

FIGURE 1A

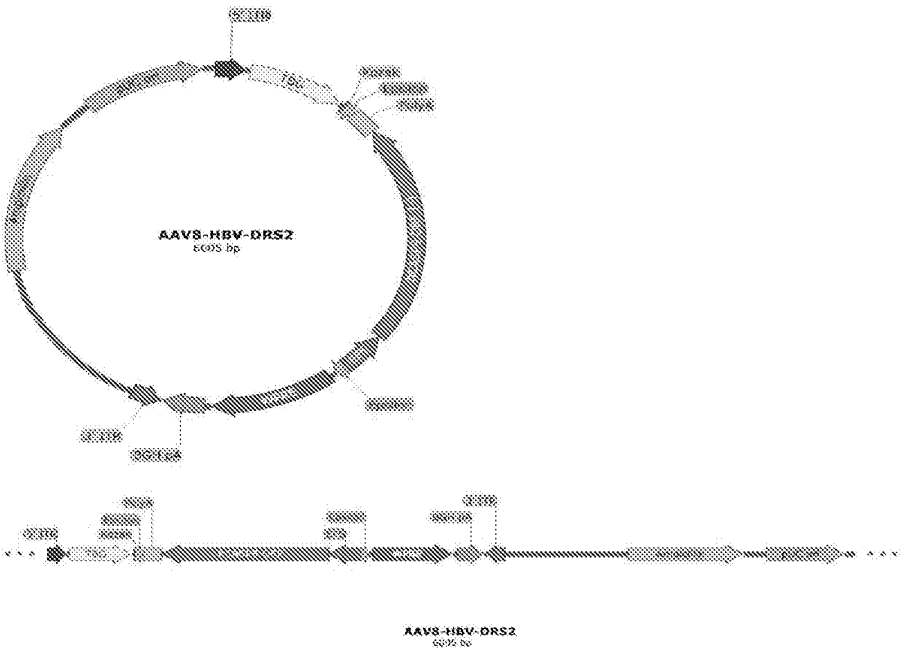


FIGURE 1B

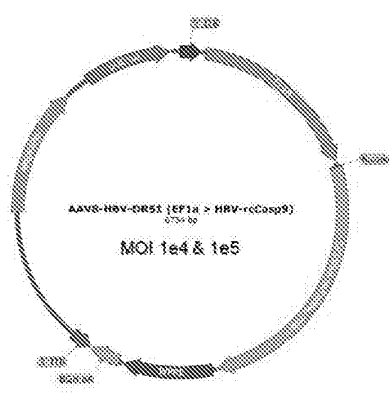


FIGURE 2A

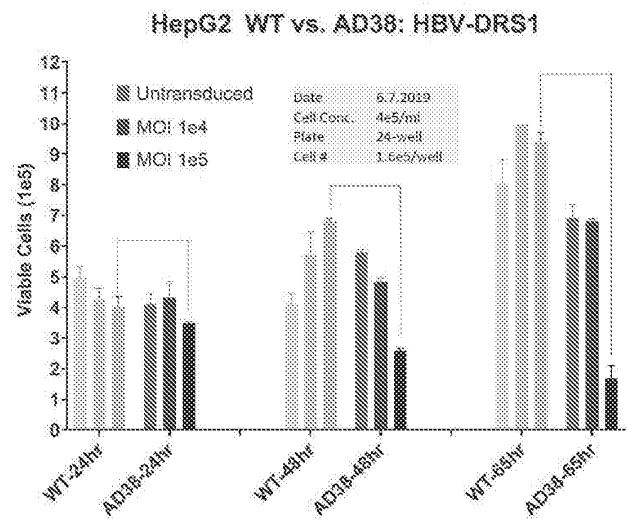


FIGURE 2B

FIGURE 2C

Experiment 1

Date 6.7.2019
 Cell Conc. 4e5/ml
 Plate 24-well
 Cell # 1.6e5/well
 AAV8-HBV-DRS1 (EF1a > HBV-rcCasp9)

Group 1 Untransduced
 Group 2 MOI 1e4
 Group 3 MOI 1e5

24h	Total (e5)	HepG2	
		Via %	Live (e5)
Group 1	5.29	98.7	5.23
	4.78	98.1	4.69
Group 2	4.11	98.2	4.03
	4.61	98	4.51
Group 3	3.82	99.2	3.79
	4.33	98.3	4.26

48h	Total (e5)	HepG2	
		Via %	Live (e5)
Group 1	5.05	86.5	4.36
	4.49	87.1	3.91

24h	Total (e5)	HepAD38	
		Via %	Live (e5)
Group 1	4.41	98.4	4.34
	4.1	94.6	3.88
Group 2	4.01	98.7	3.95
	4.86	96.7	4.7
Group 3	3.73	94.8	3.53
	3.63	85.8	3.47

48h	Total (e5)	HepAD38	
		Via %	Live (e5)
Group 1	6.12	95.7	5.86
	6	95.6	5.73

FIGURE 2C

Group 2	6.52	95.9	6.25	Group 2	5.36	92.1	4.93
	5.51	94.5	5.21		5.29	89.4	4.73
Group 3	7.08	96	6.79	Group 3	2.98	88.7	2.64
	7.1	97.1	6.89		3	84.2	2.53
HepG2				HepAD38			
65h	Total (e5)	Via %	Live (e5)	65h	Total (e5)	Via %	Live (e5)
Group 1	9.17	93.7	8.59	Group 1	7.96	90.8	7.23
	8.09	93.2	7.49		7.13	92.5	6.6
Group 2	10.3	96.9	10	Group 2	7.54	89.8	6.77
	10.2	97.7	10		7.79	88.2	6.87
Group 3	9.93	96.9	9.62	Group 3	2.05	69.5	1.42
	9.71	95	9.22		2.51	79	1.98

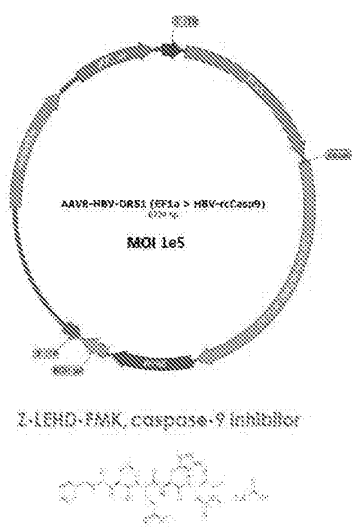


FIGURE 3A

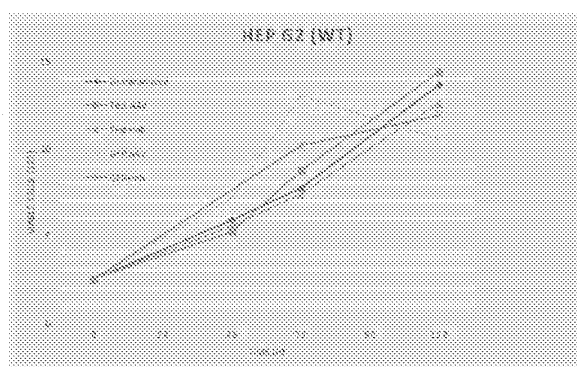


FIGURE 3B

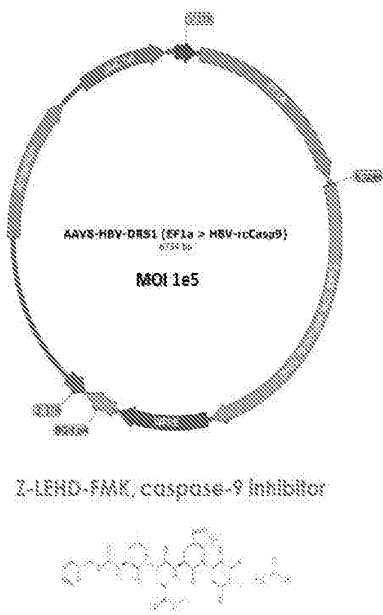


FIGURE 4A

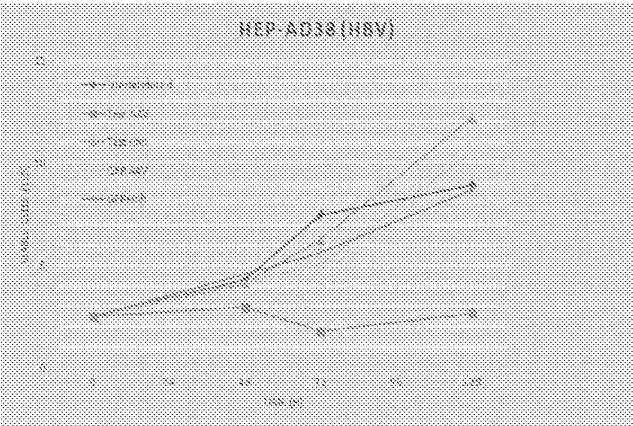


FIGURE 4B

Figure 4C
Experiment 2

Date 6.12.2019
Cell Conc. 2.5e5/ml
Plate 96-well
Cell # 25e3/well
Test Virus AAV8-HBV-DRS1 (EFla > HBV-rcCasp9)

Group 1 Untransduced
Group 2 Test AAV MOI 1e5
Group 3 Test AAV MOI 1e5 + z-LJHD.fmk
Group 4 GFP AAV MOI 1e5
Group 5 GFP AAV MOI 1e5 + z-LJHD.fmk

		HepG2	
48h	Total (e5)	Via %	Live (e5)
Group 1	5.73	93.3	5.34
	5.82	95.5	5.55
	7.14	95.7	6.84
Group 2	4.47	84.8	3.81
	6.51	87.9	5.73
	6.75	92.5	6.24
Group 3	6.84	87.6	6
	6.18	85.6	5.31
	6.54	83.6	5.46
Group 4	8.04	96.2	7.74
	8.16	97.3	7.92
	6.24	95.1	5.94
Group 5	N/A		

		HepAD38	
48h	Total (e5)	Via %	Live (e5)
Group 1	4.44	99	4.02
	4.26	92.4	3.96
	5.43	88.8	4.83
Group 2	3.63	81	2.93
	4.38	79.3	3.48
	3.48	79.1	2.44
Group 3	5.31	84	4.44
	4.41	83	3.66
	5.67	84.4	4.76
Group 4	N/A		
Group 5	N/A		

Figure 4C

		HepG2	
72h	Total (e5)	Via %	Live (e5)
Group 1	7.41	96.4	7.14
	8.58	96.9	8.31
Group 2	9.54	96	9.15
	9.72	95.3	8.31
Group 3	7.71	96.3	7.44
	7.5	98.1	7.35
Group 4	14.58	98.8	14.4
	12.09	97.4	11.76
Group 5	11.52	95.3	10.98
	9.54	98.3	9.39

		HepAD38	
72h	Total (e5)	Via %	Live (e5)
Group 1	7.23	95	6.87
	7.23	93.3	6.75
	9.18	95.4	8.76
Group 2	2.73	97.8	2.67
	1.77	96.5	1.71
	1.01	98	0.99
Group 3	6.75	94.9	6.42
	6.63	96	6.36
	6.51	92.1	6
Group 4	5.4	98.5	5.34
	5.64	97.8	5.52
	4.47	96.3	4.32
Group 5	5.91	94.3	5.55
	5.22	96.5	5.04
	6.3	98.4	6.18

		HepG2	
120h	Total (e5)	Via %	Live (e5)
Group 1	13.56	91	12.32
	15.84	94	14.88
	15.16	91.3	13.84
Group 2	13.2	94.1	12.4
	15.64	91.9	14.4
	18.28	89.9	16.44
Group 3	13.68	96.4	13.2
	13.64	95.8	13.04
	12.36	94.1	11.64
Group 4	11.24	90.1	10.12
	12.8	89	11.4
	11.52	88.3	10.2
Group 5	14.64	92.5	13.52
	13.32	92.3	12.28
	10.64	94	10

		HepAD38	
120h	Total (e5)	Via %	Live (e5)
Group 1	8.76	97.2	8.52
	9.92	97.2	9.64
	8.84	97.3	8.6
Group 2	2.7	88	2.37
	3.13	83.6	2.61
	3.3	90	2.97
Group 3	13.48	93.8	12.64
	14.64	94.5	13.84
	10.72	94.5	10.12
Group 4	11.36	95.6	10.88
	11.08	97.1	10.76
	10.32	97.3	10.04
Group 5	8.88	98.1	8.72
	12.2	97.8	9.56
	8	95.9	7.68

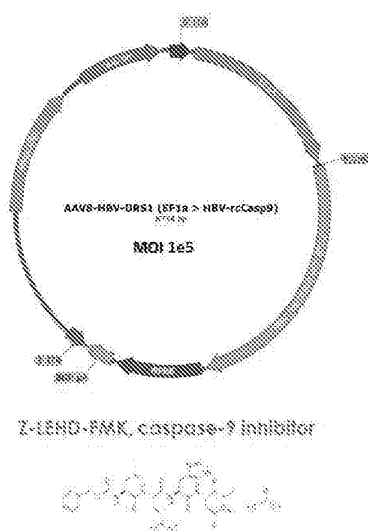


FIGURE 5A

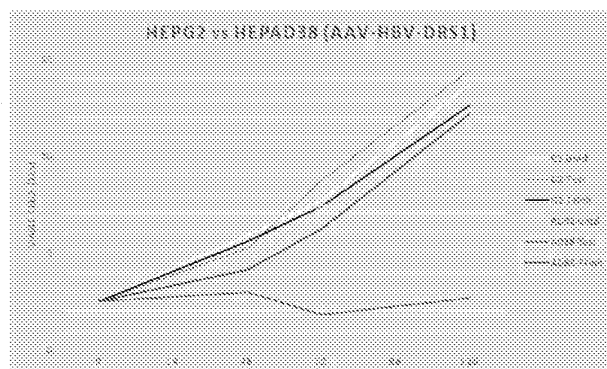


FIGURE 5B

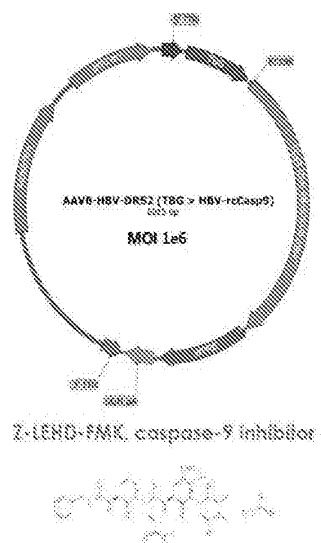


FIGURE 6A

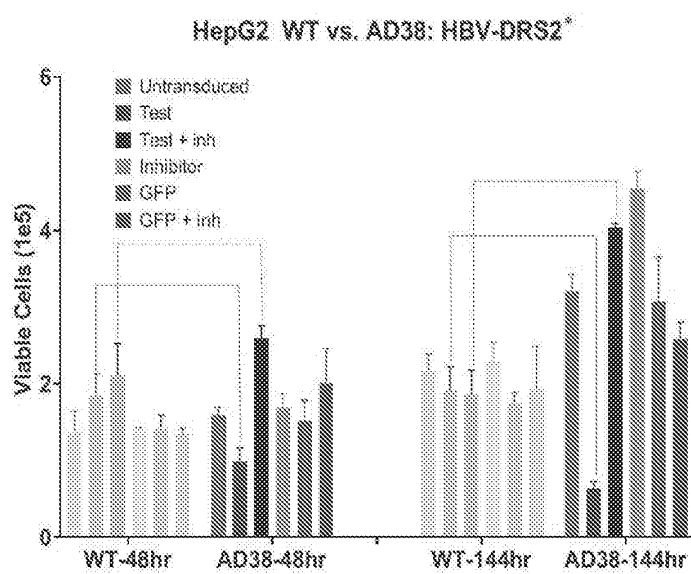


FIGURE 6B

FIGURE 6C
Experiment 3

Date 6.17.2019
Cell Conc. 2.5e5/ml
Plate 24-well
Cell # 1e5/well
Test Virus AAV8-HBV-DRS2 (TBC > HBV-rcCasp9)

Group 1 Untransduced
Group 2 Test AAV MOI 1e6
Group 3 Test AAV MOI 1e6 + z-LEHD.fmk
Group 4 z-LEHD.fmk
Group 5 GFP AAV MOI 1e6
Group 6 GFP AAV MOI 1e6 + z-LEHD.fmk

48h	HepG2		
	Total (e5)	Via %	Live (e5)
Group 1	2.2	75.2	1.66
	1.98	57.1	1.13
	1.74	76.7	1.33
Group 2	2.8	71.7	2
	2.81	71.9	2.02
	2.12	71.8	1.52
Group 3	2.67	75	2
	3.45	74.3	2.57
	2.43	72.9	1.77

48h	HepAD39		
	Total (e5)	Via %	Live (e5)
Group 1	2.28	64.6	1.47
	2.26	73.2	1.65
	2.2	75.2	1.65
Group 2	1.68	63.9	1.07
	1.9	58.5	1.11
	1.57	50	0.78
Group 3	3.6	66.9	2.41
	4.14	66.2	2.73
	3.75	70.3	2.64

FIGURE 6C

Group 4	2.1	65.4	1.37	Group 4	2.21	75.7	1.67
	2.62	71	1.43		2.34	64.7	1.52
	1.9	73.4	1.4		2.55	73.8	1.88
Group 5	2.06	61	1.26	Group 5	1.9	75.5	1.43
	1.92	83.2	1.6		2.58	70.3	1.82
	1.7	82.1	1.39		1.88	69.9	1.31
Group 6	2.04	62.6	1.28	Group 6	2.75	84.6	2.32
	2.12	66.7	1.41		2.82	78.1	2.21
	2.18	63	1.37		2.2	67.9	1.49
HepG2				HepAD38			
144h	Total (e5)	Via %	Live (e5)	144h	Total (e5)	Via %	Live (e5)
Group 1	2.28	95.2	2.18	Group 1	3.38	97.6	3.3
	1.98	98.6	1.95		3.46	96.9	3.36
	2.5	95.1	2.38		3.06	96.8	2.96
Group 2	2.44	90.1	2.2	Group 2	0.594	88.6	0.526
	2.42	80.5	1.96		0.742	90.9	0.674
	1.75	90.6	1.59		0.782	89.7	0.702
Group 3	2.4	92.7	2.22	Group 3	4.14	96.7	4
	1.93	87.4	1.68		4.16	96.8	4.02
	2.64	84.1	1.71		4.28	95.6	4.1
Group 4	2.22	97	2.14	Group 4	4.74	97.2	4.62
	2.64	97.9	2.58		4.84	97.7	4.72

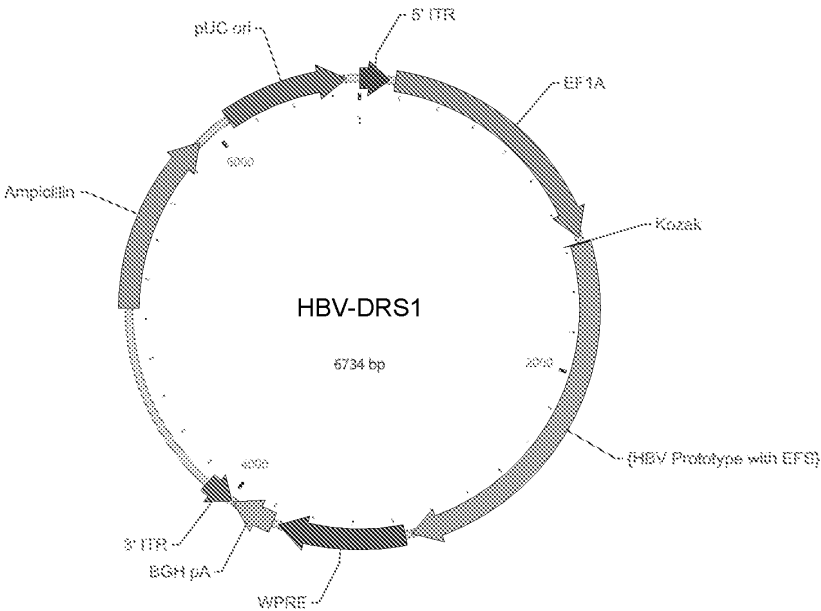
FIGURE 6C

	2.28	94.1	2.14			4.56	94.6	4.3	
Group 5	1.74	91.3	1.6	>>>>>>>>	Group 5	3.76	96	3.6	>>>>>>>> Both cells GFP expression 39%
	1.87	95	1.78			3.28	96.3	3.16	
	1.99	93.8	1.87			2.58	94.8	2.44	
Group 6	1.44	93.5	1.35	>>>>>>>>	Group 6	2.5	93.7	2.4	>>>>>>>> Both cells GFP expression 34%
	2.56	95.8	2.46			2.9	97.2	2.82	
	2.1	94.2	1.97			2.68	94.9	2.54	

Vector Summary

Vector ID	HBV-DRS1
Vector Name	pAAV[Exp]-EF1A>{HBV Prototype with EFS}:WPRE
Size	6734 bp
Vector Type	Mammalian Gene Expression AAV Vector
Inserted Promoter	EF1A
Inserted ORF	{HBV-Casp9 with EFS}
Plasmid Copy Number	High
Antibiotic Resistance	Ampicillin
Cloning Host	Stbl3 (or alternative strain)

Vector Map



Vector Components

Name	Position	Size (bp)	Type	Description	Application notes
5' ITR	■ 1-141	141	ITR	AAV 5' inverted terminal repeat (functional equivalent of wild-type 5' ITR)	Allows replication of the viral genome and its packaging into virus.
EF1A	■ 169-1347	1179	Promoter	Human eukaryotic translation elongation factor 1 α 1 promoter	Strong promoter.
Kozak	■ 1372-1377	6	Miscellaneous	Kozak translation initiation sequence	Facilitates translation initiation of ATG start codon downstream of the Kozak sequence.
{HBV-Casp9 with EFS}	■ 1378-3123	1746	ORF	None	None

Name	Position	Size (bp)	Type	Description	Application notes
WPRE	3154-3751	598	Miscellaneous	Woodchuck hepatitis virus posttranscriptional regulatory element	Enhances virus stability in packaging cells, leading to higher titer of packaged virus; enhances higher expression of transgenes.
BGH pA	3782-3989	208	PolyA_signal	Bovine growth hormone polyadenylation signal	Allows transcription termination and polyadenylation of mRNA transcribed by Pol II RNA polymerase.
3' ITR	complement (3997-4137)	141	ITR	AAV 3' inverted terminal repeat	Allows replication of the viral genome and its packaging into virus.
Ampicillin	5054-5914	861	ORF	Ampicillin resistance gene	Allows E. coli to be resistant to ampicillin.
pUC ori	6085-6673	589	Rep_origin	pUC origin of replication	Facilitates plasmid replication in E. coli; regulates high-copy plasmid number (500-700).

Vector Sequence

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1  CCTGCAGGCA GCTGCGCGCT CGCTCGCTCA CTGAGGCCGC CCGGGCAAAG CCCGGGCGTC GGGCGACCTT TGGTCGCCCC GCCTCAGTGA GCGAGCGAGC
101 GCGCAGAGAG GAGATTGGCCA ACTCCATCAC TAGGGGTTC TTCTAGACAA CTTTGTATAG AAAAGTTGGG CTCGGGTGCC CGTCAGTGGG CAGAGCGCAC
201 ATCGCCACAC GTCCCCGAGA AGTTGGGGGG AGGGGTCCGC AATTGAACCG GTGCCTAGAG AAGGTGGCGC GGGGTAACCT GGGAAAGTGA TGTGCTGTAC
301 TGGCTCCGCG TTTTCCCGA GGGTGGGGGA GAACCGTATA TAAGTGCAGT AGTCGCCGTG AACGTTCTTT TTCGCAACGG GTTTGCCGCC AGAACACAGG
401 TAAGTGCAGT GTGTGGTTCC CGCGGGCCTG GCCTCTTTAC GGGTTATGGC CCTTGCGTGC CTTGAATTAC TTCCACCTGG CTGCAGTACG TGATTCTTGA
501 TCCCGAGCTT CGGGTTGGAA GTGGGTGGGA GAGTTCGAGG CCTTGCGCTT AAGGAGCCCC TTCGCCTCGT GCTTGAGTTG AGGCCTGGCC TGGGCGCTGG
601 GGCCGCCGCG TGCGAATCTG GTGGCACCTT CGCGCCTGTC TCGTGTCTTT CGATAAGTCT CTAGCCATTT AAAATTTTGT ATGACTGCTC GCGACGCTTT
701 TTTTCTGGCA AGATAGTCTT GTAAATGCGG GCCAAGATCT GCACACTGGT ATTTGCGTTT TTGGGGCCGC GGGCGGCGAC GGGGCCCGTG CGTCCCAGCG
801 CACATGTTGCG GCGAGGCGGG GCCTGCGAGC GCGGCCACCG AGAATCGGAC GGGGGTAGTC TCAAGCTGGC CGCCCTGCTC TGGTGCCTGG TCTCGCGCCG
901 CCGTGTATCG CCCCGCCCTG GCGGGCAAGG CTGGCCCGGT CGGCACCACT TGCGTGAGCG GAAAGATGGC CGCTTCCCGG CCCTGCTGCA GGGAGCTCAA
1001 AATGGAGGAC GCGGCGCTCG GGAGAGCGGG CGGGTGAGTC ACCCACACAA AGGAAAAGGG CCTTCCGTC CTCAGCCGTC GCTTCATGTG ACTCCACGGA
1101 GTACCGGGCG CCGTCCAGGC ACCTCGATTA GTTCTCGAGC TTTTGGAGTA CGTCGTCTTT AGGTGCGGGG GAGGGGTTTT ATGCGATGGA GTTTCCCCAC
1201 ACTGAGTGGG TGGAGACTGA AGTTAGGCCA GCTTGGCACT TGATGTAATT CTCCTTGGAA TTTGCCCTTT TTGAGTTTGG ATCTTGGTTC ATTCTCAAGC
1301 CTCAGACAGT GGTTCAAAGT TTTTCTCTC CATTTAGAGT GTCGTGACAA GTTTGTACAA AAAAGCAGGC TGCCACCATT GTTTCATGTC CTACTGTTCa
1401 AGCCTCCAAG CTGTGCCTTG GGTGGCTTTG GGGCATGGAC AAGAGCCAGA CATGATAAGA TACATTGATG AGTTTGAGCA AACCACAAC AGAATGCAGT
1501 GAAAAAATG CTTTATTTGT GAAATTTGTG ATGCTATTGC TTTATTGTGA ACCATTATAA GCTGCAATAA ACAAGTTTAT GATGTTTTAA AGAAAAATTT
1601 TTTCCGGAGG AAATTAAGC AACCAGGCAT CTGTTTATAA ATCCCTTTCA CCGAAACAGC ATTAGCGACC CTAAGCAGGA GGGACTGCAG GTCTTCAGAG
1701 TGAGCCCACT GCTCAAGAT GTCGTCCAGG GTCTCAACGT ACCAGGAGCC ACTCTGGGGT TCCCTCCAGG AAACAAAACC TGGGAAAGTA GAGTAGGACA
1801 CAAAGATGTC ACTGGGTGTG GGCAAACTAG ATATGGCGTC CAGCTGGTGC AAGGTCCTCA AACCTTCCTG GAACGGGGTG GCATCTGGCT CGGGGTTACT
1901 GCCAGGGGAC TCGTCTTCAG GGGAAAGTGA GGCCACCTCA AACCCATGGT CTTTCTGCTC CCCACCACAG GCCTGGATGA AAAAGAGCTT GGGCTTCCTT
2001 CCCAGGCTGG GGCAGCTGGT CCCATTGAAG ATGTTCAACA TCTTCTCGAC CGACACAGGG CATCCATCTG TGCCGTAGAC AGCCCTGGG AACTGCAGGT
2101 GGCTGGCCTG ACAGCCGTGA GAGAGAATGA CCACCACGCA GCAGTCCAGA GCACCGTGGT CCTGCTGCGC CAGCTCCAGC AAAGCCAGCA CCATTTCTTT
2201 GGCAGTCAAG TCGCCCTTCA CCTCCACCAT GAAATGCAGC GAGGAGAAGC GACGCCGCAA CTTCTCACAG TCGATGTTGG AGCCAGTGGC GGTGCGGAGC
2301 CCGGACTCAC GGCAGAAAGT CACATTGTTG ATAATGAGGC AGTGCCACA GGGCTCCATG CTCAGGATGT AAGCCAAATC TGCAATTTCC CTCAAACCTC
2401 CAAGAGCACG GACATCACCA AATCCTCCAG AACCAATGTC CACTGGTCTG GGTGTTTCCG GTCTGAGAAC CTCTGGTTTG CGAATCTCTG GTCTGAGCAC
2501 CACTGGGGTA AGGTTTTCTA GGGTTGGCTT CGACAACTTT GCTGCTTGCC TGTTAGTTCG CAGAAACGAA GCCAGCATGT CCTGGCCTGT GTCCCTAAG
2601 CAGGAGATGA ACAAGGAAG AGCCTGACTC CCTCGAGTCT CCAGATCTAT GATCAGCTGC CTGGCCTGAT CCCGCCGAGA TCCAGAGCCT GCCCGCTGGA
2701 TGTCTTCGAT CATATGGGGC CTGAACAGCT CGCGGCTCAG CAGGGCGTCC CAGAGCTGGT CCACCTGCAG CTCTTCCACC AGCCGACGCC GGCACCGCCG
2801 CAGGAGCCGC CGATCCGCTT CGTCCATCCT GTGTTCTGGC GGCAAACCCG TTGCGAAAAA GAACGTTTAC GCGCACTACT GCACCTATAT ACGGTTCTCC
2901 CCCACCTCGG GGAAAAAGGC GGAGCCAGTA CACGACATCA CTTTCCCAGT TTACCCGCGC CCACCTTCTC TAGGCACCGG ATCAATTGCC GACCCTCCC
3001 CCAACTTCT CGGGGAGTGT GGGCGATGTG CGCTCTGCCC ACTGACGGGC ACCGGAGCCT GTTCATGTCC TACTGTTCAA GCCTCCAAGC TGTGCTTGG
3101 GTGGCTTTGG GGCATGGACA TAAACCCAGC TTTCTTGTAC AAAGTGGGAA TTCCGATAAT CAACCTCTGG ATTACAAAAT TTGTGAAAGA TTGACTGGTA
3201 TTCTTAACTA TGTTGCTCCT TTTACGCTAT GTGGATACGC TGCTTAAATG CCTTTGTATC ATGCTATTGC TTCCCGTATG GCTTTCAATT TCTCCTCCTT
3301 GTATAAATCC TGTTGCTGCT CTCTTTATGA GGAGTTGTGG CCCGTGTGTA GGCAACGTGG CGTGGTGTGC ACTGTGTTTG CTGACGCAAC CCCCACTGGT
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3501

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3601 GGACAGGGGC TCGGCTGTTG GGCAGTGACA ATTCCGTGGT GTTGTGCGGG AAGCTGACGT CCTTCCATG GCTGCTCGCC TGTGTTGCCA CCTGGATTCT
3701 GCGCGGGAGC TCCTTCTGCT ACGTCCCCTC GGCCTCAAT CCAGCGGACC TTCTTCCCG CGGCTGCTG CCGCTCTGC GGCCTCTTCC GCGTCTTCGC
3801 CTTCGCCCTC AGACGAGTCG GATCTCCCTT TGGCCGCGCT CCGCGCATCG GGAATTCCTA GAGCTCGCTG ATCAGCCTCG ACTGTGCCCT CTAGTTGCCA
3901 GCCATCTGTT GTTTCGCCCT CCCCCTGCC TTCTTGACC CTGGAAGTG CCACTCCCAC TGTCTTTCC TAATAAAATG AGGAAATTGC ATCGCATTTG
4001 CTGAGTAGGT GTCATTCTAT TCTGGGGGT GGGGTGGGC AGGACAGCAA GGGGAGGAT TGGGAAGAGA ATAGCAGGCA TGCTGGGAG GGGCGCAGGA
4101 ACCCCTAGTG ATGGAGTTGG CCACTCCCTC TCTGCGCGCT CGCTCGCTCA CTGAGGCCGG GCGACCAAAG GTCGCCGAC GCCCGGGCTT TGCCCGGGCG
4201 GCCTCAGTGA GCGAGCGAGC GCGCAGCTGC CTGACGGGCG GCCTGATGCG GTATTTCTC CTACGCATC TGTGCGGTAT TTCACACCGC ATAGCTCAAA
4301 GCAACCATAG TACGCGCCCT GTAGCGGCGC ATTAAGCGCG GCGGGGGTGG TGGTTACGCG CAGCGTGACC GCTACACTTG CCAGCGCCTT AGCCCGCGCT
4401 CCTTTCGCTT TCTTCCCTTC CTTTCTCGCC ACGTTGCGCG GCTTTCGCCG TCAAGCTCTA AATCGGGGCG TCCTTTAGG GTTCGGATTG AGTGCTTTAC
4501 GGCACCTCGA CCCCAGAAAA CTTGATTGG GTGATGGTC ACGTAGTGGG CCATCGCCCT GATAGACGGT TTTTCGCCCT TTGACGTTGG AGTCCACGTT
4601 CTTTAATAGT GGACTCTTGT TCCAACTGG AACAACTCT AACTCTATCT CGGGCTATTC TTTGATTGA TAAGGATTG TGCCGATTTC GGTCTATTGG
4701 TTAATAAATG AGCTGATTGA ACAAATTT AACGCGAATT TTAACAAAT ATTAACGTTT ACAATTTAT GGTGCACTCT CAGTACAATC TGCTCTGATG
4801 CCGCATAGTT AAGCCAGCCC CGACACCCGC CAACACCCGC TGACGCGCCC TGACGGGCTT GCTGCTCCC GGCATCCGCT TACAGACAGC CTGTGACCGT
4901 CTCCGGGAGC TGCATGTGTC AGAGGTTTTC ACCGTATCA CCGAAACGCG CGAGACGAAA GGGCCTCGTG ATACGCCTAT TTTTATAGT TAATGTGATG
5001 ATAATAATGG TTTCTTAGAC GTCAGGTGGC ACTTTTCGGG GAAATGTGCG CGGAACCCCT ATTGTTTAT TTTTCTAAAT ACATTCAAAAT ATGTATCCGC
5101 TCATGAGACA ATAACCTGTA TAAATGCTTC AATAATATTG AAAAGGGAAG AGTATGATG TTAACATTT CCGTGTCGCC CTTATTCCTT TTTTTCGGGC
5201 ATTTTCGCTT CCTGTTTTTG CTCACCCAGA AACGCTGGTG AAAGTAAAAG ATGCTGAAGA TCAGTTGGGT GCACGAGTGG GTTACATCGA ACTGGATCTC
5301 AACAGCGGTA AGATCCTTGA GAGTTTTTCG CCGAAGAAG GTTTTCCAAT GATGAGCACT TTTAAAGTTC TGCTATGTGG CCGGTATTA TCCCGTATTG
5401 ACGCCGGGCA AGAGCAATC GGTGCGCGCA TACACTATT TCAGATGAC TTGGTTGAGT ACTCACCAGT CACAGAAAAG CATCTTACGG ATGGCATGAC
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6401 GCTAATCCTG TTACCAGTGG CTGCTGCCAG TGGCGATAAG TCGTGTCTTA CCGGTTGGA CTCAAGACGA TAGTTACCGG ATAAGGCGCA GCGGTGCGGC
6501 TGAACGGGGG GTTCGTGACG ACAGCCCAGC TTGGAGCGAA CGACCTACAC CGAACTGAGA TACCTACAGC GTGAGCTATG AGAAAGCGCC ACGCTTCCCG
6601 AAGGGAGAAA GCGCGACAGG TATCCGTAA GCGGCAGGCT CGGAACAGGA GAGCGCACGA GGGAGCTTCC AGGGGGAAC GCCTGGTATC TTTATAGTCC
6701 TGTGCGGTTT CGCCACCTCT GACTTGAGCG TCGATTTTGT TGATGCTCGT CAGGGGGGCG GAGCCTATGG AAAAAGCCCA GCAACGCGGC CTTTTTACGG
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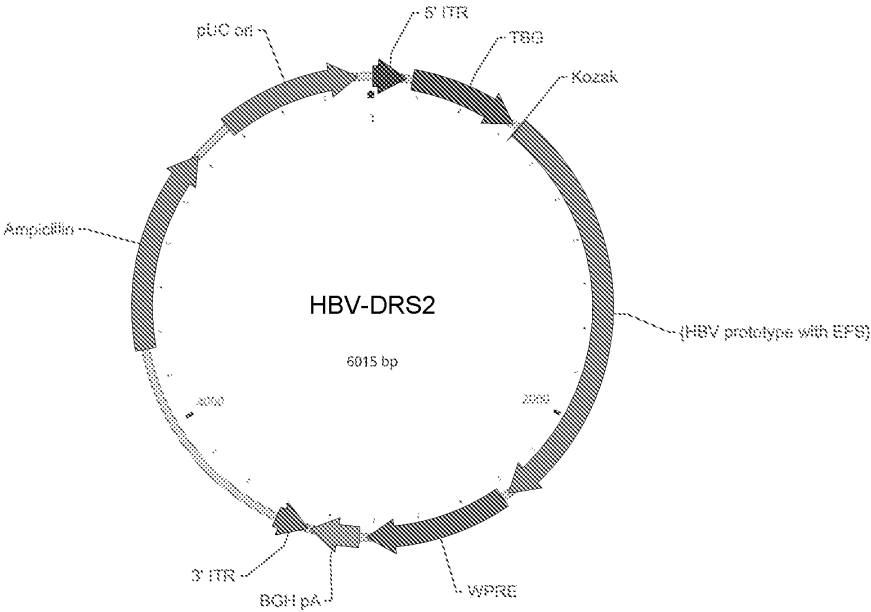
Validation by Restriction Enzyme Digestion

Restriction Enzymes	Cutting Sites	DNA Fragments (bp)
NcoI	1945, 3567	1622, 5112
ApaLI	3368, 4673, 5170, 6416	1305, 497, 1246, 3686
EcoRI	3149, 3753	604, 6130
ApaLI+NcoI	1945, 3368, 3567, 4673, 5170, 6416	1423, 199, 1106, 497, 1246, 2263
ApaLI+EcoRI	3149, 3368, 3753, 4673, 5170, 6416	219, 385, 920, 497, 1246, 3467

Vector Summary

Vector ID	HBV-DRS2
Vector Name	pAAV[Exp]-TBG>{HBV prototype with EFS}:WPRE
Size	6015 bp
Vector Type	Mammalian Gene Expression AAV Vector
Inserted Promoter	TBG
Inserted ORF	{HBV-Casp9 with EFS}
Plasmid Copy Number	High
Antibiotic Resistance	Ampicillin
Cloning Host	Stbl3 (or alternative strain)

Vector Map



Vector Components

Name	Position	Size (bp)	Type	Description	Application notes
5' ITR	■ 1-141	141	ITR	AAV 5' inverted terminal repeat (functional equivalent of wild-type 5' ITR)	Allows replication of the viral genome and its packaging into virus.
TBG	■ 169-628	460	Promoter	Human thyroxine-binding globulin promoter	Tissue specificity: Liver. Cell type specificity: Hepatocytes.
Kozak	■ 653-658	6	Miscellaneous	Kozak translation initiation sequence	Facilitates translation initiation of ATG start codon downstream of the Kozak sequence.
{HBV-Casp9 with EFS}	■ 659-2404	1746	ORF	None	None

Name	Position	Size (bp)	Type	Description	Application notes
WPRE	2435-3032	598	Miscellaneous	Woodchuck hepatitis virus posttranscriptional regulatory element	Enhances virus stability in packaging cells, leading to higher titer of packaged virus; enhances higher expression of transgenes.
BGH pA	3063-3270	208	PolyA_signal	Bovine growth hormone polyadenylation signal	Allows transcription termination and polyadenylation of mRNA transcribed by Pol II RNA polymerase.
3' ITR	complement (3278-3418)	141	ITR	AAV 3' inverted terminal repeat	Allows replication of the viral genome and its packaging into virus.
Ampicillin	4335-5195	861	ORF	Ampicillin resistance gene	Allows E. coli to be resistant to ampicillin.
pUC ori	5366-5954	589	Rep_origin	pUC origin of replication	Facilitates plasmid replication in E. coli; regulates high-copy plasmid number (500-700).

Vector Sequence

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1  CCTGCAGGCA GCTGCGCGCT CGCTCGCTCA CTGAGGCCGC CCGGGCAAAG CCCGGGCGTC GGGCGACCTT TGGTCGCCCG GCCTCAGTGA GCGAGCGAGC
101 GCGCAGAGAG GGAGTGGCCA ACTCCATCAC TAGGGGTTC TTCTAGACAA CTTTGTATAG AAAAGTTGGG GCTGGAAGCT ACCTTTGACA TCATTTCTCT
201 TGCGAATGCA TGTATAATTT CTACAGAACC TATTAGAAAG GATCACCAGC CCTCTGCTTT TGTACAACTT TCCTTAAAAA AACTGCCAAT TCCACTGCTG
301 TTTGGCCCAA TAGTGAGAAC TTTTTCCTGC TGCTCTTGG TGCTTTTGCC TATGGCCCTT ATTCTGCCTG CTGAAGACAC TCTTGCCAGC ATGGACTTAA
401 ACCCCTCCAG CTCTGACAAT CCTCTTTCTC TTTTGTTTTA CATGAAGGGT CTGGCAGCCA AAGCAATCAC TCAAAGTTCA AACCTTATCA TTTTTTGCTT
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601 ACAGGACATG CTATAAAAAA GGAAAGATCA AGTTTGTACA AAAAAGCAGG CTGCCACCAT GTGTTTATGT CCTACTGTTT AAGCCTCCAA GCTGTGCCTT
701 GGGTGGCTTT GGGGCGATGA CAAGAGCCAG ACATGATAAG ATACATTGAT GAGTTTGGAC AAACCACAAC TAGAATGCAG TGAAAAAAT GCTTTATTTG
801 TGAAATTTGT GATGCTATTG CTTTATTGTG AACCATTTATA AGCTGCAATA AACAAAGTTA TGATGTTTTA AAGAAAAGTT TTTTCCGGAG GAAATTAAAG
901 CAACCAGGCA TCTGTTTTATA AATCCCTTTC ACCGAAACAG CATTAGCGAC CCTAAGCAGG AGGGACTGCA GGTCTTCAGA GTGAGCCAC TGCTCAAAGA
1001 TGTCTCTCAG GGTCTCAACG TACCAGGAGC CACTCTTGGG GTCCCTCCAG GAAACAAAC CTGGGAAAGT AGAGTAGGAC ACAAGATGT CACTGGGTGT
1101 GGGCAAACTA GATATGGCGT CCAGCTGGTC GAAGTCCTC AAACCTTCTT GGAACGGGGT GGCATCTGGC TCGGGGTTAC TGCCAGGGGA CTCGTCTTCA
1201 GGGGAAGTGG AGGCCACCTC AAACCCATGG TCTTCTGTCT CCCCACCACA GGCCTGGATG AAAAAGAGCT TGGGCTTCCC TCCCAGGCTG GGGCAGCTGG
1301 TGCCATTGAA GATGTTTACA ATCTTCTCGA CCGACACAGG GCATCCATCT GTGCCGTAGA CAGCCCTTGG GAACTGCAGG TGGCTGGCCT GACAGCCGTG
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1601 TCACATTGTT GATAATGAGG CAGTGGCCAC AGGGCTCCAT GCTCAGGATG TAAGCCAAAT CTGCATTTC CTCTAAACTC TCAAGAGCAC CGACATCACC
1701 AAATCCTCCA GAACCAATGT CCACTGGTCT GGGTGTTTTC GGTCTGAGAA CCTCTGTTTT GCGAATCTCT GGTCTGAGCA CCACTGGGGT AAGGTTTTCT
1801 AGGGTTGGCT TCGACAACCT TGCTGCTTGC CTGTTAGTTC GCAGAAACGA AGCCAGCATG TCCTGGCCTG TGTCTCTTAA GCAGGAGATG AACAAAGGAA
1901 GAGCCTGACT CCCTCGAGTC TCCAGATCTA TGATCAGCTG CCTGGCCTGA TCCCAGCGAG ATCCAGAGCC TGCCCGCTGG ATGTCTCTGA TCATATGGGG
2001 CCTGAACAGC TCGCGGCTCA GCAGGGCGTC CCAGAGCTGG TCCACCTGCA GCTCTTCCAC CAGCCGCAGC CGGCACCGCC GCAGGAGCCG CCGATCCGCT
2101 TCGTCCATCC TGTGTTCTGG CGGCAAAACC GTTGCGAAAA AGAACGTTCA CGGCGACTAC TGCACTTATA TACGGTTCTC CCCCACCTCT GGGAAAAAGG
2201 CGGAGCCAGT ACACGACATC ACTTTCCTCAG TTTACCCCGC GCCACCTTCT CTAGGCACCG GATCAATTGC CGACCCCTCC CCCCACCTTC TCGGGGACTG
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3501

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3801 ACTTGATTGG GGTGATGGTT CACGTAGTGG GCCATCGCCC TGATAGACGG TTTTTCGCCC TTTGACGTTG GAGTCCACGT TCTTTAATAG TGGACTCTTG
3901 TTCCAAACTG GAACAACACT CAACTCTATC TCGGGCTATT CTTTGTATT ATAAGGAGTT TTGCCGATT CGGTCTATTG GTTAAAAAAT GAGCTGATTT
4001 AACAAAAAT TAACGCGAAT TTTAACAAAA TATTAACGTT TACAATTTTA TGGTGCACCT TCAGTACAAT CTGCTCTGAT GCCGCATAGT TAAGCCAGCC
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4201 CAGAGGTTTT CACGTCATC ACCGAAACGC GCGAGACGAA AGGGCTCGT GATACGCCTA TTTTATAGG TTAATGTCAT GATAATAATG GTTCTTAGA
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5101 CTCCGGCTG GCTGGTTTAT TGCTGATAAA TCTGGAGCCG GTGAGCGTGG AAGCCGCGGT ATCATTGCAG CACTGGGGCC AGATGGTAAG CCCTCCCGTA
5201 TCGTAGTTAT CTACACGACG GGGAGTCAGG CAACTATGGA TGAACGAAAT AGACAGATCG CTGAGATAGG TGCTCACTG ATTAAGCATT GGTAACTGTC
5301 AGACCAAGTT TACTCATATA TACTTTAGAT TGATTTAAAA CTTCAATTTT AATTAAAAAG GATCTAGGTG AAGATCCTTT TTGATAATCT CATGACCAA
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5701 GCTGCTGCCA GTGGCGATAA TGTGTGTCTT ACCGGGTGG ACTCAAGACG ATAGTTACCG GATAAGGCGC AGCGGTCGGG CTGAACGGGG GGTTCGTGCA
5801 CACAGCCCAG CTTGGAGCGA ACGACCTACA CCGAACTGAG ATACCTACAG CGTGAGCTAT GAGAAAGCGC CACGCTTCCC GAAGGGAGAA AGGCGGACAG
5901 GTATCCGGTA AGCGGCAGGG TCGGAACAGG AGAGCGCAGC AGGGAGCTTC CAGGGGGAAA CGCTTGGTAT CTTTATAGTC CTGTGGGGTT TCGCCACCTC
6001 TGACTTGAGC GTCGATTTTT GTGATGCTCG TCAGGGGGGC GGAGCCTATG GAAAACGCC AGCAACGCGG CCTTTTACG GTTCTTGGCC TTTTGCTGGC
CTTTTGCTCA CATGT

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Validation by Restriction Enzyme Digestion

Restriction Enzymes	Cutting Sites	DNA Fragments (bp)
XhoI	1914	6015
NdeI	1994	6015
XmnI	322, 1313, 4523	991, 3210, 1814
NcoI	1226, 2848	1622, 4393
ApaLI	2649, 3954, 4451, 5697	1305, 497, 1246, 2967
ApaLI+XhoI	1914, 2649, 3954, 4451, 5697	735, 1305, 497, 1246, 2232
ApaLI+NdeI	1994, 2649, 3954, 4451, 5697	655, 1305, 497, 1246, 2312
ApaLI+XmnI	322, 1313, 2649, 3954, 4451, 4523, 5697	991, 1336, 1305, 497, 72, 1174, 640
ApaLI+NcoI	1226, 2649, 2848, 3954, 4451, 5697	1423, 199, 1106, 497, 1246, 1544

FIGURE 9

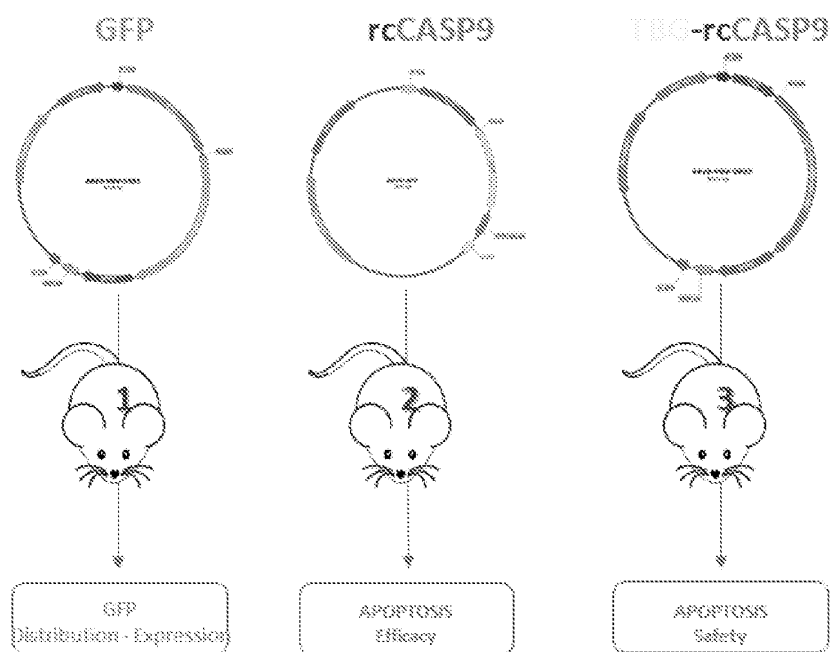


FIGURE 10A

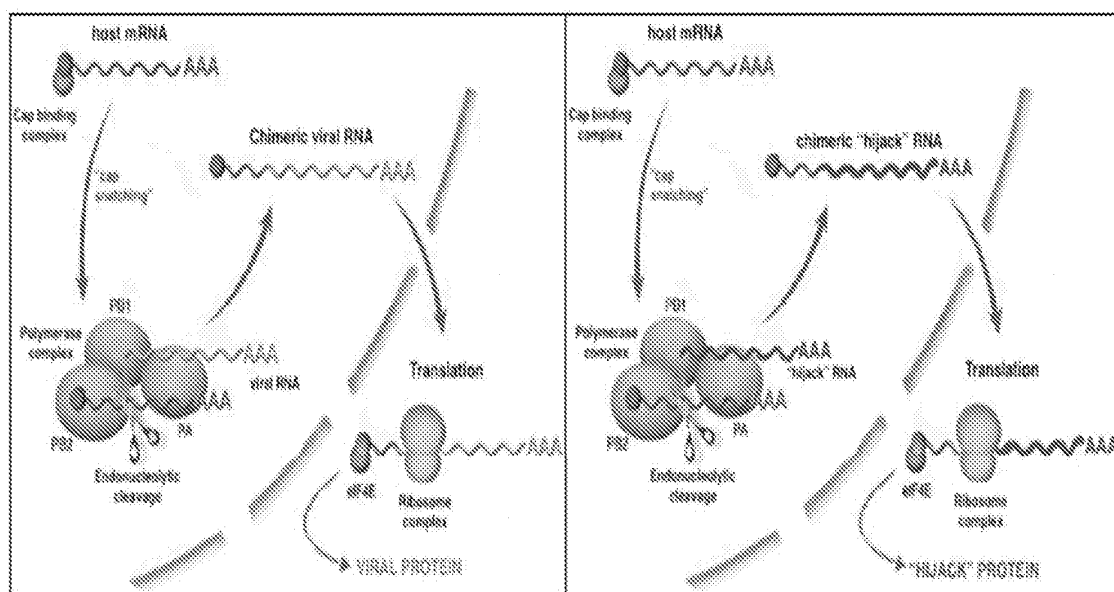


FIGURE 11A

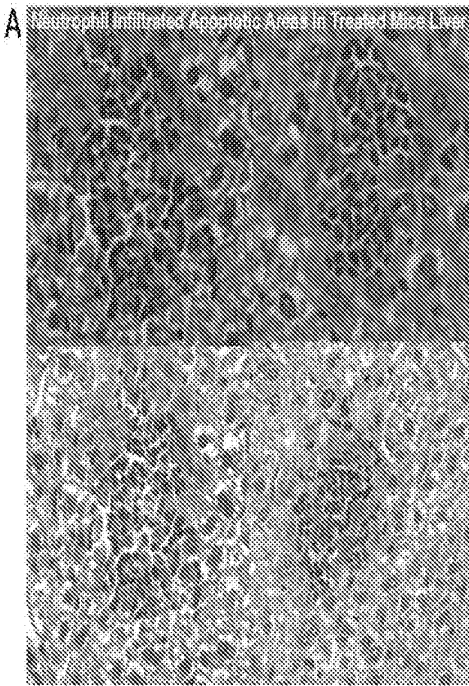


FIGURE 11B

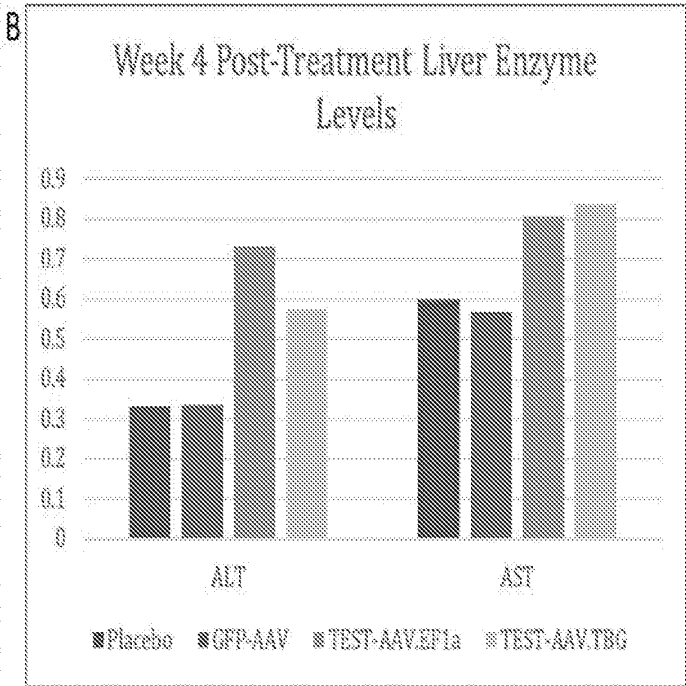
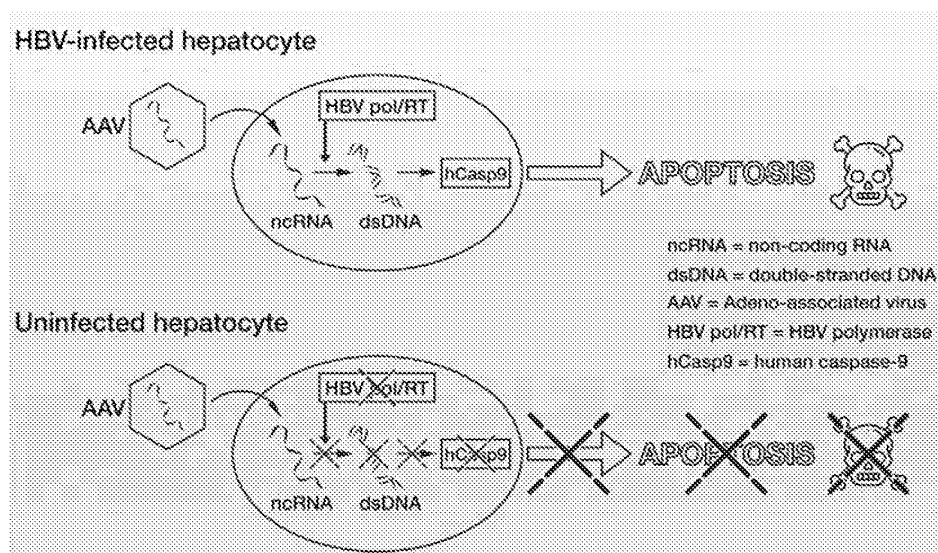


FIGURE 11C



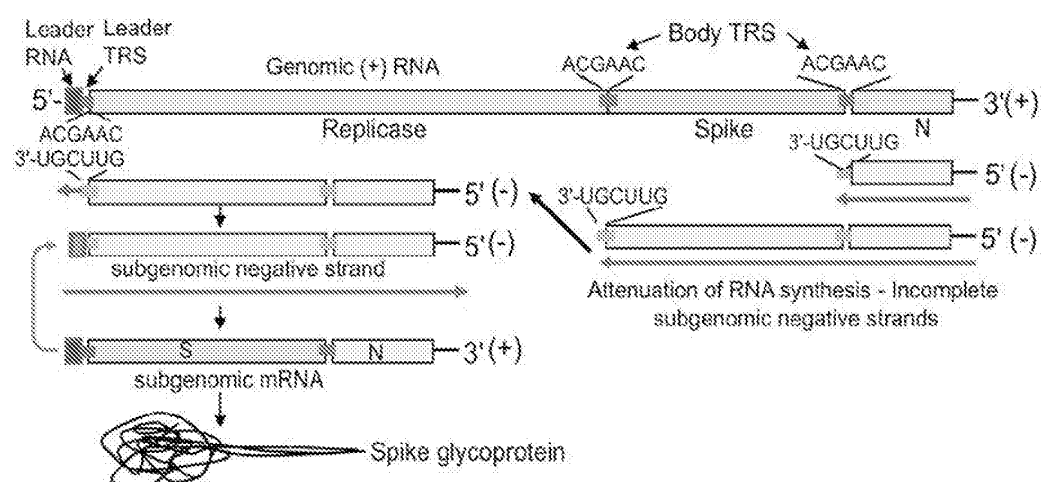


FIGURE 12A

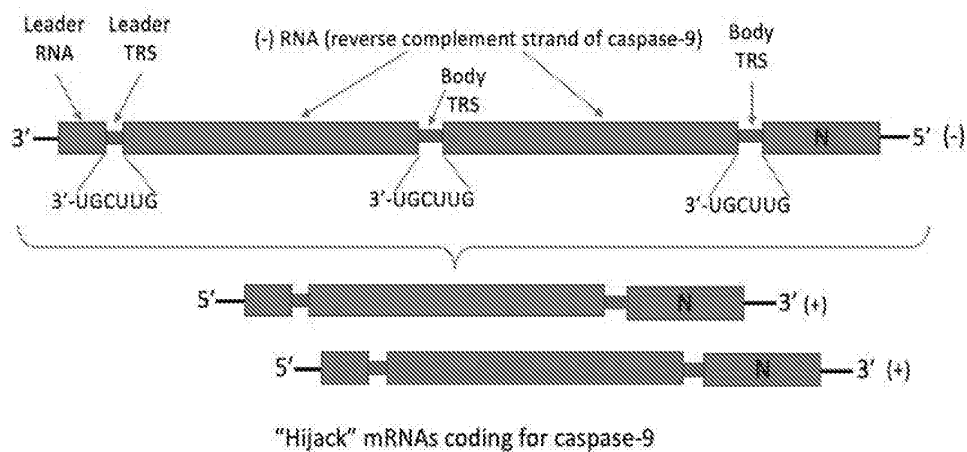
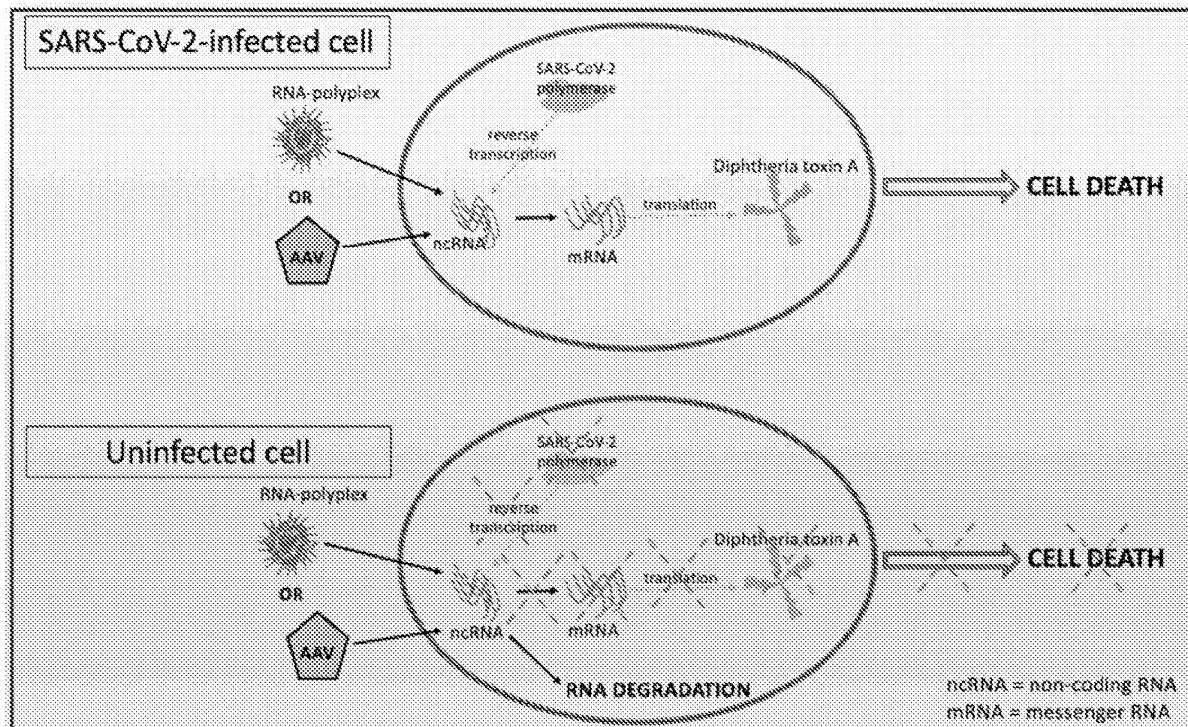


FIGURE 12B

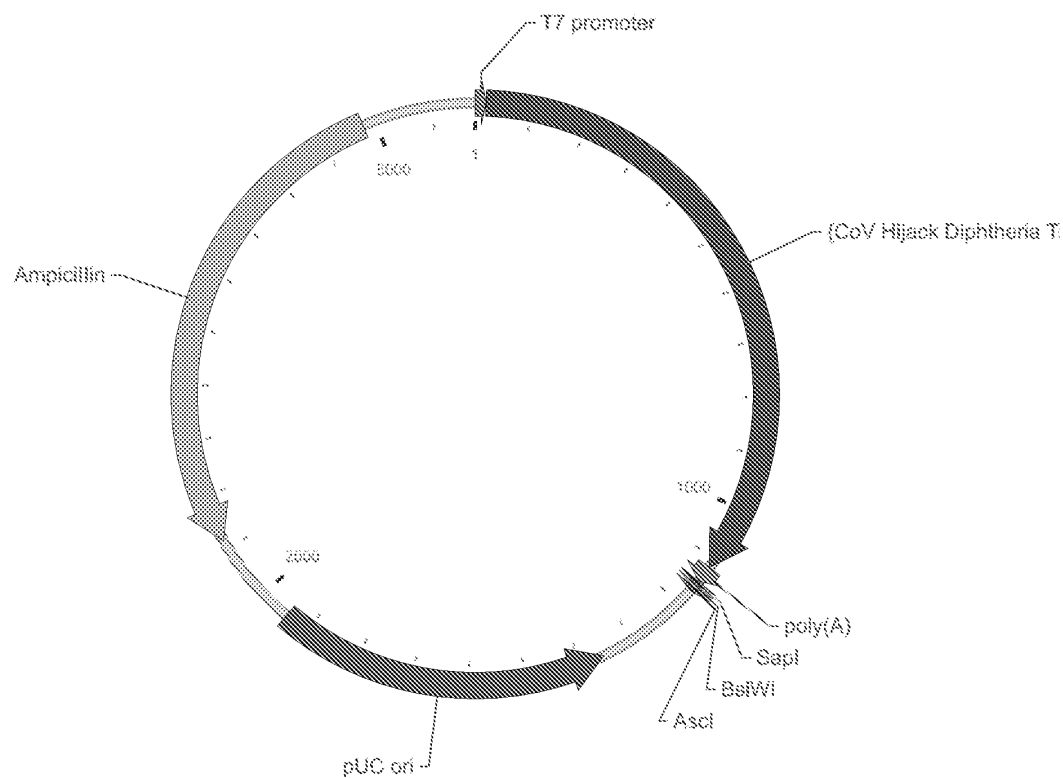
FIGURE 13



Vector Summary

Vector ID	CoV-2 Hijack DTA
Vector Name	pT7[mRNA]-{CoV Hijack Diphtheria Toxin A}
Vector Size	3177 bp
Vector Type	In Vitro Transcription Vector (for mRNA)
Inserted Transcribed Sequence	{CoV Hijack Diphtheria Toxin A}
Plasmid Copy Number	High
Antibiotic Resistance	Ampicillin
Cloning Host	VB UltraStable (or alternative strain)

Vector Map



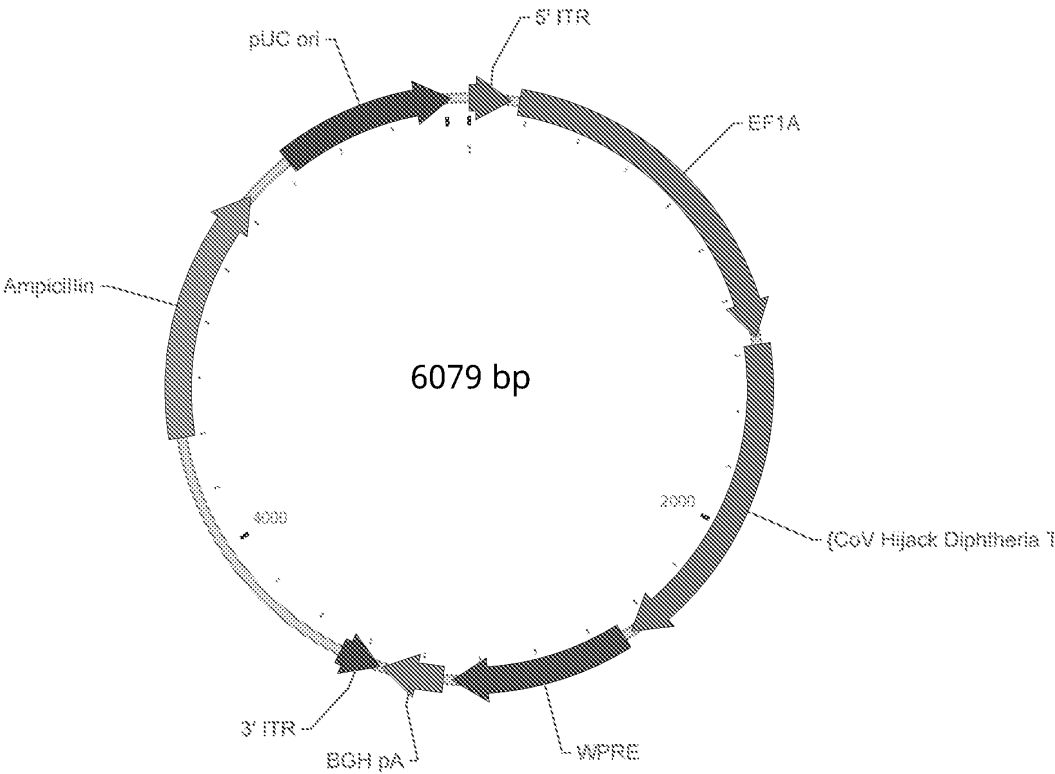
Name	Position	Size (bp)	Type	Description	Application notes
T7 promoter	■ 1-19	19	Promoter	T7 promoter	Drives high-level transcription of downstream gene in E. coli host cells that express T7 RNA polymerase; can also be used for in vitro transcription.
{CoV Hijack Diphtheria Toxin A...	■ 20-1116	1097	Transcribed Sequence	None	None
poly(A)	■ 1117-1146	30	Miscellaneous	Polyadenylation	Allows to stability of mRNA.
SapI	■ 1148-1154	7	Miscellaneous	SapI restriction site	Allows linearization of vector.
BsiWI	■ 1155-1160	6	Miscellaneous	BsiWI restriction site	Allows linearization of vector.
AscI	■ 1161-1168	8	Miscellaneous	AscI restriction site	Allows linearization of vector.
pUC ori	■ complement (1358-1946)	589	Rep_origin	pUC origin of replication	Facilitates plasmid replication in E. coli; regulates high-copy plasmid number (500-700).
Ampicillin	■ complement (2117-2977)	861	ORF	Ampicillin resistance gene	Allows E. coli to be resistant to ampicillin.

1	TAATACGACT	CACATATAGGC	ATGAAGACAG	TGTTTAGCAA	GATTGTTTTT	TTGTCATTCT	CCTAAGAAGC	TATTAAAAATC
81	ACATGGGGAT	AGCACTACTA	AAATTAATTT	TACACATTAG	GGCTCTTCCA	TATAGGCAGC	TCTCCCTAGC	ATTGTTCACT
161	GTACACTCGA	TCGTACTCCG	CGTGGCCTCG	GTGAAAATGT	GGTGGCTCTT	TCAAGTCCTC	CCTAATGTTA	CACACTGATT
241	AAAGATTGTT	ACAATGAGCT	ACCTACTGAT	CGCCTGACAC	GATTTCTTGC	ACAGGCTTGA	GCCATATACT	CATACATCGC
321	ATCTTGGCCA	CGTTTTCCAC	GGGTTTCAAA	ATTAATCTCA	AGTTCTACGC	TTAACGCTTT	CGCCTGTTCC	CAGTTATTAA
401	TATATTCAAC	GCTAGAACTC	CCCTCAGCGA	AGGGAAGGCT	GAGCACTACA	CGCGAAGCAC	CATCACCAGAA	CCTTTTGATA
481	AACTCTTCCG	TTCCGACTTG	CTCCATCAAC	GGTTCAGTGA	GACTTAAACC	TAACTCTTTC	TTAATAGTTT	CGGCATTATC
561	CACTTTTAGT	GCGAGAACCT	TCGTCACTCC	TGGATACGTC	ACTTTGACCA	CGCCTCCAGC	TTTTCCAGAG	AGCGGGTTTT
641	CATTATCTAC	AGAGTATCCC	GCAGCGTCGT	ATTATTGTTC	GGTACTATAA	AACCTTTTCC	AATCATCGTC	ATAATTTCCCT
721	TGTGTACCAG	ATTTTGGCTT	TTGTATACCT	TTTGAATGG	AATCTACATA	ACCAGGTTTA	GTCCCGTGGT	ACGAAGAAAA
801	GTTTTCCATC	ACAAAAGATT	TAGAAGAATC	AACAACATCA	TCAGCGCCCA	TCTTACCTTT	CGGTACACCC	CGGACGAAAC
881	CTAGATGTGC	TGATGATCGG	CTGCAACACG	GACGAAACCG	TAAGCAGCCT	GCAGAAGATA	GACGAGTTAC	TCGTGTCCTG
961	TCAACGACAG	TAATTAGTTA	TTAATTATAC	TGCGTGAGTG	CACTAAGCAT	GCAGCCGAGT	GACAGCCACA	CAGATTTTAA
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1361	CCATAGGCTC	CGCCCCCTCG	ACGAGCATCA	CAAAAATCGA	CGCTCAAGTC	AGAGGTGGCG	AAACCCGACA	GGACTATAAA
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1521	TTTCTCCCTT	CGGGAAGCGT	GGCGCTTCTT	CATAGCTCAC	GCTGTAGGTA	TCTCAGTTCC	GTGTAGGTCC	TTCGCTCCAA
1601	GCTGGGCTGT	GTGCACGAAC	CCCCCGTTCA	GCCCGACCGC	TGCGCCTTAT	CCGTAACATA	TCGTCTTGAG	TCCAACCCGG
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1841	CGGAAAAAGA	GTTGGTAGCT	CTTGATCCGG	CAAAACAAACC	ACCGCTGGTA	GCGGTGGTTT	TTTTGTTTGC	AAGCAGCAGA
1921	TTACCGCGCAG	AAAAAAAGGA	TCTCAAGAAG	ATCCTTTGAT	CTTTTCTACG	GGGTCTGACG	CTCAGTGGAA	CGAAAACTCA
2001	CGTTAAGGGA	TTTTGGTCAT	GAGATTATCA	AAAAGGATCT	TCACCTAGAT	CCTTTTAAAT	TAAAAATGAA	GTTTTAAATC
2081	AATCTAAAGT	ATATATGAGT	AAACTTGGTC	TGACAGTTAC	CAATGCTTAA	TCAGTGAGGC	ACCTATCTCA	GCGATCTGTC
2161	TATTTCTGTT	ATCCATAGTT	GCCTGACTCC	CCGTCTGTGA	GATAACTACG	ATACGGGAGG	GCTTACCATC	TGGCCCCAGT
2241	GCTGCAATGA	TACCGCGAGA	TCCACGCTCA	CCGCTCCAGT	ATTTATCAGC	AATAAACCCAG	CCAGCCGGAA	GGGCCGAGCG
2321	CAGAAGTGGT	CCTGCAACTT	TATCCGCCTC	CATCCAGTCT	ATTAATTGTT	GCCGGGAAGC	TAGAGTAAGT	AGTTCGCCAG
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2561	CGTTGTCAGA	AGTAAGTTGG	CCGCAGTGTT	ATCACTCATG	GTTATGGCAG	CACTGCATAA	TTCTCTTACT	GTCAIGCCAT
2641	CCGTAAAGATG	CTTTTCTGTG	ACTGGTGAGT	ACTCAACCAA	GTCAITCTGA	GAATAGTGTA	TGCGGCGACC	GAGTTGCTCT
2721	TGCCCGGCGT	CAATACGGGA	TAATACCGCG	CCACATAGCA	GAACITTTAA	AGTGCTCATC	ATTGGAAAAC	GTTCTTCGGG
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2881	CTTTTACTTT	CACCAGCGTT	TCTGGGTGAG	CAAAAACAGG	AAGGCAAAAT	GCCGCAAAAA	AGGGAATAAG	GGCGACACGG
2961	AAATGTTGAA	TACTCATACT	CTTCCTTTTT	CAATATTATT	GAAGCATTTA	TCAGGGTTAT	TGTCTCATGA	GCGGATACAT
3041	ATTTGAATGT	ATTTAGAAAA	ATAAACAAAT	AGGGGTTCCG	CGCACATTTT	CCCGAAAAAGT	GCCACCTGAC	GTCTAAGAAA
3121	CCATTATTAT	CATGACATTA	ACCTATAAAA	ATAGGCGTAT	CACGAGGCC	TTTCGTCT		

Vector Summary

Vector Name	pAAV[ncRNA]-EF1A>{CoV Hijack Diphtheria Toxin A};WPRE
Vector Size	6079 bp
Viral Genome Size	3482 bp
Vector Type	Mammalian ncRNA Expression AAV Vector
Inserted Promoter	EF1A
Inserted Non-coding RNA	{CoV Hijack Diphtheria Toxin A}
Inserted Regulatory Element	WPRE
Plasmid Copy Number	High
Antibiotic Resistance	Ampicillin
Cloning Host	VB UltraStable (or alternative strain)

Vector Map



Name	Position	Size (bp)	Type	Description	Application notes
5' ITR	■ 1-141	141	ITR	AAV 5' inverted terminal repeat (functional equivalent of wild-type 5' ITR)	Allows replication of the viral genome and its packaging into virus.
EF1A	■ 169-1347	1179	Promoter	Human eukaryotic translation elongation factor 1 α 1 promoter	Strong promoter.
{CoV Hijack Diphtheria Toxin A...	■ 1372-2468	1097	Non-coding RNA	None	None
WPRE	■ 2499-3096	598	Regulatory Element	Woodchuck hepatitis virus posttranscriptional regulatory element	Enhances virus stability in packaging cells, leading to higher titer of packaged virus; enhances higher expression of transgenes.
BGH pA	■ 3127-3334	208	PolyA_signal	Bovine growth hormone polyadenylation signal	Allows transcription termination and polyadenylation of mRNA transcribed by Pol II RNA polymerase.
3' ITR	■ complement (3342-3482)	141	ITR	AAV 3' inverted terminal repeat	Allows replication of the viral genome and its packaging into virus.
Ampicillin	■ 4399-5259	861	ORF	Ampicillin resistance gene	Allows E. coli to be resistant to ampicillin.
pUC ori	■ 5430-6018	589	Rep_origin	pUC origin of replication	Facilitates plasmid replication in E. coli; regulates high-copy plasmid number (500-700).

Vector Sequence

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1  CCTGCAGGCA GCTGCGCGCT CGCTCGCTCA CTGAGGCCGC CCGGGCAAAG CCCGGGCGTC GGGCGACCTT TGGTCGCCCG
61  GCCTCAGTGA GCGAGCGAGC GCGCAGAGAG GGAGTGGCCA ACTCCATCAC TAGGGGTTCC TTCTAGACAA CTTTGTATAG
161 AAAAGTTGGG CTCCGGTGCC CGTCAGTGGG CAGAGCGCAC ATCGCCACAC GTCCCCGAGA AGTTGGGGGG AGGGGTCGGC
241 AATTGAACCG GTGCC TAGAG AAGGTGGCGC GGGGTAAACT GGGAAAGTGA GTTCGTGTAC TGGCTCCGCC TTTTCCCCGA
321 GGGTGGGGGA GAACCGTATA TAAGTGACGT AGTCGCCGTG AACGTTCTTT TTCGCAACGG GTTTGCCGCC AGAACACAGG
401 TAAGTGCCGT GTGTGGTTCC CGCGGGCCTG GCCTCTTTAC GGGTTATGGC CCTTGCGTGC CTGAATTAC TTCCACCTGG
481 CTGCAGTACG TGATTCTTGA TCCCGAGCTT CCGGTTGGAA GTGGGTGGGA GAGTTCGAGG CCTTGCCTT AAGGAGCCCC

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561 TTGCGCTCGT GCTTGAGTTG AGGCCTGGCC TGGGCGCTGG GCGCGCGCGG TGCGAATCTG GTGGCACCTT CGCGCCTGTC
561 TCGCTGCTTT CGATAAGTCT CTAGCCATTT AAAATTTTTG ATGACCTGCT GCGACGCTTT TTTTCTGGCA AGATAGTCTT
721 GTAAATGCGG GCCAAGATCT GCACACTGGT ATTTGCGTTT TTGGGGCCGC GGGCGGCGAC GGGGCCCGTG CGTCCCAGCG
801 CACATGTTCG GCGAGGCGGG GCCTGCGAGC GCGGCCACCG AGAATCGGAC GGGGGTAGTC TCAAGCTGGC CGGCCTGCTC
881 TGGTGCCTGG TCTCGCGCGG CCGTGTATCG CCCC GCCCTG GCGCGCAAGG CTGGCCCGGT CGGCACCACT TCGGTGAGCG
961 GAAAGATGGC CGCTTCCCGG CCCTGCTGCA GGGAGCTCAA AATGGAGGAC GCGCGCTCG GGAGAGCGGG CGGTGAGTC
1041 ACCCACACAA AGGAAAAGGG CCTTTCGTC CTCAGCCGTC GCTTCATGTG ACTCCACGGA GTACCGGGCG CCGTCCAGGC
1121 ACCTCGATTA GTTCTCGAGC TTTTGAGTA CGTCGTCTTT AGGTTGGGGG GAGGGGTTTT ATGCGATGGA GTTTCCCCAC
1201 ACTGAGTGGG TGAGACTGA AGTTAGGCCA GCTTGGCACT TGATGTAATT CTCCTTGGAA TTGCGCTTTT TTGAGTTTGG
1281 ATCTTGGTTC ATCTCAAGC CTCAGACAGT GGTTCAAAGT TTTTTCTTC CATTTAGGT TCGTGACAA GTTTGTACAA
1361 AAAAGCAGGC TCATGAAGAC AGTGTTAGC AAGATTGTT TTTTGTCACT CTCCTAAGAA GCTATTAAAA TCACATGGGG
1441 ATAGCACTAC TAAATTAAT TTTACACATT AGGGCTCTTC CATATAGGCA GCTCTCCCTA GCATTGTTC CTGTACACTC
1521 GATCGTACTC CGGTGGGCT CGGTGAAAAT GTGGTGGCTC TTTCAAGTCC TCCCTAATGT TACACACTGA TTAAAGATTG
1601 TTACAATGAG CTACCTACTG ATCGCTGAC ACGATTTCTT GCACAGGCTT GAGCCATATA CTATACATC GCATCTTGGC
1681 CACGTTTTCC ACGGGTTTCA AAATTAATCT CAAGTTCTAC GCTTAACGCT TTCGCTGT TCCAGTTATT AATATATTCA
1761 ACGCTAGAAC TCCCTCAGC GAAGGGAAGG CTGAGCACTA CACGCGAAGC ACCATCACCG AACCTTTGA TAACTCTTC
1841 CGTTCGACT TGCTCCATCA ACGGTTCACT GAGACTTAA CCTAACTCTT TCTTAATAGT TTCGGCATT TCCACTTTTA
1921 GTGCGAGAAC CTTGTCAGT CCTGGATACG TCACTTTGAC CACGCCTCCA GCTTTTCCAG AGAGCGGGTT TTCATTATCT
2001 ACAGAGTATC CCGCAGCGTC GTATTATTG TCGGTACTAT AAAACCCCTT CCAATCATCG TCATAATTC CTTGTGTACC
2081 AGATTTTGGC TTTTGTATAC CTTTTGAAT GGAATCTACA TAACCAGGTT TAGTCCCGTG GTACGAAGAA AAGTTTCCA
2161 TCACAAAAGA TTTAGAAGAA TCAACAACAT CATCAGCGCC CATCTTACCT TTCGGTCACA CCCGGACGAA ACCTAGATGT
2241 GCTGATGATC GGTGCAACA CGGACGAAAC CGTAAGCAGC CTGAGAAGA TAGACGAGTT ACTCGTGTCC TGTCAACGAC
2321 AGTAATTAGT TATTAATTAT ACTGCGTGAG TGCACTAAGC ATGCAGCCGA GTGACAGCCA CACAGATTTT AAAGTTCGTT
2401 TAGAGAACAG ATCTACAAGA GATCGAAAGT TGGTTGGTTT GTTACCTGGG AAGGTATAAA CCTTTAATAC CCAGCTTTCT
2481 TGTACAAAGT GGAATTCGG ATAATCAACC TCTGGATTAC AAAATTGTG AAAGATTGAC TGGTATCTT AACTATGTG
2561 CTCCCTTTAC GCTATGTGGA TACGCTGCTT TAATGCTTTT GTATCATGCT ATTGCTTCCC GTATGCTTTT CATTTCTCC
2641 TCCTTGATA AATCTGGTT GCTGTCTCTT TATGAGGAGT TGTGGCCCGT TGTAGGCAA CGTGGCGTGG TGTGCACTGT
2721 GTTTGCTGAC GCAACCCCA CTGGTTGGGG CATTGCCACC ACCTGTCAGC TCCTTTCCGG GACTTTGCTT TTCCCTCC
2801 CTATTGCCAC GCGGGAATC ATCGCCGCTT GCCTTGCCCG CTGCTGGACA GGGGCTCGGC TGTGGGCAC TGACAATTCC
2881 GTGGTGTGT CCGGGAAGCT GACGTCTTTT CCATGGCTGC TCGCCTGTGT TGCCACCTGG ATTCTGCGCG GGACGTCTTT
2961 CTGTACGTC CCTTCGGCCC TCAATCCAGC GGACCTTCTT TCCCGCGGCC TGTGCGCGC TCTGCGCCT CTTCCGCGTC
3041 TTCGCTTCG CCTCAGACG AGTCGGATCT CCCTTTGGGC CGCCTCCCG CATCGGAAT TCCTAGAGCT CGCTGATCAG
3121 CCTCGACTGT GCCTTCTAGT TGCCAGCCAT CTGTGTTTG CCCCTCCCC GTGCTTCTT TGACCTTGA AGGTGCCACT
3201 CCCACTGTCC TTTCTAATA AAATGAGGAA ATTGCATCGC ATTGTCTGAG TAGGTGTCT TCTATTCTGG GGGGTGGGGT
3281 GGGGCAGGAC AGCAAGGGGG AGGATTGGGA AGAGAATAGC AGGCATGCTG GGGAGGGCCG CAGGAACCCC TAGTGATGGA
3361 GTTGGCCACT CCTCTCTGCG GCGCTCGCTC GCTCACTGAG GCGGGGCGAC CAAAGGTGCG CGGACGCCCC GGCTTTGCC
3441 GGGCGGCCCTC AGTGAGCGAG CGAGCGCGCA GCTGCTGCA GGGCGCCTG ATGCGGTATT TTCTCCTTAC GCATCTGTGC
3521 GGTATTTCAC ACCGCATACG TCAAAGCAAC CATAGTACGC GCCCTGTAGC GCGCATTAAG GCGCGCGGGG GGTGGTGGTT
3601 ACGCGCAGCG TGACCGCTAC ACTTGCCAGC GCCTTAGCGC CCGCTCCTTT CGCTTCTTC CCTTCCTTC TCGCCACGTT
3681 CGCCGGCTTT CCCCCTCAAG CTCTAAATCG GGGCTCCCT TTAGGGTTCC GATTAGTGC TTTACGGCAC CTCGACCCCA
3761 AAAAATTGA TTTGGGTGAT GGTTCACGTA GTGGCCATC GCCCTGATAG ACGGTTTTTC GCCCTTGAC GTTGGAGTCC
3841 ACGTTCTTTA ATAGTGACT CTTGTCCAA ACTGGAACAA CACTCAACTC TATCTCGGGC TATTCTTTT ATTTATAAGG
3921 GATTTTGCCG ATTTGCTCT ATTGGTTAAA AAATGAGCTG ATTTAACAAA AATTTAACGC GAATTTTAAC AAAATATTAA
4001 CGTTTACAAT TTTATGGTGC ACTCTCAGTA CAATCTGCTC TGATGCCGCA TAGTTAAGCC AGCCCCGACA CCCGCCAACA
4081 CCCGCTGACG CGCCCTGACG GGCTTGTCTG CTCCCGGCAT CCGCTTACAG ACAAGCTGTG ACCGTCTCCG GGAGCTGCAT
4161 GTGTACAGAG TTTTACCCTG CATCACCAGG ACGCGCGAGA CGAAAGGGCC TCGTGATACG CCTATTTTTA TAGGTTAATG
4241 TCATGATAAT AATGGTTTCT TAGACGTCAG GTGGCACTTT TCGGGGAAAT GTGCGCGGAA CCCCTATTTG TTTATTTTTT
4321 TAAATACATT CAAATATGTA TCCGCTCATG AGACAATAAC CCTGATAAAT GCTTCAATAA TATTGAAAAA GGAAGAGTAT

4401	GAGTATTCAA	CATTTCCGTG	TCGCCCTTAT	TCCCTTTTTT	GCGGCATTTT	GCCTTCCTGT	TTTTGCTCAC	CCAGAAACGC
4481	TGGTGAAAGT	AAAAGATGCT	GAAGATCAGT	TGGGTGCACG	AGTGGGTAC	ATCGAACTGG	ATCTCAACAG	CGGTAAGATC
4561	CTTGAGAGTT	TTCGCCCCGA	AGAACGTTTT	CCAATGATGA	GCACTTTAA	AGTTCTGCTA	TGTGGCGCGG	TATTATCCCG
4641	TATTGACGCC	GGGCAAGAGC	AACTCGGTGC	CCGCATACAC	TATTCTCAGA	ATGACTTGGT	TGAGTACTCA	CCAGTCACAG
4721	AAAAGCATCT	TACGGATGGC	ATGACAGTAA	GAGAATTATG	CAGTGTGCC	ATAACCATGA	GTGATAACAC	TGCGGCCAAC
4801	TTACTTCTGA	CAACGATCGG	AGGACCGAAG	GAGCTAACCG	CTTTTTTGCA	CAACATGGGG	GATCATGTAA	CTCGCCTTGA
4881	TCGTTGGGAA	CCGGAGCTGA	ATGAAGCCAT	ACCAAACGAC	GAGCGTGACA	CCACGATGCC	TGTAGCAATG	GCAACAACGT
4961	TGCGCAAAC	ATTAACCTGG	GAACACTTAA	CTCTAGCTTC	CCGGCAACAA	TTAATAGACT	GGATGGAGGC	GGATAAAGTT
5041	GCAGACCAC	TTCTGCGCTC	GGCCCTTCCG	GCTGGCTGGT	TTATTGCTGA	TAAATCTGGA	GCCGGTGAGC	GTGGAAGCCG
5121	CGGTATCATT	GCAGCACTGG	GGCCAGATGG	TAAGCCCTCC	CGTATCGTAG	TTATCTACAC	GACGGGGAGT	CAGGCAACTA
5201	TGGATGAACG	AAATAGACAG	ATCGCTGAGA	TAGGTGCCTC	ACTGATTAAG	CATTGGTAAC	TGTCAGACCA	AGTTTACTCA
5281	TATATACTTT	AGATTGATTT	AAAACCTCAT	TTTTAATTTA	AAAGGATCTA	GGTGAAGATC	CTTTTGTATA	ATCTCATGAC
5361	CAAAATCCCT	TAACGTGAGT	TTTCGTTCCT	CTGAGCGTCA	GACCCCGTAG	AAAAGATCAA	AGGATCTTCT	TGAGATCCTT
5441	TTTTTCTGCG	CGTAATCTGC	TGCTTGCAAA	CAAAAAACC	ACCGCTACCA	GCGGTGGTTT	GTTTGCCGGA	TCAAGAGCTA
5521	CCAATCTTTT	TTCCGAAGGT	AACTGGCTTC	AGCAGAGCGC	AGATACCAAA	TACTGTTCTT	CTAGTGTAGC	CGTAGTTAGG
5601	CCACCACTTC	AAGAATCTTG	TAGCACCGCC	TACATACCTC	GCTCTGCTAA	TCCTGTTACC	AGTGGCTGCT	GCCAGTGGCG
5681	ATAAGTCGTG	TCTTACCGGG	TTGGACTCAA	GACGATAGTT	ACCGGATAAG	GCGCAGCGGT	CGGGCTGAAC	GGGGGGTTCTG
5761	TGCACACAGC	CCAGCTTGGA	GCGAACGACC	TACACCGAAC	TGAGATACCT	ACAGCGTGAG	CTATGAGAAA	GCGCCACGCT
5841	TCCCGAAGGG	AGAAAGGCGG	ACAGGTATCC	GGTAAGCGGC	AGGGTCGGAA	CAGGAGAGCG	CACGAGGGAG	CTTCCAGGGG
5921	GAAACGCCTG	GTATCTTTAT	AGTCCTGTGC	GGTTTCGCCA	CCTCTGACTT	GAGCGTCGAT	TTTTGTGATG	CTCGTCAGGG
6001	GGGCGGAGCC	TATGGAAAAA	CGCCAGCAAC	GCGGCCTTTT	TACGGTTCCT	GGCCTTTTGC	TGGCCTTTTG	CTCACATGT

FIGURE 16A

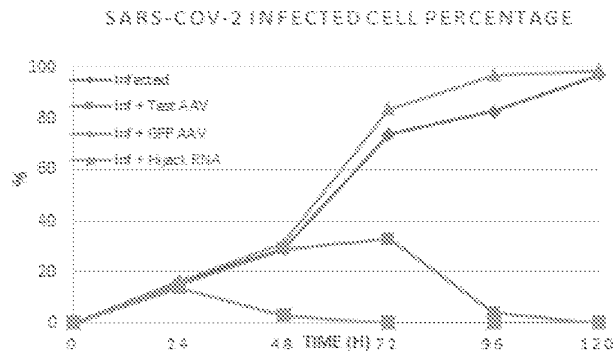


FIGURE 16B

