

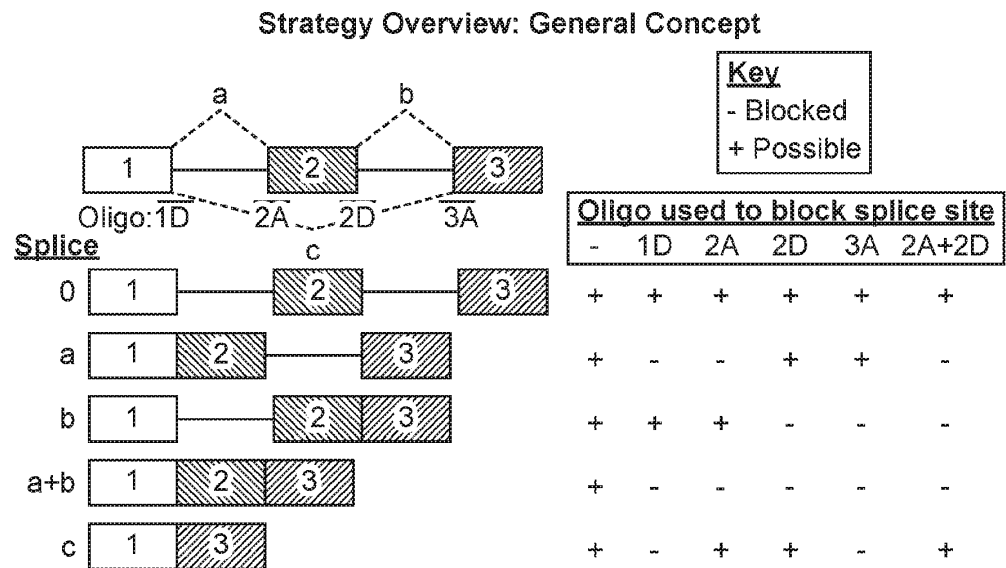


FIG. 1

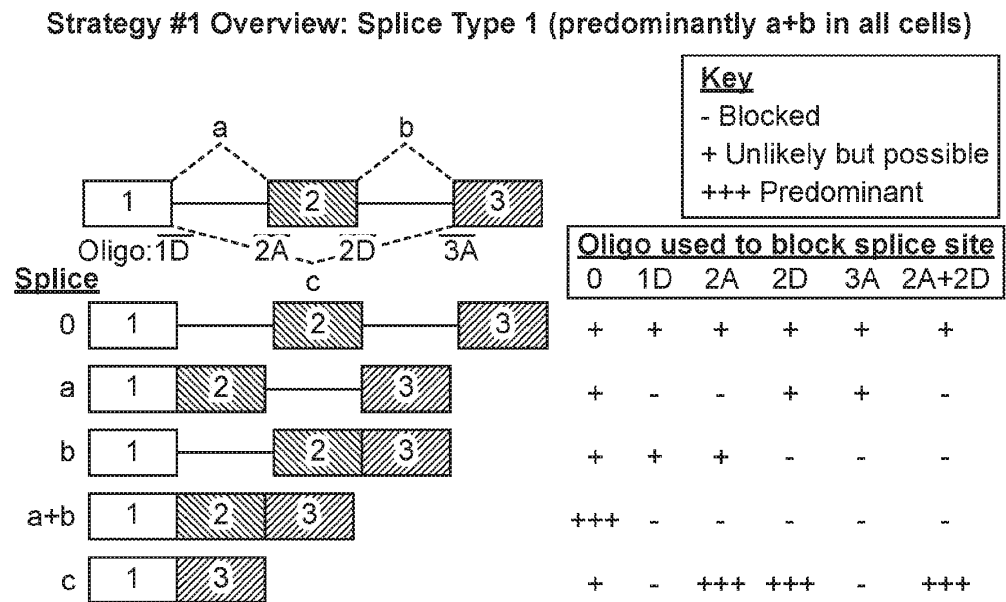


FIG. 2

Strategy #1 Overview: Splice Type 1 (predominantly a+b in all cells)

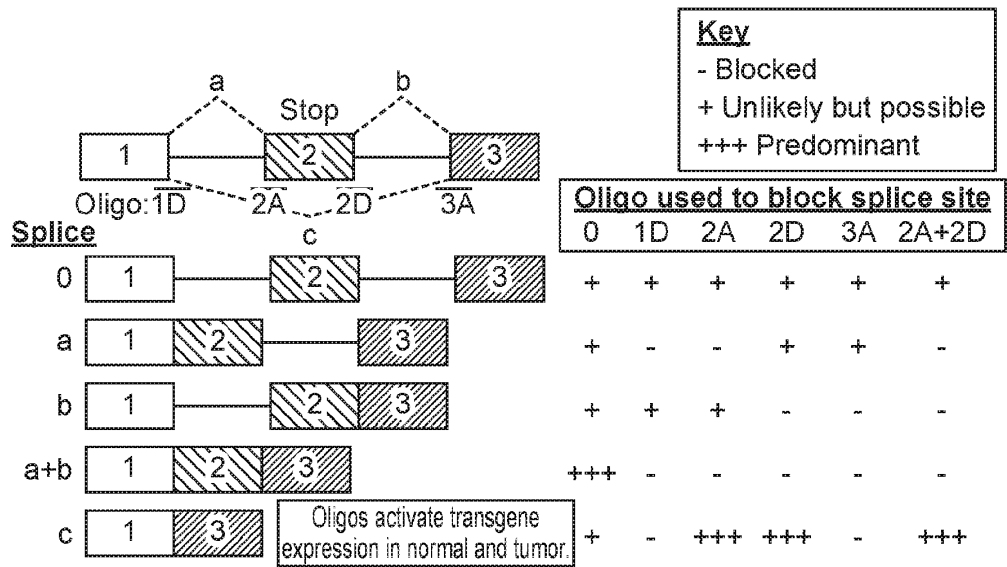


FIG. 3

Strategy #1 Construction Plan

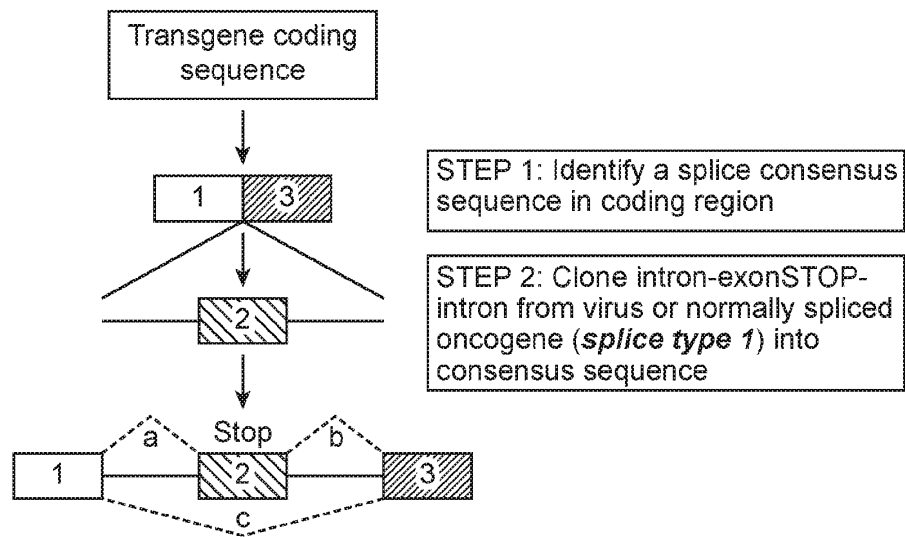


FIG. 4

Strategy #2 Overview: Splice Type 2 (a+b in normal cells, c in tumor cells)

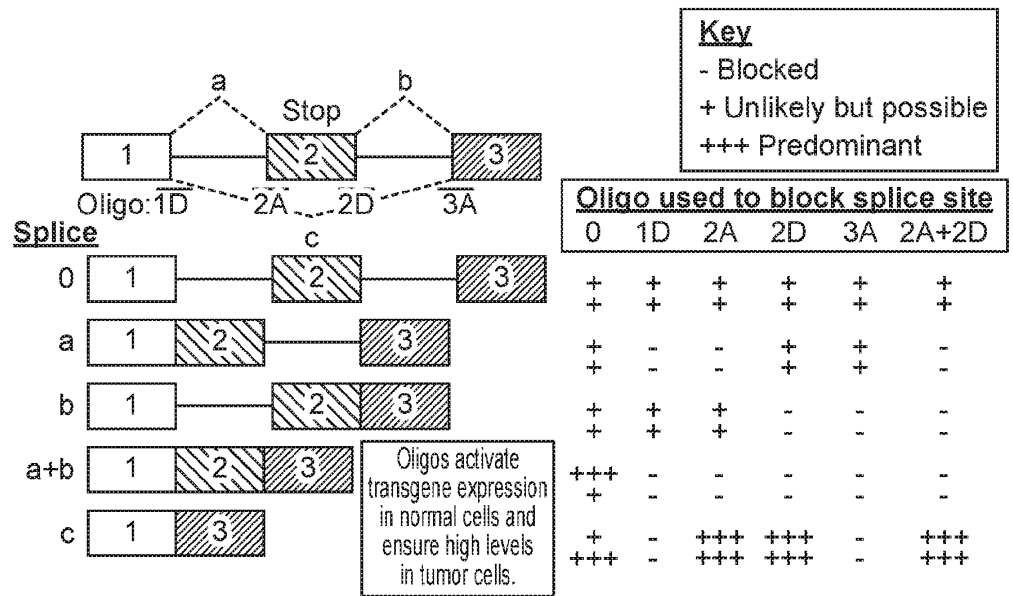


FIG. 5

Strategy #3 Overview: Splice Type 3 (c in normal cells, a+b in tumor cells)

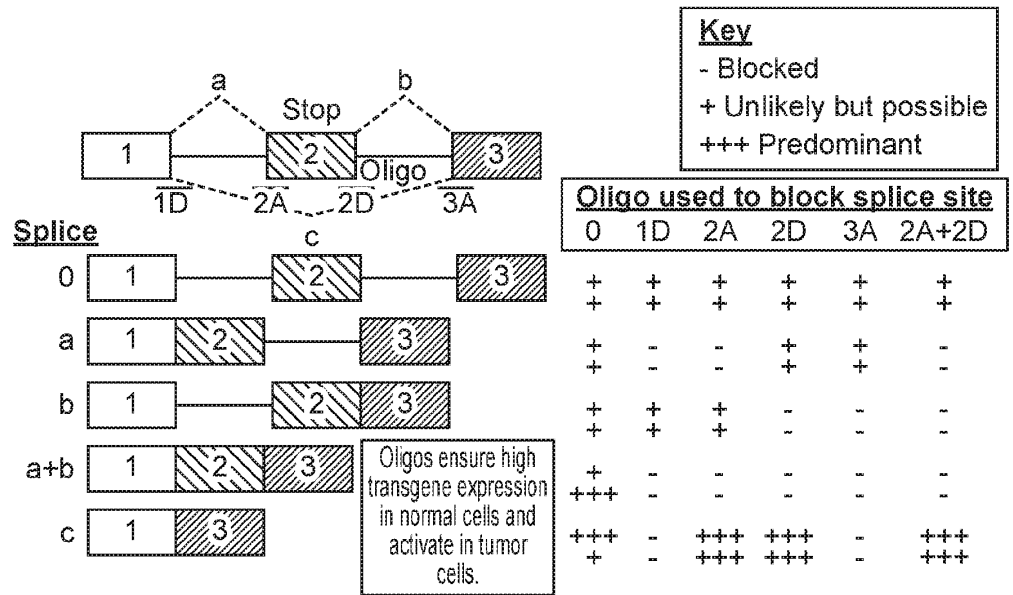


FIG. 6

CD3xGD2-HDD TransJoins: AAVs Expressing Linked Anti-CD3 and Anti-GD2 Single Chain Variable Fragments Linked to Secretion Peptides

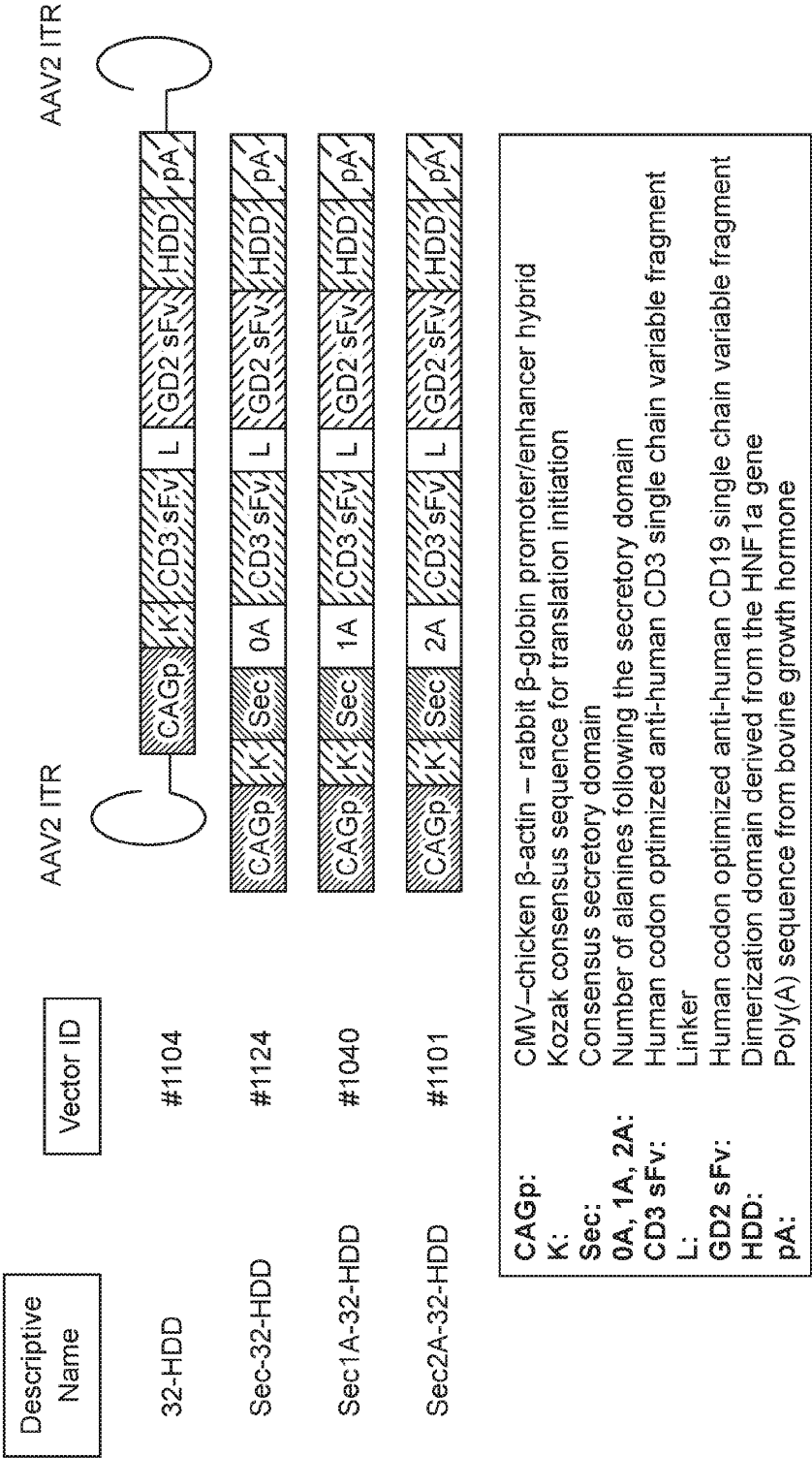


FIG. 7

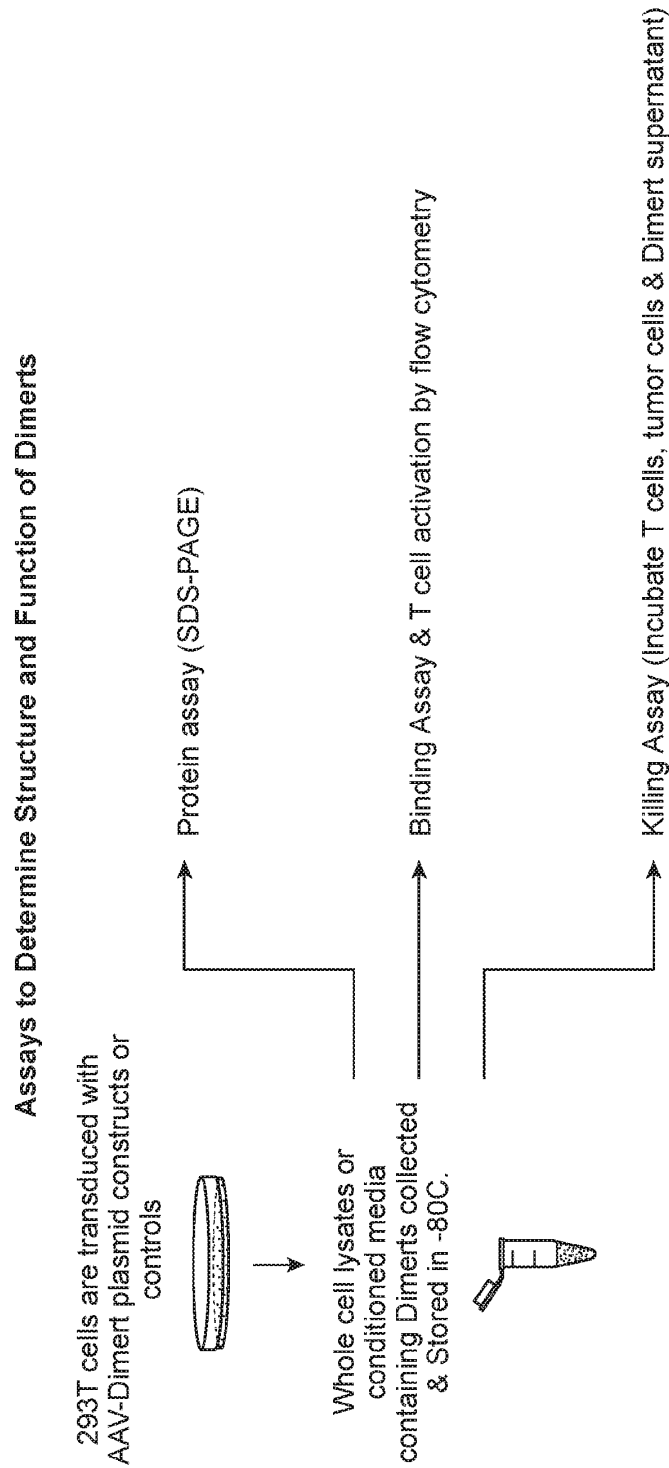


FIG. 8

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SDS-PAGE of Whole Cell Lysates from Transfected 293T Cells

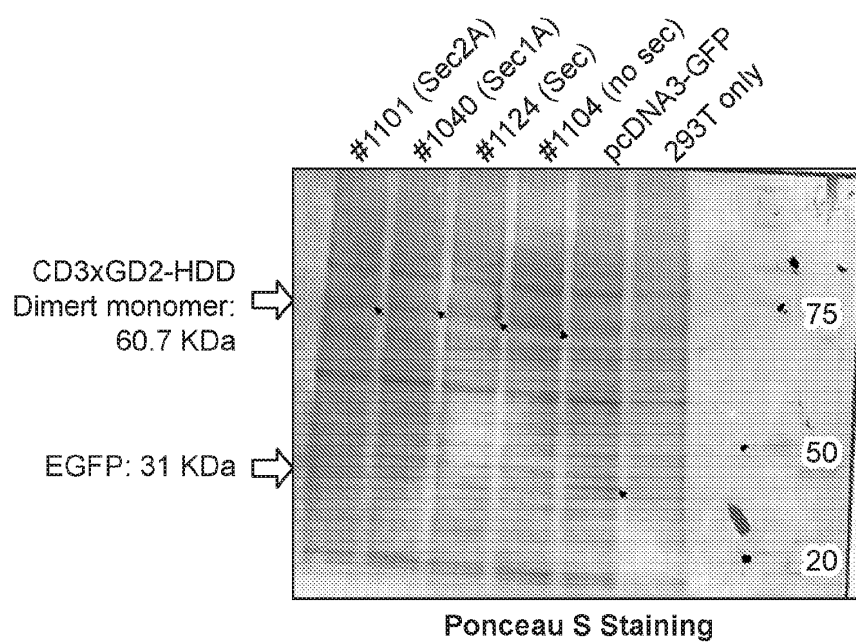


FIG. 9

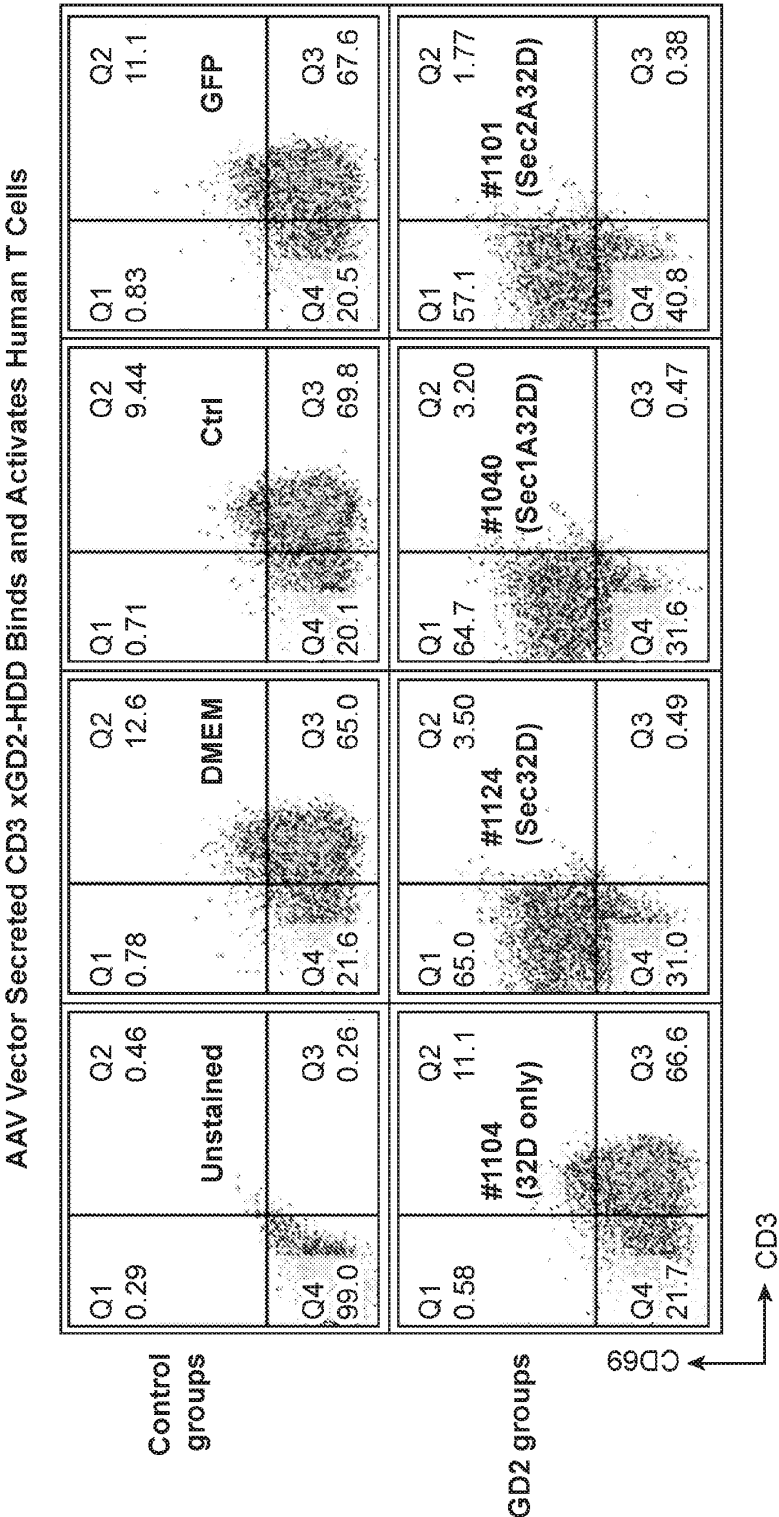


FIG. 10

Secreted CD3 xGD2-HDD Activates Human T Cells

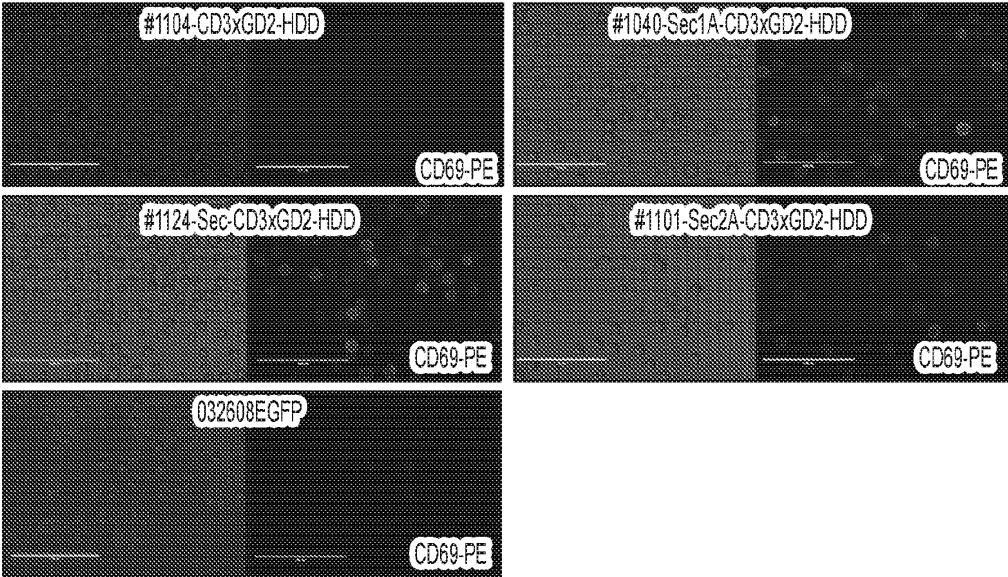


FIG. 11

Binding of CD3xGD2-HDD to T Cells is Dose-Dependent

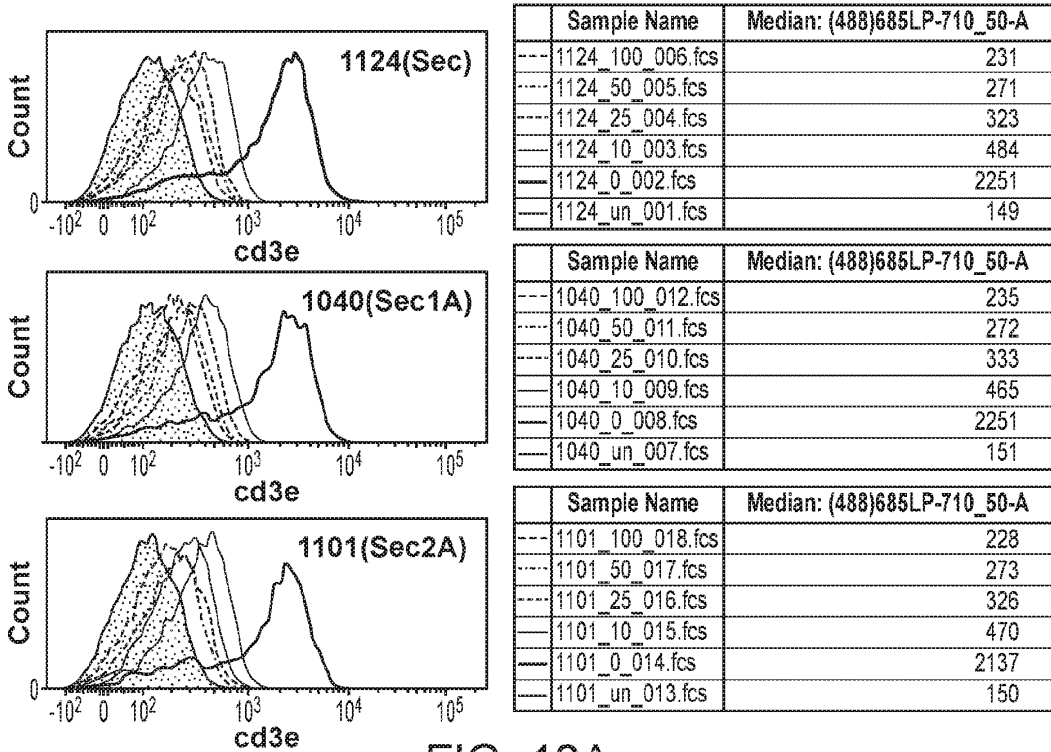


FIG. 12A

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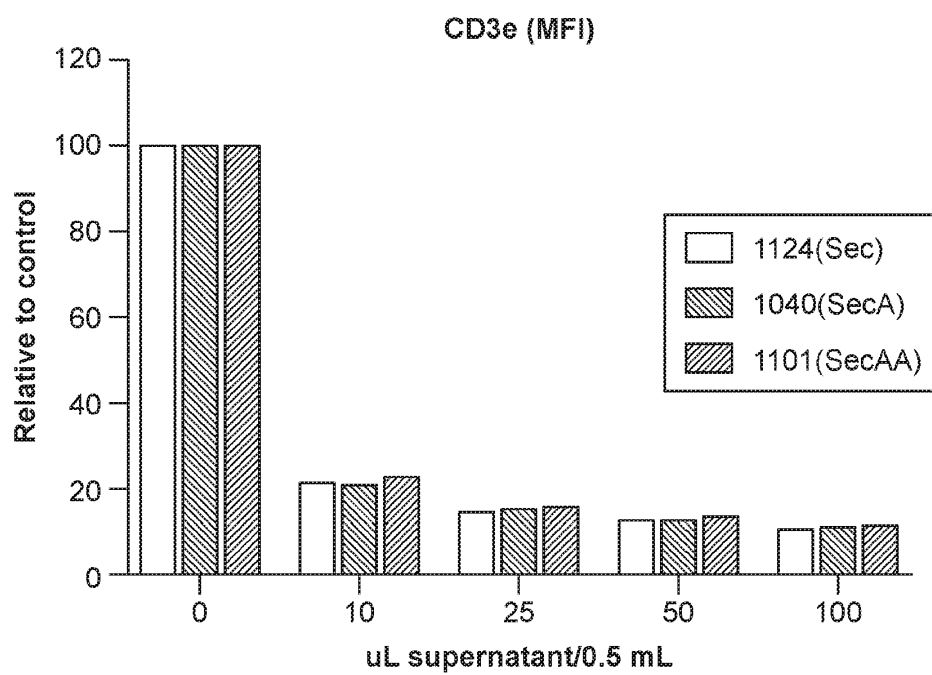


FIG. 12B

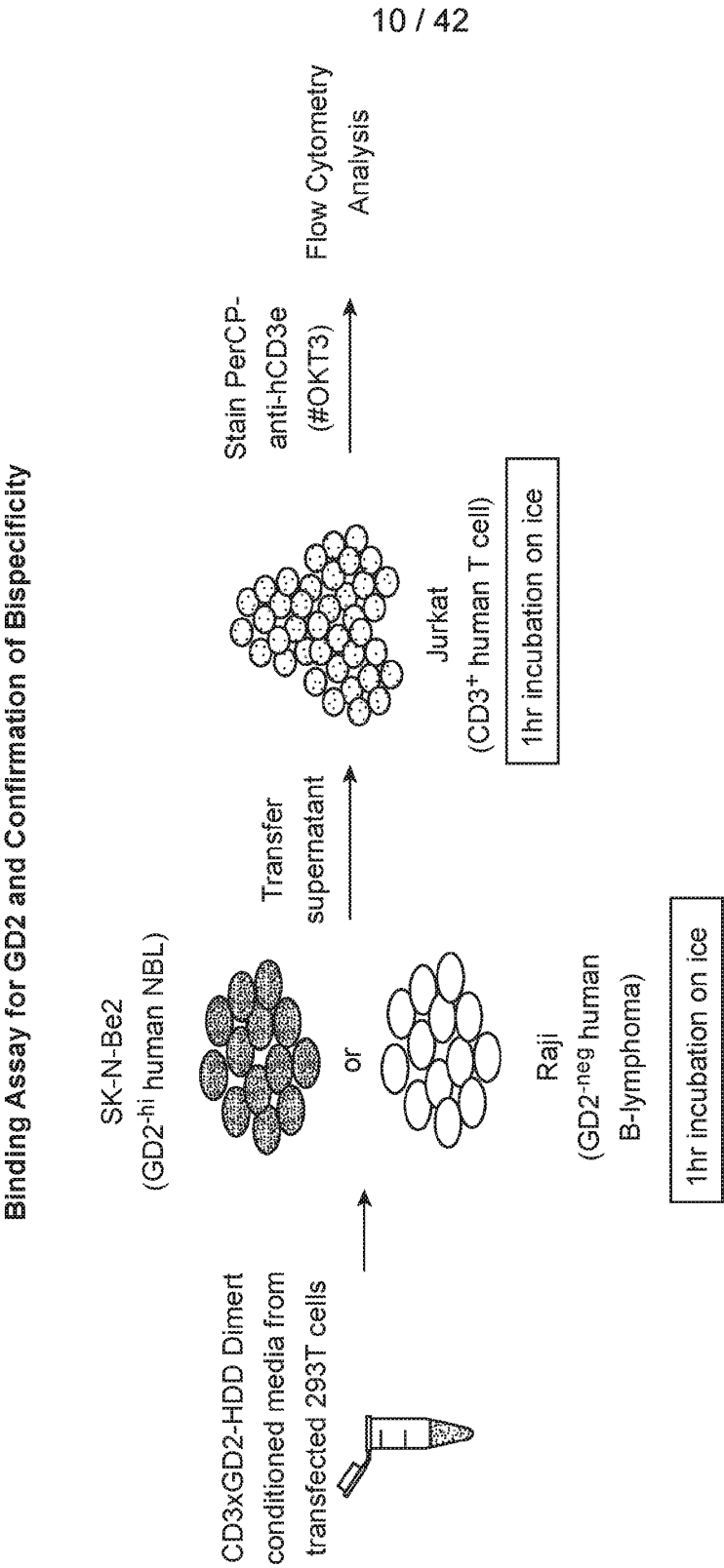
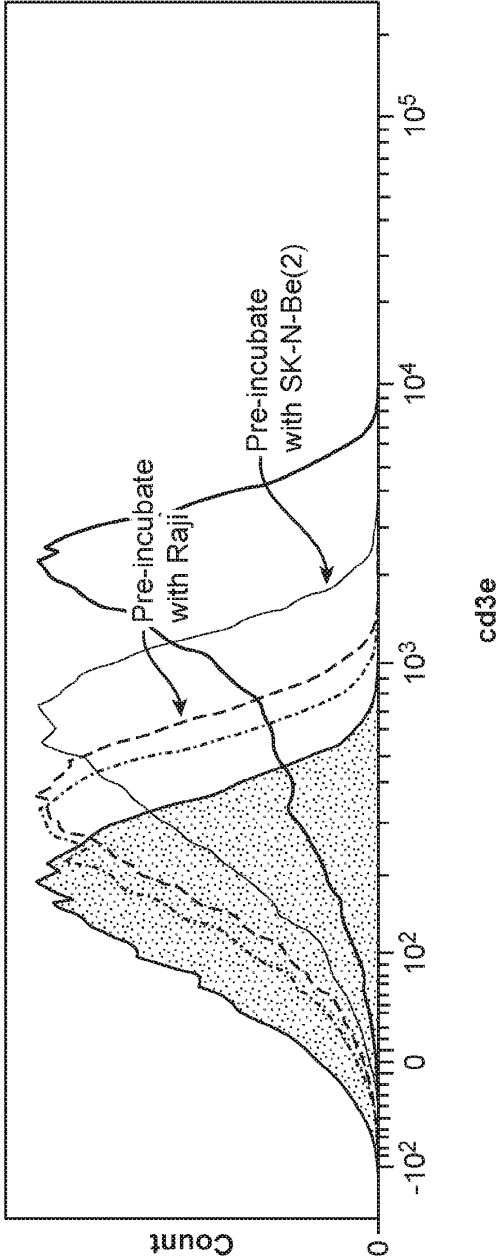


FIG. 13

CD3xGD2-HDD Binds Both CD3 and GD2



	Sample Name	Median : (488)685LP-710_50-A
-----	Jurkat_cd3e sknbe2 CD3xGD2-HDD Dimert	643
----	Jurkat_cd3e raji CD3xGD2-HDD Dimert	394
----	Jurkat_cd3e CD3xGD2-HDD Dimert	334
----	Jurkat_cd3e_002.fcs	1828
----	Jurkat_un_001.fcs	220

FIG. 14

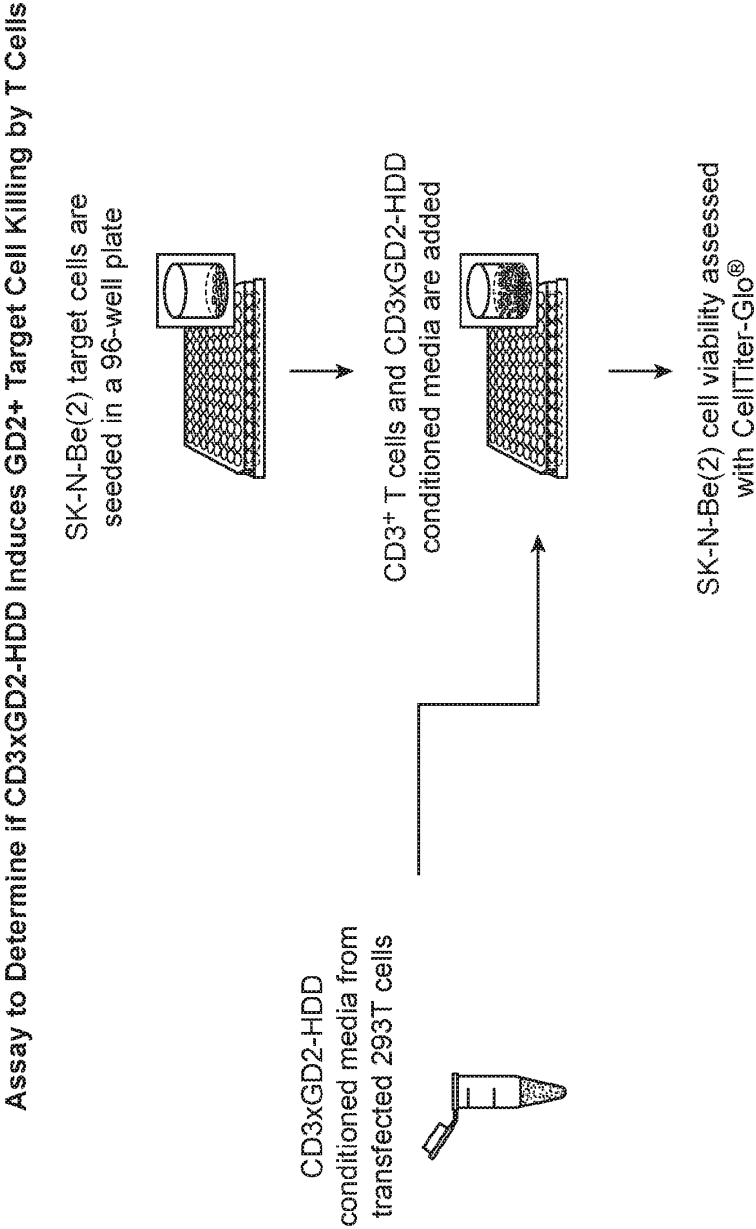


FIG. 15

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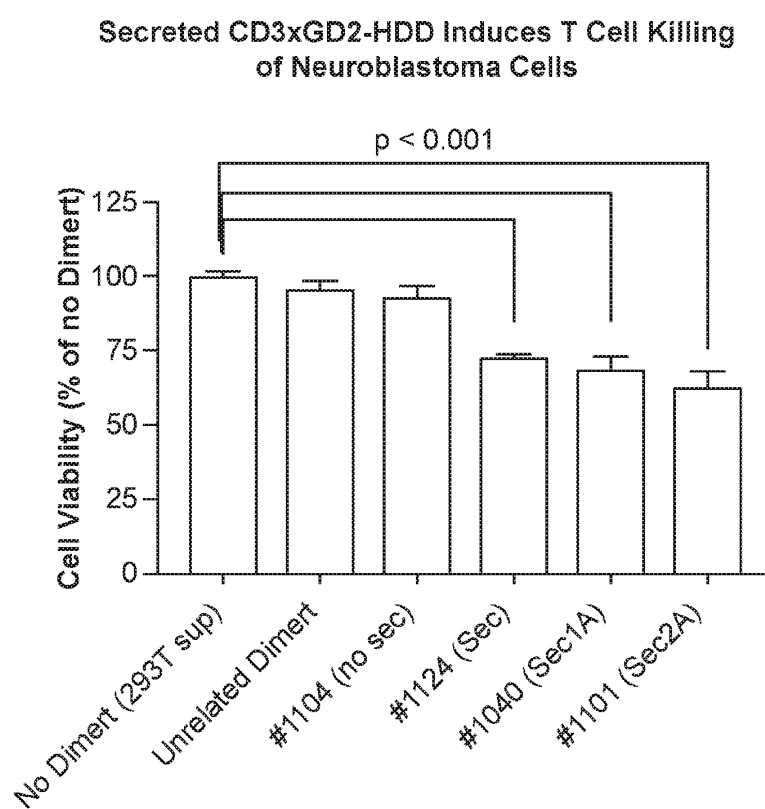


FIG. 16

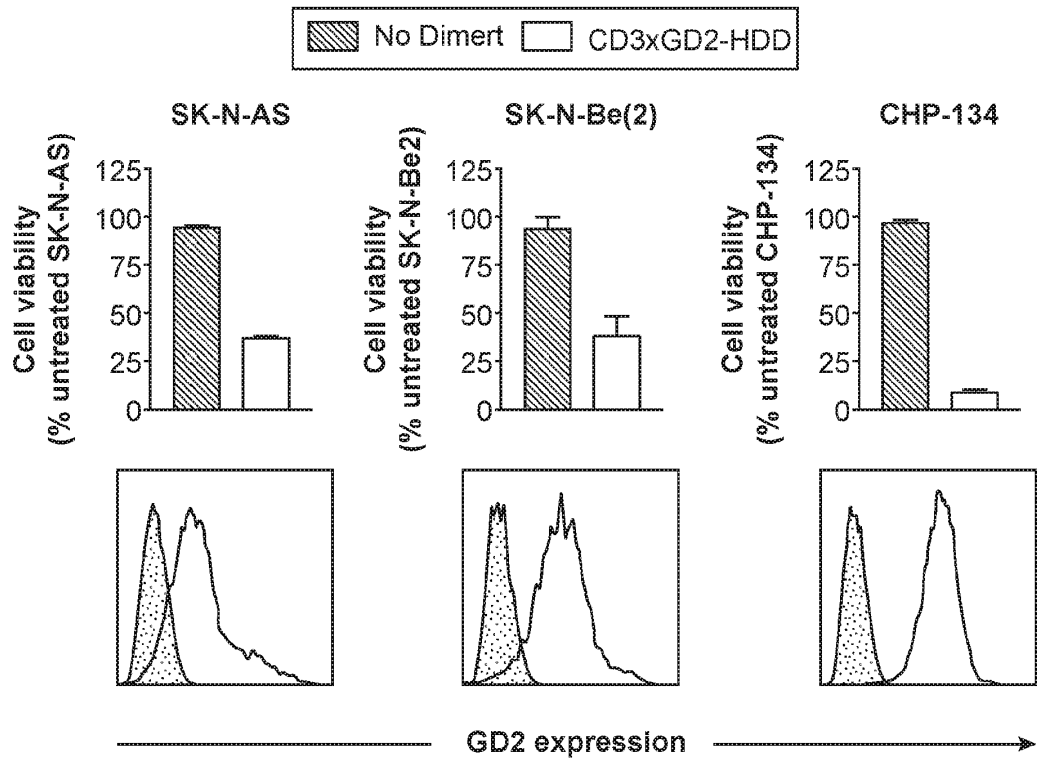


FIG. 17

CD19xCD3 TransJoin: AAV Expressing anti-CD19 and anti-CD3 Linked Single Chain Variable Fragments with Secretion Peptides

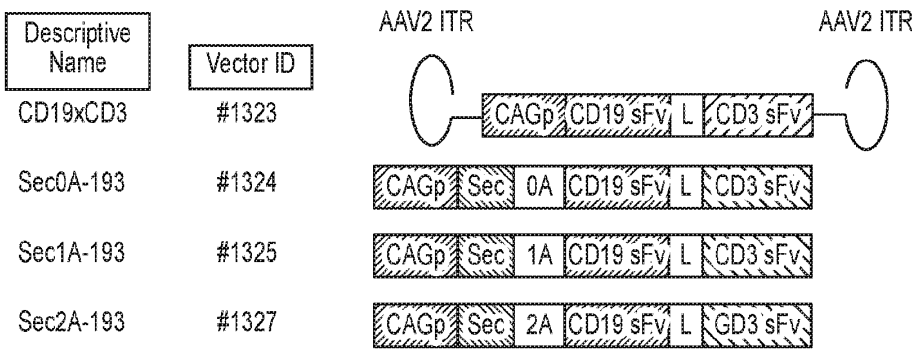


FIG. 18A

CD19 TransJoin: an exemplary genomic structure

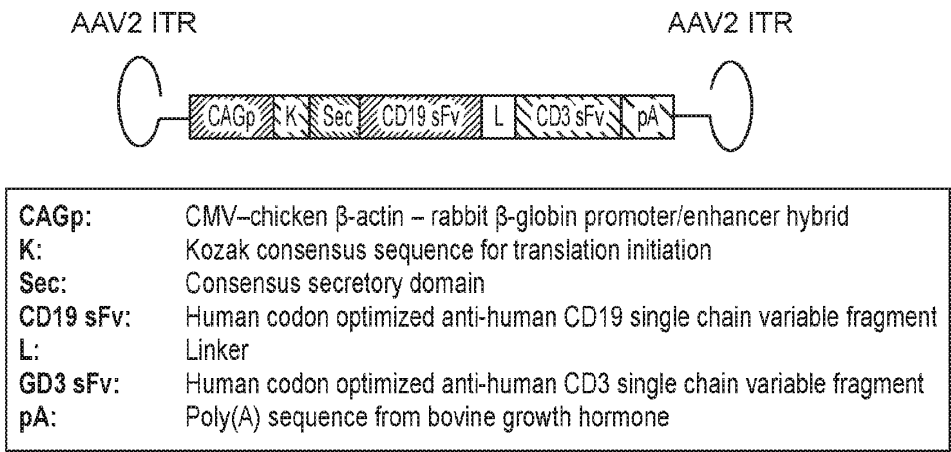


FIG. 18B

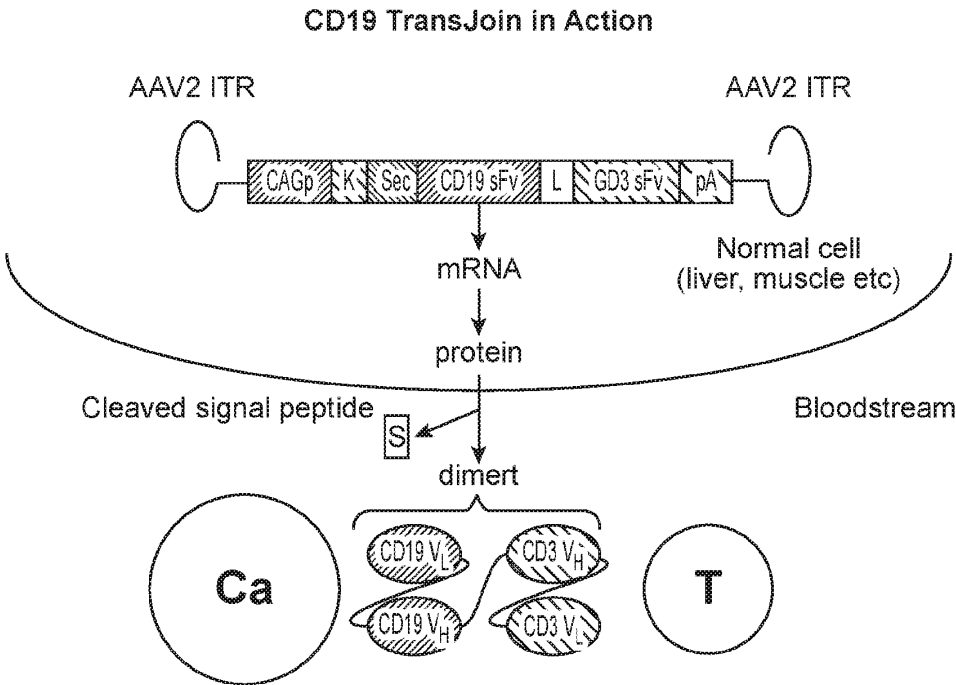


FIG. 18C

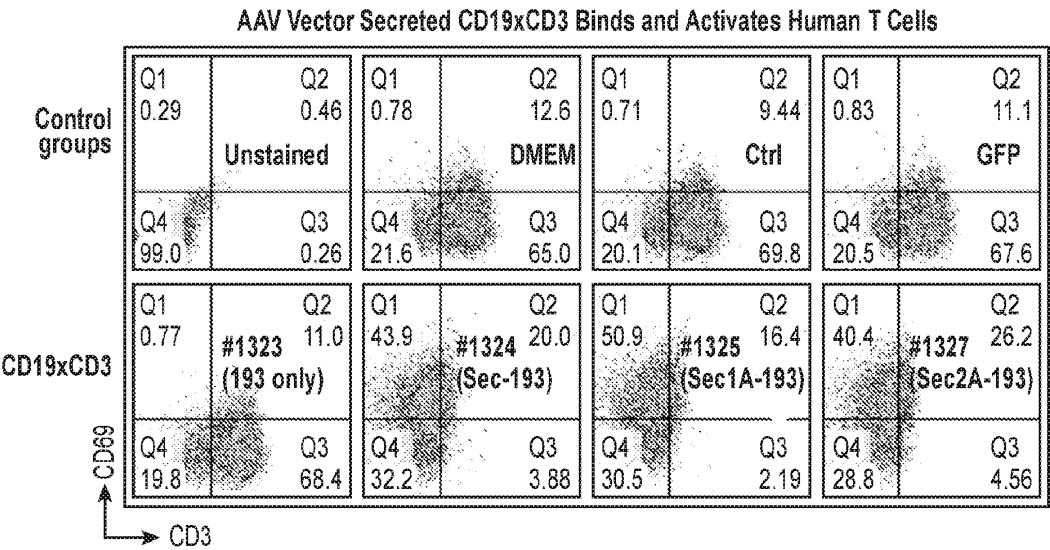


FIG. 19

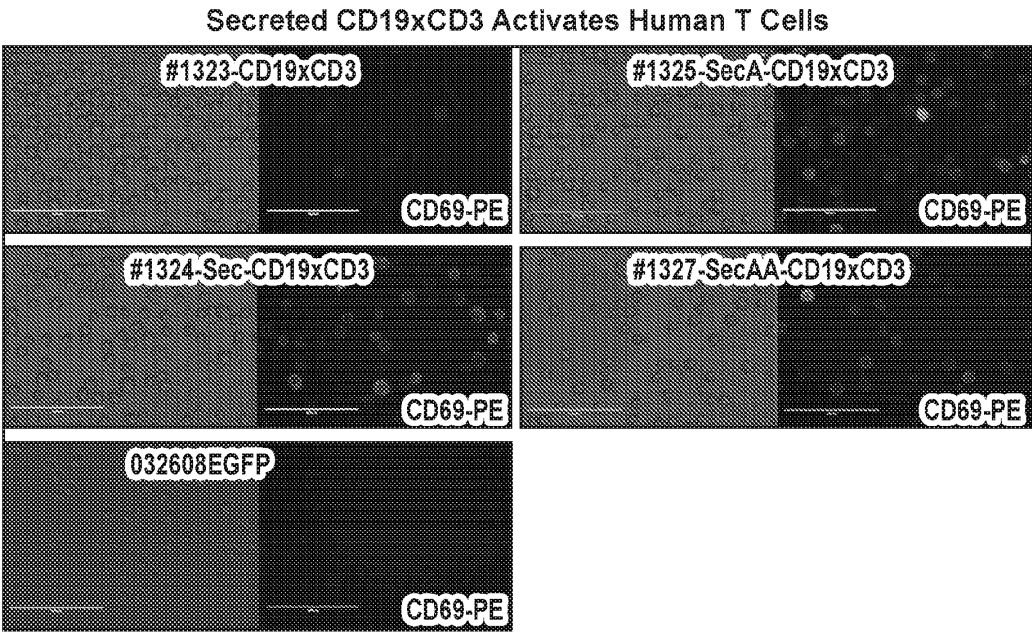


FIG. 20

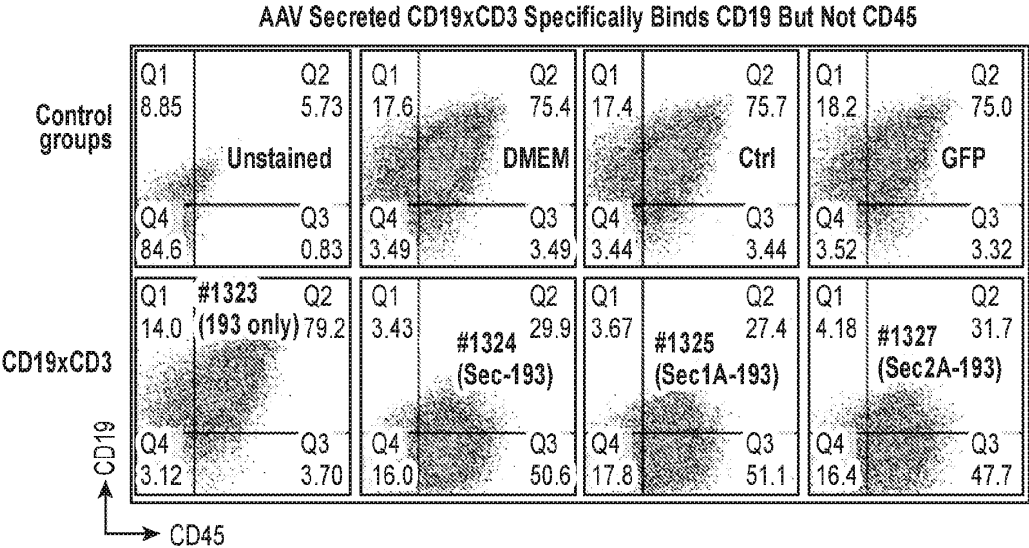


FIG. 21

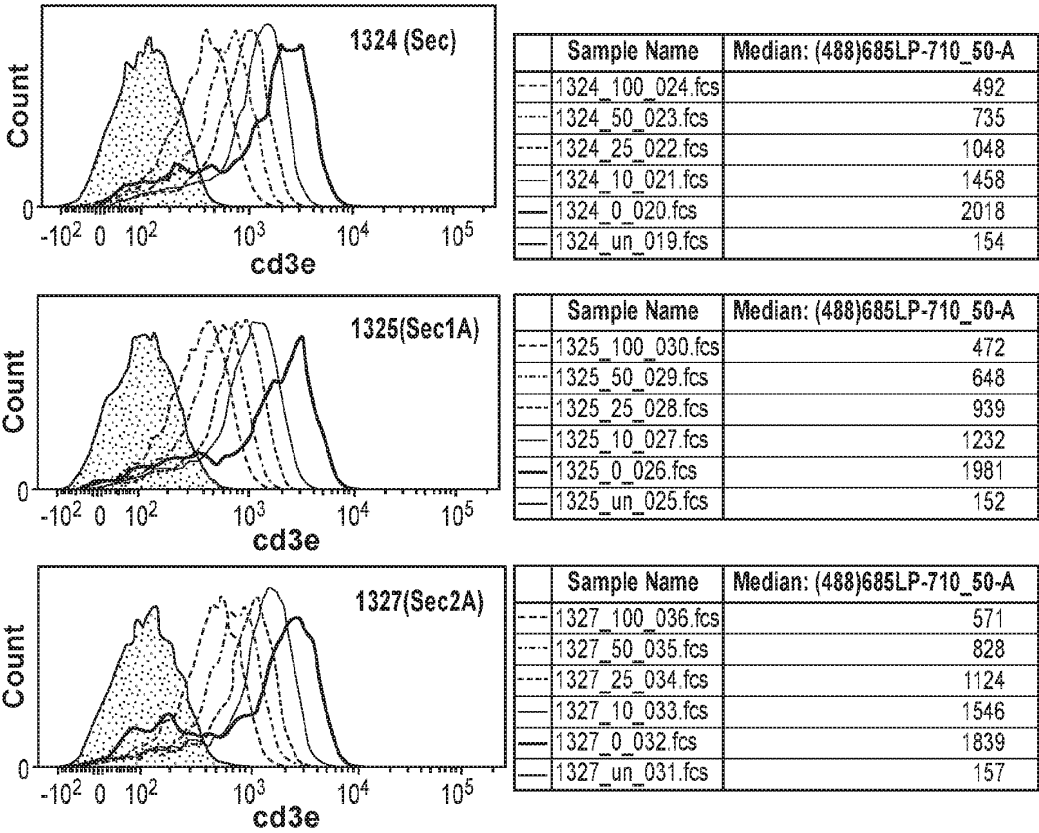


FIG. 22A

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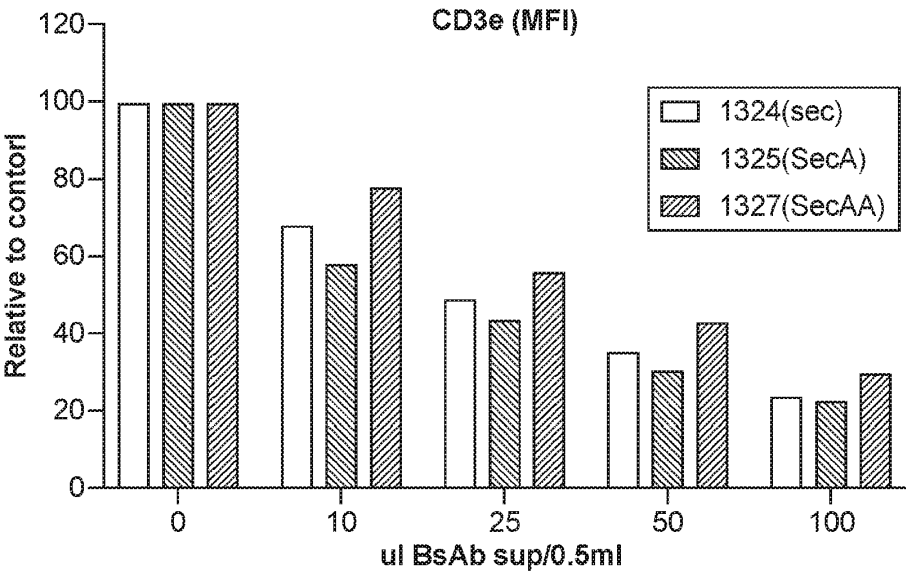
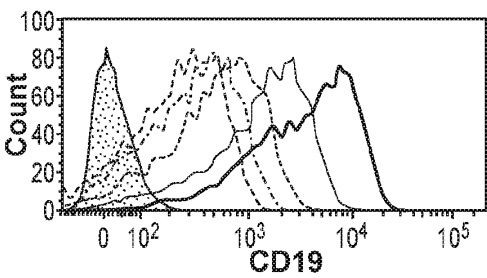
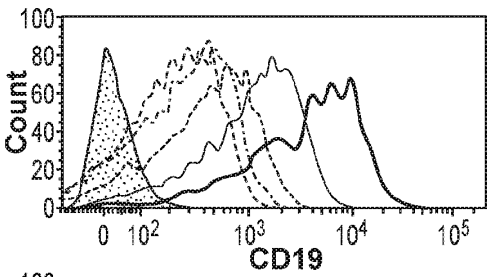


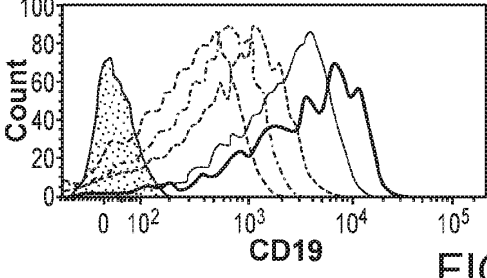
FIG. 22B



Sample Name	Median: (633)655LP-670_14-A
1324_100_001.fcs	239
1324_50_002.fcs	325
1324_25_003.fcs	542
1324_10_004.fcs	1504
1324_0_005.fcs	4129
1324_UN_006.fcs	5.50



Sample Name	Median: (633)655LP-670_14-A
1325_100_007.fcs	210
1325_50_008.fcs	271
1325_25_009.fcs	442
1325_10_010.fcs	1202
1325_0_011.fcs	4296
1325_UN_012.fcs	5.63



Sample Name	Median: (633)655LP-670_14-A
1327_100_013.fcs	273
1327_50_014.fcs	460
1327_25_015.fcs	768
1327_10_016.fcs	2331
1327_0_017.fcs	3904
1327_UN_018.fcs	6.15

FIG. 23A

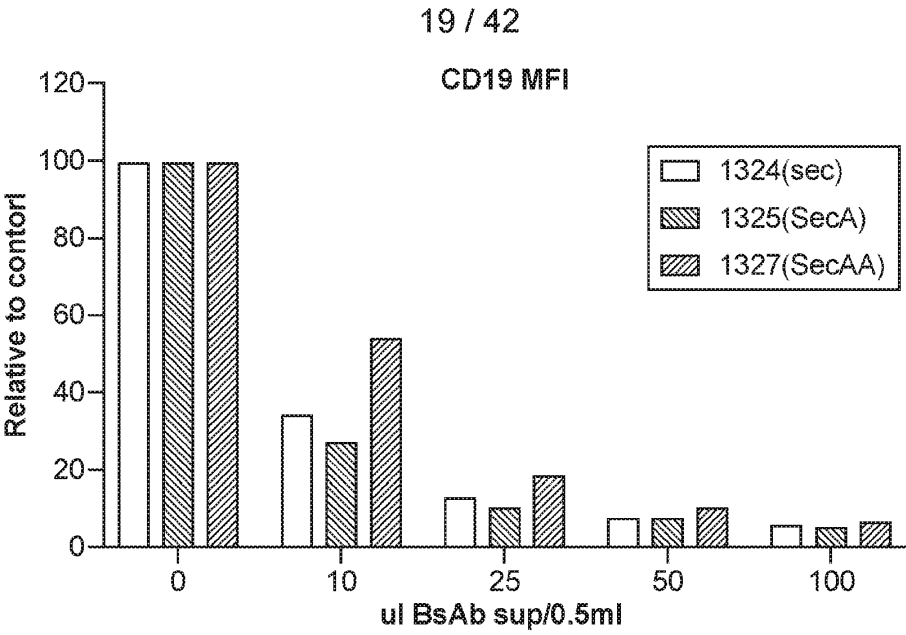


FIG. 23B

CD3 Dimerts Activate T Cells With Anti-CD28 Co-Stimulation
Better Than Anti-CD3 Antibodies

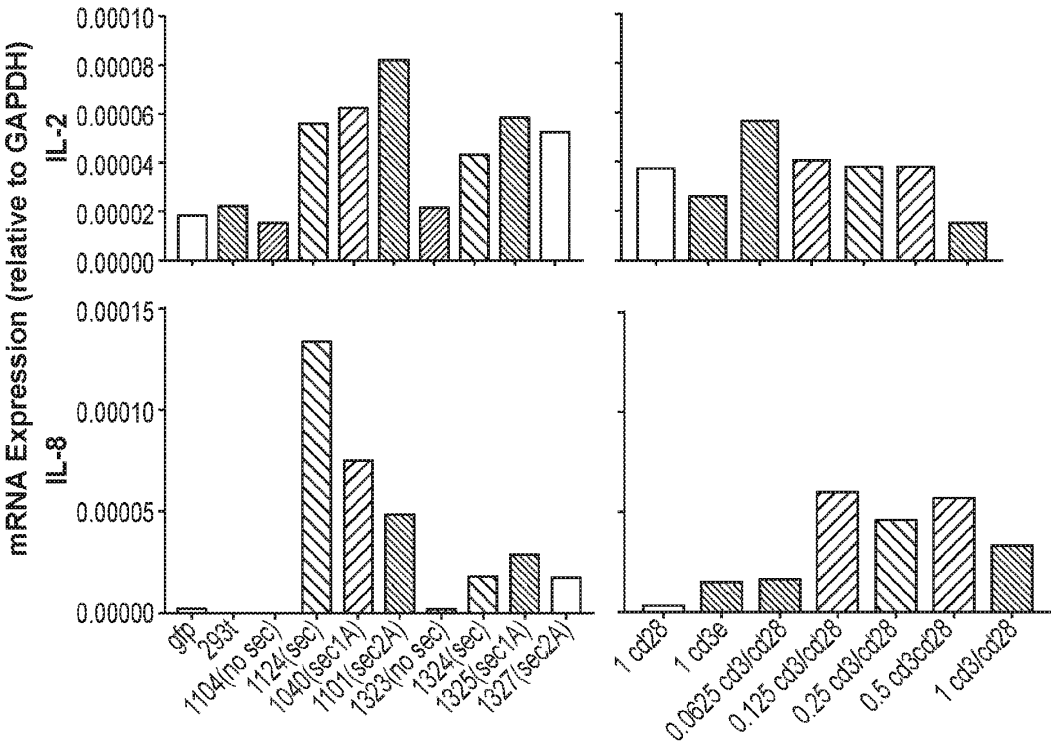


FIG. 24

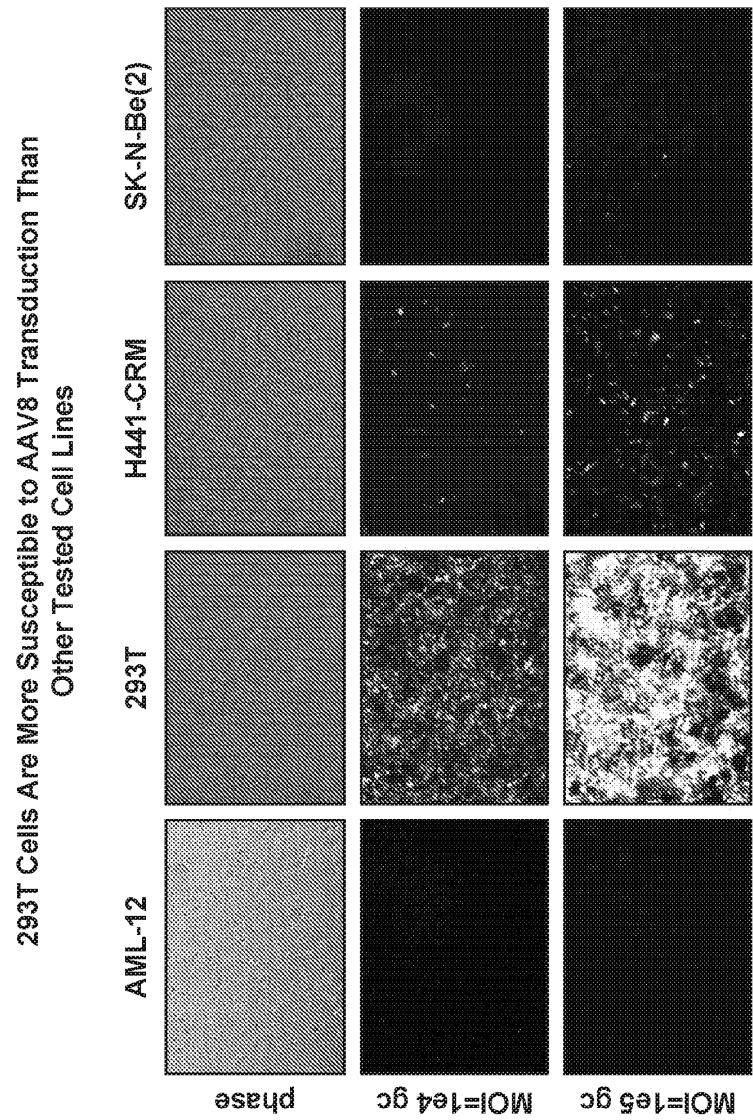


FIG. 25

Dimert Concentration in Supernatant from AAV8-infected Cells is
Dependent on Dose and Transduction Efficiency

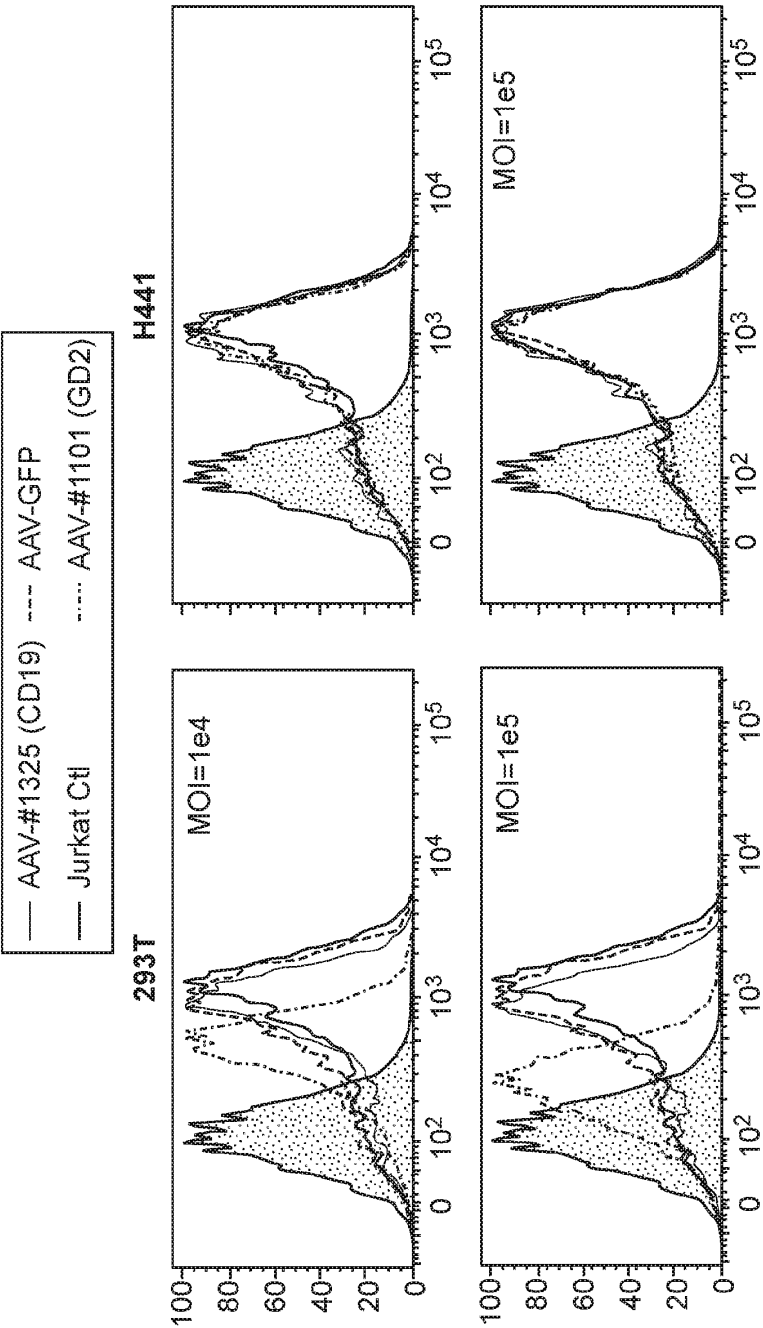


FIG. 26

A Single Intravenous Injection of CD19xCD3 TransJoin Selectively Eliminates B Cells in Humanized Mice

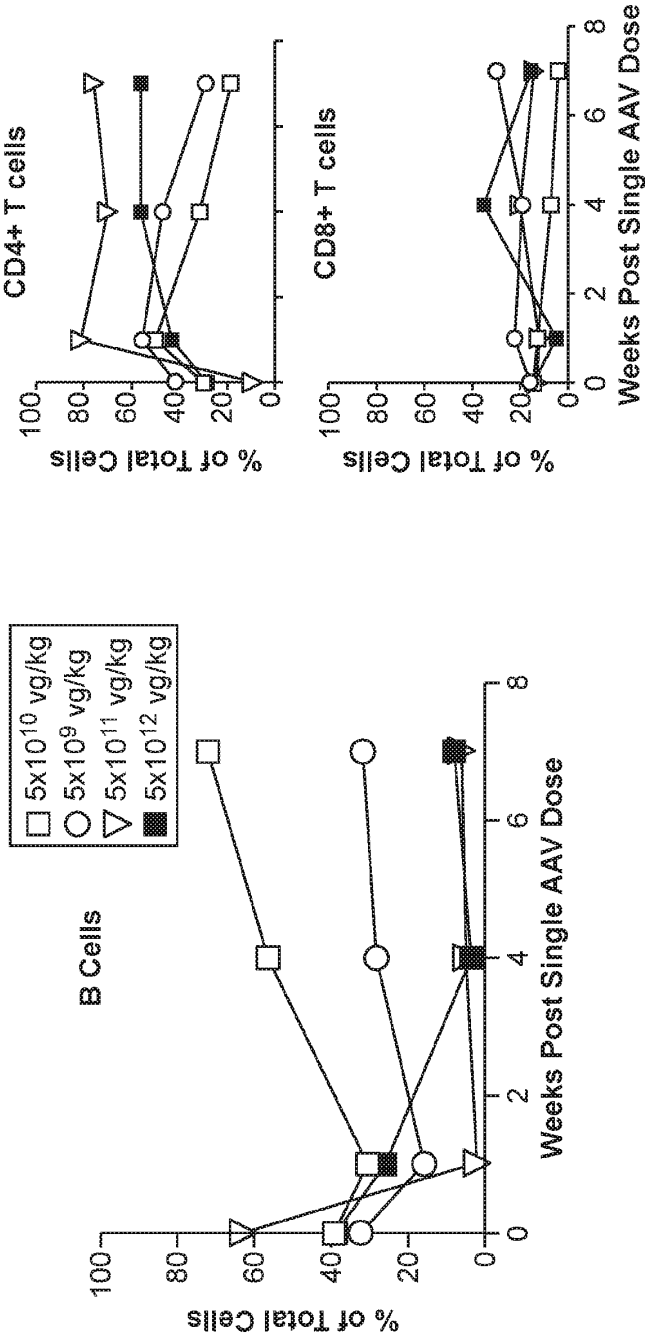


FIG. 27

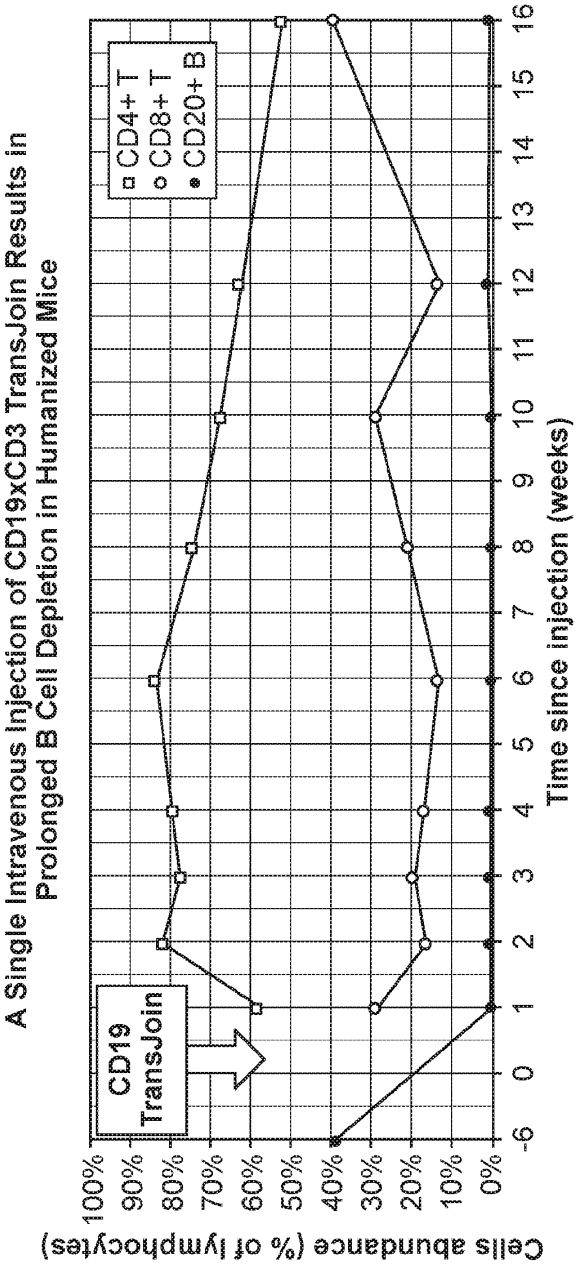


FIG. 28

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A Single Intravenous Injection of CD19xCD3 TransJoin Eliminates
CD19+ Lymphoma in Humanized Mice
AAVCD3xCD19 or AAVGFP
(5.0×10^{12} gc/Kg)

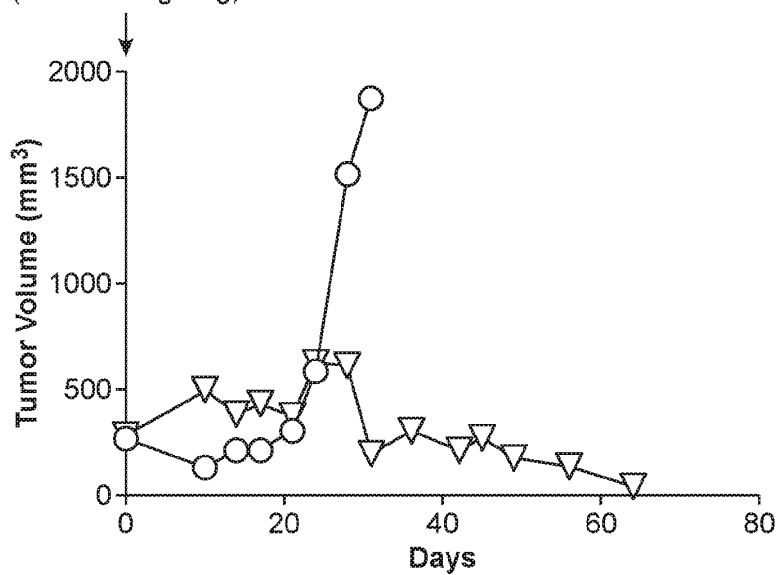


FIG. 29

OncoSkip and TransSkip: Novel Technologies Designed to Simultaneously Target
Oncogene Expression and Activate Therapeutic Transgene Expression

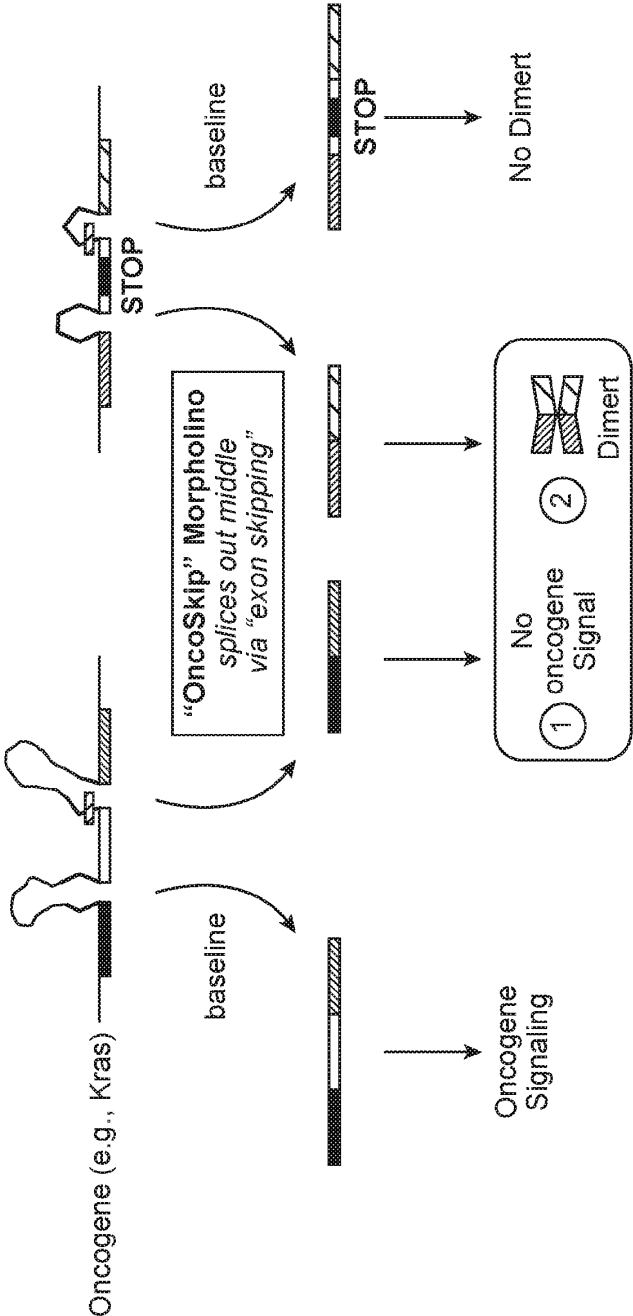


FIG. 30

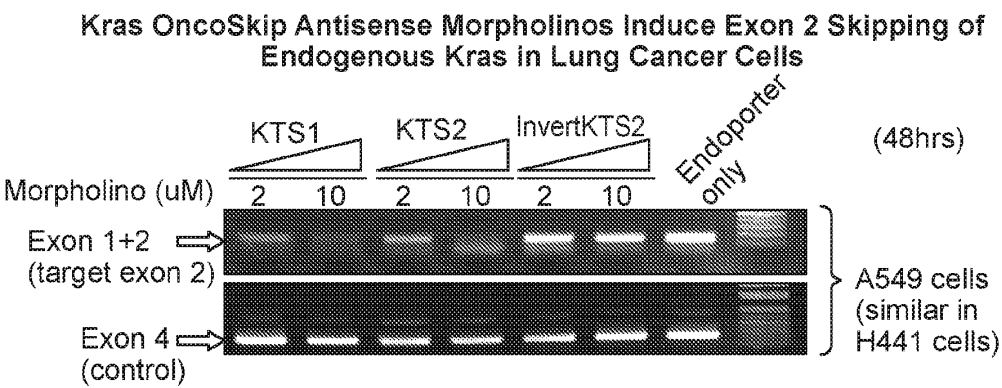


FIG. 31

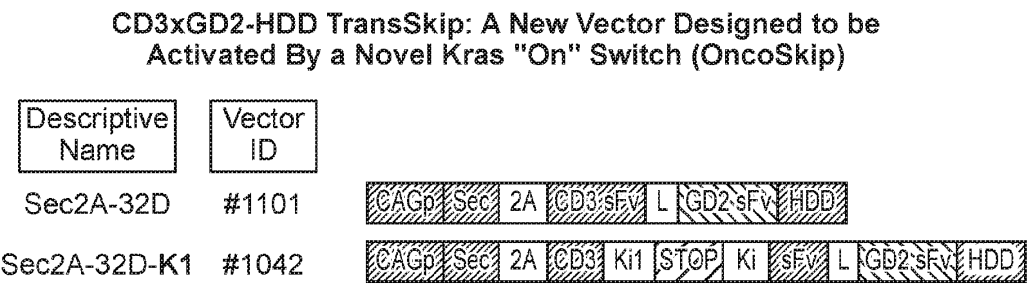


FIG. 32

Strategy for Testing Activity of OncoSkip and TransSkip

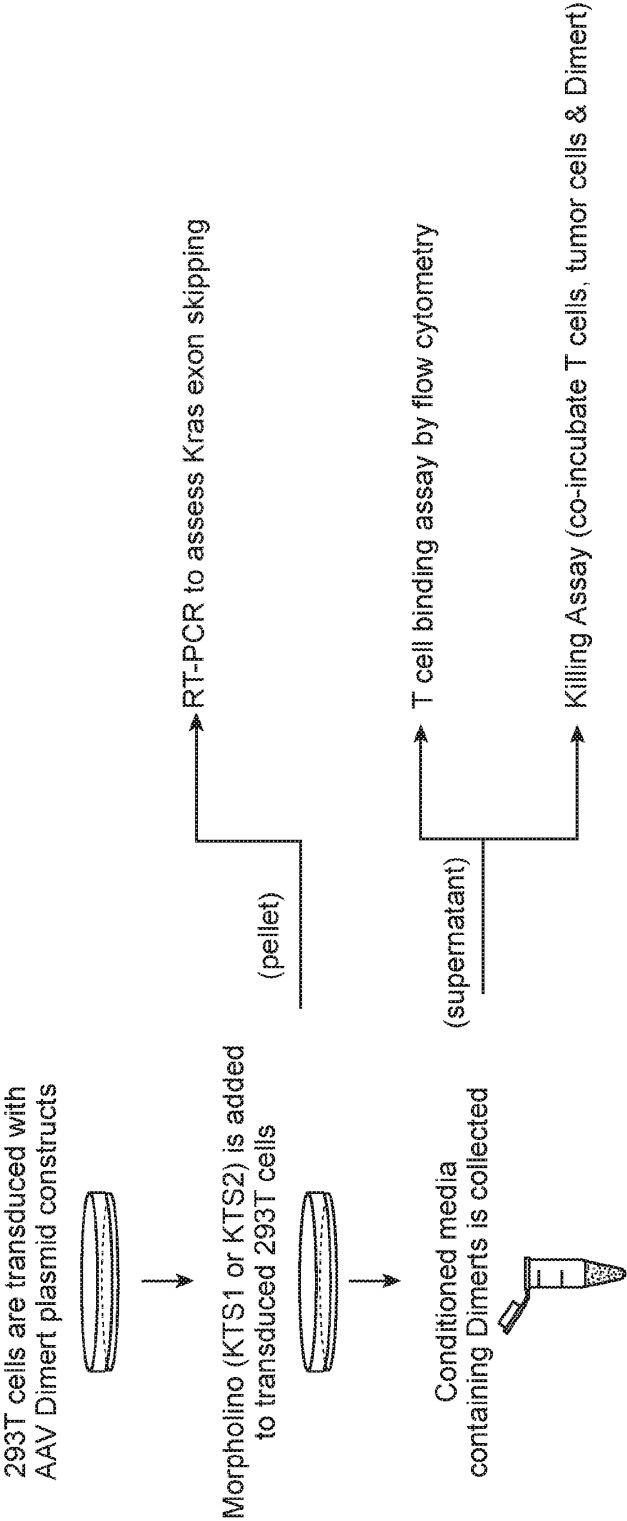


FIG. 33

Antisense Morpholinos Induce Exon Skipping
of the CD3xGD2-HDD TransSkip Transgene

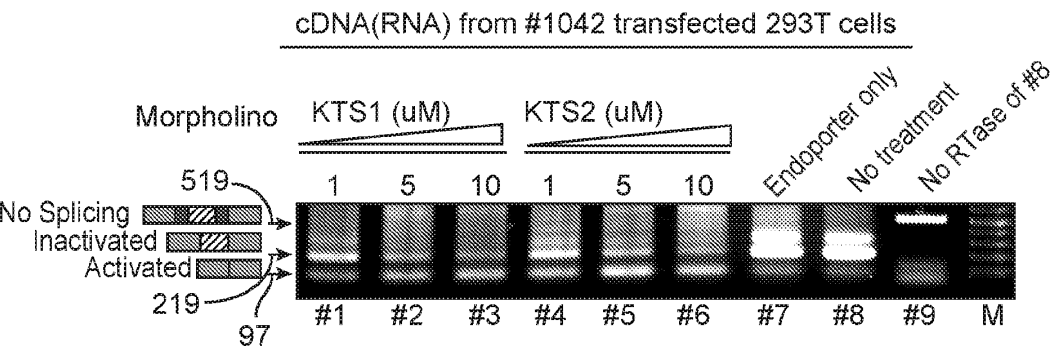
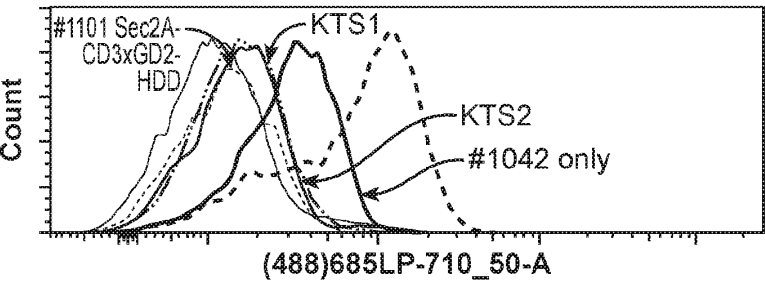


FIG. 34

Kras OncoSkip Induces Secreted Expression of CD3xGD2-HDD
Dimert in Cells Transfected With the CD3xGD2-HDD
TransSkip AAV Vector



	Sample Name	Median: (488)685LP-710_50-A
---	Jurkat_cd3e_002.fcs	1007
----	Jurkat_1101_003.fcs	172
—	Jurkat_1042 only_008.fcs	403
----	Jurkat_1042 with kts1-1_004.fcs	194
—	Jurkat_1042 with kts2-1_006.fcs	204
—	Jurkat_unstain_001.fcs	144

FIG. 35

Exon Skipping of CD3xGD2-HDD TransSkip by Kras OncoSkip is an On-Target Effect

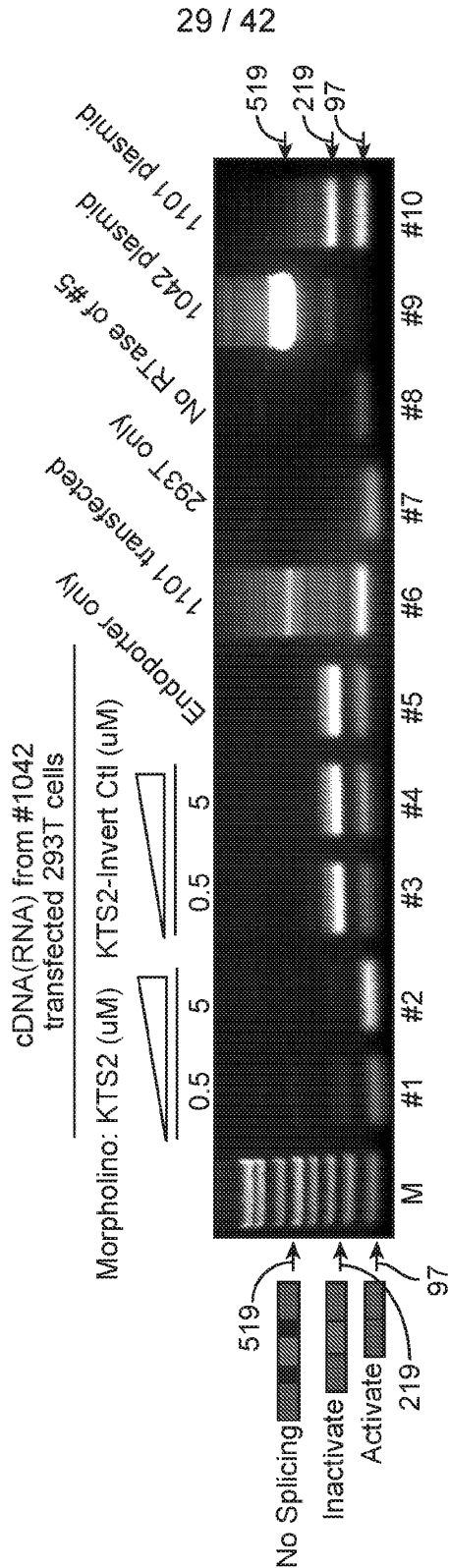


FIG. 36

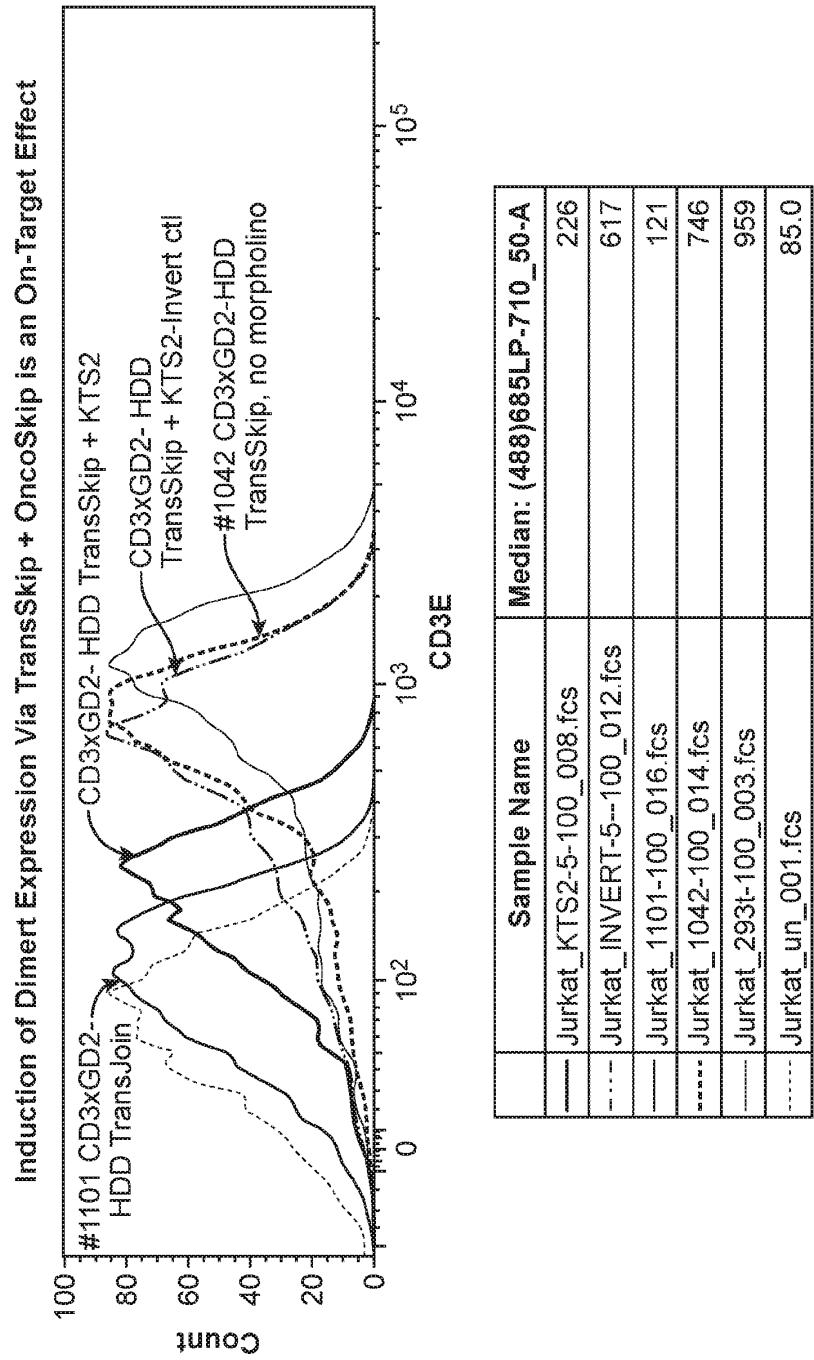


FIG. 37

AAV Genome Maps of CD3xGD2-HDD TransSkip Splice Variants
(Ki2-5 are variants of the upstream splice binding site)

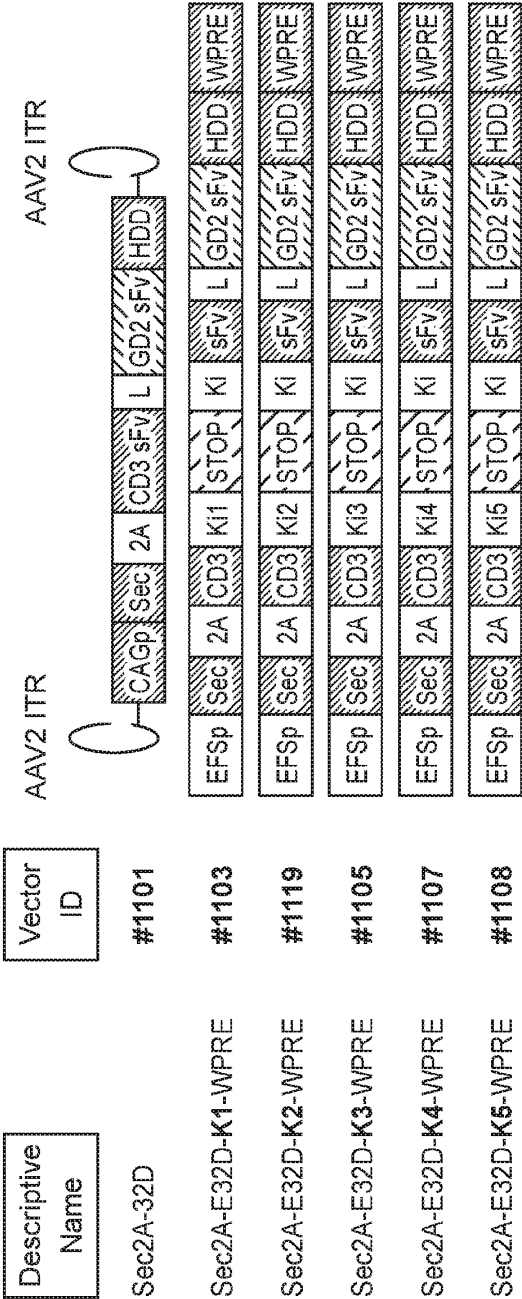


FIG. 38

CD3xGD2-HDD TransSkip Splice Variants K3 Eliminates Baseline Yet
Maintains Inducible Exon Skipping

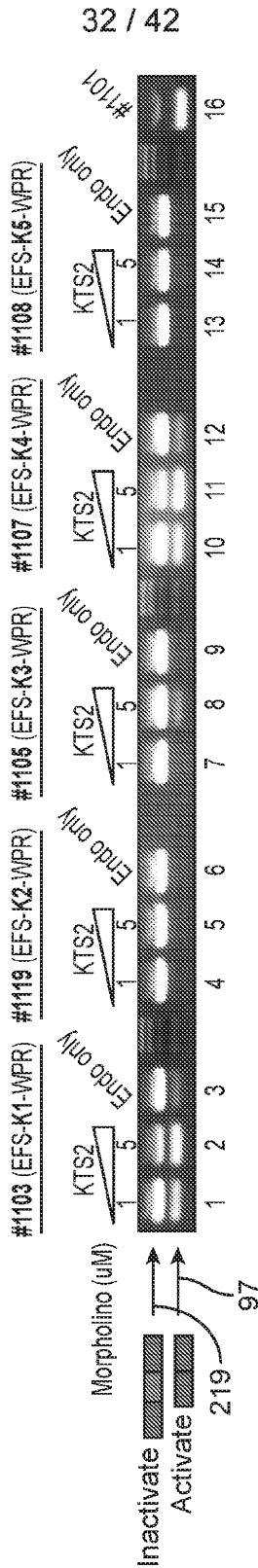


FIG. 39

CD3xGD2-HDD TransSkip Variant K3 Shows No Baseline Dimert Production
But is Most Inducible by the Kras Antisense Morpholino OncoSkip KTS2

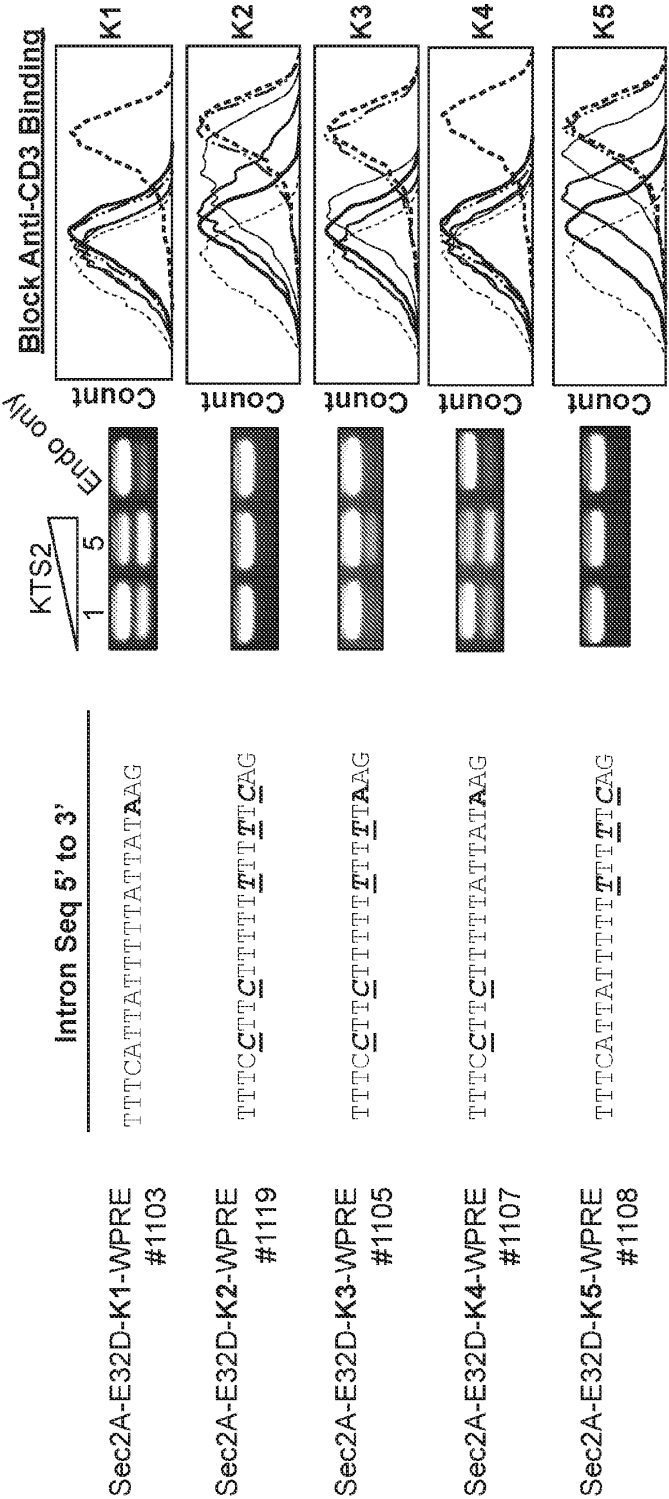


FIG. 40

OncoSkip-Mediated Induction of Dimert Expression from
CD3xGD2-HDD TransSkip Variants K3 and K5 is an On-Target Effect

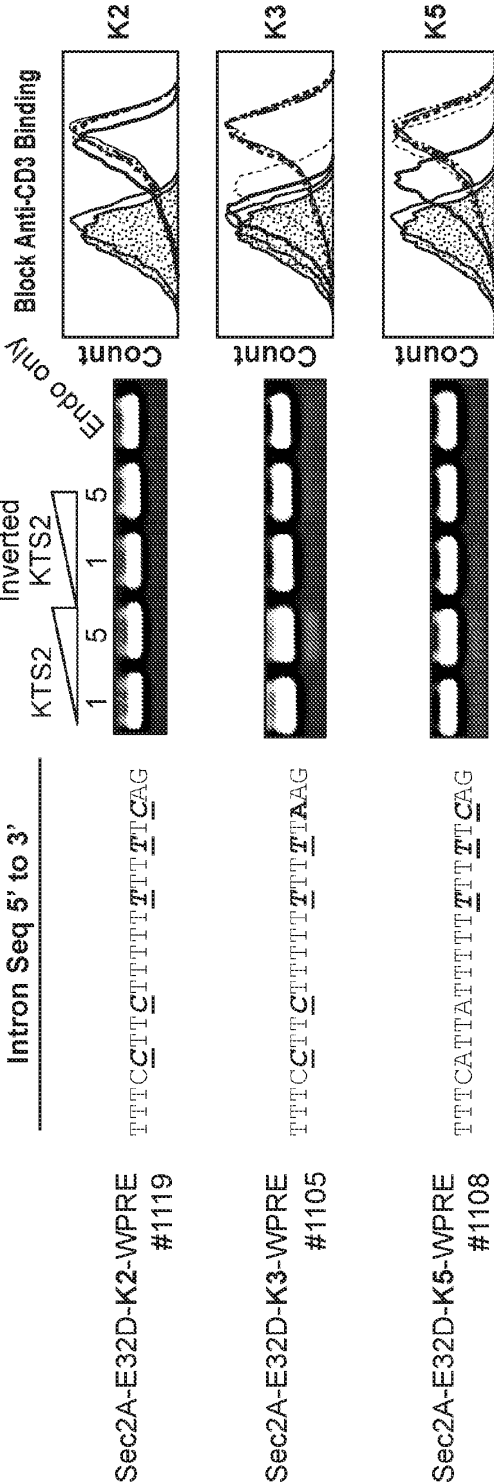
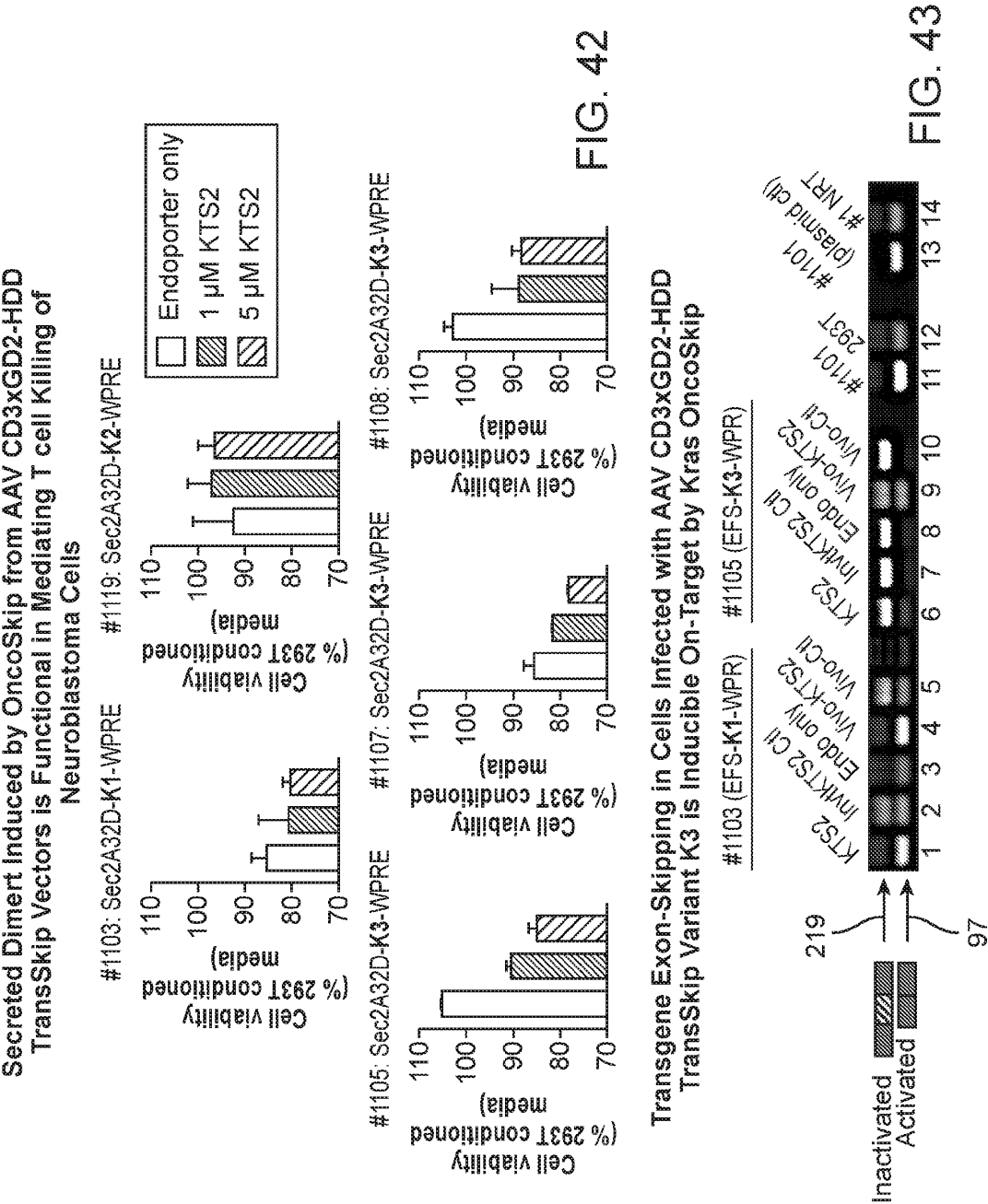


FIG. 41



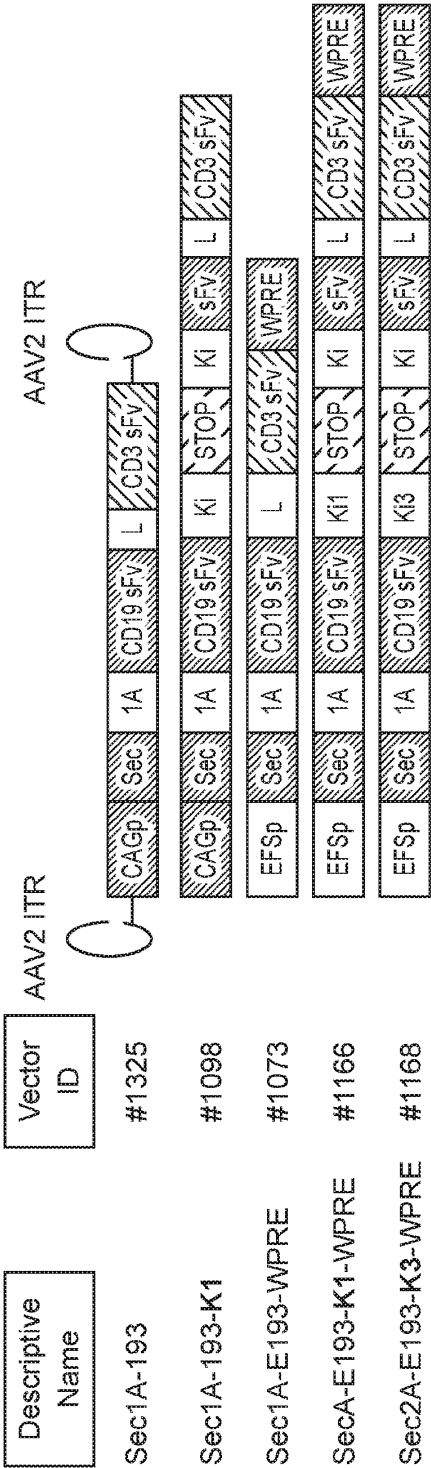


FIG. 44A

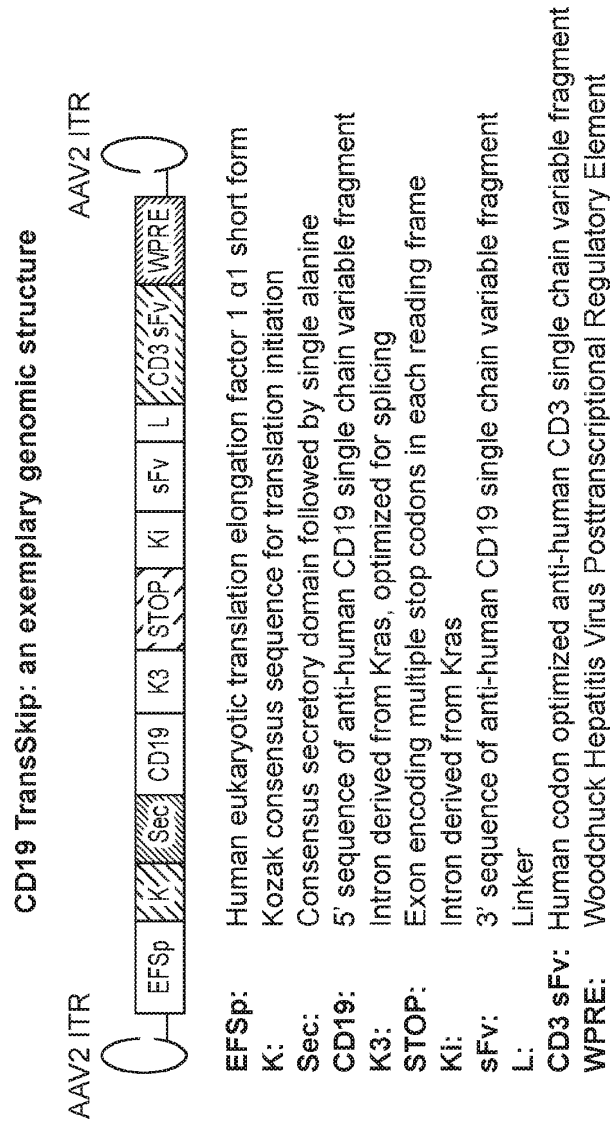


FIG. 44B

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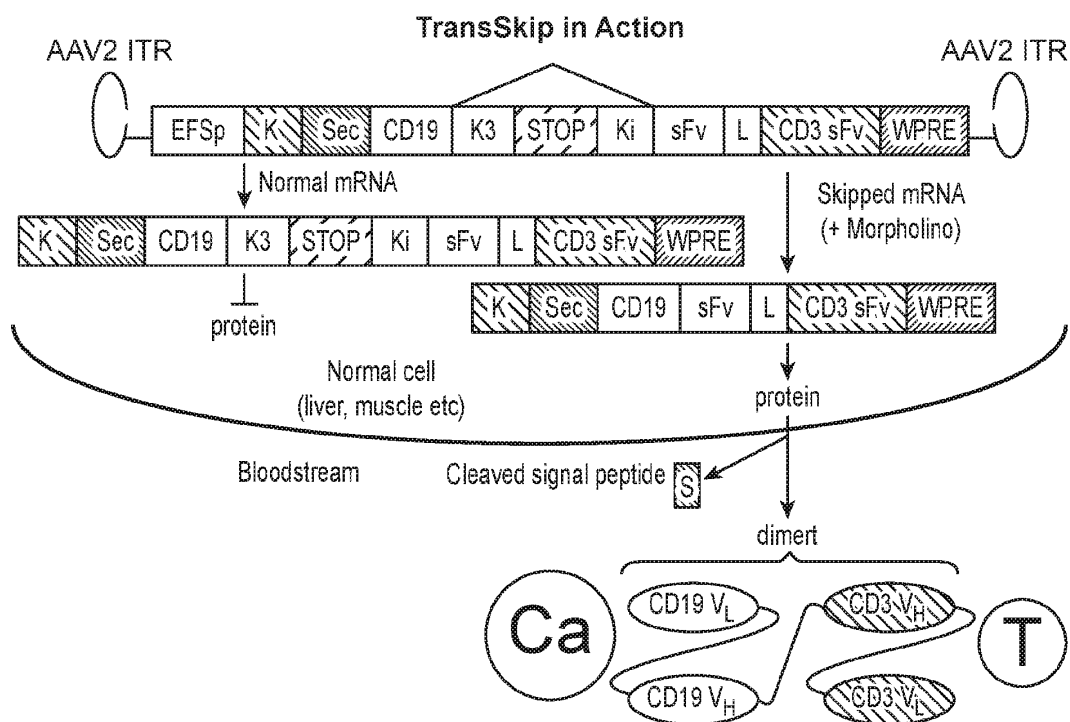


FIG. 44C

Both OncoSkip Morpholinos KTS1 and KTS2 Induce On-Target Exon Skipping of CD19xCD3 TransSkip K1
 #1098 transfected

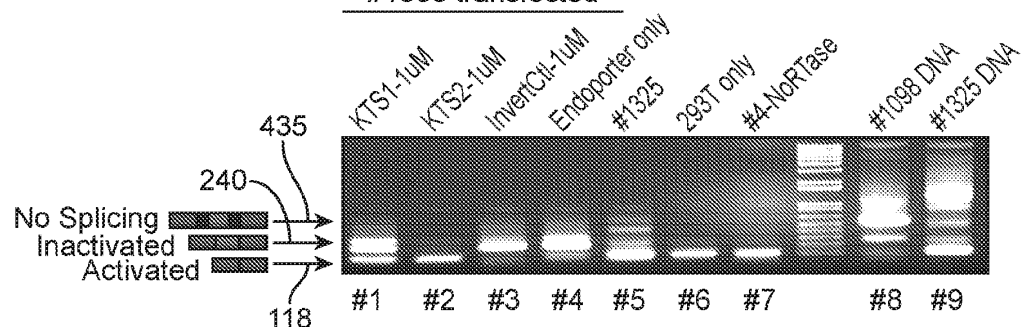


FIG. 45

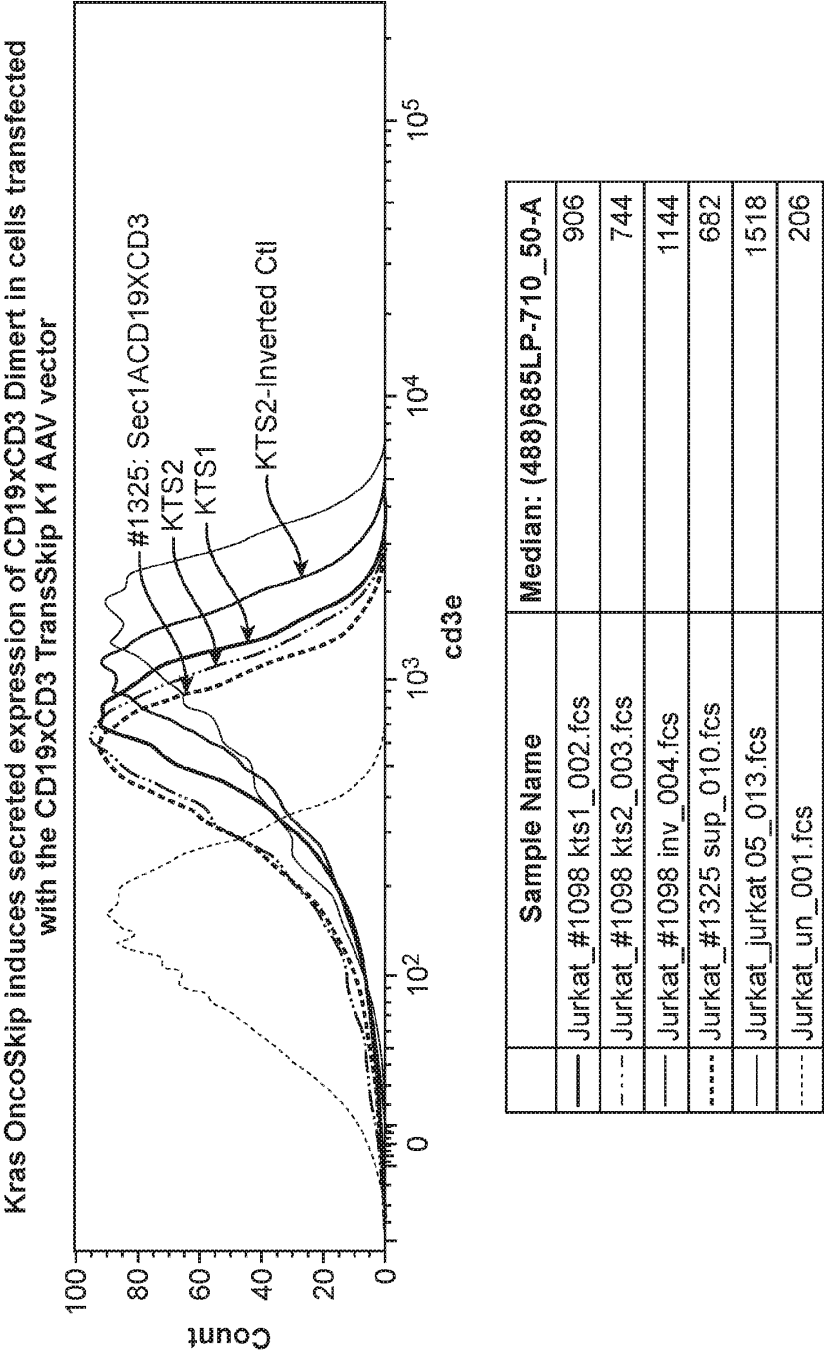


FIG. 46

CD19xCD3 TransSkip Splice Variant K3 Eliminates Baseline Yet Maintains Inducible Exon Skipping

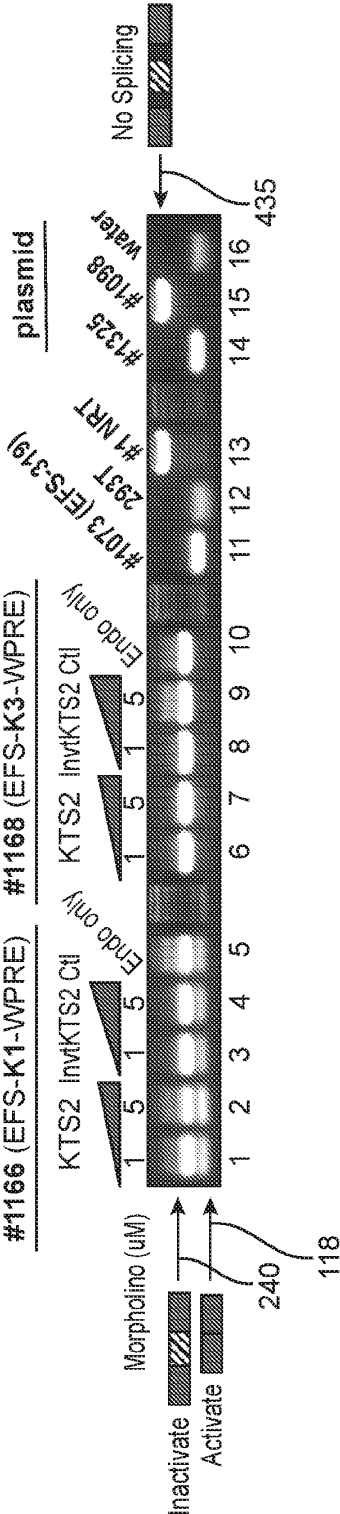


FIG. 47

Induction of CD19xCD3 Dimert Expression From CD19xCD3 TransSkip K3 as Determined by T Cell Binding is an On-Target Effect

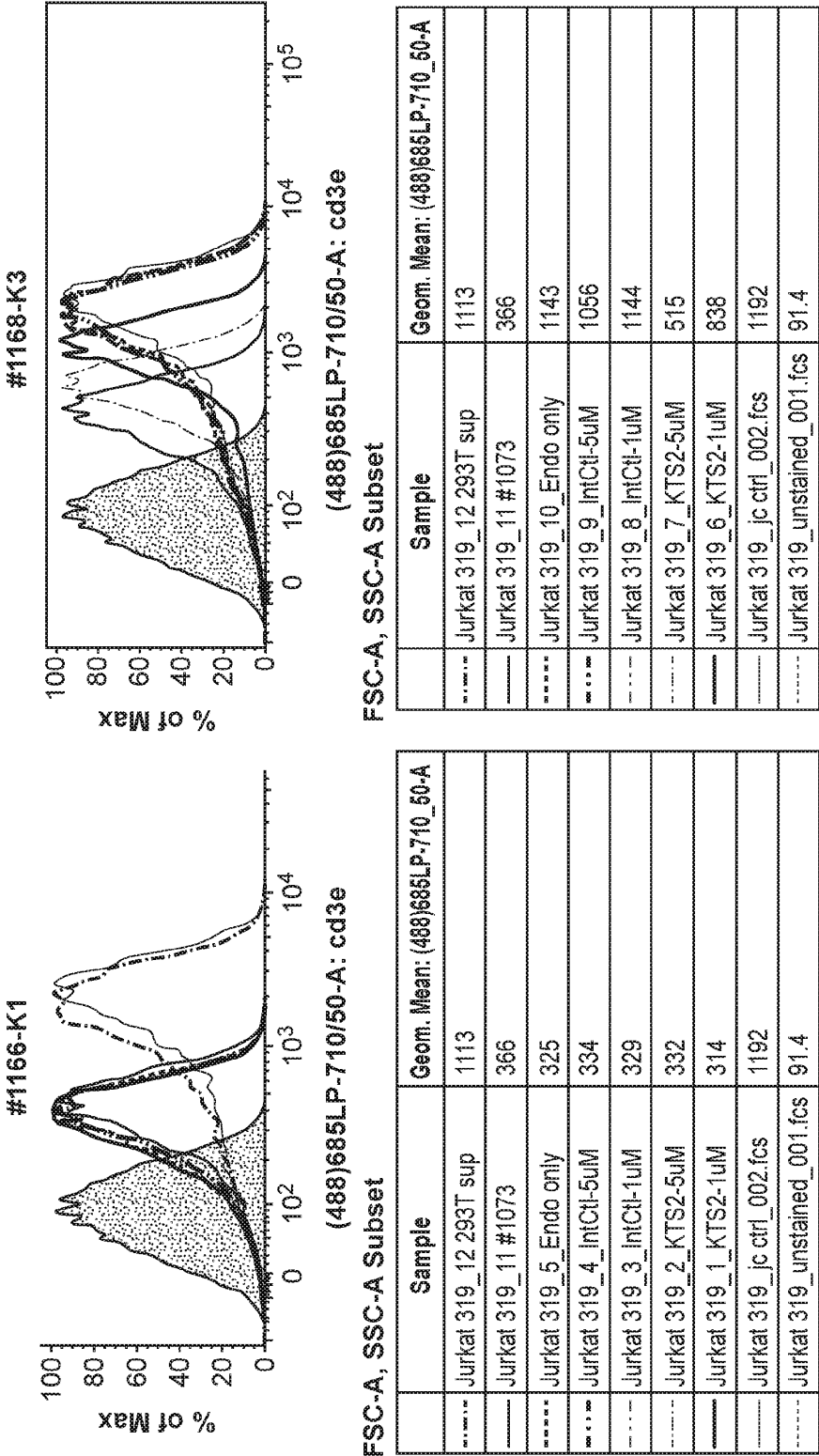


FIG. 48

Induction of CD19xCD3 Dimert Expression From CD19xCD3 TransSkip K3 Is Repeatable

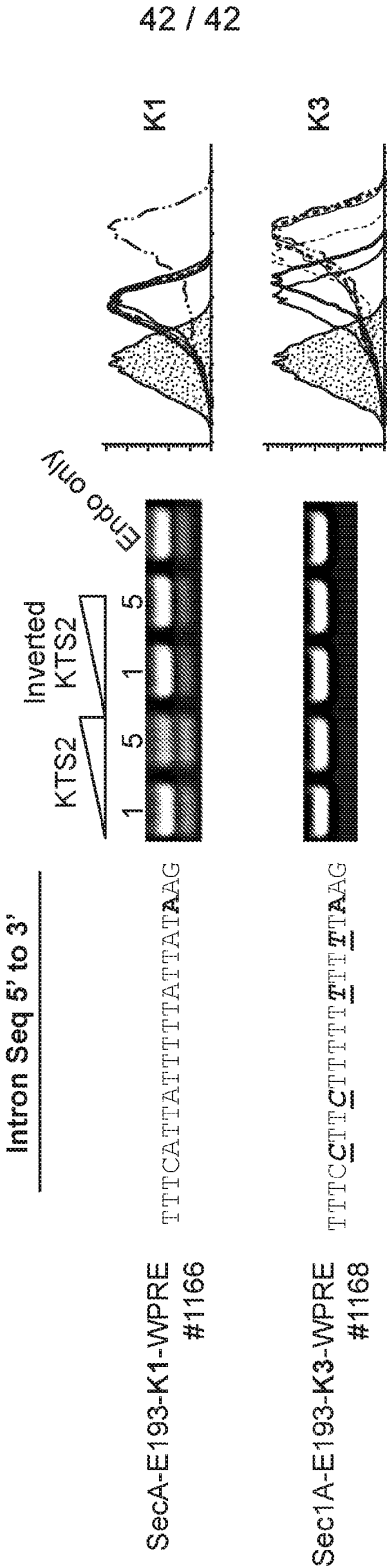


FIG. 49