

FIG. 1

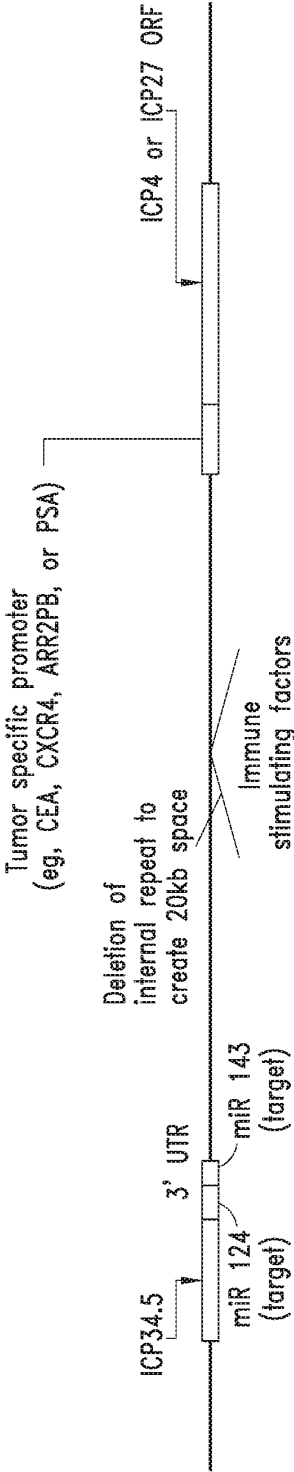
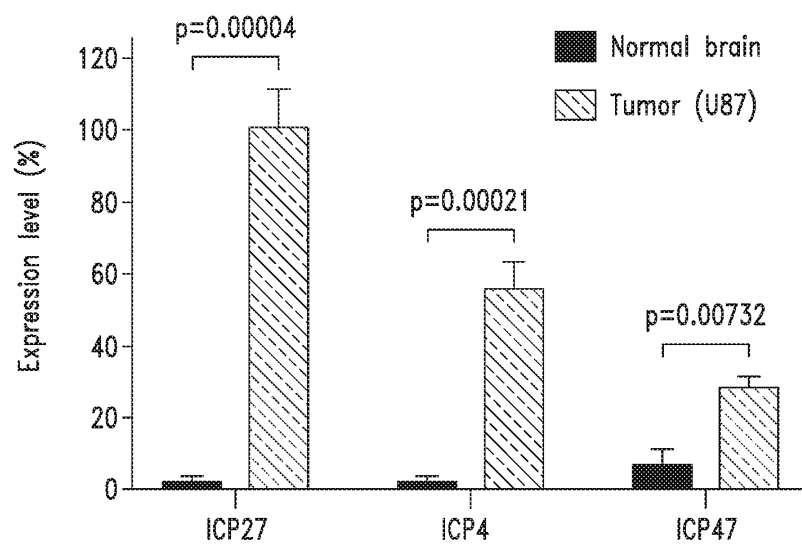


FIG. 2

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*FIG. 3*

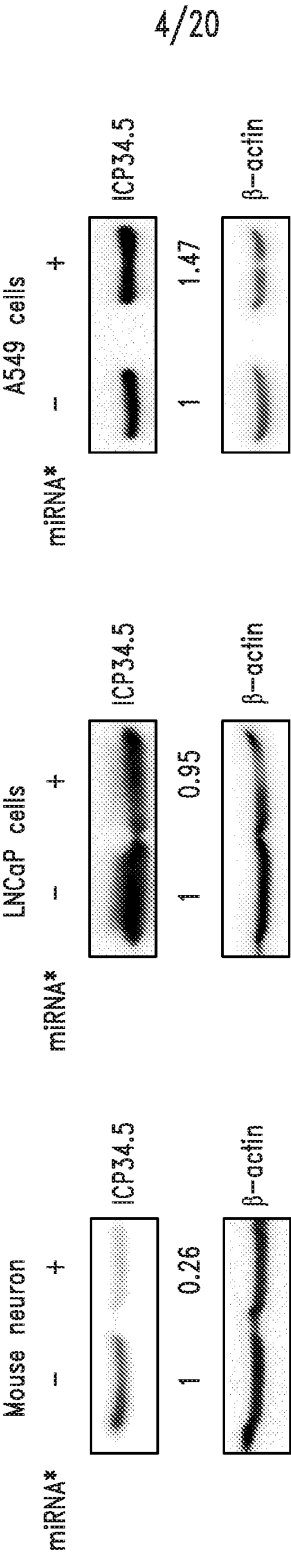


FIG. 4

Transcriptional and translational dual-regulated virus (TTDR)

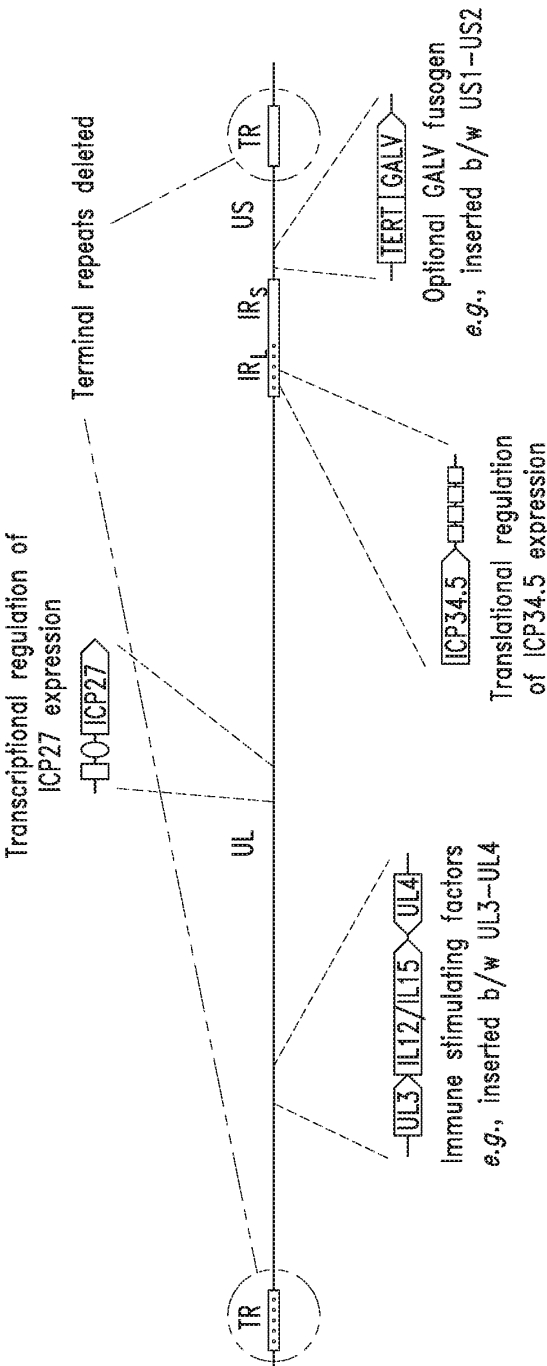
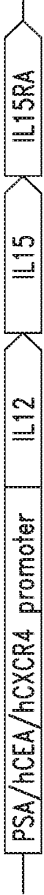


FIG. 5

Transcriptional and translational dual-regulated virus (TTDR)

- Transcriptional regulation of ICP27 expression via prostate-specific PSA or Probasin (ARR2PB) promoters, or tumor-specific hCEA or hCXCR4 promoters

- Transcriptional regulation of IL12/IL15/IL15RA expression cassette inserted between viral genes such as US1/US2, UL3/UL4, or UL50/UL51 via prostate-specific PSA promoter or tumor-specific hCEA or hCXCR4 promoters

- Transcriptional regulation of fusogen (GALV) expression cassette inserted between viral genes such as US1/US2, UL3/UL4, or UL50/UL51 via tumor-specific hTERT promoter

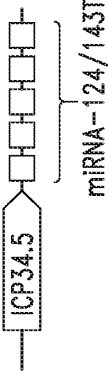
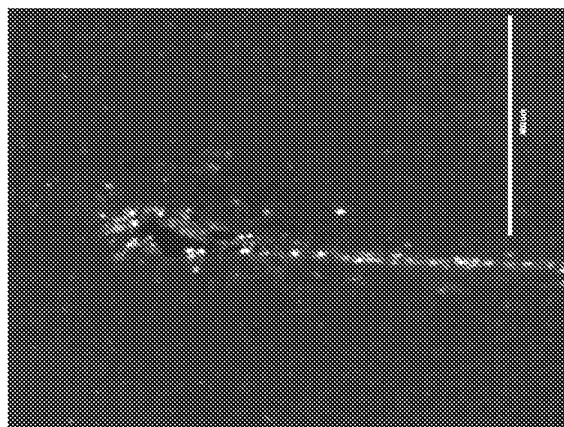
- Translational regulation of ICP34.5 via multiple copies of miRNA-124/143 response elements incorporated into 3' UTR of ICP34.5

- Terminal repeats deleted while preserving native ICP47 promoter

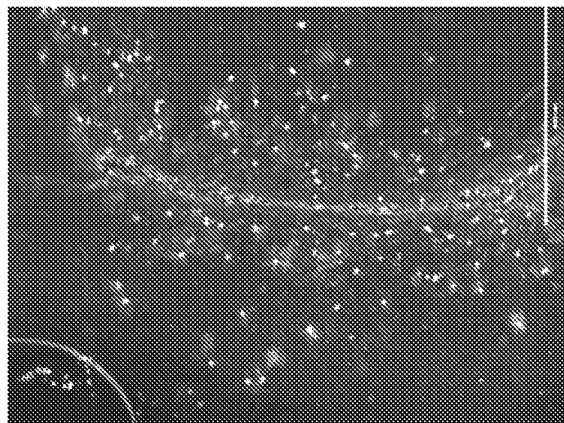
FIG. 6

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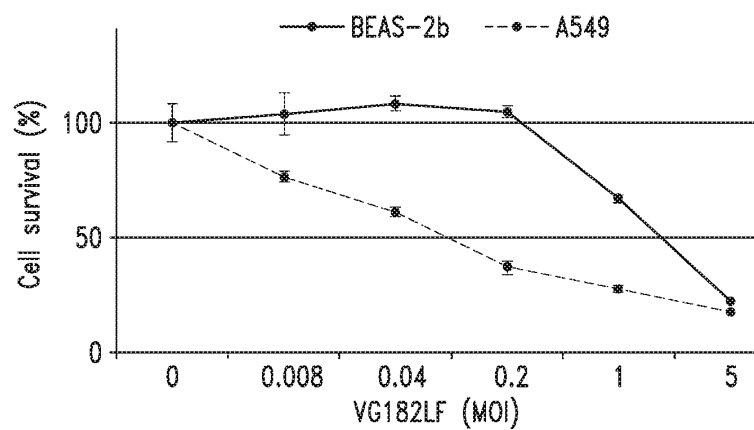
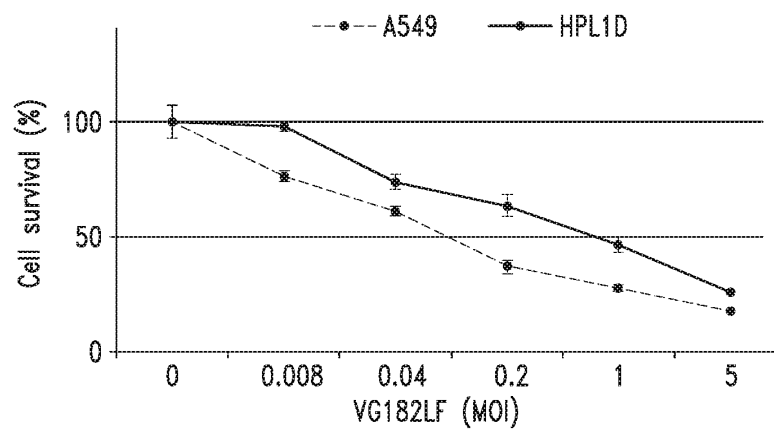
Virus: CXCR4-TF-Fc-h1215-miR
• CXCR4 transcriptional and ICP34.5
3' miR translational dual control



Virus: CXCR4-TF-Fc-h1215
• CXCR4 transcriptional control only

*FIG. 7*

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*FIG. 8A**FIG. 8B*

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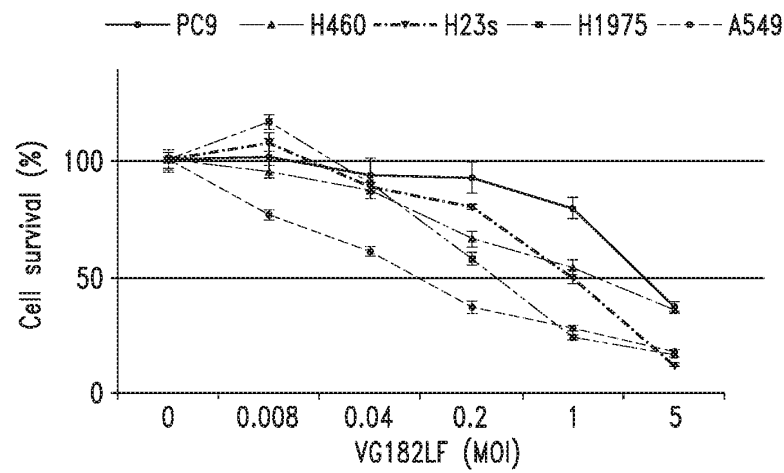


FIG. 8C

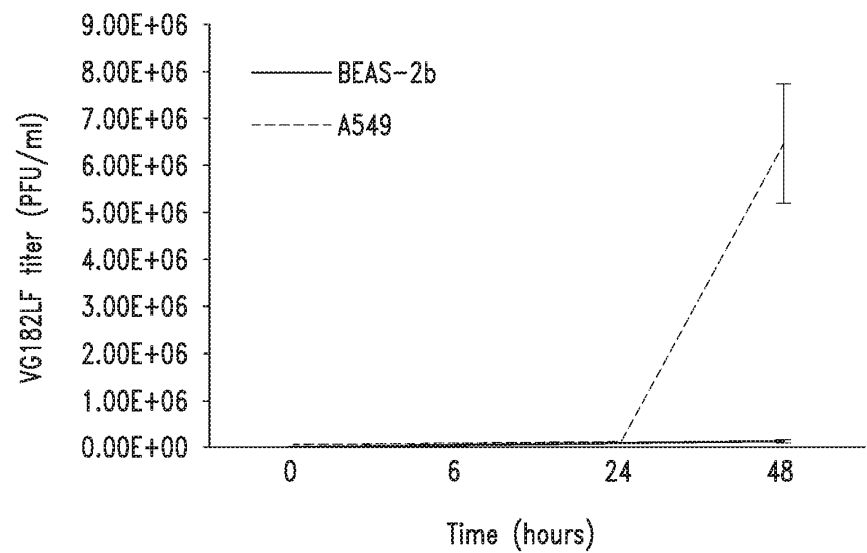
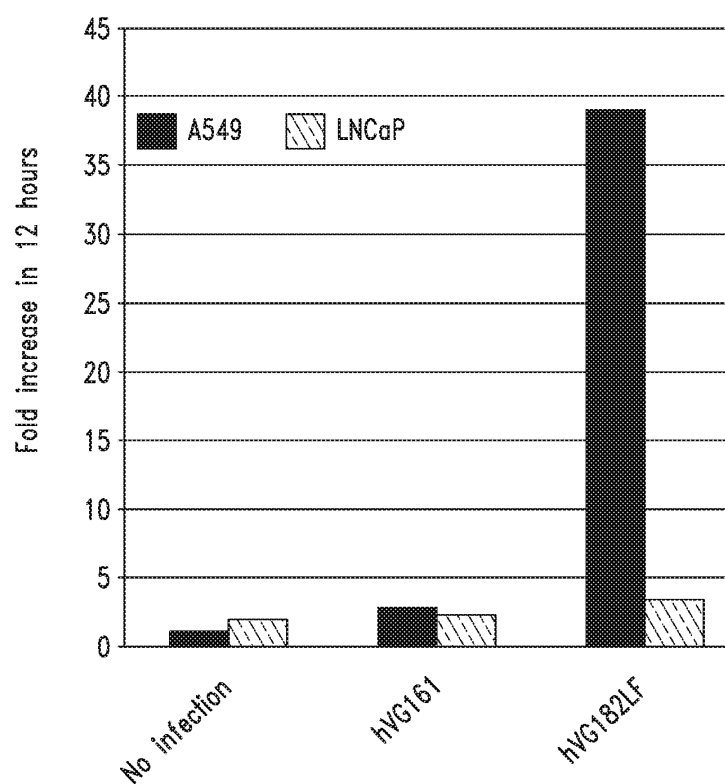


FIG. 9

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*FIG. 10*

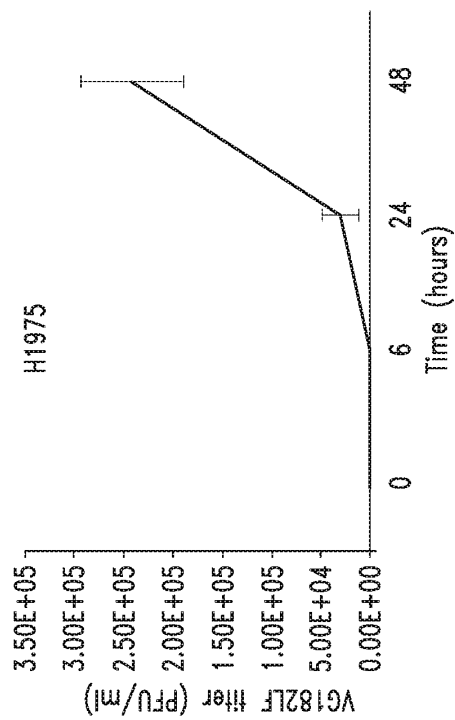


FIG. 11A

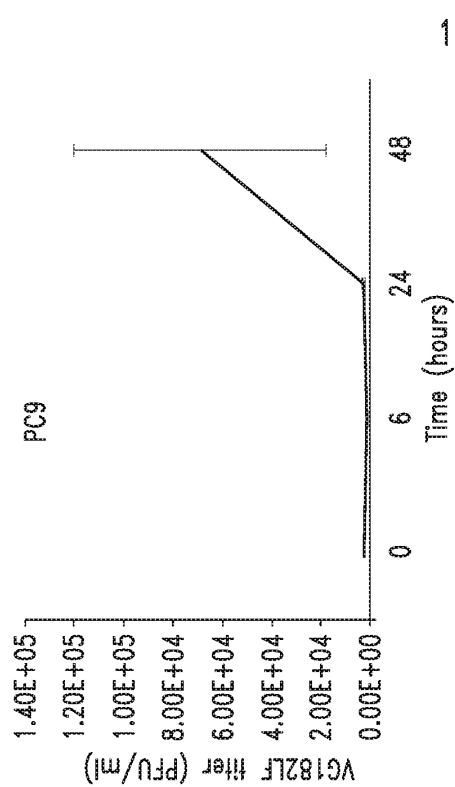


FIG. 11C

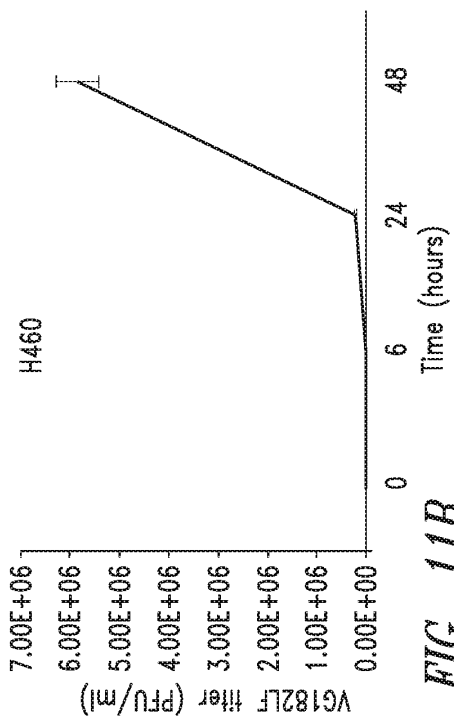


FIG. 11B

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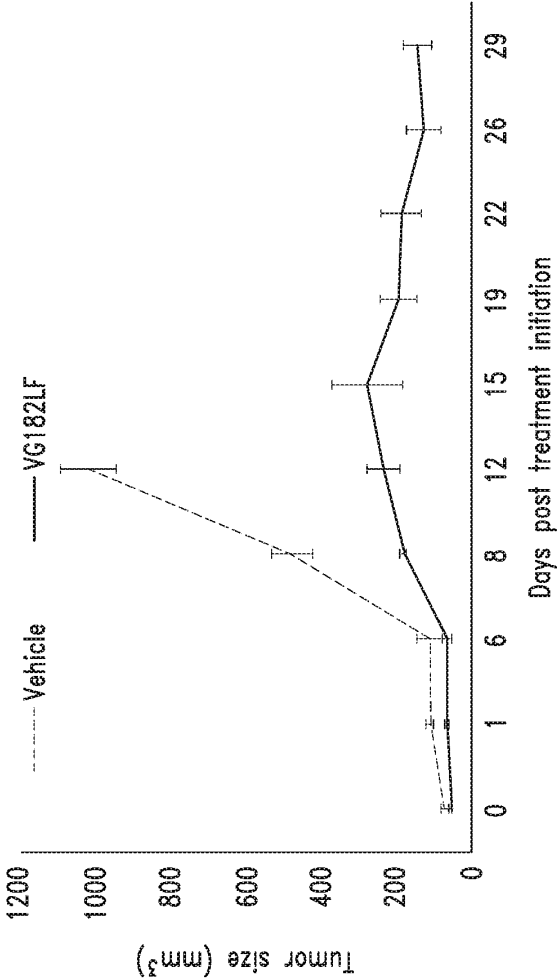


FIG. 12

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Tumor type	Downregulated miRs
Brain	let-7, miR-100, miR-101, miR-105, miR-106a, miR-107, miR-122, miR-124, miR-124-3p, miR-124-5p, miR-125a, miR-125a-5p, miR-125b, miR-126, miR-127-3p, miR-127-5p, miR-128, miR-128-3p, miR-129, miR-129-5p, miR-1297, miR-133a, miR-133b, miR-134, miR-135b, miR-136, miR-137, miR-139, miR-139-5p, miR-141, miR-142-3p, miR-143, miR-144-3p, miR-145, miR-146a, miR-146b, miR-146b-5p, miR-149, miR-150-5p, miR-152, miR-153, miR-154, miR-15b, miR-16, miR-181a, miR-181b, miR-181c, miR-181d, miR-184, miR-185, miR-194, miR-195, miR-197, miR-198, miR-199a-3p, miR-199b-5p, miR-200a, miR-200b, miR-200b-3p, miR-200c, miR-203a, miR-204, miR-204-3p, miR-205, miR-206, miR-21, miR-212-3p, miR-214, miR-216a, miR-217, miR-218, miR-219a, miR-22, miR-221, miR-222, miR-223b, miR-26b, miR-27a, miR-27c, miR-29a, miR-29b, miR-29c, miR-300-3p, miR-300-5p, miR-31, miR-3189-3p, miR-320a, miR-320d, miR-323, miR-323a-3p, miR-326, miR-328, miR-330, miR-331-3p, miR-335, miR-337-3p, miR-337-5p, miR-338-3p, miR-338-5p, miR-340, miR-342, miR-34a, miR-34c-3p, miR-34c-5p, miR-361-5p, miR-362-5p, miR-369-3p, miR-369-5p, miR-370-3p, miR-373, miR-375, miR-376a, miR-376a*, miR-376b-3p, miR-376b-5p, miR-378a-3p, miR-378a-5p, miR-383, miR-384, miR-409-3p, miR-409-5p, miR-422a, miR-429, miR-433-3p, miR-433-5p, miR-449a, miR-451a, miR-452, miR-454, miR-483-5p, miR-495, miR-497, miR-503, miR-506, miR-508-5p, miR-517c, miR-519a, miR-520c, miR-542-3p, miR-544a, miR-548b, miR-564, miR-577, miR-584, miR-590-3p, miR-610, miR-622, miR-656, miR-661, miR-663a, miR-7, miR-7-5p, miR-873, miR-885-5p, miR-98, miR-99a, miR-99b
Lung	miR-132, miR-376c, miR-451, miR-329, miR-382*, miR-541-5p, miR-541-3p, miR-758, miR-1207-5p, miR-1238, miR-1244, miR-1247, miR-125a-3p, miR-126*, miR-1271, miR-1304, miR-135a, miR-140, miR-140-3p, miR-1469, miR-146a-5p, miR-148b, miR-16-5p, miR-181a-5p, miR-182, miR-187-5p, miR-1908, miR-193a, miR-1976, miR-199a, miR-20a-5p, miR-215, miR-224, miR-302b, miR-30a-5p, miR-30b, miR-30d, miR-30d-5p, miR-30e-5p, miR-32, miR-328-3p, miR-345, miR-361-3p, miR-377, miR-382, miR-3940-5p, miR-424-3p, miR-432, miR-449b, miR-4500, miR-455, miR-4782-3p, miR-499-5p, miR-509-5p, miR-511, miR-512-3p, miR-512-5p, miR-526b, miR-545, miR-585, miR-588, miR-590, miR-592, miR-614, miR-623, miR-625*, miR-635, miR-660, miR-7515, miR-92b, miR-944, miR-9500, miR-96
Liver	miR-188-3p, miR-188-5p, miR-431, miR-485-3p, miR-485-5p, miR-539, miR-122*, miR-1269a, miR-127-5p, miR-1299, miR-152-3p, miR-15a-5p, miR-15b-5p, miR-187-3p, miR-21-3p, miR-22-3p, miR-302c, miR-324-5p, miR-325, miR-33a-3p, miR-379-5p, miR-450a, miR-502-3p, miR-520a, miR-520b, miR-520c-3p, miR-548p, miR-589-5p, miR-599, miR-612, miR-615-5p, miR-637, miR-655-3p, miR-675, miR-874-3p, miR-941, miR-98-5p
Pancreas	miR-410, miR-1181, miR-150-3p, miR-150-5p, miR-663b, miR-101, miR-124, miR-1247, miR-1271, miR-133a, miR-138-5p, miR-141, miR-145, miR-146a, miR-148a, miR-148b, miR-152, miR-15a, miR-198, miR-203a, miR-214, miR-215, miR-216a, miR-29a, miR-29c, miR-329, miR-335, miR-33a, miR-34a, miR-34b, miR-34c, miR-373, miR-375, miR-494, miR-497, miR-506, miR-615-5p, miR-630, miR-96

FIG. 13A

Breast	miR-411, miR-1258, miR-127, miR-130b-3p, miR-132, miR-147a, miR-148b-3p, miR-1826, miR-191, miR-193a-3p, miR-19a-3p, miR-210, miR-27b-3p, miR-30a, miR-329, miR-339-5p, miR-33b, miR-362-3p, miR-374a, miR-379, miR-381, miR-410-3p, miR-411-5p, miR-421, miR-450b-3p, miR-485-3p, miR-485-5p, miR-489, miR-489-5p, miR-490, miR-498, miR-502-5p, miR-517a, miR-519d, miR-520a-3p, miR-567, miR-574-3p, miR-601, miR-630, miR-638, miR-652-3p, miR-671-5p, miR-802, miR-874, miR-892b
Prostate	miR-466, miR-466b, miR-543, miR-543*, let-7a-3p, miR-103a-3p, miR-1296, miR-154-5p, miR-34b-3p, miR-3619-5p, miR-4723-5p, miR-628-5p, miR-642a-5p, miR-765
Gastrointestinal	miR-551a, miR-551b, miR-551b-3p, miR-299-3p, miR-299-5p, miR-29c-5p, miR-1254, miR-1295b-3p, miR-1307, miR-140-5p, miR-145-5p, miR-1827, miR-187, miR-193a-5p, miR-196a, miR-202-3p, miR-24-3p, miR-25, miR-28-3p, miR-28-5p, miR-296, miR-302a, miR-30a-3p, miR-342-5p, miR-34a-5p, miR-378a-5p, miR-423-5p, miR-4282, miR-433, miR-4458, miR-448, miR-4487, miR-450b-5p, miR-483, miR-486, miR-487b-3p, miR-502, miR-518a-3p, miR-520d-5p, miR-526b-3p, miR-551a, miR-574-5p, miR-582-5p, miR-598, miR-627, miR-93, miR-96-5p, miR-106a-5p, miR-1285, miR-1291, miR-129-1-3p, miR-135a-5p, miR-149-5p, miR-182-5p, miR-200a-3p, miR-20b-5p, miR-211-5p, miR-508-3p, miR-509-3p, miR-510-5p, miR-708, miR-100-5p, miR-101-3p, miR-1294, miR-133a-3p, miR-143-3p, miR-214-3p, miR-424-5p, miR-491, miR-518b, miR-644a, miR-718, miR-103a, miR-1225-5p, miR-1228*, miR-122-5p, miR-1266, miR-1284, miR-128-2-5p, miR-129-2-3p, miR-1296-5p, miR-149-3p, miR-155-5p, miR-15a-3p, miR-208a-3p, miR-29a-3p, miR-330-3p, miR-335-5p, miR-338, miR-339, miR-367, miR-376c-3p, miR-410, miR-4328, miR-449c, miR-455-5p, miR-488, miR-513b, miR-520d-3p, miR-520f, miR-524-5p, miR-551b-3p, miR-561, miR-647, miR-935, miR-940

FIG. 13B

6 Hours				Ct Mean
Sample Number	Cell Line	Virus Infection	Transfection Condition	miR143
4R-1	293FT	No	Blank	32.756
5R-1			Negative (scrambled)	32.845
6R-1			miRNA	19.832
7R-1		Yes	Blank	31.923
8R-1			Negative (scrambled)	30.073
9R-1			miRNA	18.025

FIG. 14A

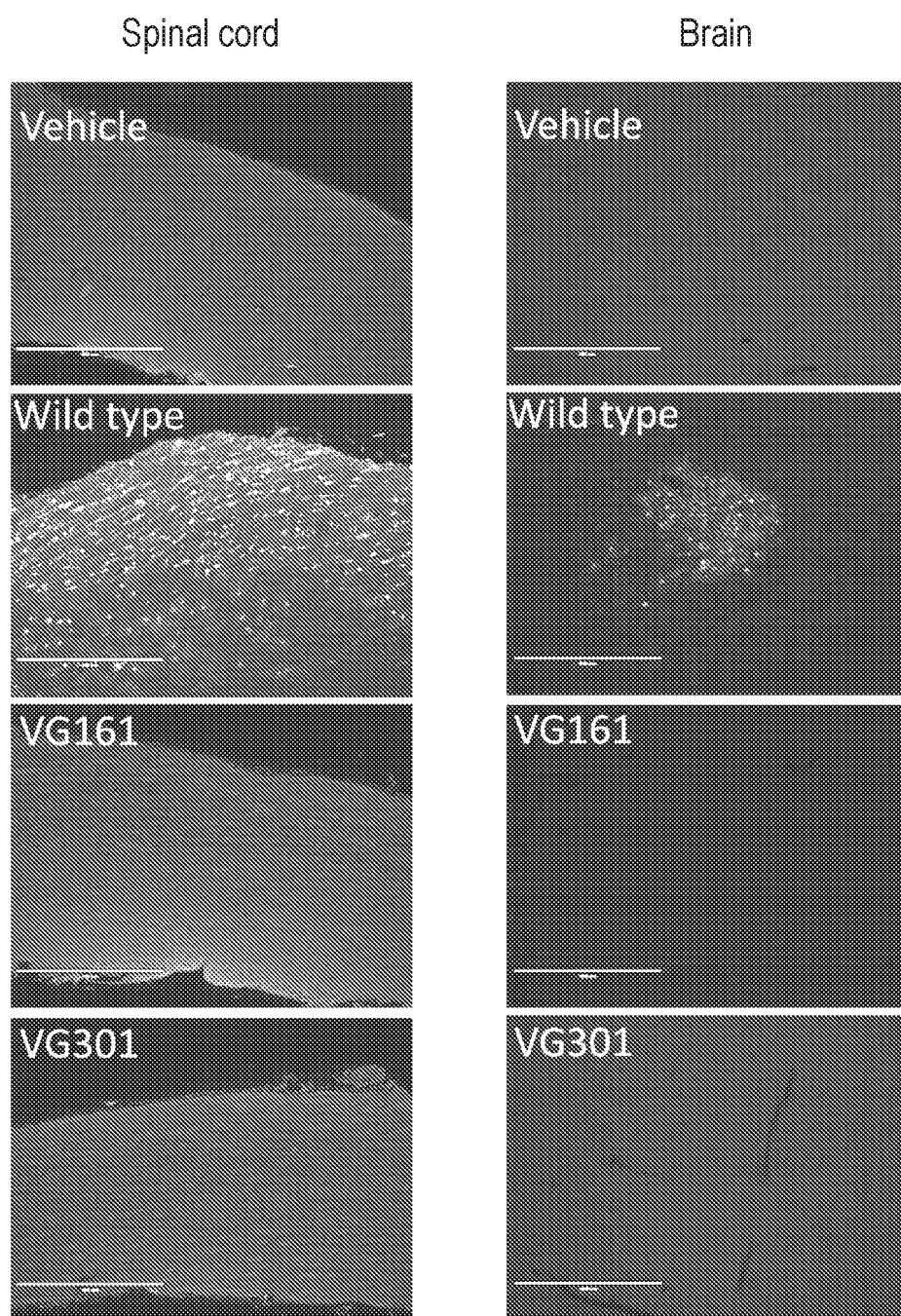
6 Hours						Quantity Mean		Ct Mean	
Sample Number	Cell Line	Virus Infection	Transfection Condition	ICP27 Copies (Copies/uL)	ICP34.5 Copies (Copies/uL)	ICP34.5 Copies (Copies/uL)	Actin	LAT	
4R-1	293FT	No	Blank	0	0	0	16.549	38.989	
5R-1			Negative (scrambled)	0	0	0	16.389	Undetermined	
6R-1			miRNA	0	0	0	16.469	Undetermined	
7R-1		Yes	Blank	109847	5700	5700	16.661	30.075	
8R-1			Negative (scrambled)	56840	3811	3811	16.728	30.315	
9R-1			miRNA	68277	1688	1688	16.704	30.682	

FIG. 14B

24 Hours				
Sample Number	Cell Line	Transfection Condition	Virus Infection	ICP27 Copies (Copies/uL)
13D-1	293FT	Blank	No	0
14D-1		Negative (scrambled)	No	0
15D-1		miRNA	No	0
16D-1		Blank	Yes	2518
17D-1		Negative (scrambled)	Yes	1471
18D-1		miRNA	Yes	1156

FIG. 14C

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*FIG. 15*

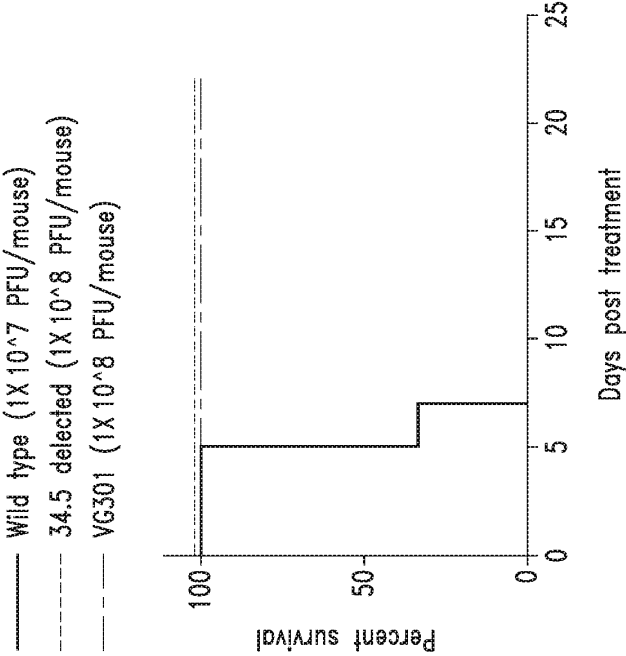


FIG. 16

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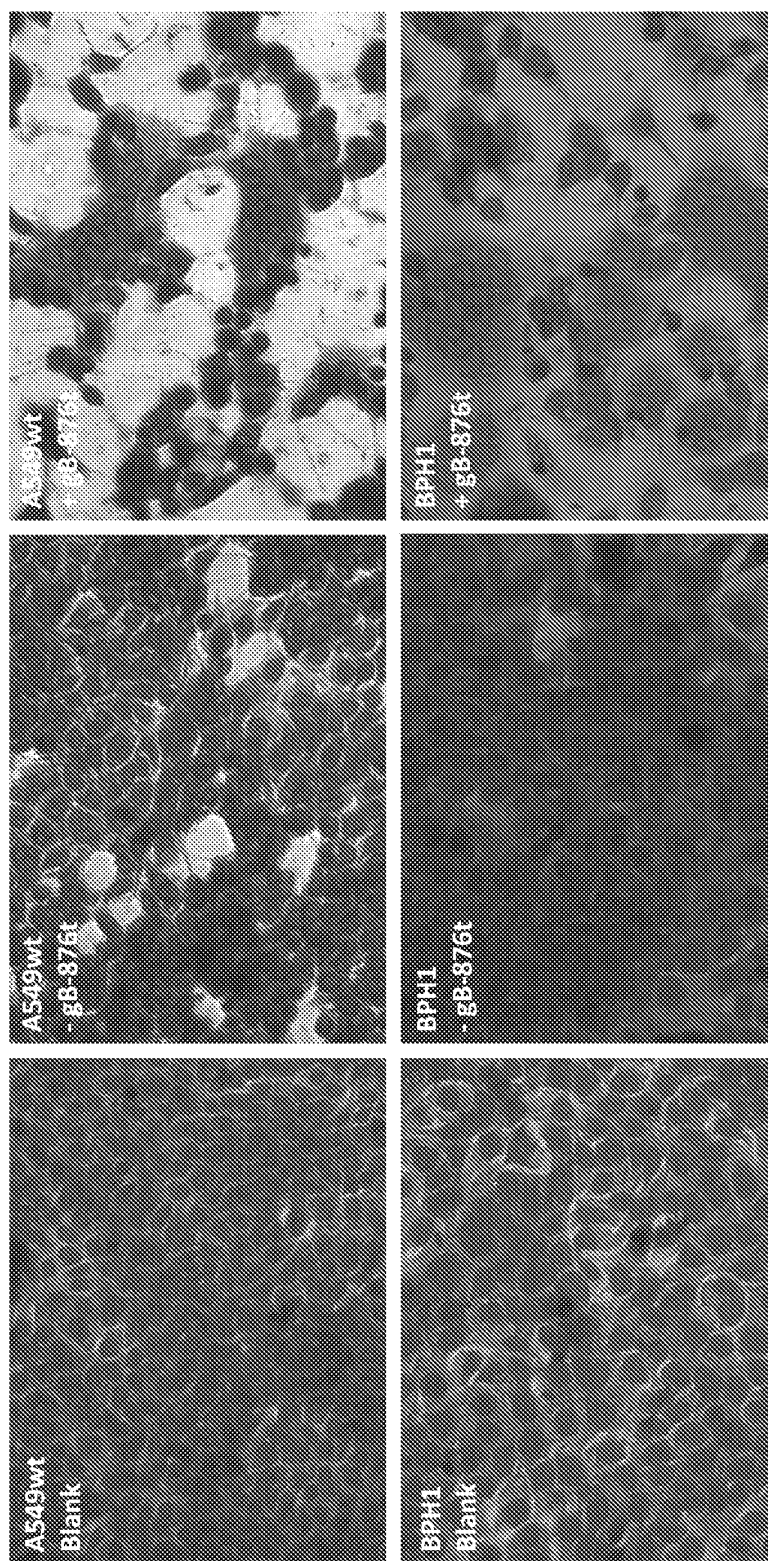


FIG. 17