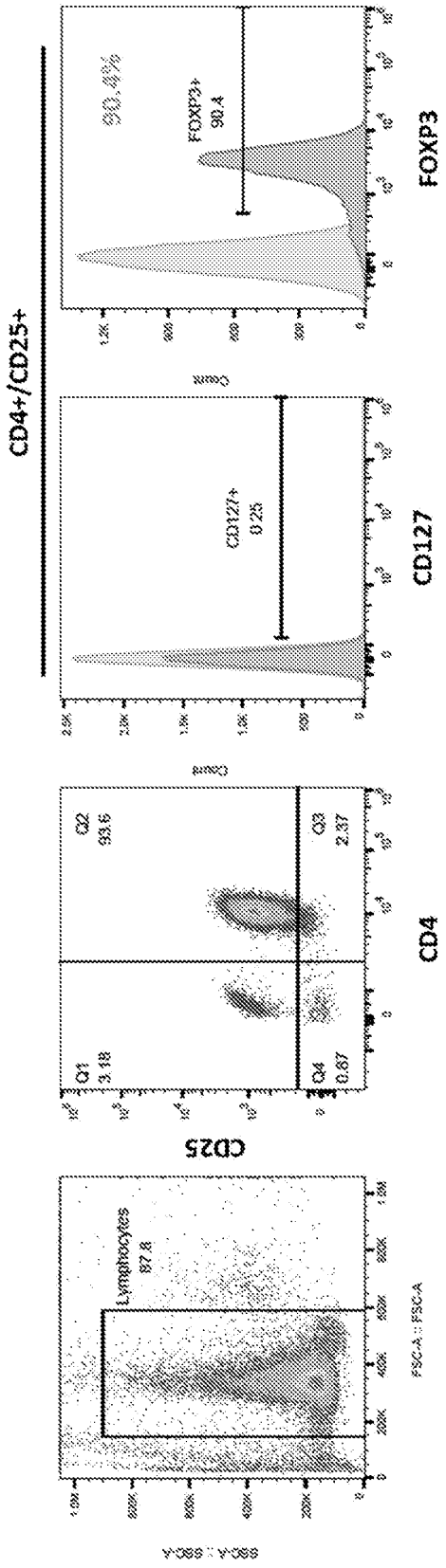


FIG. 1A FIG. 1B FIG. 1C FIG. 1D

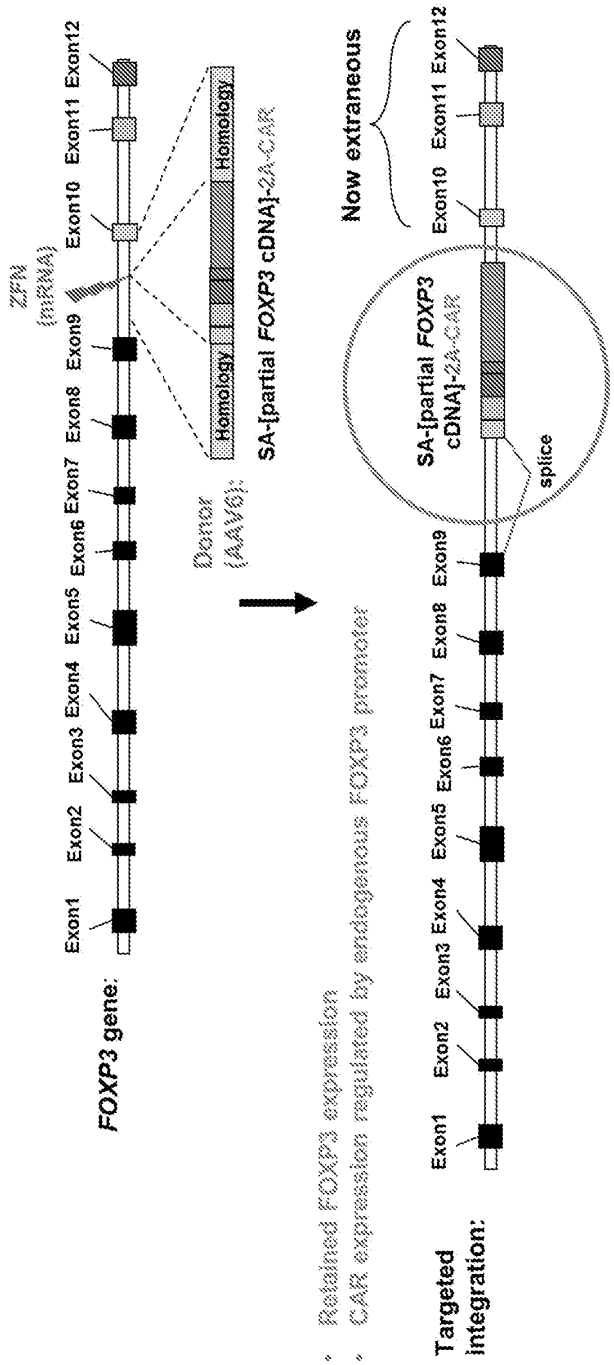

FOXP3 gene:
Exon1
Exon2
Exon3
Exon4
Exon5
Exon6
Exon7
Exon8
Exon9
Exon10
Exon11
Exon12
ZFN (mRNA)
Donor (AAV6):
Homology
Homology
SA-[partial FOXP3 cDNA]-2A-CAR
Now extraneous
SA-[partial FOXP3 cDNA]-2A-CAR
splice
Targeted integration:
• Retained FOXP3 expression
• CAR expression regulated by endogenous FOXP3 promoter

FIG. 2A

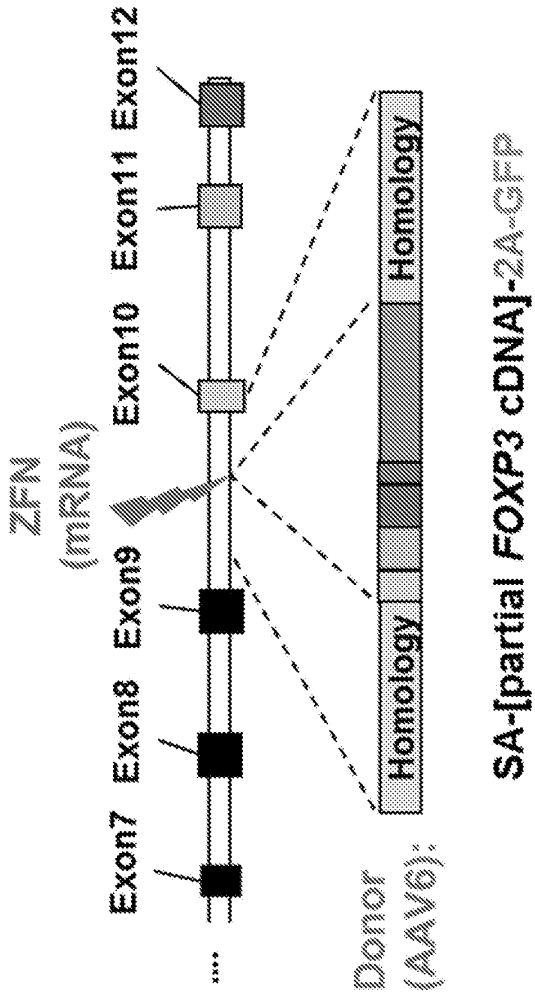

Exon7
Exon8
Exon9
Exon10
Exon11
Exon12
ZFN
(mRNA)
Donor
(AAV6):
Homology
Homology
SA-[partial FOXP3 cDNA]-2A-GFP

FIG. 2B

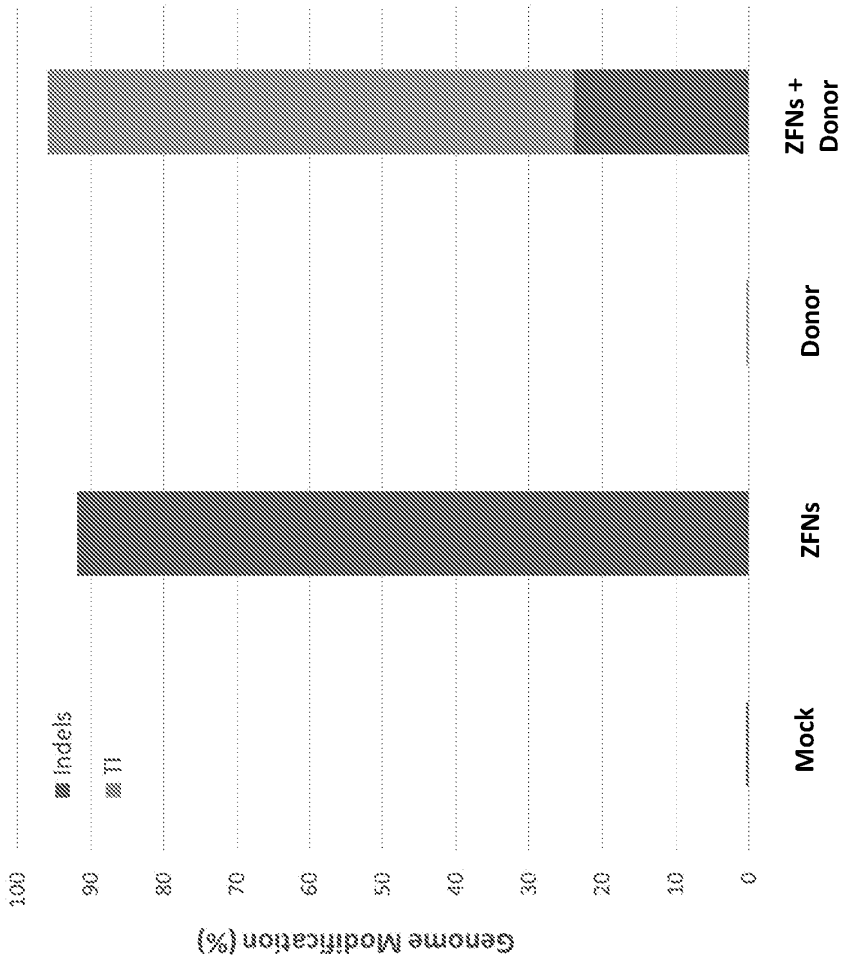

Genome Modification (%)
100
90
80
70
60
50
40
30
20
10
0
Indels
TI
Mock
ZFNs
Donor
ZFNs + Donor

FIG. 2C

FOXP3 Site	Sample	Dose (mRNA per ZFP (ug/mL)	Indels (%)	TI (%)	Total Editing (%)
A	75591/75592	20	37.3	60.7	98.0
A	**Donor only**		0.4	3.1	3.5
A	*GFP*		0.1	0.0	0.1
B	75683/75684	20	60.1	31.8	92.0
B	**Donor only**		0.8	1.0	1.7
B	*GFP*		0.4	0.0	0.4
C	75714/75715	20	54.7	36.0	90.7
C	**Donor only**		0.4	0.6	1.0
C	*GFP*		0.5	0.0	0.5
D	75806/75808	20	42.9	46.7	89.5
D	**Donor only**		1.0	1.5	2.5
D	*GFP*		0.7	0.0	0.7
E	75893/75895	20	52.1	43.0	95.0
E	**Donor only**		0.2	4.0	4.2
E	*GFP*		0.8	0.0	0.8
F	76695/76698	20	47.9	46.7	94.5
F	**Donor only**		0.2	0.0	0.2
F	*GFP*		0.2	0.0	0.2

FIG. 2D

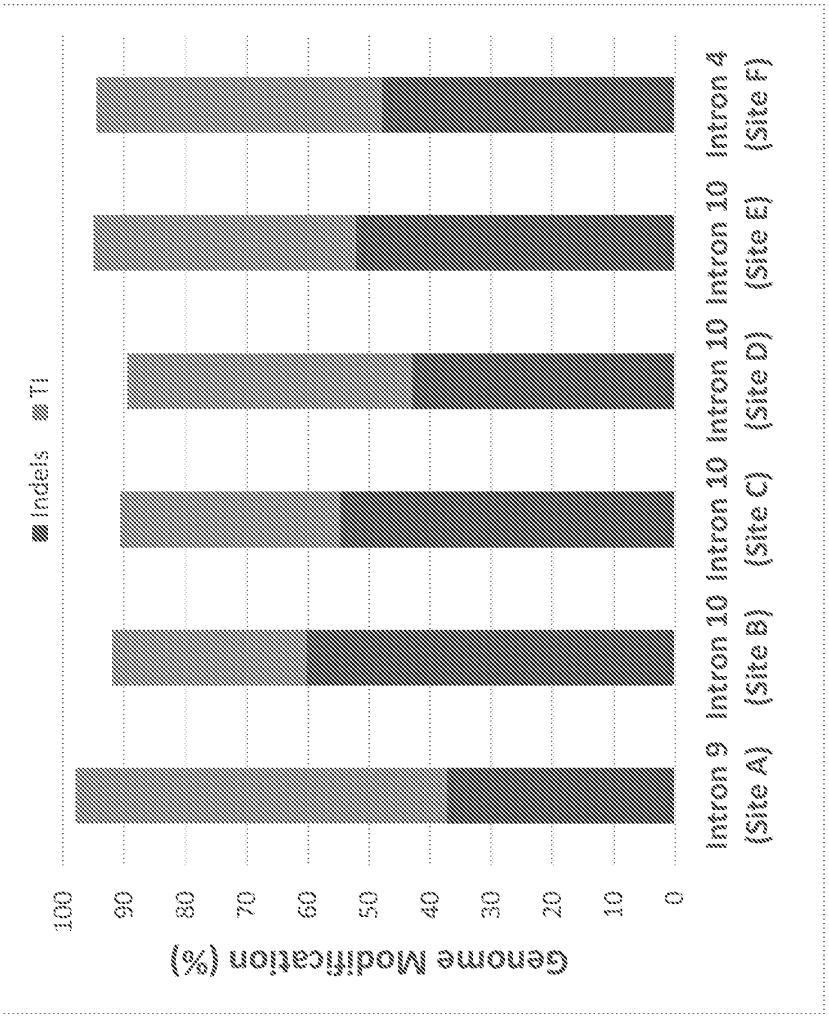

Indels
TI
Genome Modification (%)
100
90
80
70
60
50
40
30
20
10
0
Intron 9 (Site A)
Intron 10 (Site B)
Intron 10 (Site C)
Intron 10 (Site D)
Intron 10 (Site E)
Intron 4 (Site F)

FIG. 2E

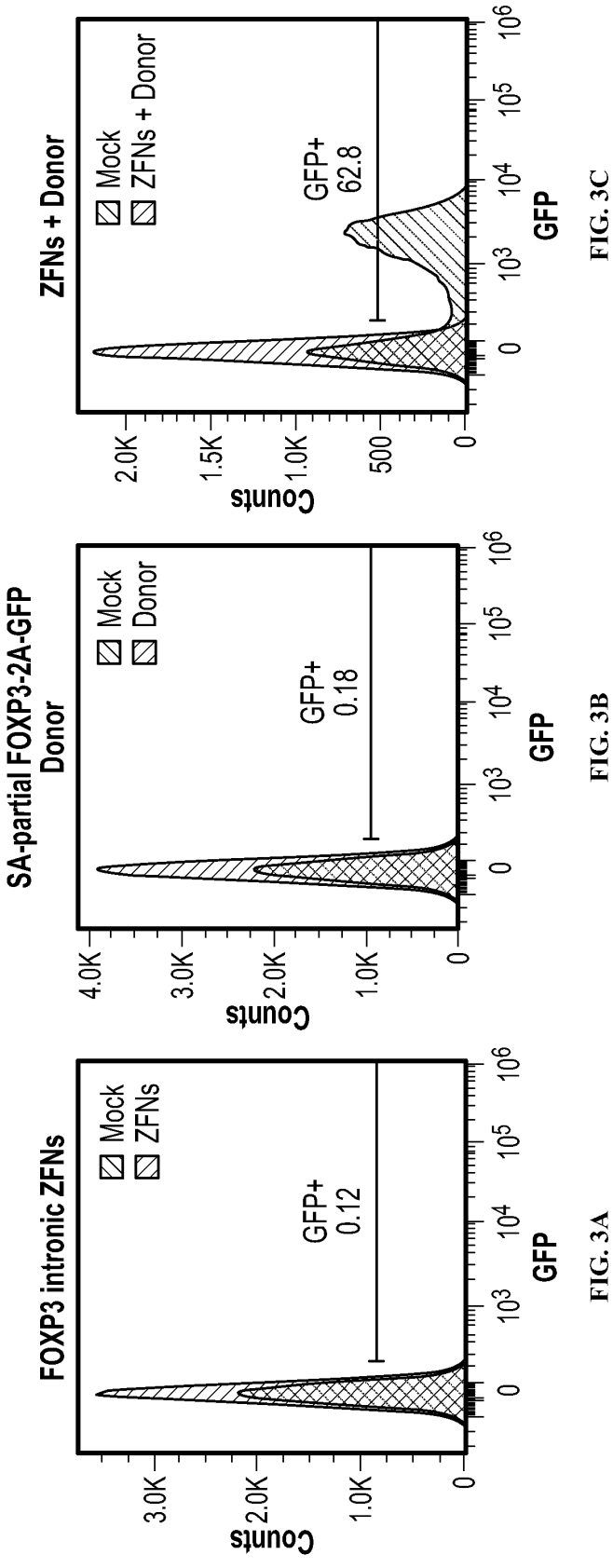
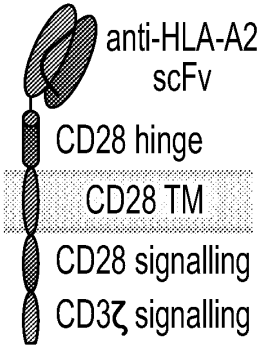


FIG. 3A

FIG. 3B

FIG. 3C



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FIG. 4A

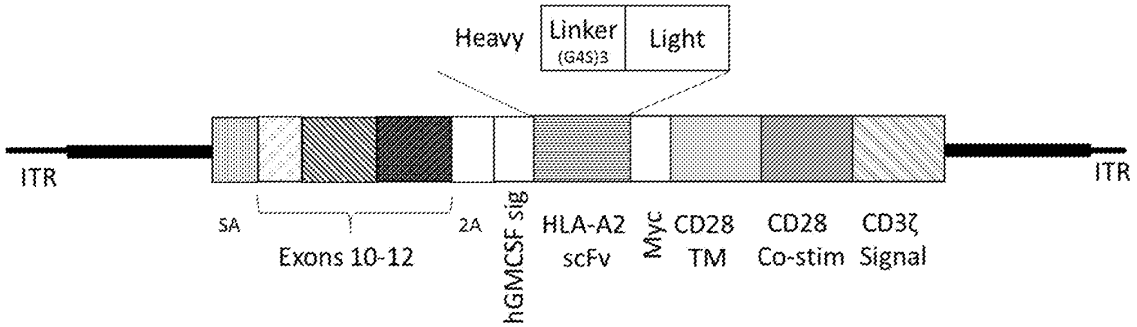


FIG. 4C

HLA-A2 scFv Heavy chain (3PB2)

	FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4
	1 10 20 30		40	50 60	70 80 90	100	103
Cos-3	QVQLVESGGGVVQPGGSLRLSCAASGFTFS	SYGMH	WVRQAPGKGLEWVA	FIRYDGSNKYYADSVKG	RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK		
3PB2	-----q----------V------V-L-	D---h	----------a	---N---D-------	-------n--EKtVS--Ss-l---e--------	NGESGPLDYWYLDL	WGRGT

HLA-A2 scFv Light chain (DPK1)

	FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4
	1 10 20	30	40	50	60 70 80	90	102
DPK1	DIQMTQSPSSLSASVGDRVTITC	QASQDISNYLN	WYQQKPGKAPKLLIY	DASNLET	GVPSRFSGSGSGTDFTFTISSLQPEDIATYYC	QQYDNLP	

FIG. 4B

SUBSTITUTE SHEET (RULE 26)

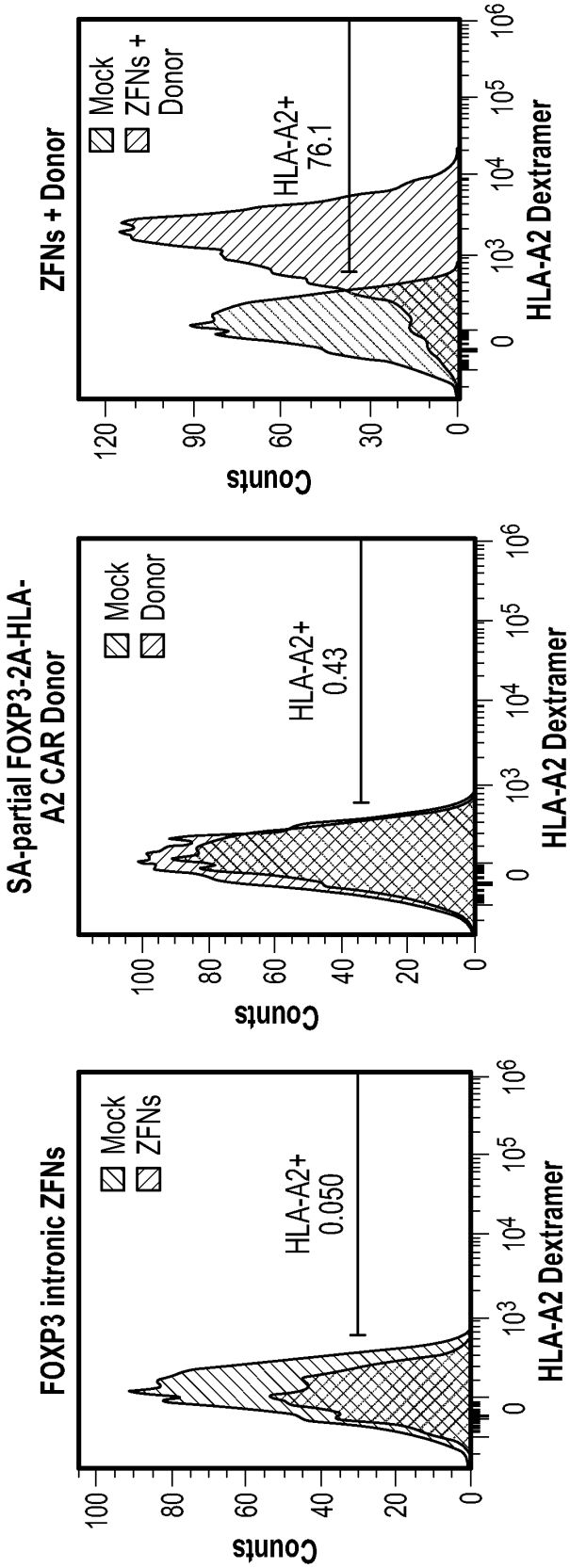


FIG. 5A

FIG. 5B

FIG. 5C

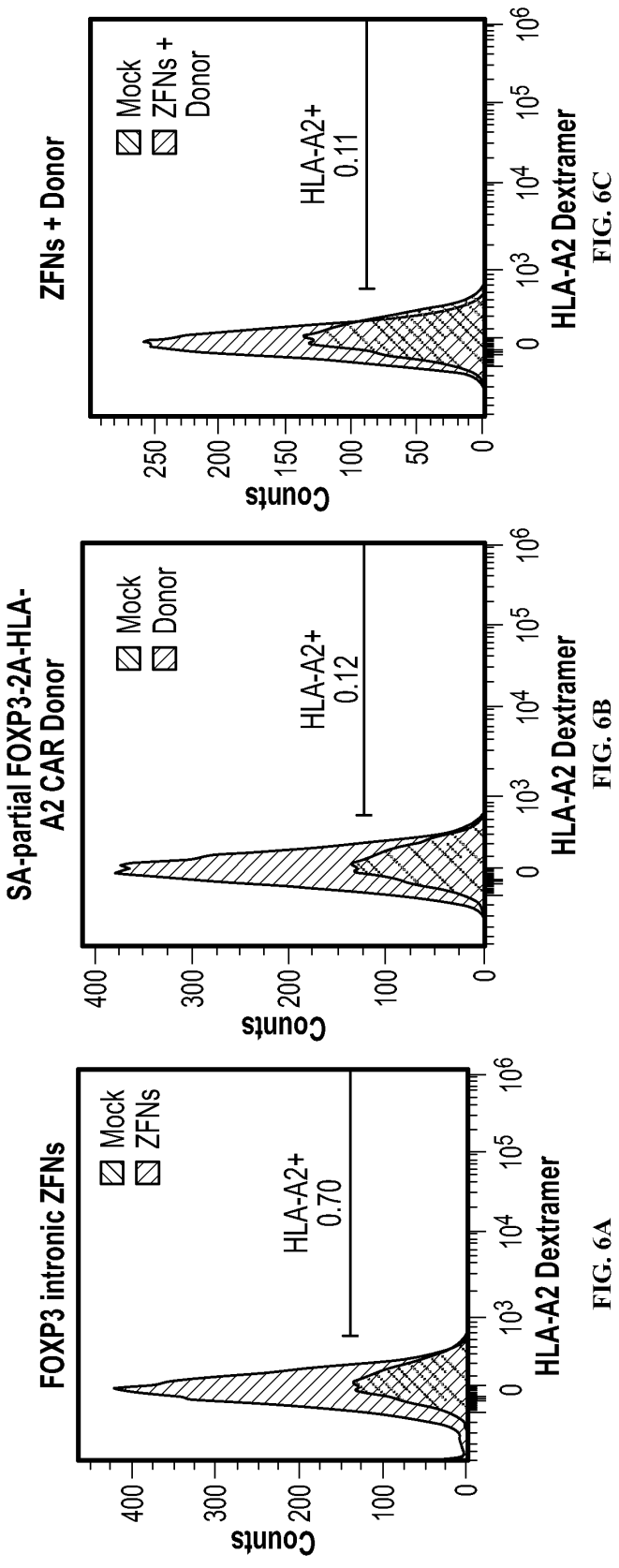


FIG. 6A

FIG. 6B

FIG. 6C

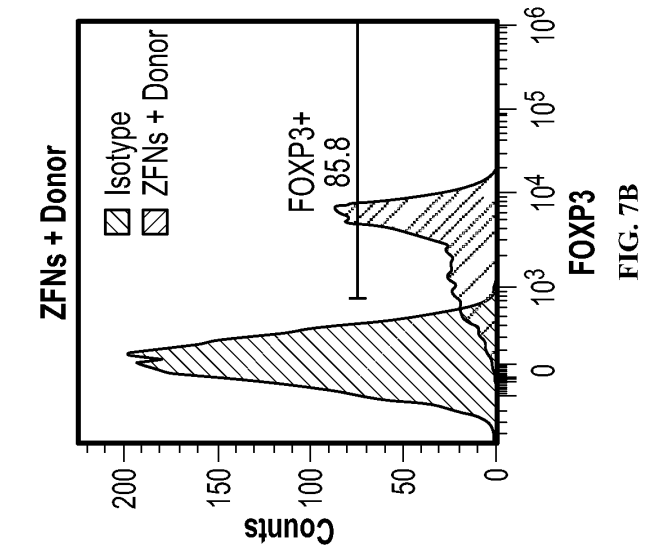

ZFNs + Donor
Isotype
ZFNs + Donor
FOXP3+
85.8
Counts
FOXP3
0
50
100
150
200
0
10^3
10^4
10^5
10^6

FIG. 7B

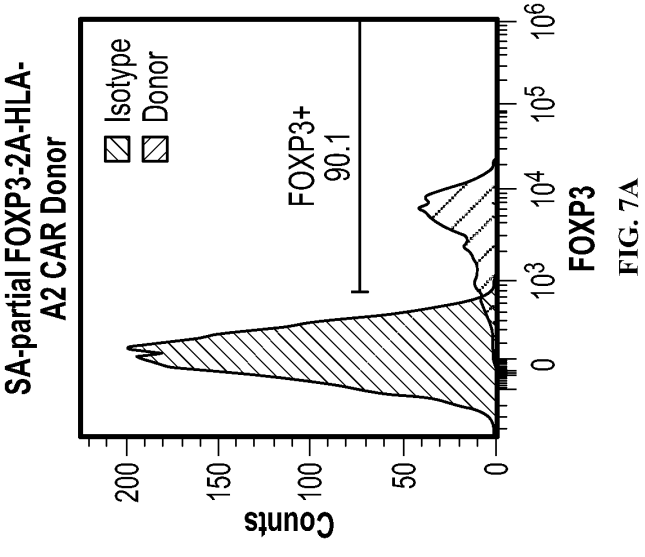

SA-partial FOXP3-2A-HLA-A2 CAR Donor
Isotype
Donor
FOXP3+
90.1
Counts
FOXP3
0
50
100
150
200
0
10^3
10^4
10^5
10^6

FIG. 7A

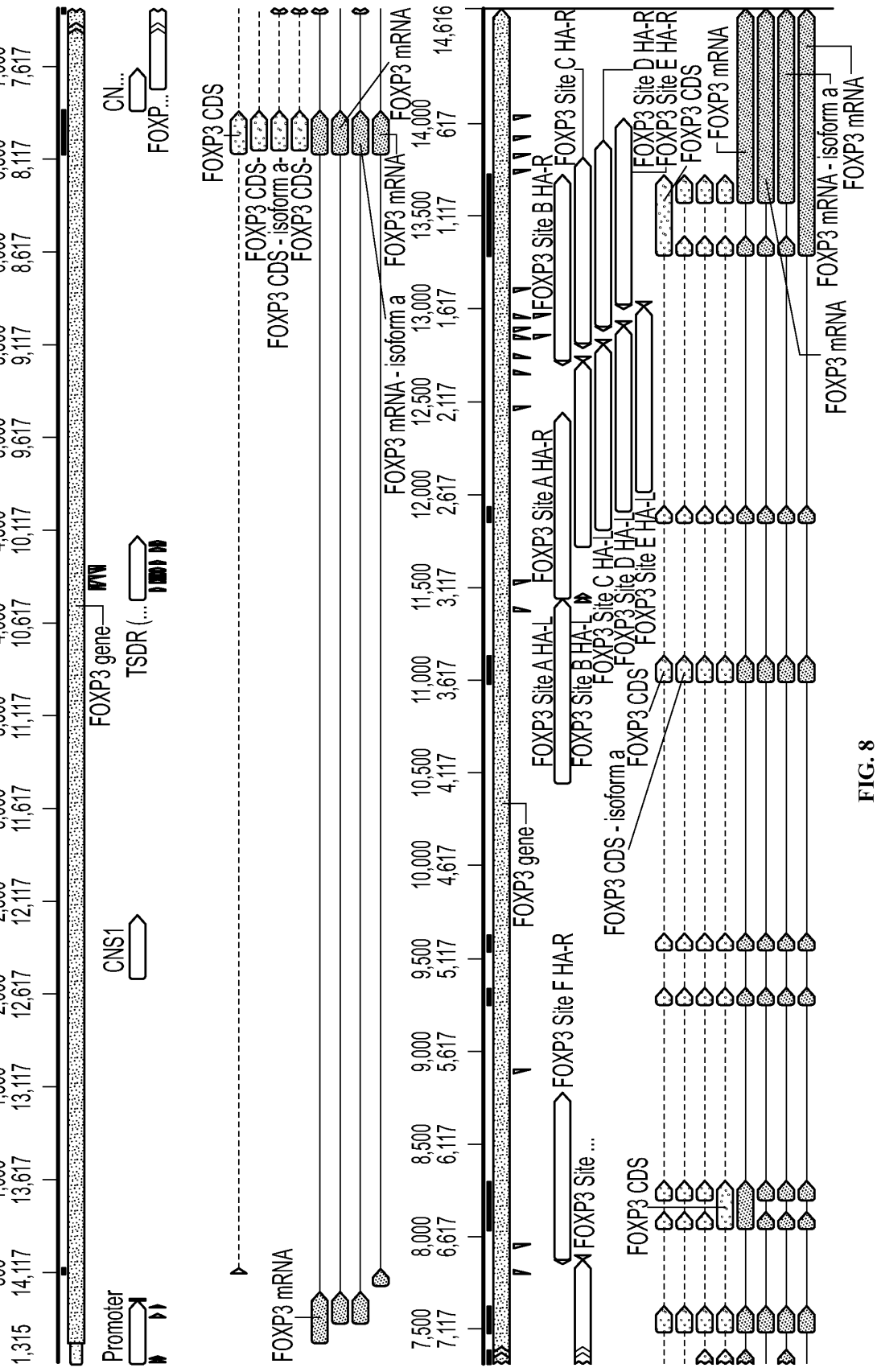

Promoter
CNS1
FOXP3 gene
TSDR (...
CN...
FOXP...
FOXP3 mRNA
FOXP3 CDS
FOXP3 CDS- isoform a-
FOXP3 CDS-
FOXP3 mRNA - isoform a
FOXP3 mRNA
FOXP3 Site A HA-L
FOXP3 Site A HA-R
FOXP3 Site B HA-L
FOXP3 Site B HA-R
FOXP3 Site C HA-L
FOXP3 Site C HA-R
FOXP3 Site D HA-L
FOXP3 Site D HA-R
FOXP3 Site E HA-L
FOXP3 Site E HA-R
FOXP3 Site F HA-R
FOXP3 Site ...
FOXP3 CDS - isoform a
FOXP3 CDS
FOXP3 mRNA - isoform a
FOXP3 mRNA

FIG. 8