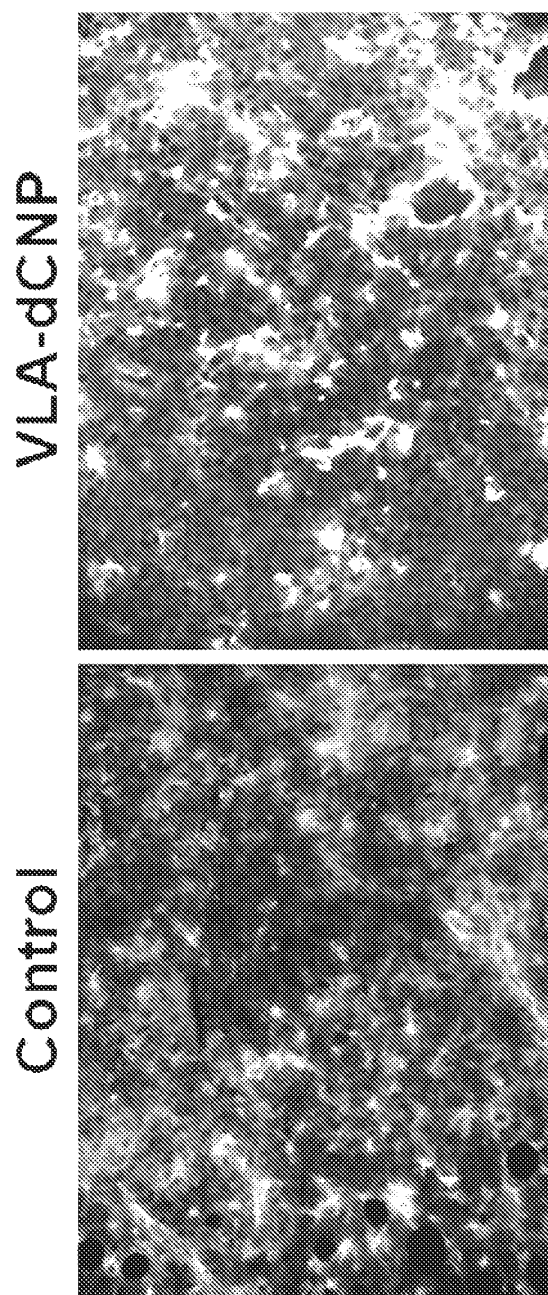
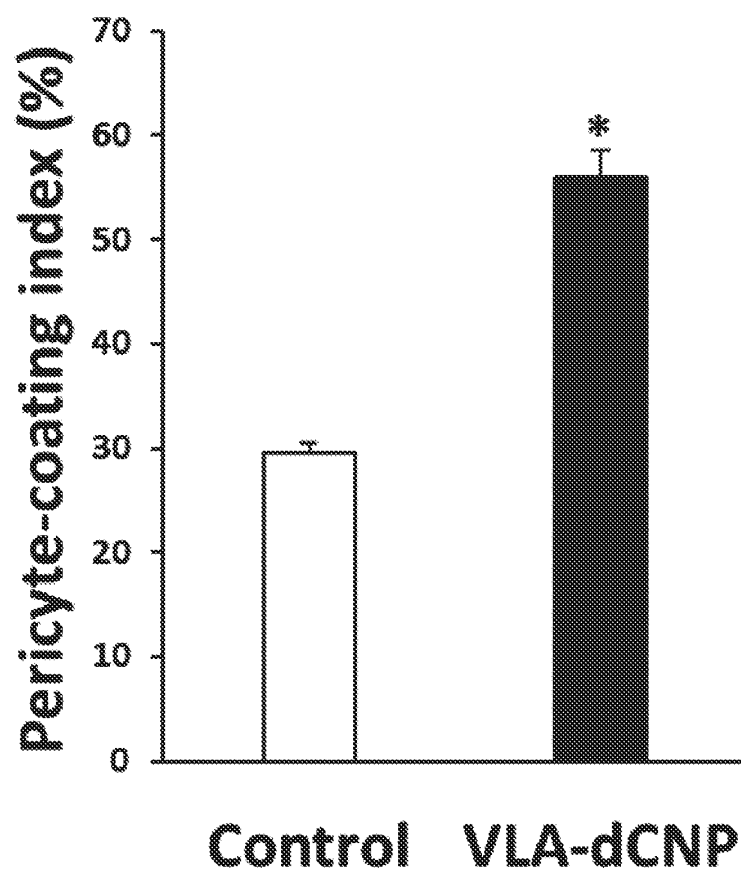


FIG. 9A

15/50***FIG. 9B***

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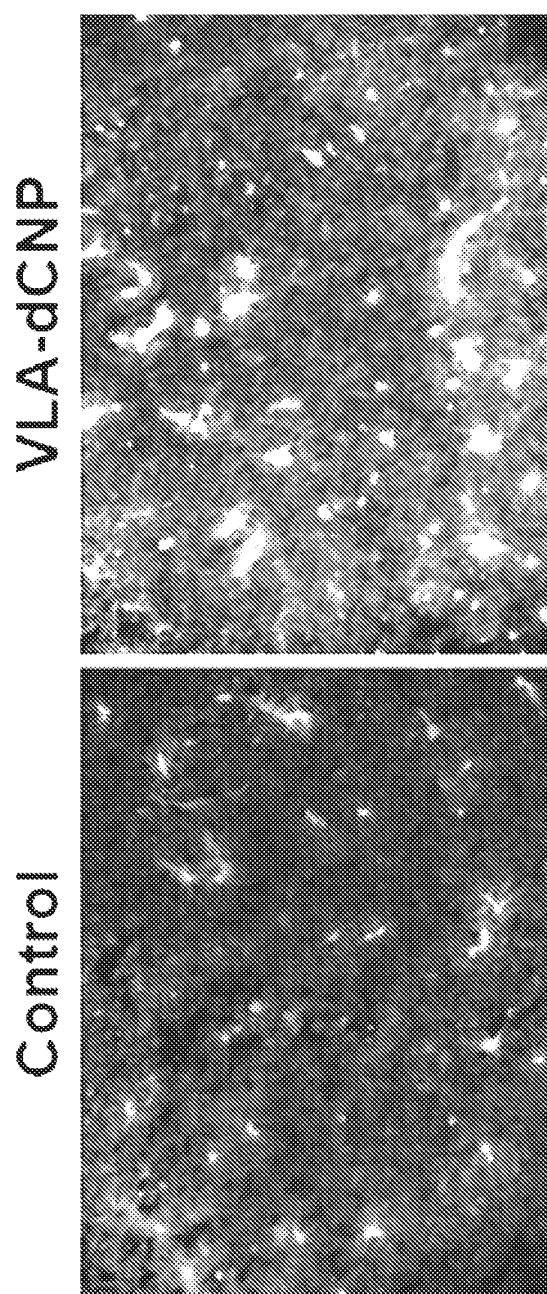
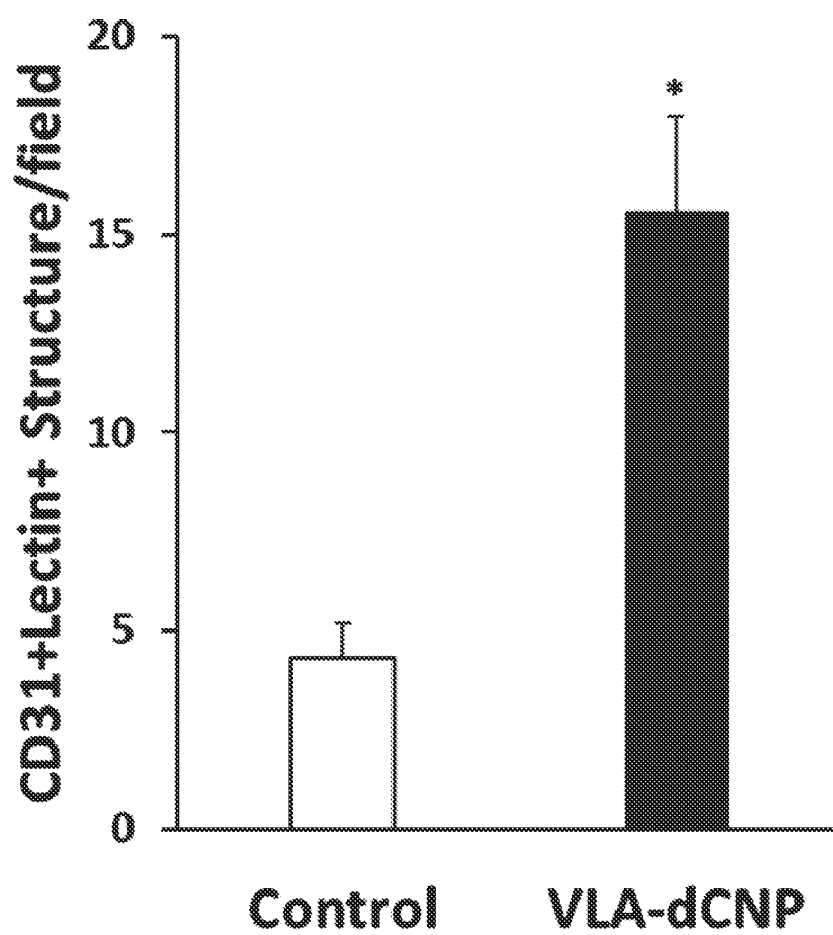


FIG. 10A

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***FIG. 10B***

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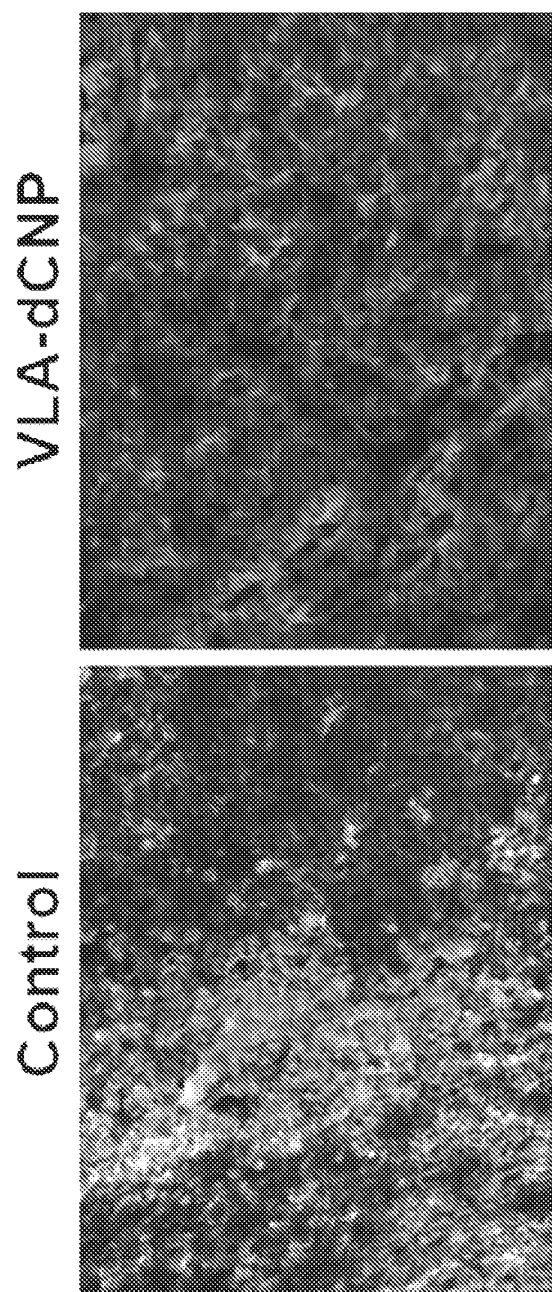


FIG. 11A

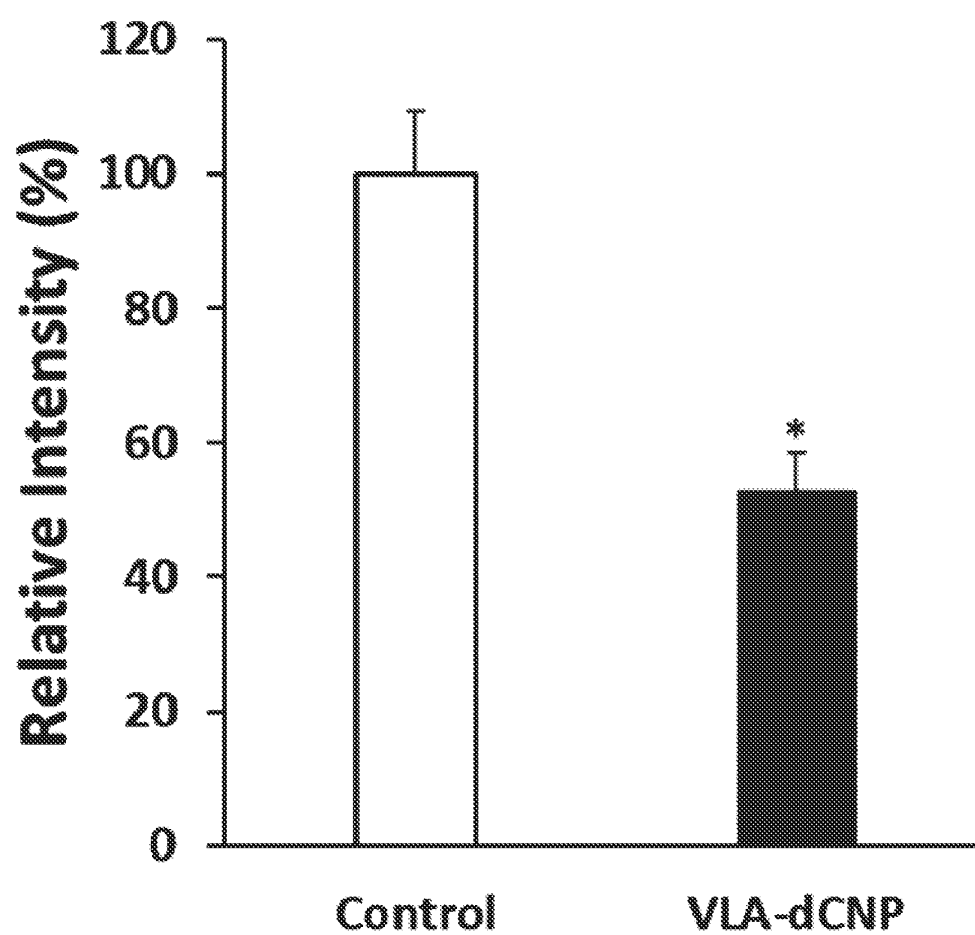
19/50***FIG. 11B***

FIG. 12

Tumor volume (mm3)	Day 8	Day 11	Day 15	Day 18/19	Day 21/22
Control	22.2 (5.1)	222.1 (68.1)	260.3 (42.8)	526.4 (81.0)	777.1 (150.6)
CTLA 4	26.7 (4.6)	239.5 (32.6)	179.8 (23.9)	199.4 (31.3)	275.8† (123.1)
VLA-dCNP + CTLA 4	30.1 (5.6)	137.3 (37.2)	20.0 (15.1)	23.1 (21.6)	29.6* (23.7)
VLA-dCNP	17.2 (5.0)	334.8 (75.0)	172.6 (43.7)	132.4 (39.3)	86.4* (44.9)
dCNP + CTLA 4	19.0 (3.3)	50.2 (16.9)	52.5 (7.2)	62.7 (18.6)	37.9* (14.0)
dCNP	23.2 (5.1)	210.4 (29.3)	162.2 (32.1)	165 (33.2)	182.3* (37.9)
ANP	31.2 (4.4)	267.7 (32.7)	326.8 (43.7)	632.3 (49.0)	771.2 (96.7)
BNP	21.4 (3.2)	199.1 (30.7)	217.7 (42.7)	531 (98.9)	510.9 (72.7)
CNP	14.8 (1.0)	272.7 (24.7)	301.3 (22.2)	588.7 (84.9)	690.3 (113.7)
TNFα	24.8 (2.5)	263 (13.3)	285.4 (30.1)	475.6 (29.3)	781.4 (74.4)
VDN	19.1 (2.9)	192.1 (18.3)	300.3 (19.4)	606.8 (67.2)	641.0 (68.9)

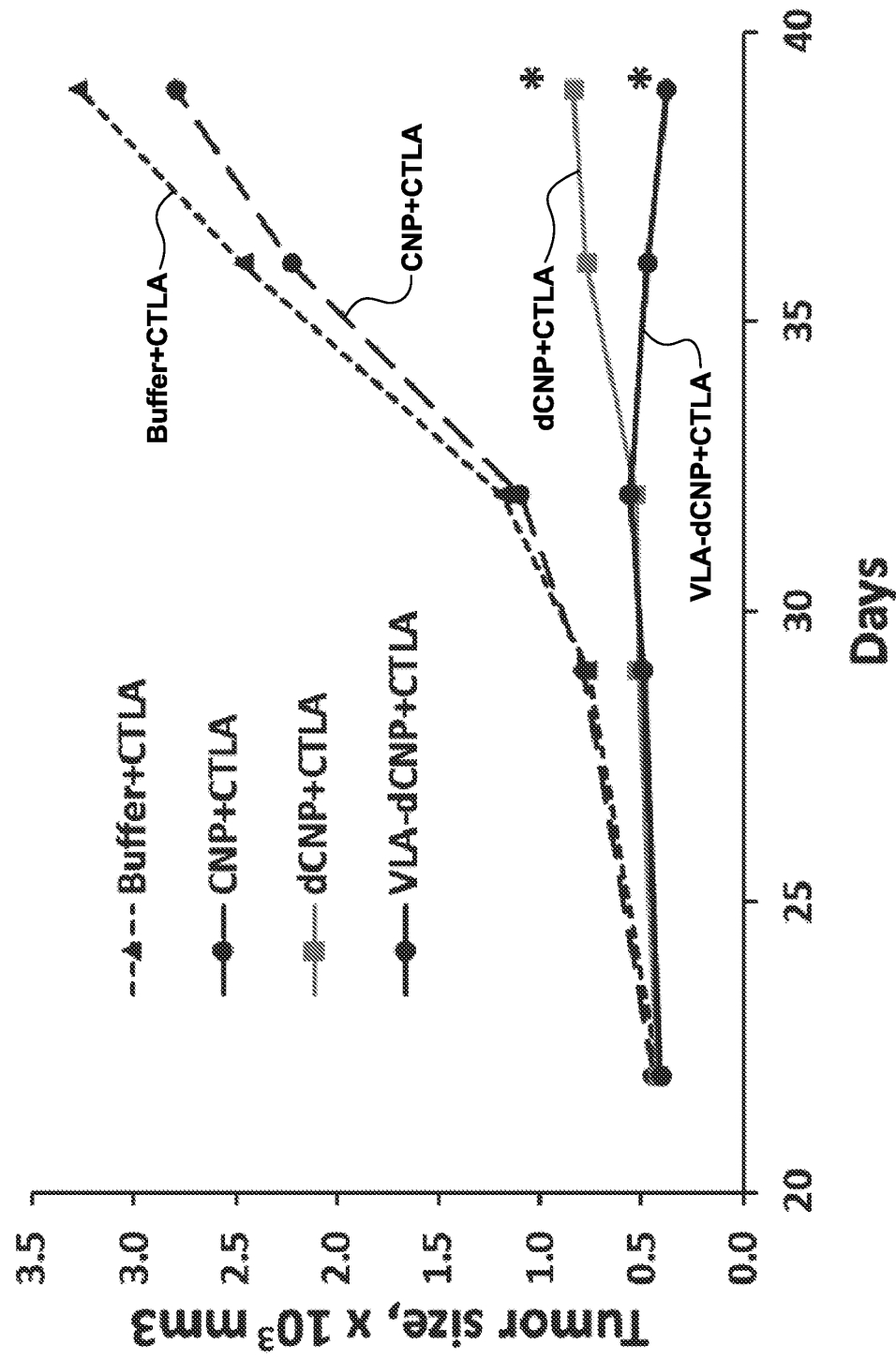


FIG. 13A

Tumor volume (x10 ³ mm ³)	Day 22	Day 29	Day 32	Day 36	Day 39
CTLA 4 n=6 (SEM)	0.4 (0.04)	0.8 (0.05)	1.2 (0.09)	2.5 (0.17)	3.3 (0.28)
CNP + CTLA 4 n=6 (SEM)	0.4 (0.07)	0.8 (0.07)	1.1 (0.13)	2.2 (0.15)	2.8 (0.36)
dCNP + CTLA 4 n=7 (SEM)	0.4 (0.03)	0.5 (0.06)	0.5 (0.09)	0.8 (0.14)	0.8* (0.54)
VLA-dCNP + CTLA 4 n=5 (SEM)	0.4 (0.15)	0.5 (0.13)	0.6 (0.07)	0.5 (0.13)	0.4* (0.13)

FIG. 13B

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FIG. 14

Tumor volume (mm ³)	Day 0	Day 8	Day 11	Day 15	Day 18	Day 21	Day 26
Control; n=10 (SEM)	0.0 (0.0)	34.2 (4.1)	48.1 (6.2)	136.0 (8.5)	240.5 (17.6)	743.6 (69.0)	878.1 (81.9)
PD-1; n=10 (SEM)	0.0 (0.0)	34.4 (5.2)	27.4 (3.7)	101.6 (15)	217.2 (55.6)	337.3 (72.5)	885.9 (320.5)
VLA-dCNP + PD-1; n=10 (SEM)	0.0 (0.0)	40.6 (5.5)	24.5 (3.4)	70.1 (21.1)	127.8 (39.0)	110.1 (32.8)	163.5*† (57.0)
VLA-dCNP; n=10 (SEM)	0.0 (0.0)	37.0 (4.5)	36.8 (4.5)	123.9 (21.7)	208.6 (41.5)	294.1 (74.1)	681.7 (200.3)
dCNP + PD-1; n=10 (SEM)	0.0 (0.0)	52.2 (7.5)	67.7 (8.2)	34.9 (12.5)	80.5 (12.5)	81.4 (13.3)	133.6*† (32.6)
dCNP; n=10 (SEM)	0.0 (0.0)	49.2 (7.5)	68.4 (7.4)	140.5 (7.9)	227.7 (22.0)	612.1 (62.6)	635.6 (102.4)
BNP + PD-1; n=10 (SEM)	0.0 (0.0)	36.0 (3.6)	41.3 (3.7)	152.5 (18.5)	234.0 (42.5)	521.5 (85.5)	837.3 (101.4)
BNP; n=10 (SEM)	0.0 (0.0)	40.3 (4.4)	51.3 (3.8)	138.4 (14.1)	229.7 (16.1)	653.0 (84.0)	766.7 (126.9)
CNP + PD-1; n=10 (SEM)	0.0 (0.0)	36.0 (5.2)	47.8 (5.5)	122.5 (10.9)	267.3 (34.6)	704.1 (49.0)	686.5 (75.9)
CNP; n=10 (SEM)	0.0 (0.0)	43.4 (4.5)	54.1 (4.4)	151.1 (11.1)	225.2 (11.4)	802.0 (36.8)	955.5 (122.4)

FIG. 15

Tumor volume (mm3)	Day 0	Day 6	Day 12	Day 15	Day 19
Control; n=10 (SEM)	0.0 (0.0)	57.5 (4.7)	97.9 (9.9)	257.0 (36.7)	1092.5 (100.1)
CTLA-4; n=10 (SEM)	0.0 (0.0)	60.0 (7.1)	96.6 (6.4)	207.1 (43.2)	735.2 (130.6)
VLA-dCNP + CTLA-4; n=8 (SEM)	0.0 (0.0)	56.8 (8.5)	112.0 (10.2)	95.9 (39.7)	250.4* (126.2)
VLA-dCNP; n=8 (SEM)	0.0 (0.0)	75.3 (10.5)	127.4 (20.3)	128.2 (36.7)	321.6* (128.4)
dCNP + CTLA-4; n=10 (SEM)	0.0 (0.0)	25.2 (7.6)	94.4 (15.0)	171.2 (44.6)	336.1* (85.5)
dCNP; n=10 (SEM)	0.0 (0.0)	77.7 (6.3)	91.4 (8.4)	233.2 (41.2)	424.7 (77.1)
BNP + CTLA-4; n=10 (SEM)	0.0 (0.0)	75.0 (12.8)	114.4 (8.2)	241.6 (29.1)	781.4 (49.2)
BNP; n=10 (SEM)	0.0 (0.0)	89.6 (11.1)	105.6 (6.7)	304.4 (30.7)	922.5 (74.8)
CNP + CTLA-4; n=10 (SEM)	0.0 (0.0)	69.8 (5.8)	119.2 (13.4)	274.6 (39.6)	792.9 (120.0)
CNP; n=10 (SEM)	0.0 (0.0)	58.6 (3.4)	104.8 (10.1)	282.5 (31.7)	918.7 (77.2)

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Tumor volume (mm ³)	Day 0	Day 4	Day 7	Day 11	Day 14
Control; n=10 (SEM)	0.0 (0.0)	33.3 (5.5)	36.1 (3.6)	178.4 (10.9)	429.3 (29.6)
PD-1; n=10 (SEM)	0.0 (0.0)	29.9 (2.5)	39.1 (4.4)	118.7 (16.7)	371.5 (53.5)
VLA-dCNP + PD-1; n=7 (SEM)	0.0 (0.0)	46.4 (4.5)	2.1 (1.2)	15.2 (8.7)	29.5*† (15.4)
VLA-dCNP; n=7 (SEM)	0.0 (0.0)	43.2 (3.7)	44.2 (3.7)	162.6 (37.5)	292.5† (51.7)
dCNP + PD-1; n=10 (SEM)	0.0 (0.0)	29.9 (3.2)	25.7 (3.0)	7.4 (3.0)	22.8*† (7.5)
dCNP; n=10 (SEM)	0.0 (0.0)	32.1 (4.1)	36.7 (4.5)	113.7 (16.3)	310.1† (37.8)
BNP + PD-1; n=10 (SEM)	0.0 (0.0)	24.0 (2.8)	31.2 (4.2)	120.0 (17.8)	456.5 (30.3)
BNP; n=10 (SEM)	0.0 (0.0)	28.2 (2.7)	31.7 (4.2)	152.5 (15.0)	431.0 (26.8)
CNP + PD-1; n=10 (SEM)	0.0 (0.0)	28.5 (4.3)	35.5 (4.0)	159.2 (18.7)	318.8† (28.2)
CNP; n=10 (SEM)	0.0 (0.0)	27.9 (3.5)	34.4 (1.2)	161.5 (13.5)	387.2 (22.0)
TNFα + PD-1; n=10 (SEM)	0.0 (0.0)	30.6 (4.7)	30.3 (4.8)	149.3 (18.6)	371.4 (30.9)
TNFα; n=10 (SEM)	0.0 (0.0)	29.5 (2.0)	37.5 (3.0)	163.6 (7.4)	438.4 (19.9)
VDN + PD-1; n=10 (SEM)	0.0 (0.0)	32.5 (4.3)	35.6 (3.9)	165.4 (6.5)	349.7 (31.3)
VDN; n=10 (SEM)	0.0 (0.0)	35.1 (5.4)	34.0 (4.1)	164.5 (21.1)	420.1 (27.1)

FIG. 16

Tumor volume (mm ³)	Day 0	Day 4	Day 7	Day 11	Day 14
Control	0.0 (0.0)	33.2 (4.4)	62.2 (5.7)	171.4 (27.8)	532 (84.7)
Buffer with PD-1	0.0 (0.0)	55.8 (5.3)	32.8 (7.4)	138.2 (43.4)	371.2 (68.7)
VLA-dCNP + PD-1 (L)	0.0 (0.0)	46.4 (4.5)	18.9 (11.3)	34.4 (16.3)	79.1 (34.0)
VLA-dCNP (L)	0.0 (0.0)	38.6 (4.2)	62.4 (11.6)	235.5 (57.9)	434.6 (53.9)
VLA-dCNP + PD-1 (M)	0.0 (0.0)	46.4 (4.5)	3.6 (2.0)	14.6 (8.4)	36.6 (19.1)
VLA-dCNP (M)	0.0 (0.0)	43.2 (3.7)	76.1 (6.4)	156.2 (36.0)	362.5 (64.1)
VLA-dCNP + PD-1 (H)	0.0 (0.0)	32.3 (2.8)	2.1 (1.9)	6.1 (2.1)	27.4 (10.3)
VLA-dCNP (H)	0.0 (0.0)	57.6 (6.0)	59.3 (12.6)	65.1 (15.8)	246.8 (26.7)

FIG. 17

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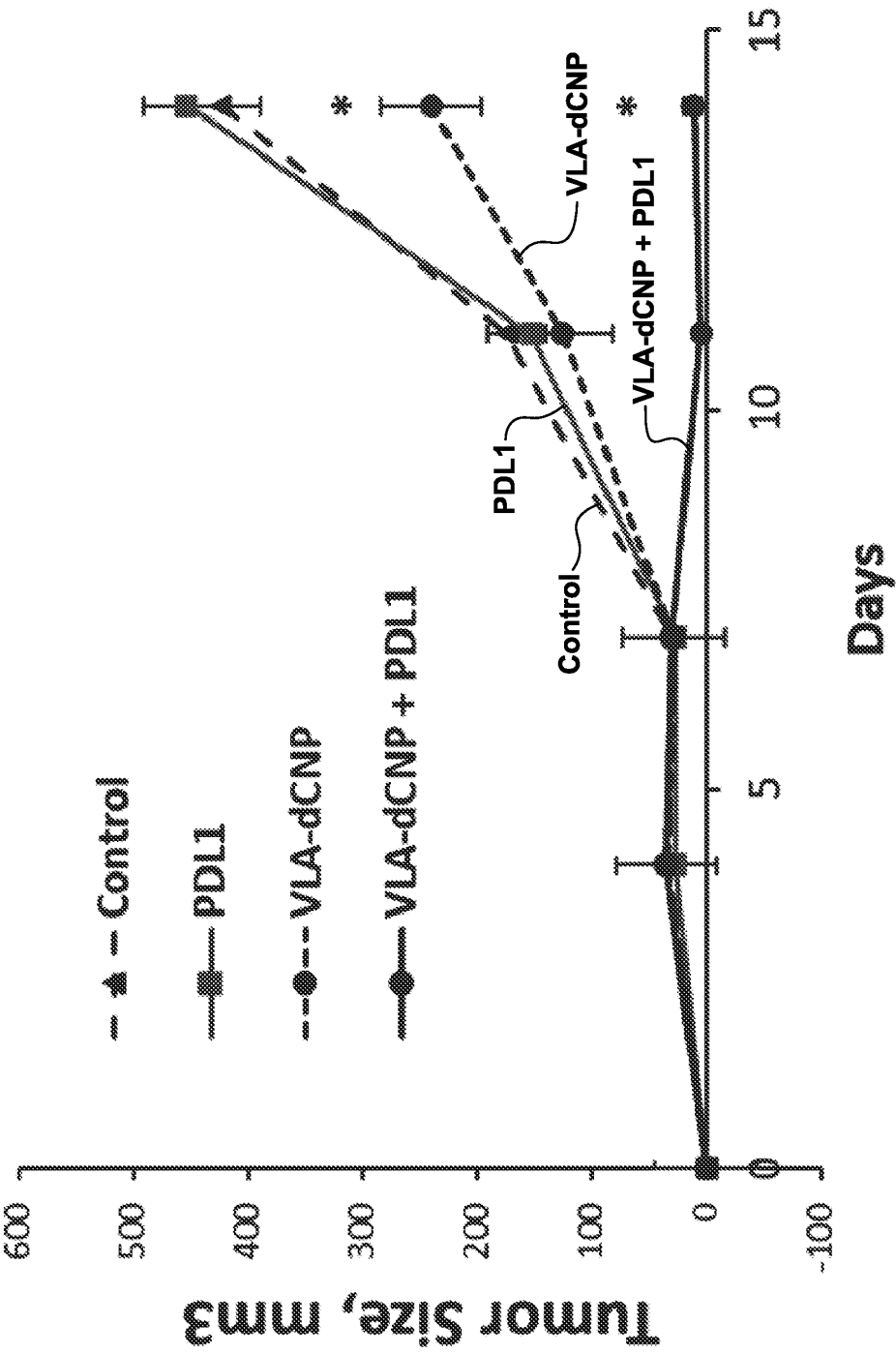


FIG. 18A

Tumor volume (mm3)	Day 0	Day 4	Day 7	Day 11	Day 14
Control; (SEM) n=8	0.0	32.3	30.6	174.4	423.9
	(0.0)	(2.4)	(2.0)	(15.7)	(35.7)
PDL-1; (SEM) n=8	0.0	27.2	27.2	152.5	453.2
	(0.0)	(3.3)	(3.3)	(12.4)	(37.7)
VLA-dCNP + PDL-1; (SEM) n=8	0.0	35.7	30.0	4.5	11.4*
	(0.0)	(5.4)	(3.5)	(1.6)	(6.7)
VLA-dCNP; (SEM) n=9	0.0	33.8	28.3	125.0	240.3*
	(0.0)	(5.3)	(2.8)	(16.5)	(25.7)

FIG. 18B

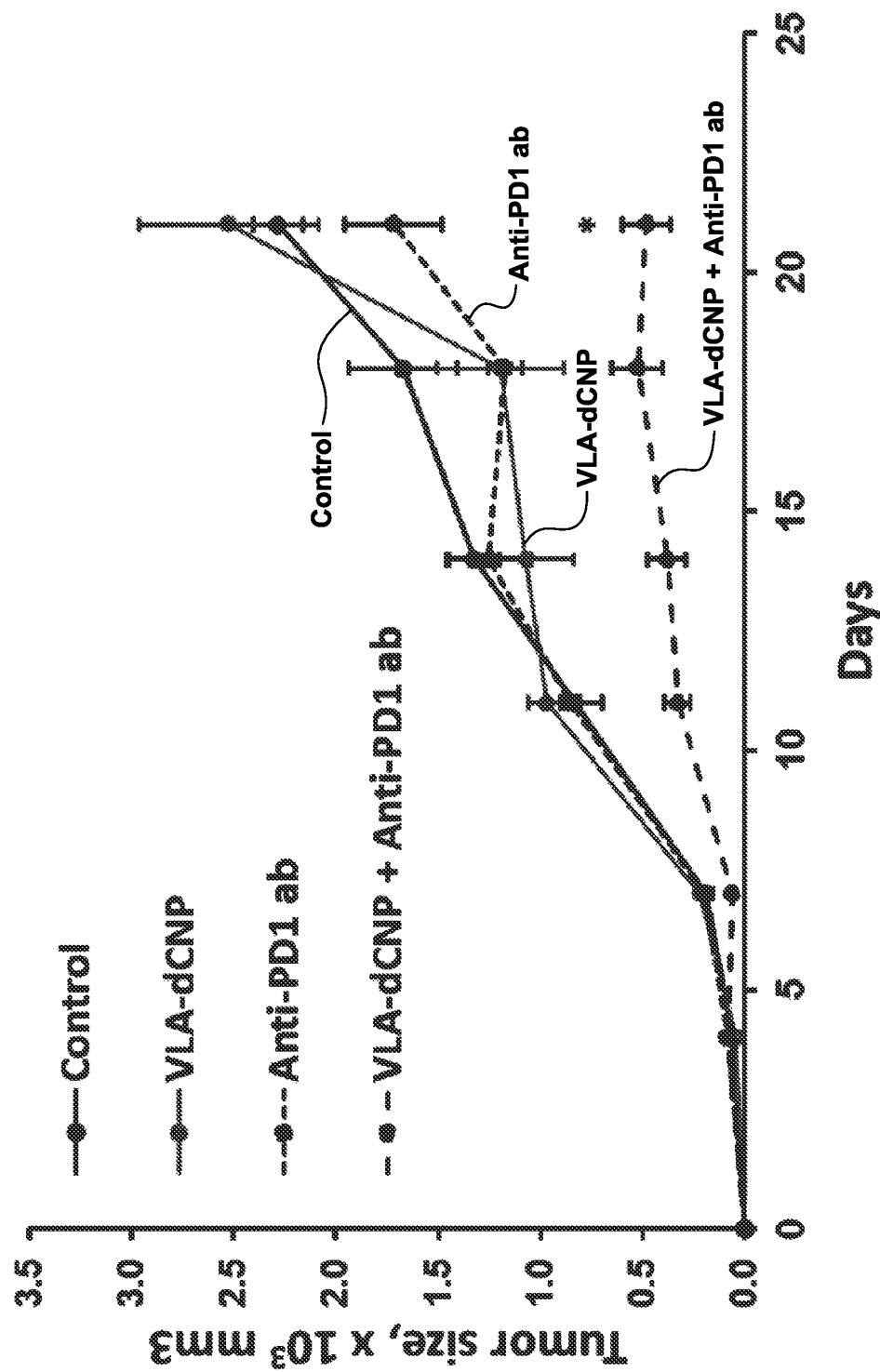


FIG. 19A

Tumor volume (mm ³)	Day 0	Day 4	Day 7	Day 11	Day 14	Day 18	Day 21
Control; (SEM) n=9	0.0 (0.0)	0.06 (2.4)	0.19 (2.0)	0.83 (15.7)	1.33 (35.7)	1.67 (0.27)	2.28 (0.12)
Anti-PD-1 ab; (SEM) n=7	0.0 (0.0)	0.09 (0.02)	0.2 (0.03)	0.85 (0.04)	1.25 (0.2)	1.17 (0.09)	1.72 (0.24)
VLA-dCNP + Anti-PD-1 ab; (SEM) n=7	0.0 (0.0)	0.08 (0.02)	0.06 (0.01)	0.33 (0.07)	0.38 (0.09)	0.53 (0.12)	0.48 (0.12)
VLA-dCNP; (SEM) n=7	0.0 (0.0)	0.05 (0.01)	0.22 (0.02)	0.97 (0.09)	1.07 (0.23)	1.20 (0.31)	2.52 (0.44)

FIG. 19B

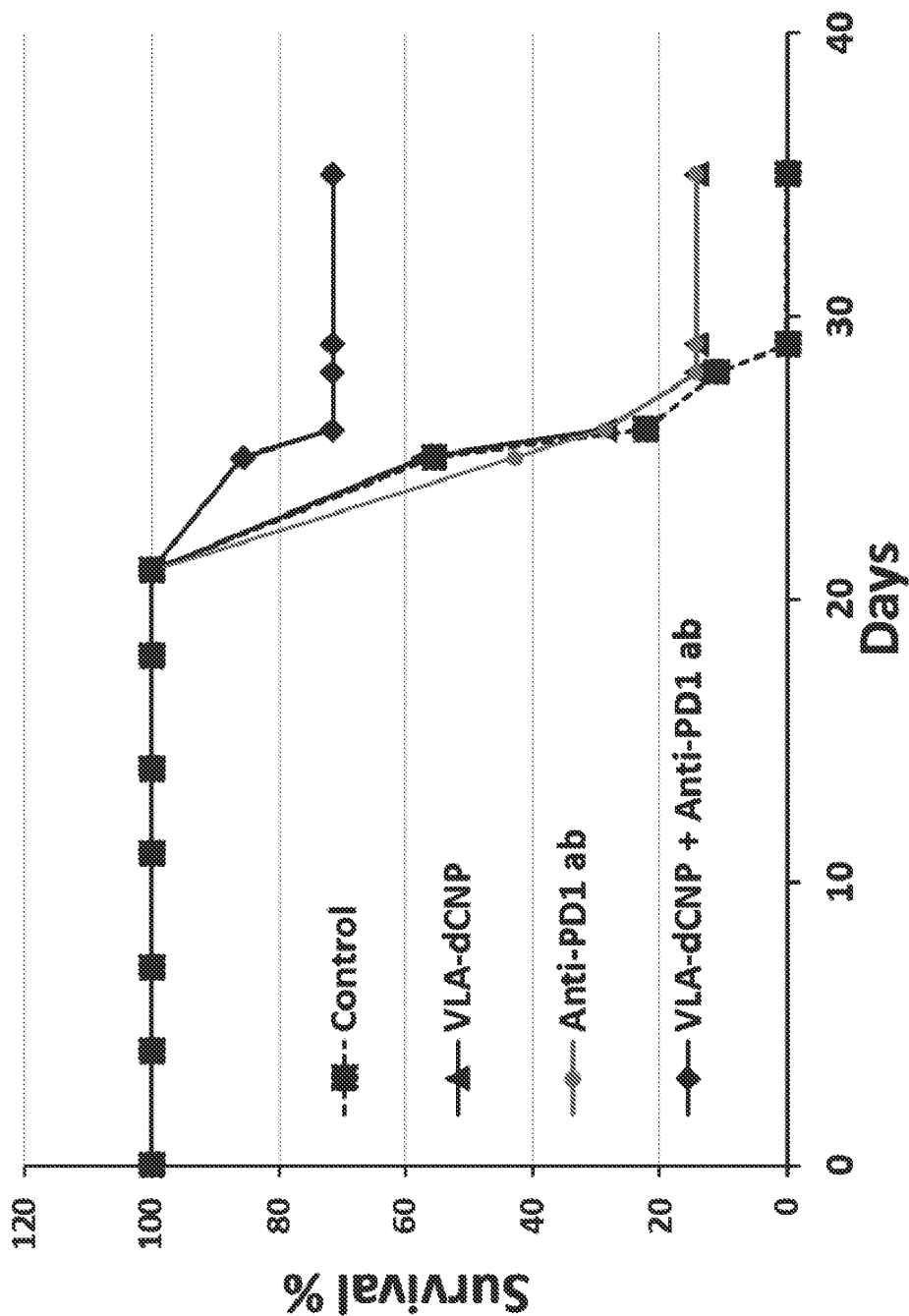


FIG. 20

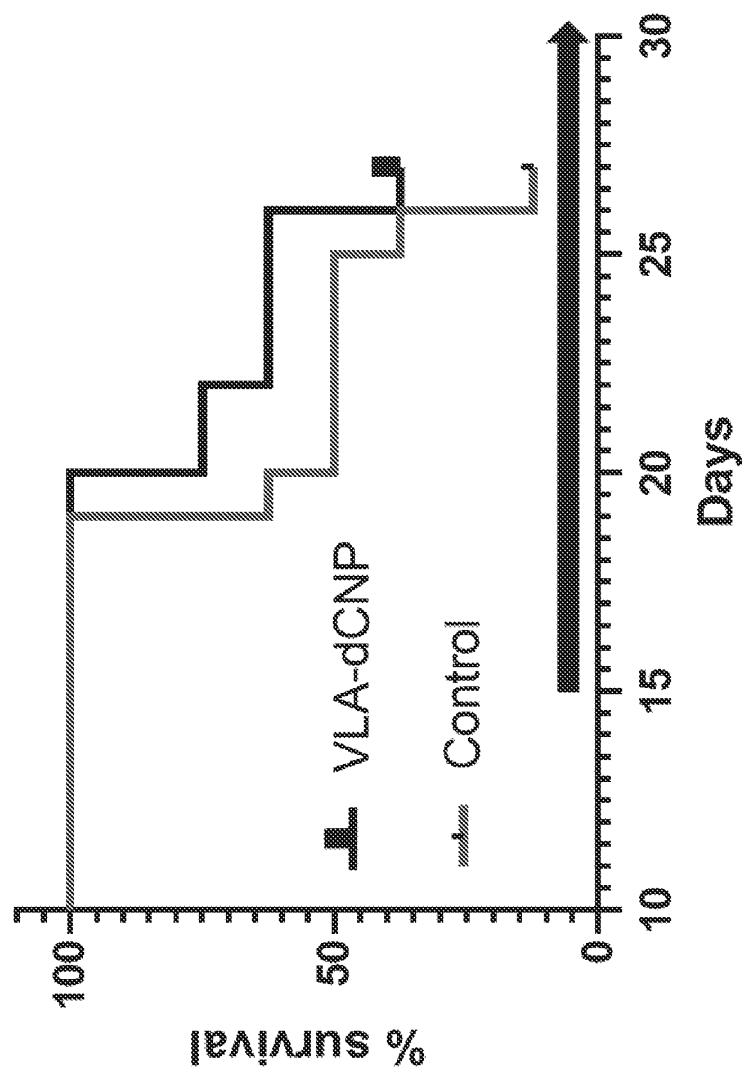
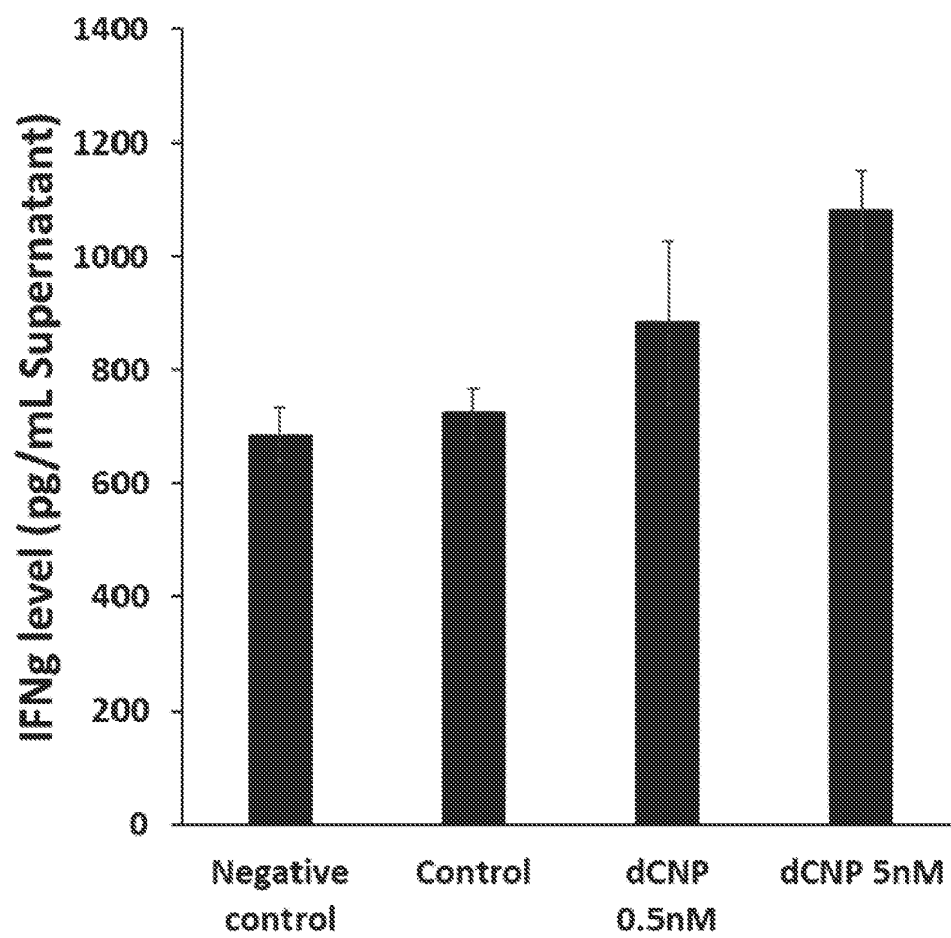


FIG. 21

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**FIG. 22**

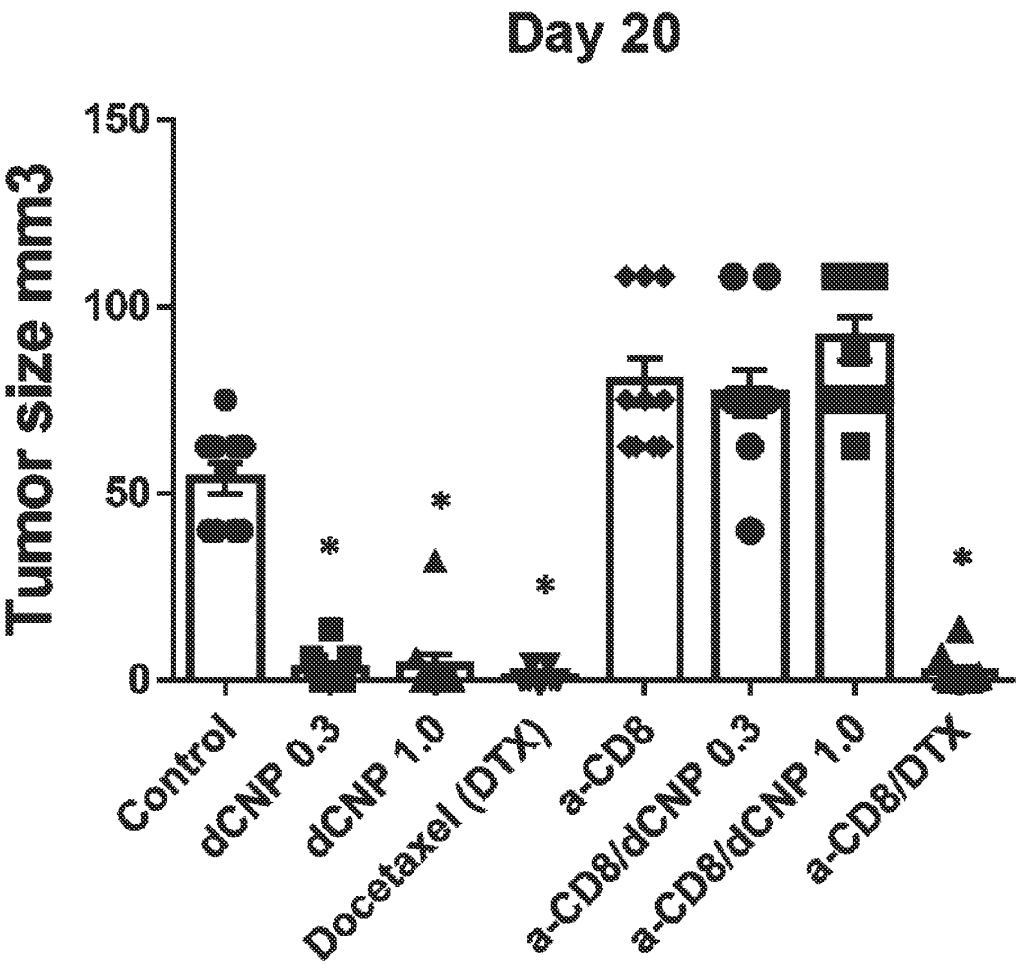


FIG. 23A

FIG. 23B

Tumor volume (mm3)	Day 0	Day 6	Day 8	Day 11	Day 13	Day 15	Day 18	Day 20	Tumor Eradication At Day 20
Control; (SEM) n=10	0.0 (0.0)	0.8 (0.4)	2.8 (0.5)	14.5 (5.5)	19.9 (2.2)	30.2 (3.5)	44.6 (4.6)	54.1 (4.1)	0/10
dCNP 0.3 mg/Kg; (SEM) n=10	0.0 (0.0)	0.5 (0.1)	0.6 (0.1)	6.9 (1.6)	1.3 (0.5)	1.1 (0.6)	1.9 (1.3)	3.0* (1.4)	6/10
dCNP 1.0 mg/Kg; (SEM) n=10	0.0 (0.0)	0.5 (0.1)	0.5 (0.2)	3.2 (1.3)	0.4 (0.1)	0.35 (0.1)	0.15 (0.1)	3.8* (3.2)	8/10
Docetaxel (DTX); (SEM) n=10	0.0 (0.0)	0.4 (0.1)	1.6 (0.6)	2.3 (1.3)	0.2 (0.1)	0.6 (0.4)	1.5 (1.3)	0.8* (0.5)	8/10
a-CD8; (SEM) n=10	0.0 (0.0)	0.6 (0.1)	3.15 (0.7)	13.4 (2.5)	29.5 (4.3)	42.0 (3.9)	67.3 (5.4)	79.9 (6.4)	0/10
a-CD8/dCNP 0.3; (SEM) n=10	0.0 (0.0)	1.2 (0.5)	2.95 (0.6)	9.75 (1.8)	29.2 (1.9)	40.8 (5.4)	55.6 (5.1)	76.9 (6.3)	0/10
a-CD8/dCNP 1.0; (SEM) n=10	0.0 (0.0)	0.5 (0.1)	3.0 (0.5)	12.1 (1.1)	25.0 (3.8)	44.4 (4.1)	64.0 (3.3)	91.5 (5.8)	0/10
a-CD8/DTX; (SEM) n=10	0.0 (0.0)	0.6 (0.1)	2.3 (0.6)	7.9 (1.6)	28.0 (2.9)	4.8 (1.5)	0.5 (0.1)	2.2* (1.4)	5/10

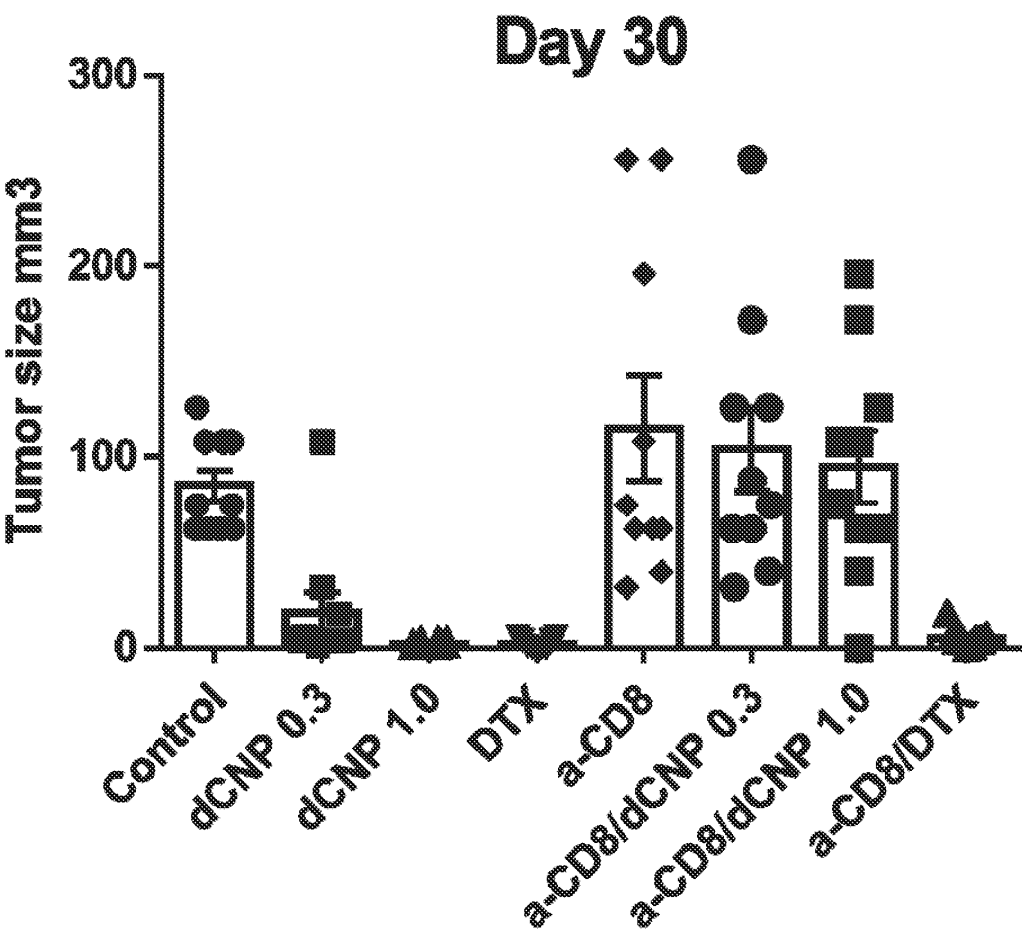


FIG. 24A

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FIG. 24B

Tumor volume (mm ³)	Day 0	Day 19	Day 21	Day 23	Day 26	Day 28	Day 30	Tumor Eradication At Day 30
Control; (SEM) n=10	0.0 (0.0)	53.8 (5.0)	65.1 (6.1)	68.6 (5.5)	66.3 (6.2)	76.2 (7.9)	85 (7.8)	0/10
dCNP 0.3 mg/Kg; (SEM) n=10	0.0 (0.0)	60.1 (3.0)	56.2 (5.5)	65.9 (5.8)	5.8 (3.0)	10.8 (5.8)	18.5* (10.4)	0/10
dCNP 1.0 mg/Kg; (SEM) n=10	0.0 (0.0)	58.8 (5.0)	44.4 (5.3)	54.6 (6.0)	4.6 (3.1)	3.7 (1.8)	2.3* (0.9)	5/10
Docetaxel (DTX); (SEM) n=10	0.0 (0.0)	57.8 (8.5)	44.0 (5.5)	56.7 (5.1)	4.1 (1.7)	4.4 (1.4)	2.3* (0.9)	4/9 (1 dead at Day 28)
a-CD8; (SEM) n=10	0.0 (0.0)	53.2 (6.8)	59.3 (6.9)	79.9 (6.4)	69.8 (5.4)	78.7 (11.9)	115.1 (27.6)	0/10
a-CD8/dCNP 0.3; (SEM) n=10	0.0 (0.0)	55.2 (7.0)	61.8 (4.0)	77.7 (7.4)	66.2 (9.0)	71.4 (10.9)	103.9 (21.7)	0/10
a-CD8/dCNP 1.0; (SEM) n=10	0.0 (0.0)	57.3 (4.2)	66.9 (5.0)	79.1 (5.1)	64.8 (2.6)	61.5 (8.4)	95.0 (18.8)	1/10
a-CD8/DTX; (SEM) n=10	0.0 (0.0)	63.4 (3.1)	58.8 (3.0)	77.3 (6.9)	36.3 (6.6)	11.4 (4.8)	5.2* (1.7)	1/9 (1 dead at Day 26)

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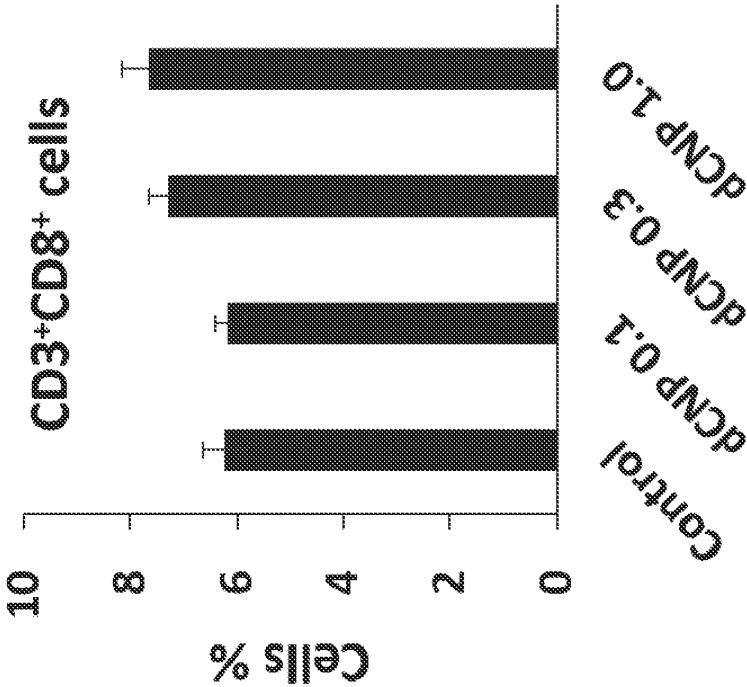


FIG. 25B

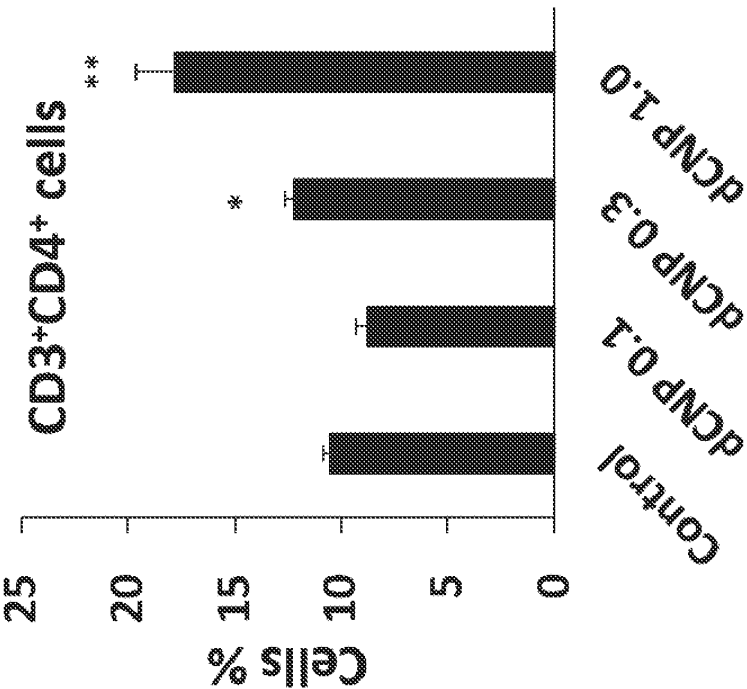


FIG. 25A

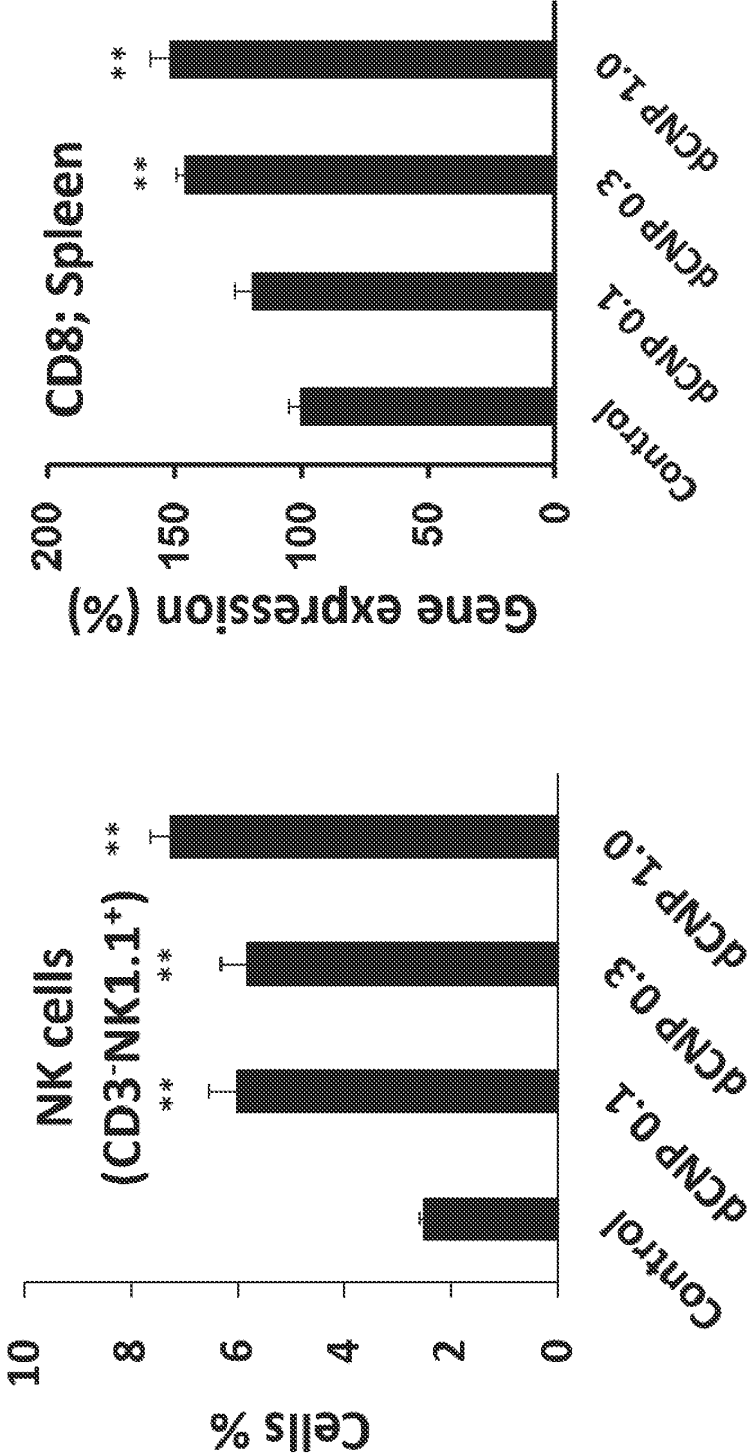


FIG. 25D

FIG. 25C

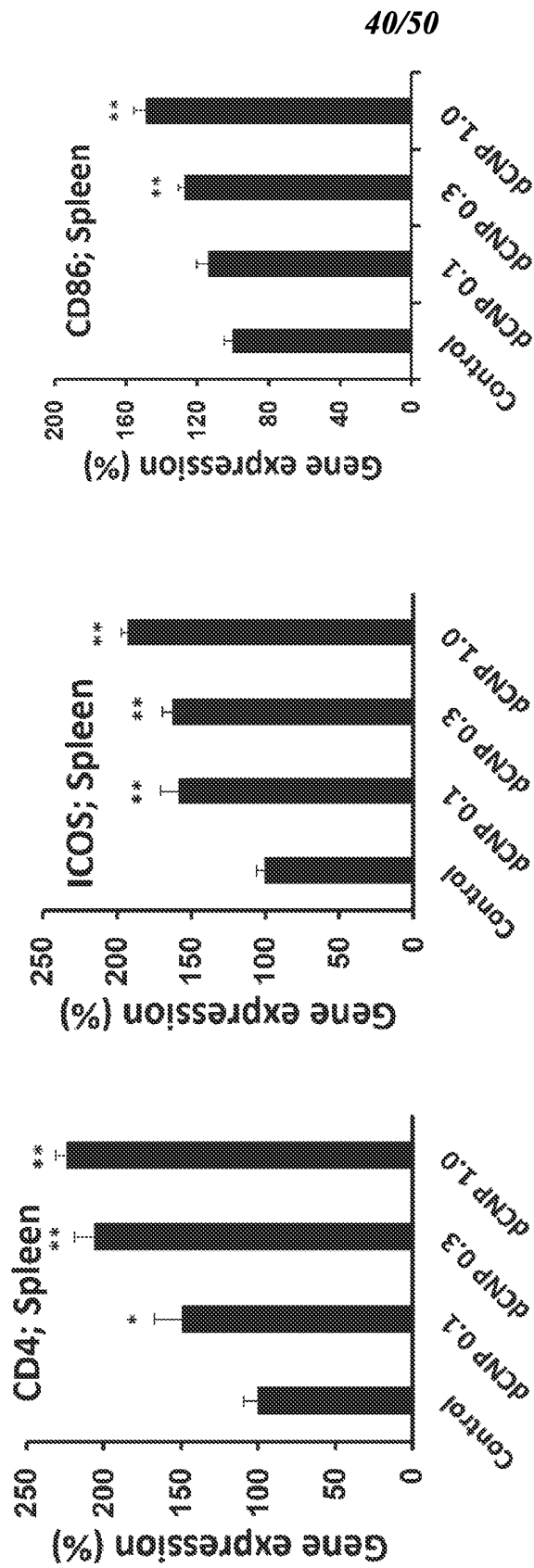


FIG. 25E

FIG. 25F

FIG. 25G

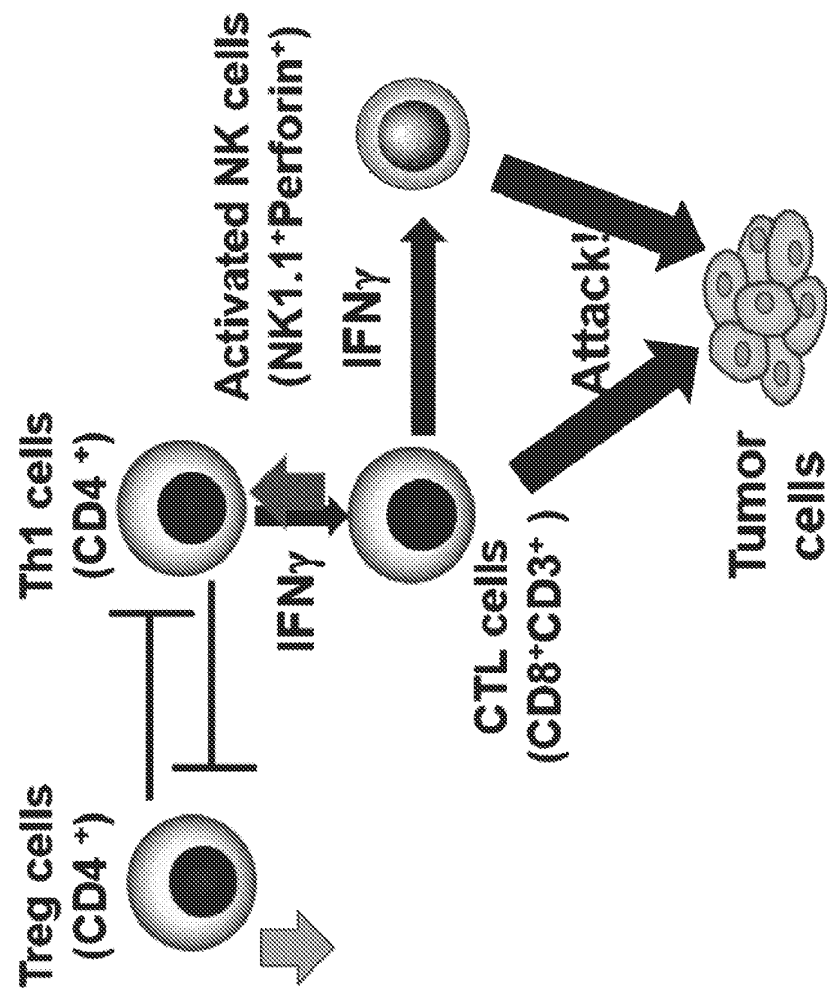
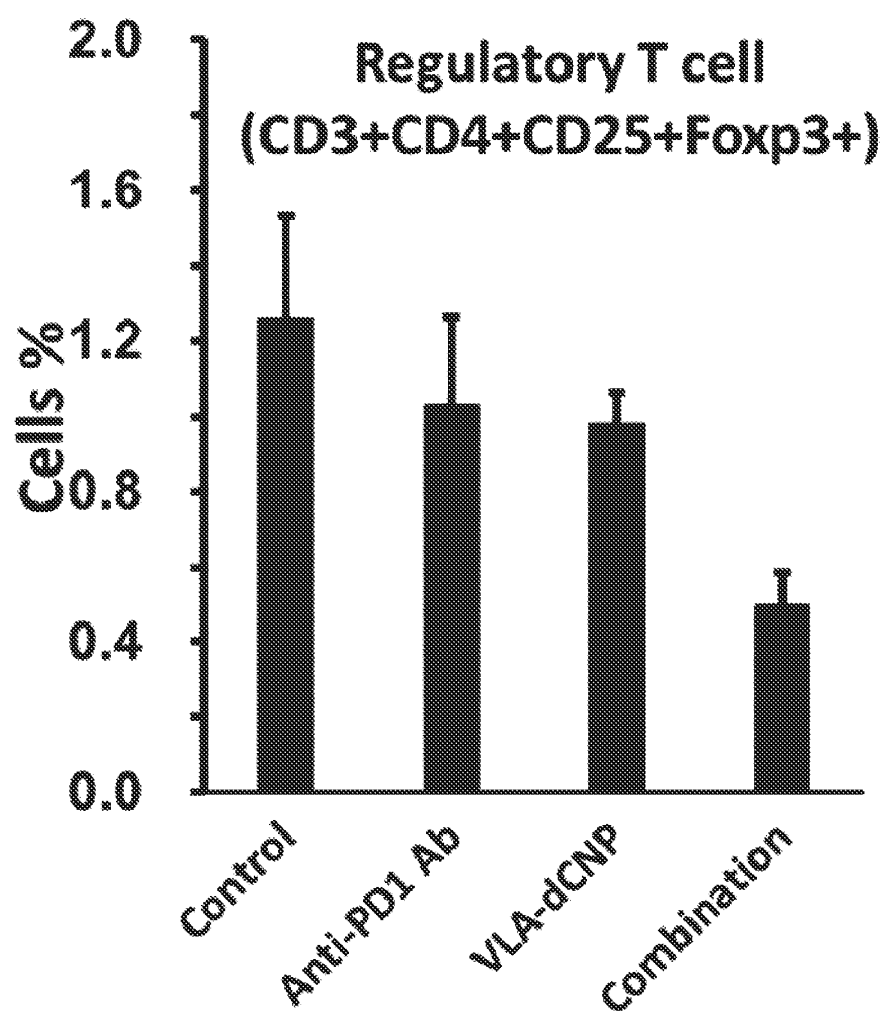
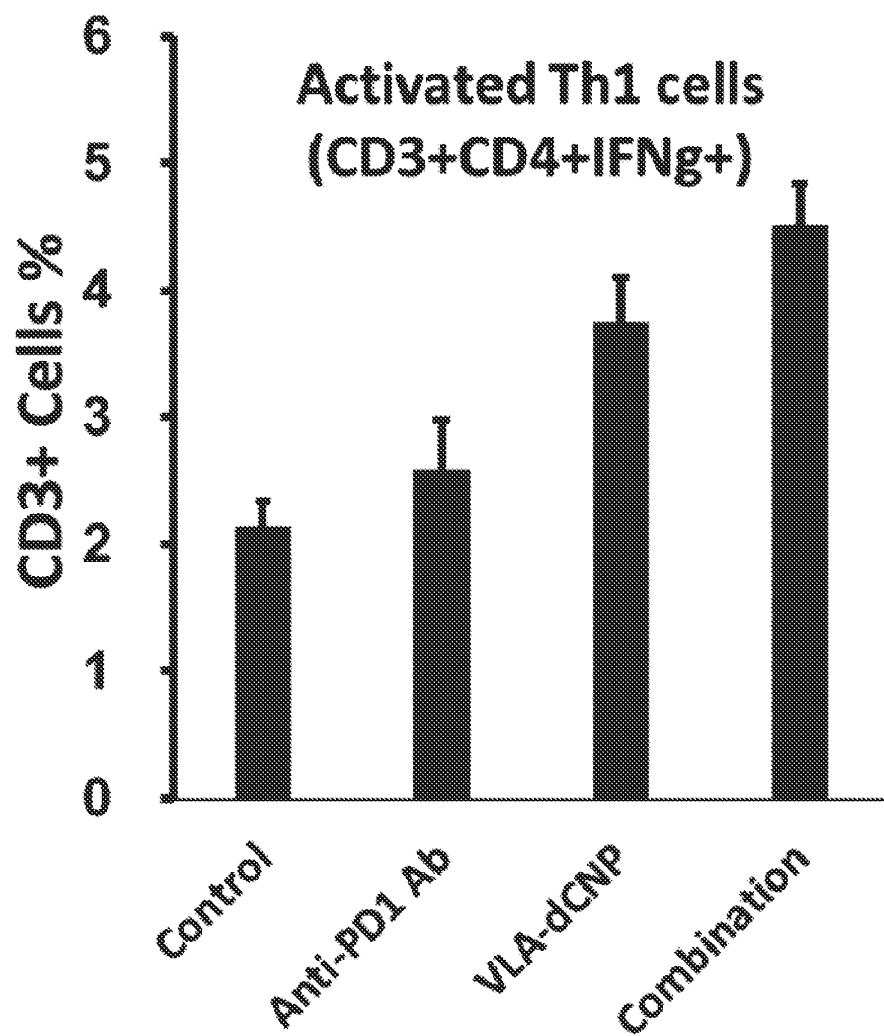


FIG. 26A

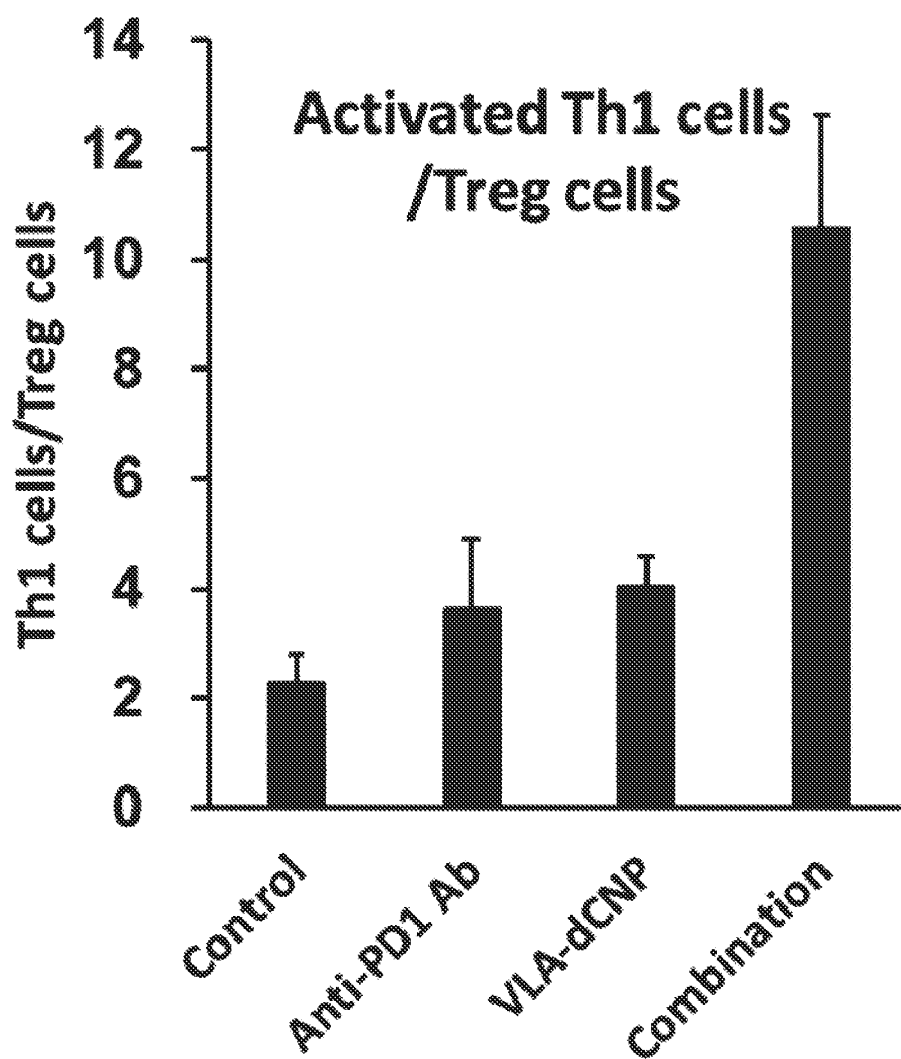
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**FIG. 26B**

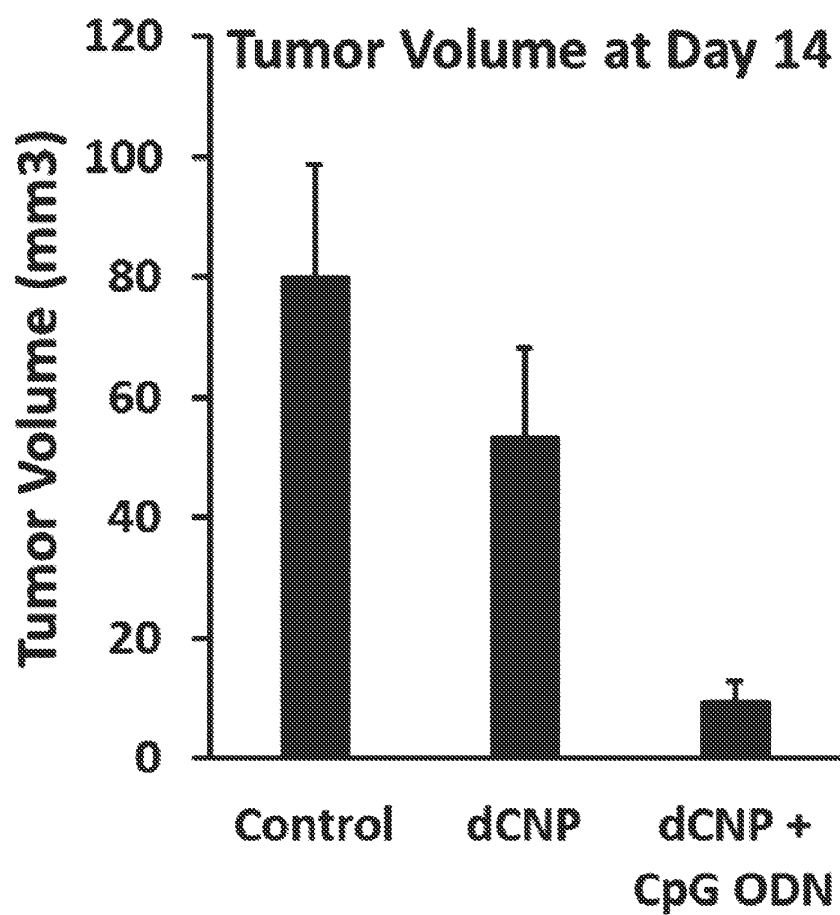
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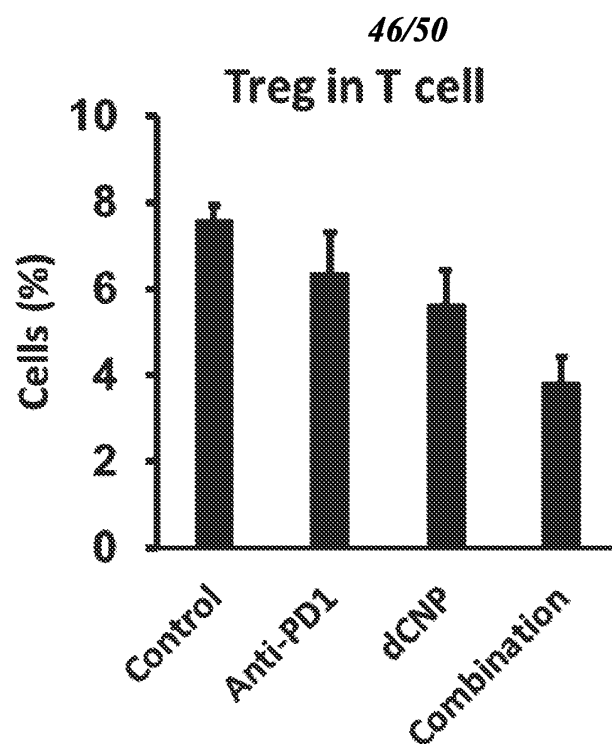
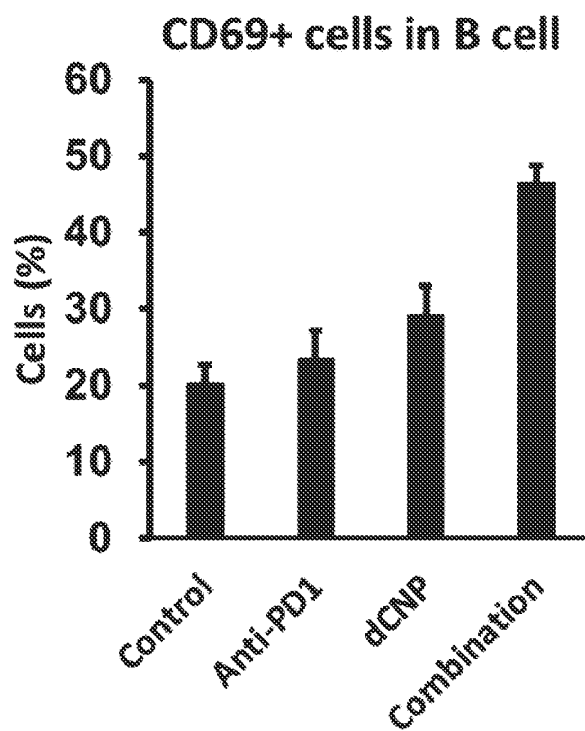
**FIG. 26C**

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**FIG. 26D**

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**FIG. 27**

**FIG. 28A****FIG. 28B**

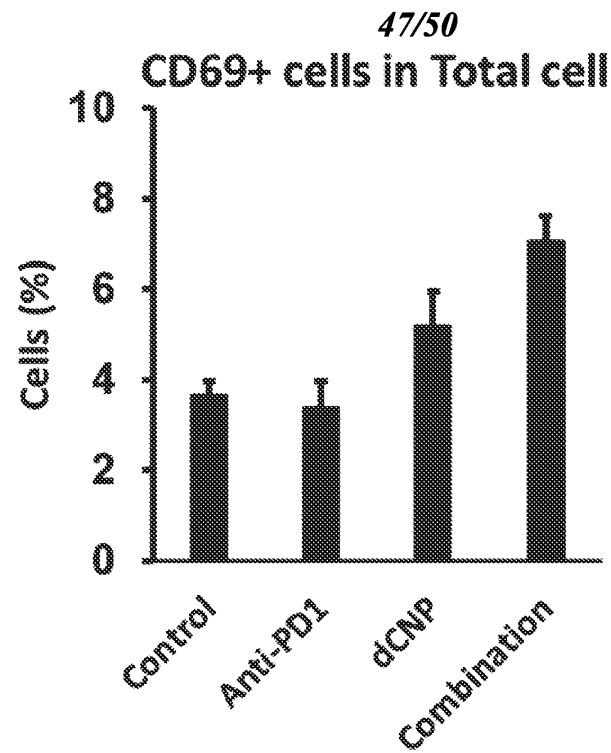


FIG. 28C

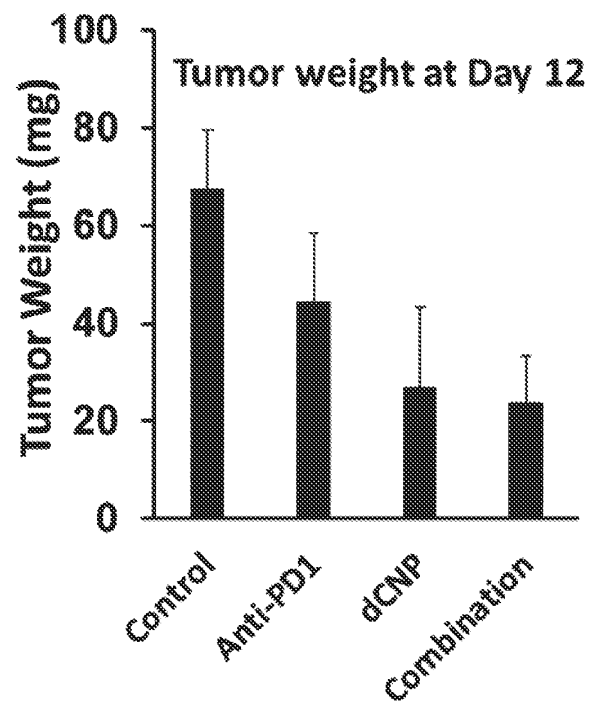
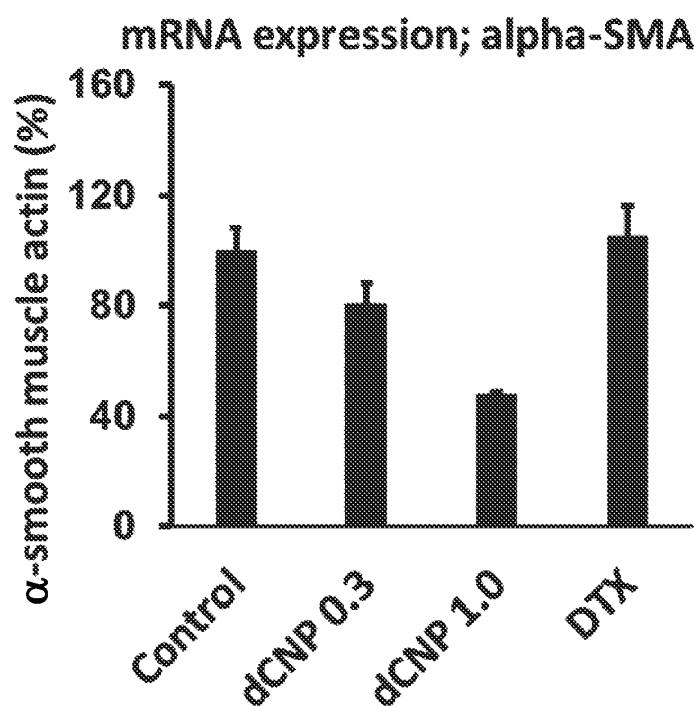
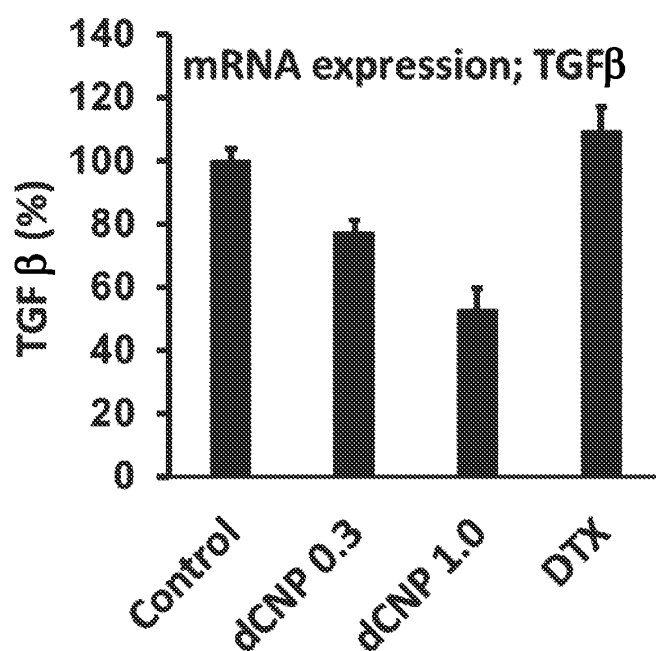
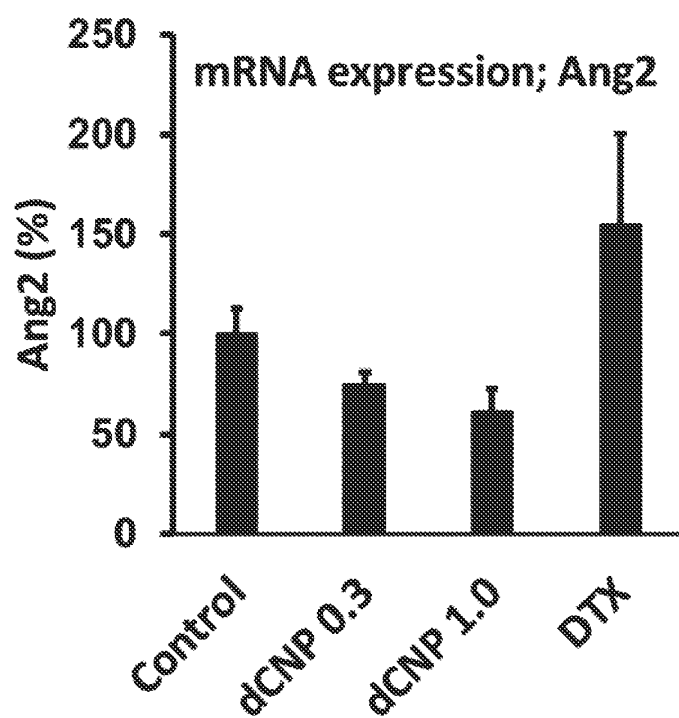


FIG. 28D

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**FIG. 29A****FIG. 29B**

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***FIG. 29C***

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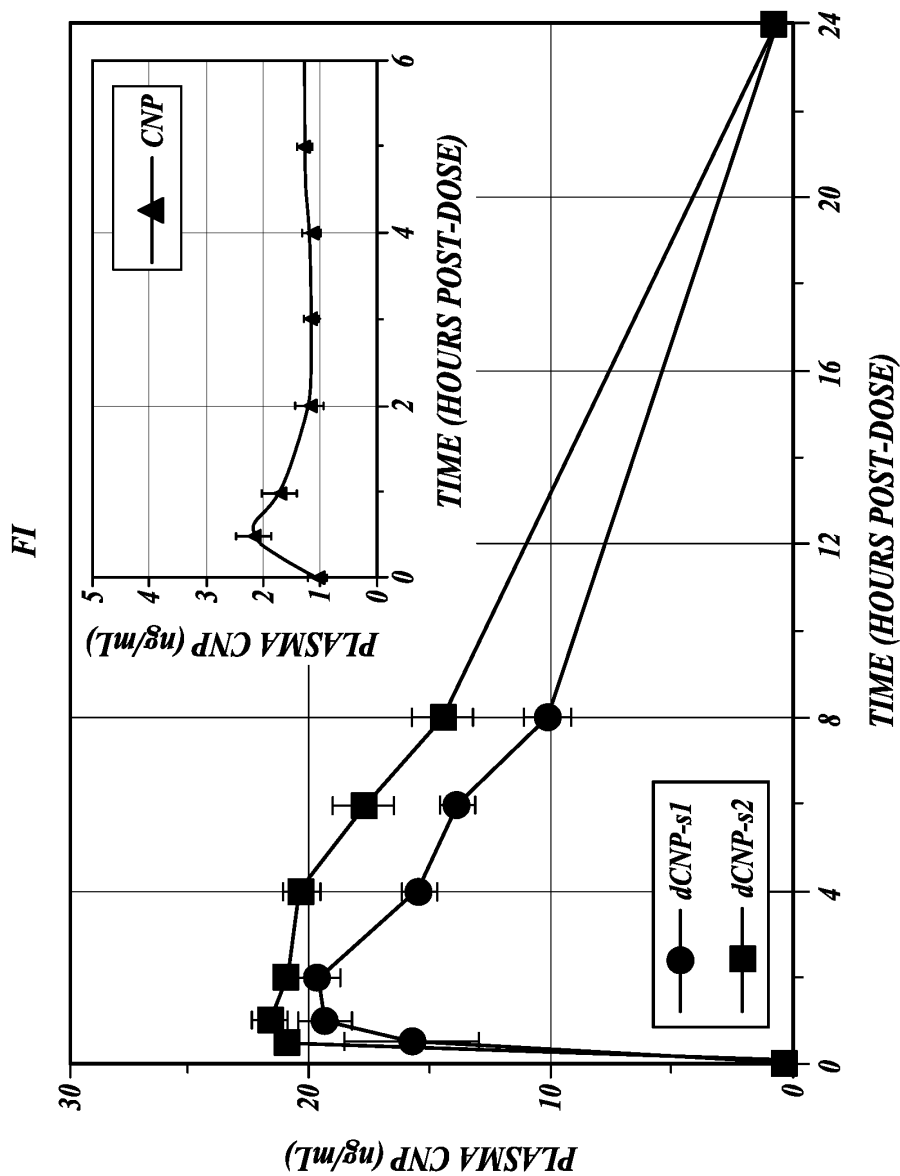


FIG. 30