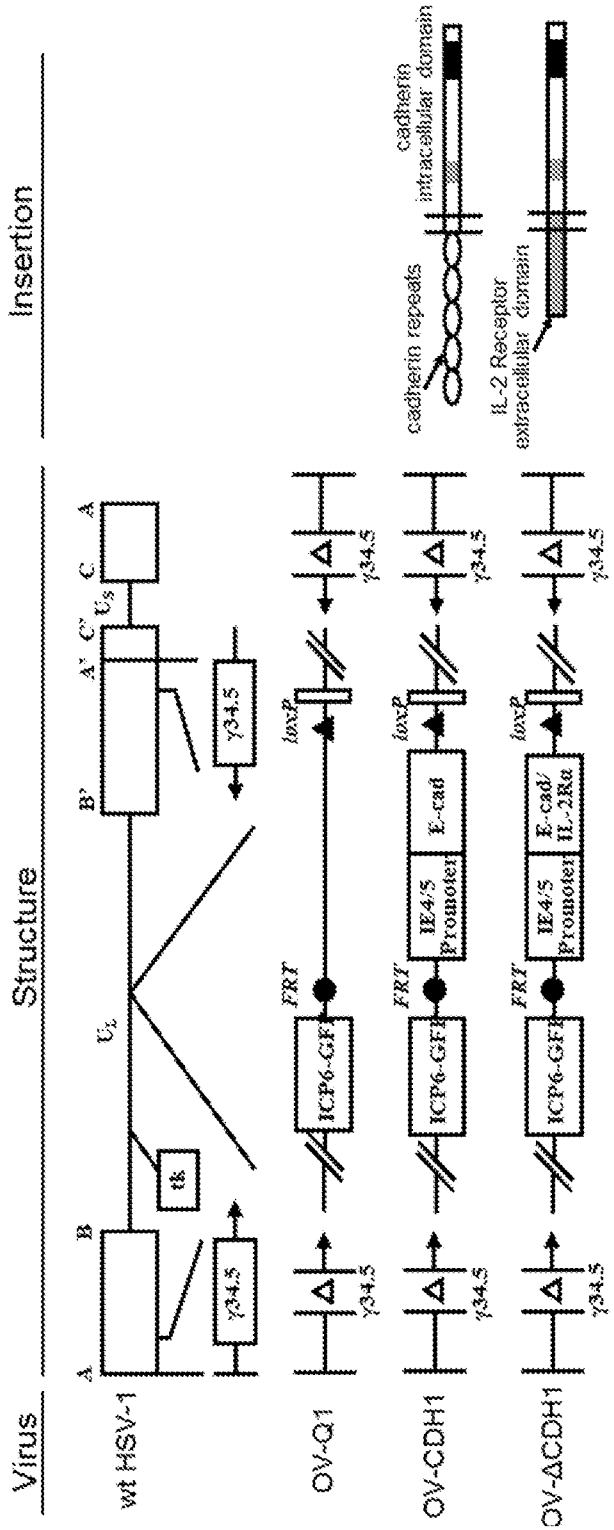

Virus
Structure
Insertion
wt HSV-1
OV-Q1
OV-CDH1
OV-ΔCDH1
cadherin repeats
cadherin intracellular domain
IL-2 Receptor extracellular domain
FRT
loxP
ICP6-GFP
IE4/5 Promoter
E-cad
E-cad/IL-2Rα
γ34.5

FIG. 1A

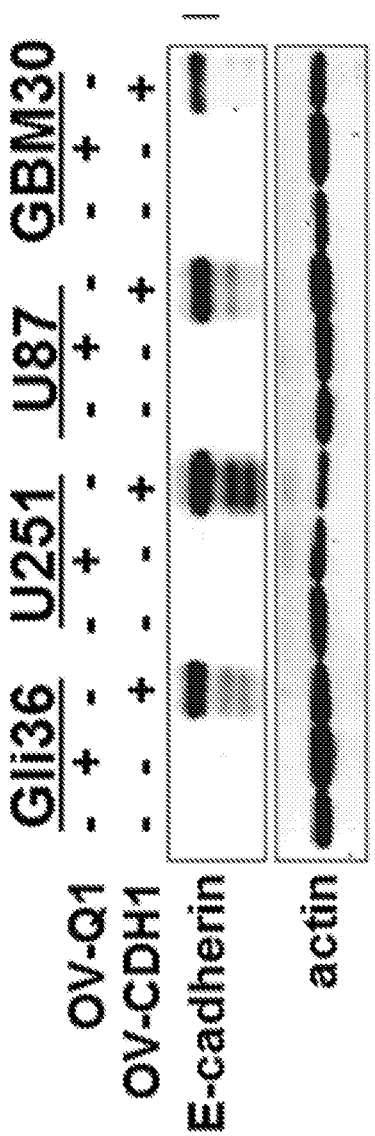

Gli36 U251 U87 GBM30
OV-Q1 - + - - + - - +
OV-CDH1 - - + - - + - -
E-cadherin
actin

FIG. 1B

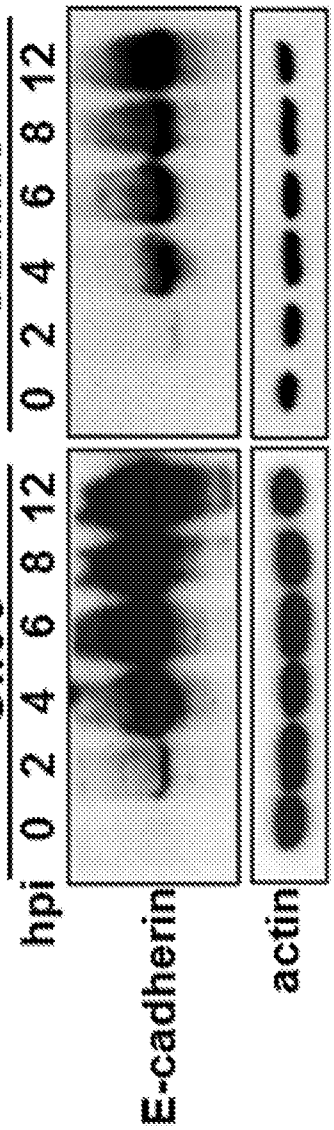

Gli36
GBM30
hpi 0 2 4 6 8 12 0 2 4 6 8 12
E-cadherin
actin

FIG. 1C

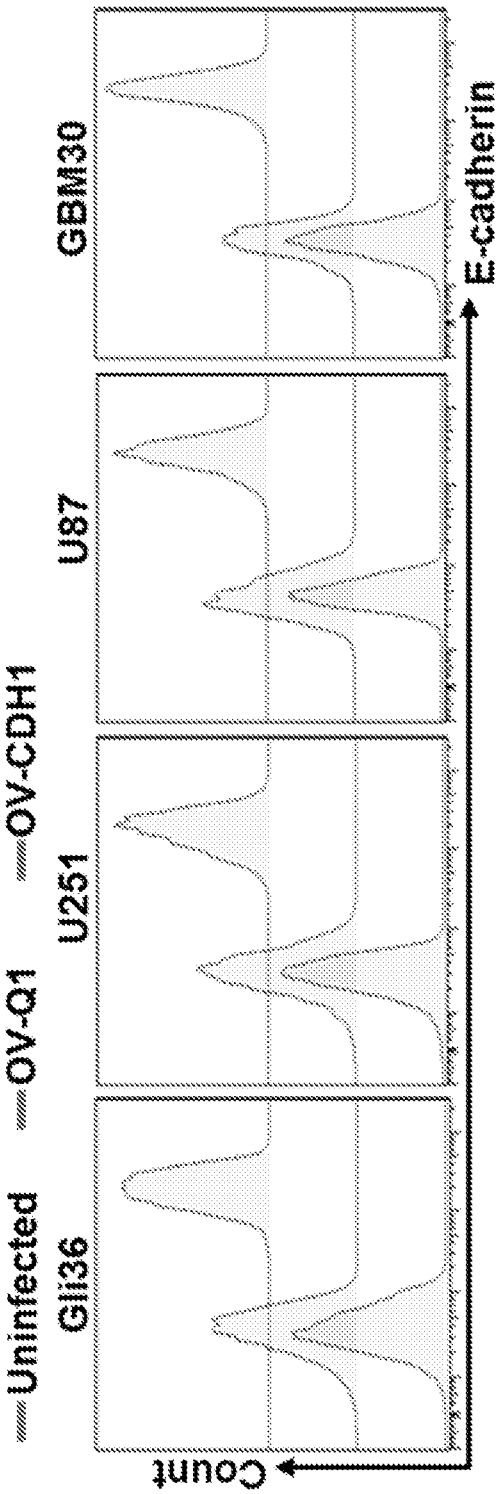

Uninfected
OV-Q1
OV-CDH1
Gli36
U251
U87
GBM30
Count
E-cadherin

FIG. 1D

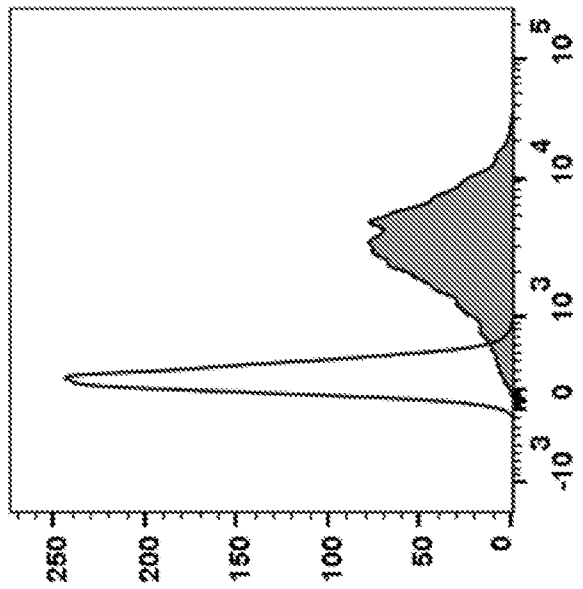

250
200
150
100
50
0
-10^3
0
10^3
10^4
10^5

FIG. 1F

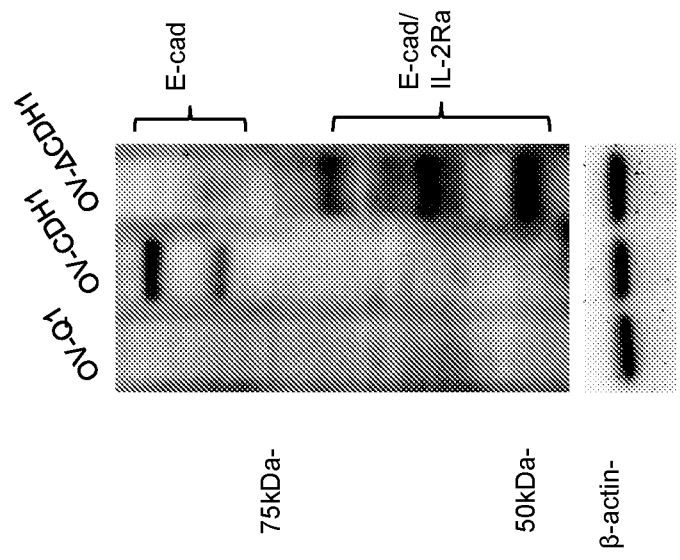

OV-Cl
OV-CDH1
OV-ΔCDH1
E-cad
E-cad/
IL-2Ra
75kDa-
50kDa-
β-actin-

FIG. 1E

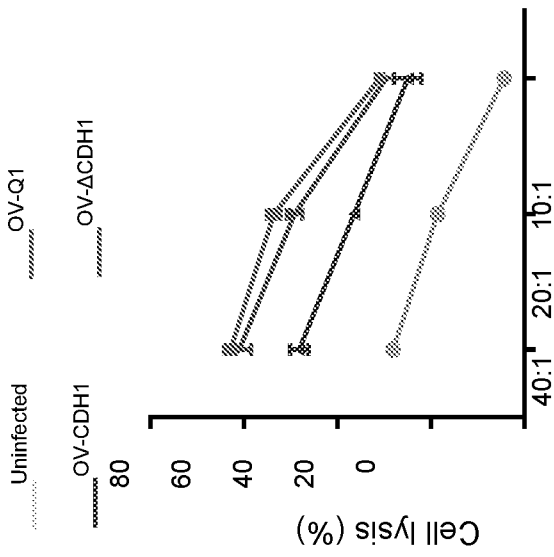

Uninfected
OV-Q1
OV-CDH1
OV-ΔCDH1
Cell lysis (%)
80
60
40
20
0
40:1
20:1
10:1

FIG. 1G

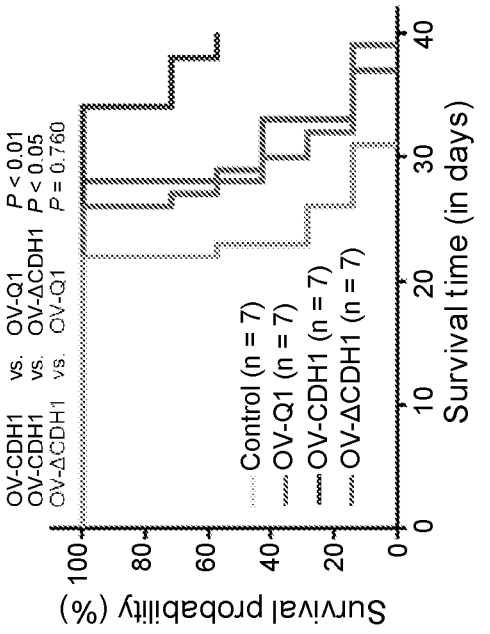

OV-CDH1 vs. OV-Q1 P < 0.01
OV-CDH1 vs. OV-ΔCDH1 P < 0.05
OV-ΔCDH1 vs. OV-Q1 P = 0.760
Control (n = 7)
OV-Q1 (n = 7)
OV-CDH1 (n = 7)
OV-ΔCDH1 (n = 7)
Survival probability (%)
100
80
60
40
20
0
0
10
20
30
40
Survival time (in days)

FIG. 1H

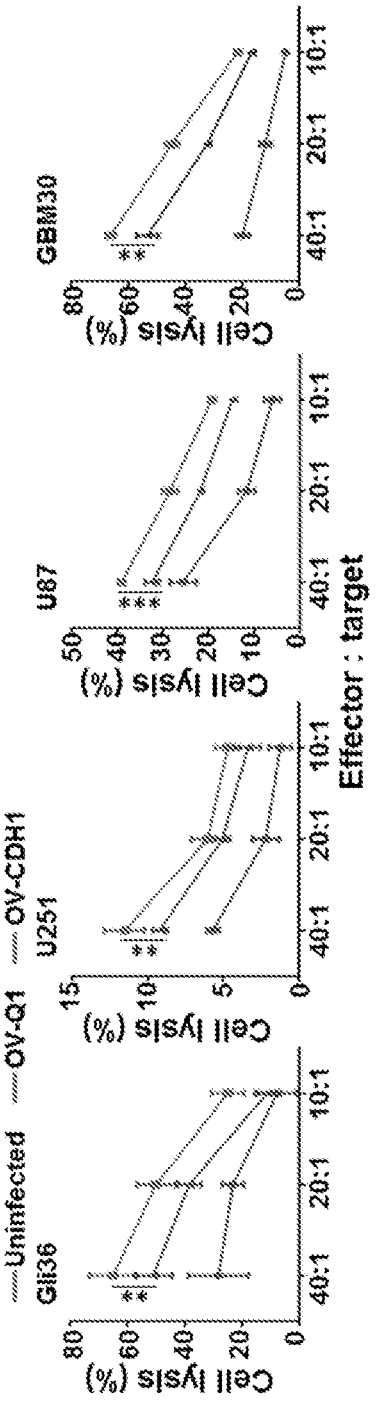

Uninfected
OV-Q1
OV-CDH1
GBM36
U251
U87
GBM30
Cell lysis (%)
Effector : target
40:1
20:1
10:1

FIG. 2A

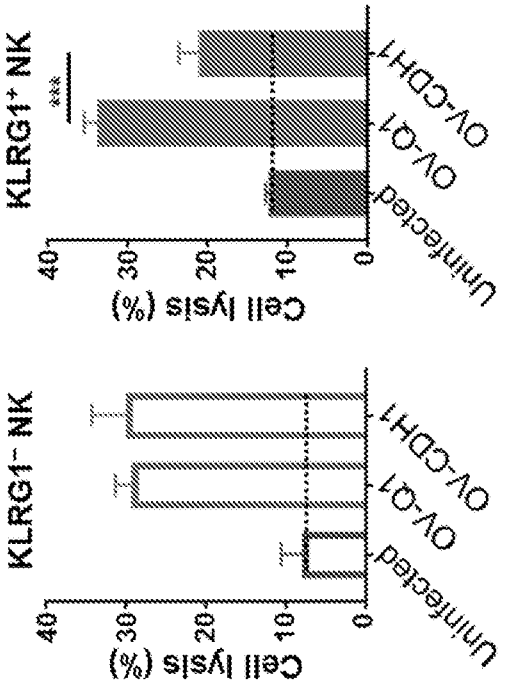

KLRG1⁻ NK
KLRG1⁺ NK
Cell lysis (%)
Uninfected
OV-Q1
OV-CDH1
***

FIG. 2B

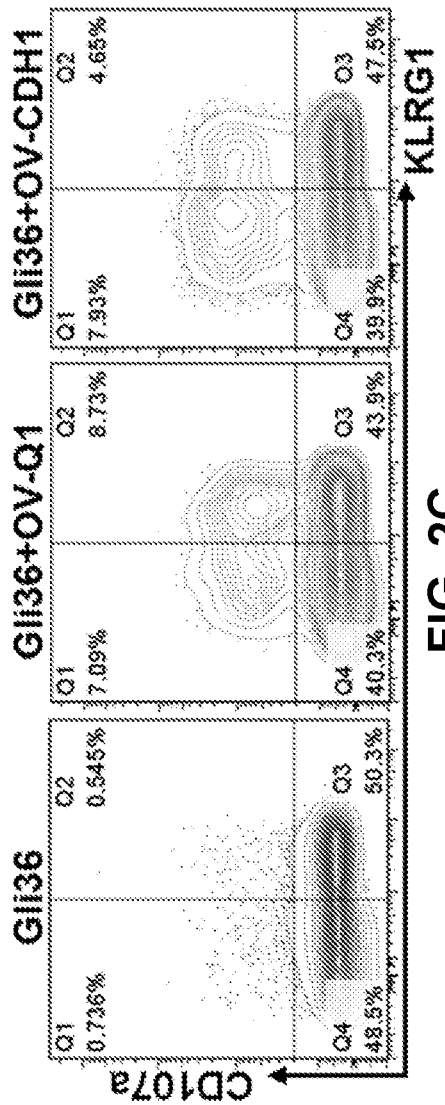


FIG. 2C

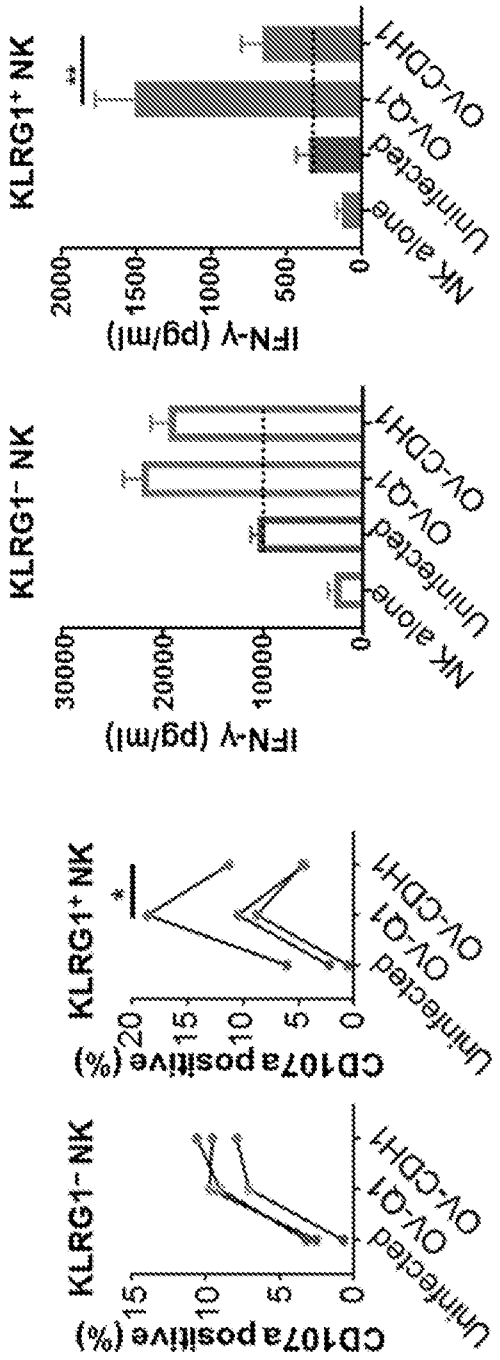


FIG. 2D

FIG. 2E

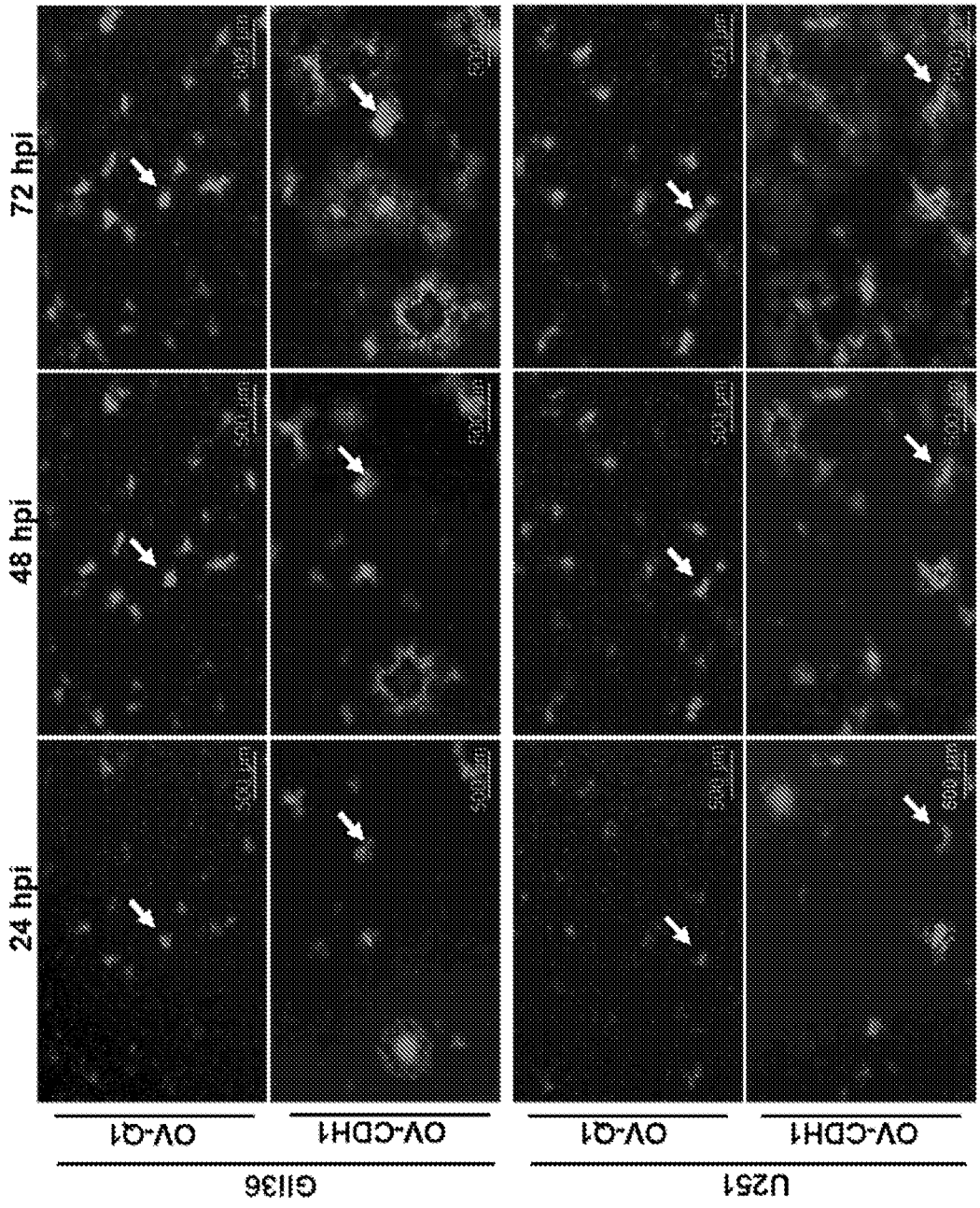


FIG. 3A

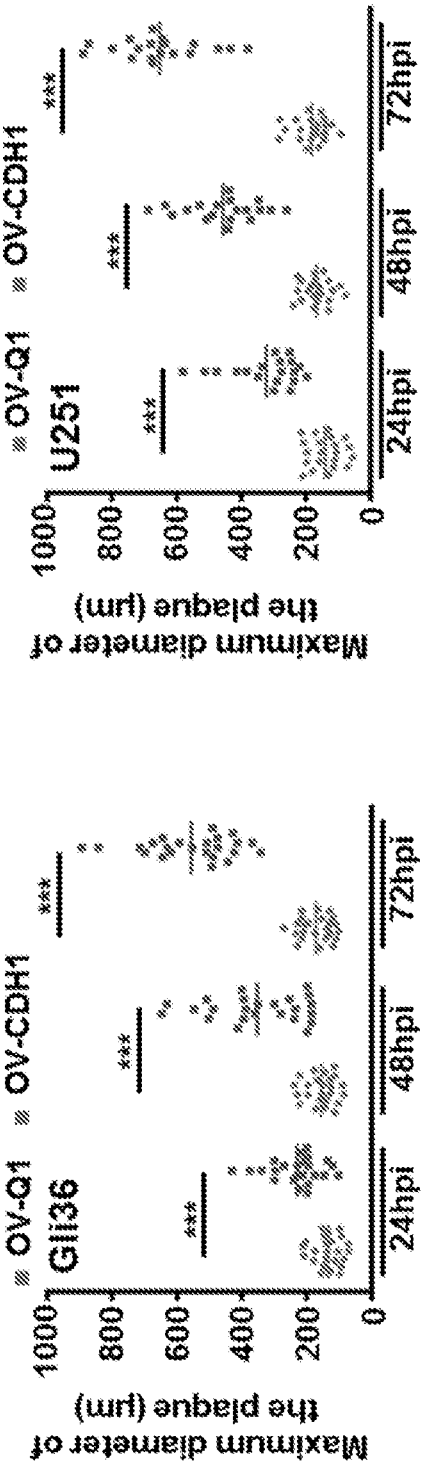

Maximum diameter of the plaque (μm)
1000
800
600
400
200
0
OV-Q1
OV-CDH1
Gli36
U251
***
24hpi
48hpi
72hpi

FIG. 3B

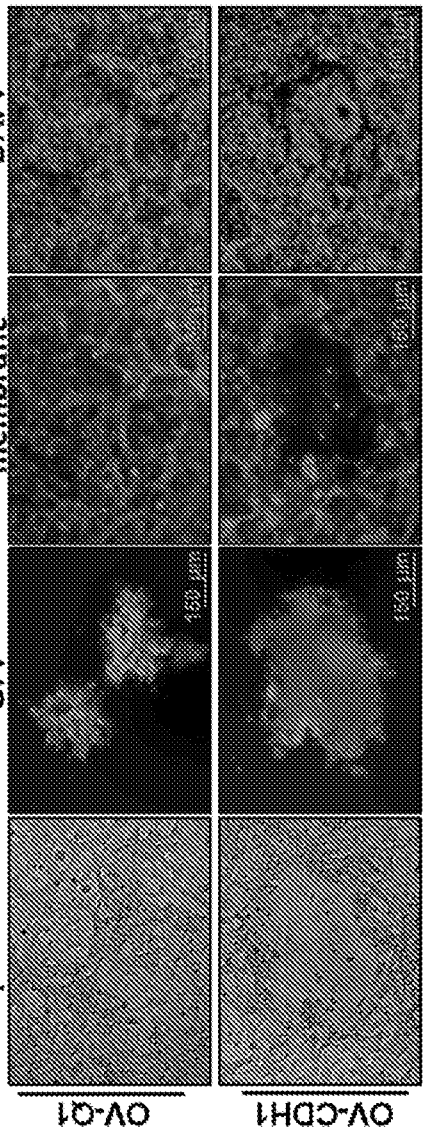

phase
GFP
membrane
DAPI
OV-Q1
OV-CDH1

FIG. 3C

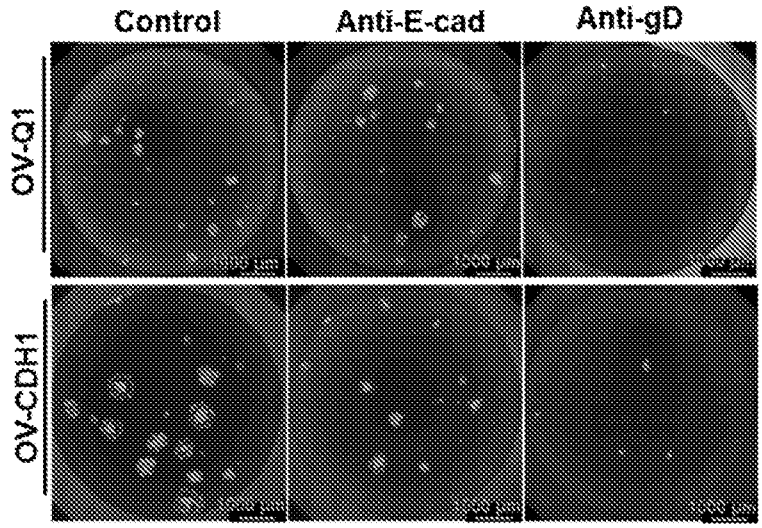

Control
Anti-E-cad
Anti-gD
OV-Q1
OV-CDH1

FIG. 4A

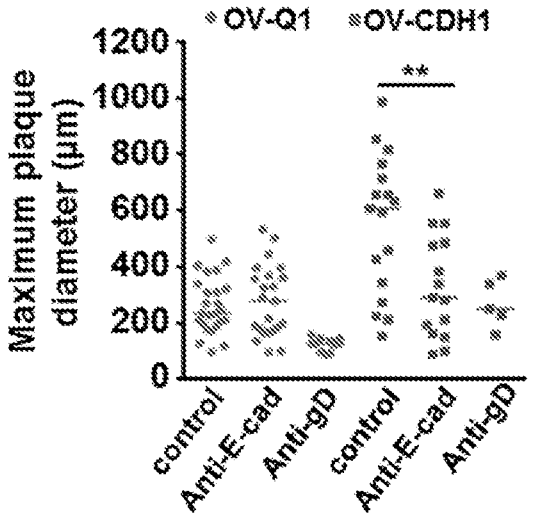

OV-Q1
OV-CDH1
Maximum plaque diameter (μm)
1200
1000
800
600
400
200
0
**
control
Anti-E-cad
Anti-gD
control
Anti-E-cad
Anti-gD

FIG. 4B

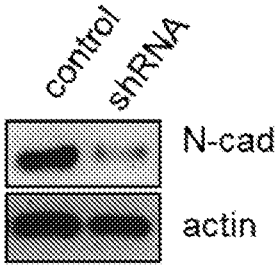


FIG. 4C

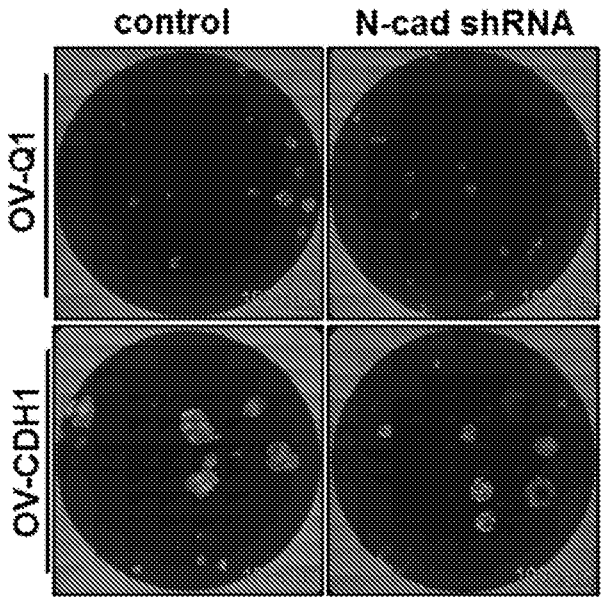


FIG. 4D

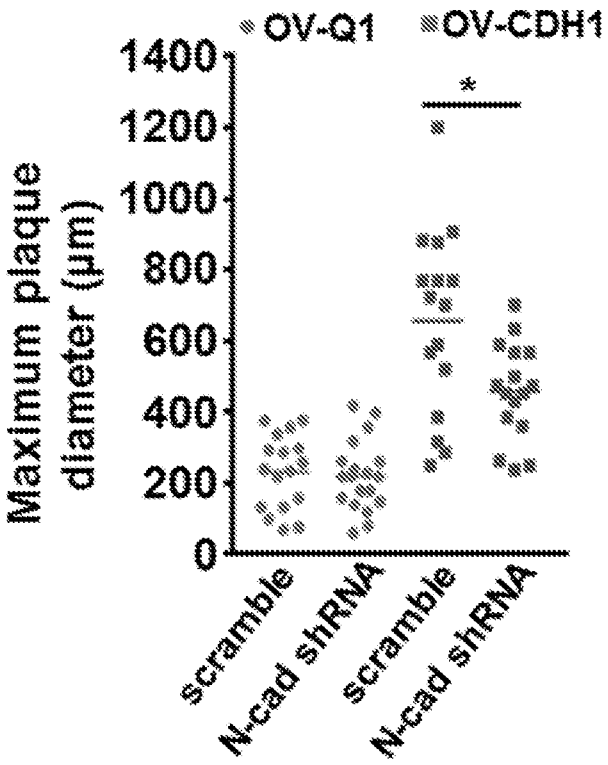

OV-Q1
OV-CDH1
Maximum plaque diameter (µm)
1400
1200
1000
800
600
400
200
0
*
scramble
N-cad shRNA
scramble
N-cad shRNA

FIG. 4E

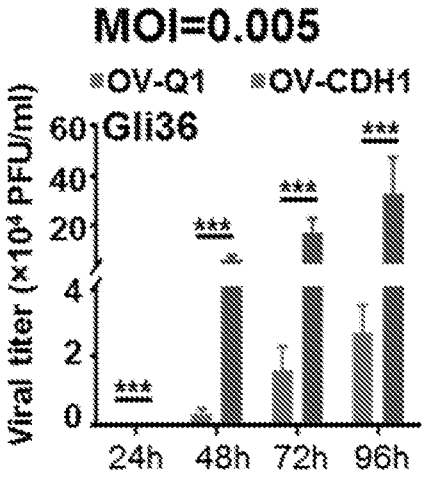


FIG. 5A

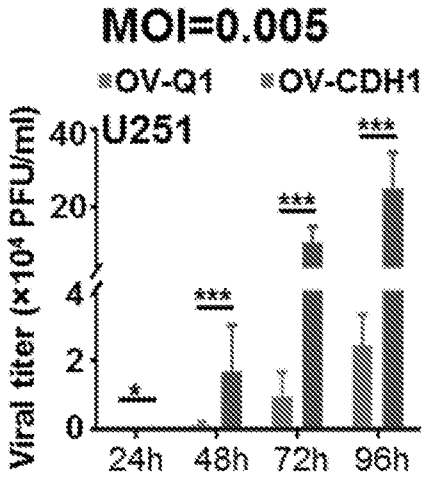


FIG. 5B

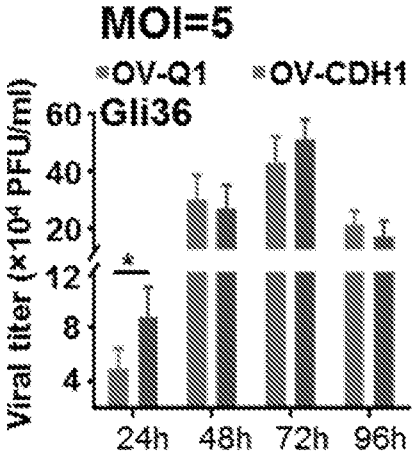


FIG. 5C

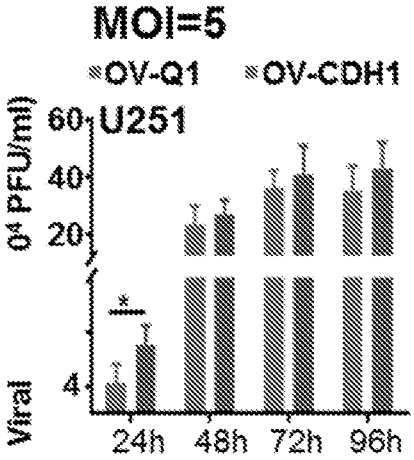


FIG. 5D

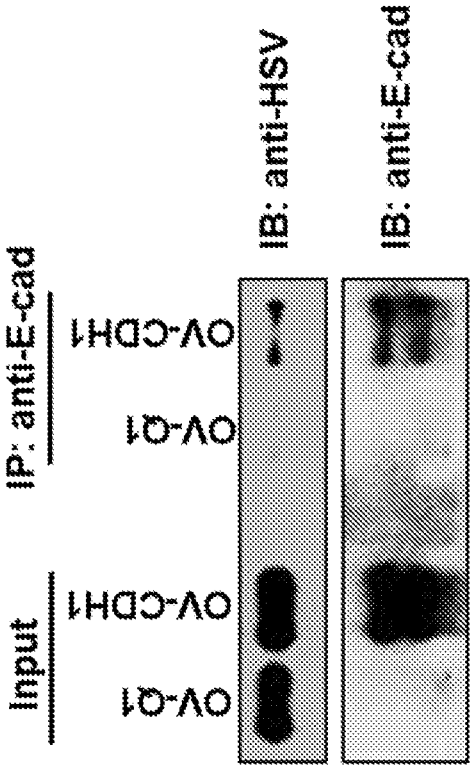

IB: anti-HSV
IB: anti-E-cad
IP: anti-E-cad
OV-CDH1
OV-Q1
Input
OV-CDH1
OV-Q1

FIG. 6B

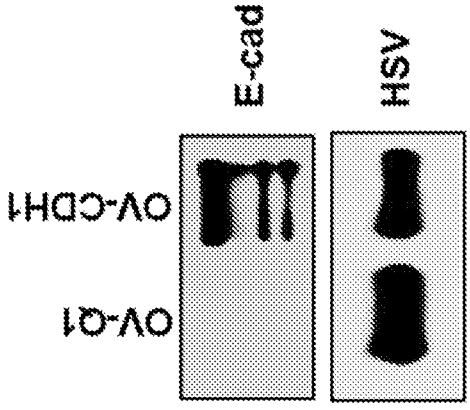

E-cad
HSV
OV-CDH1
OV-Q1

FIG. 6A

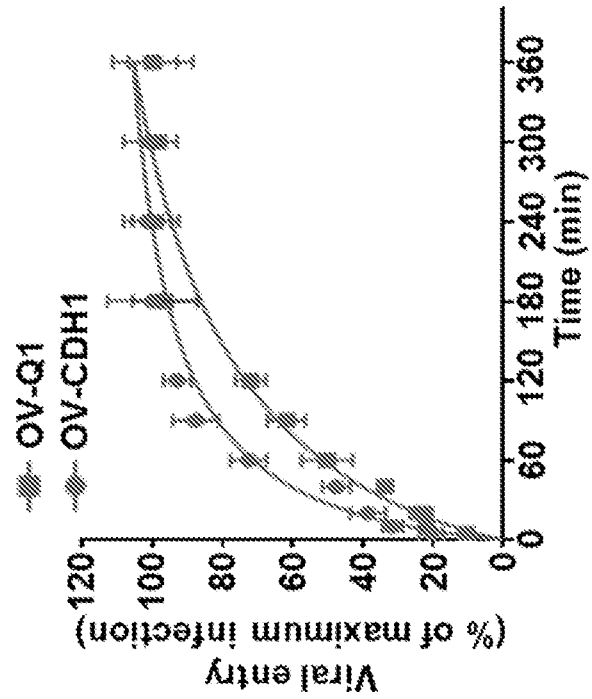

Viral entry
(% of maximum infection)
120
100
80
60
40
20
0
0
60
120
180
240
300
360
Time (min)
OV-Q1
OV-CDH1

FIG. 6D

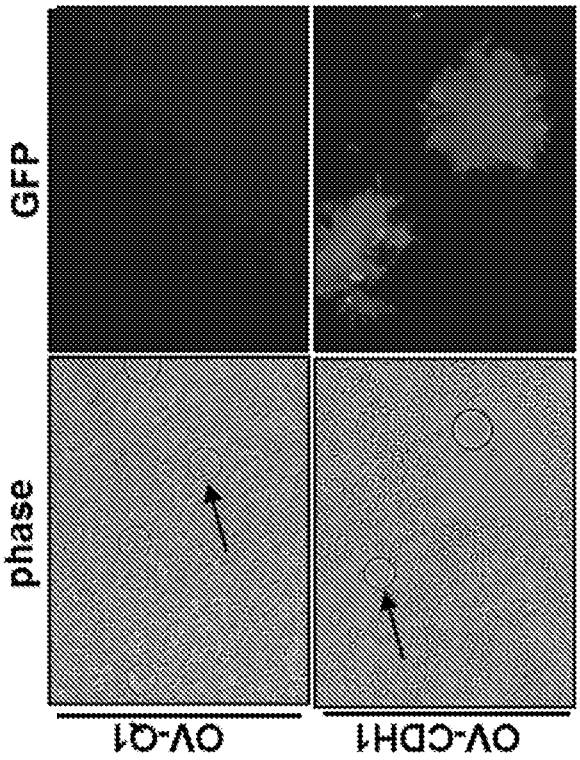

GFP
phase
OV-Q1
OV-CDH1

FIG. 6C

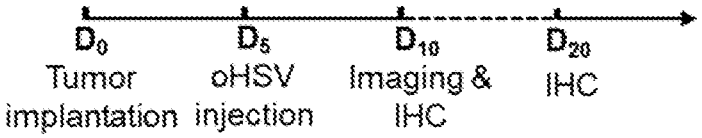

D0
Tumor implantation
D5
oHSV injection
D10
Imaging & IHC
D20
IHC

FIG. 7A

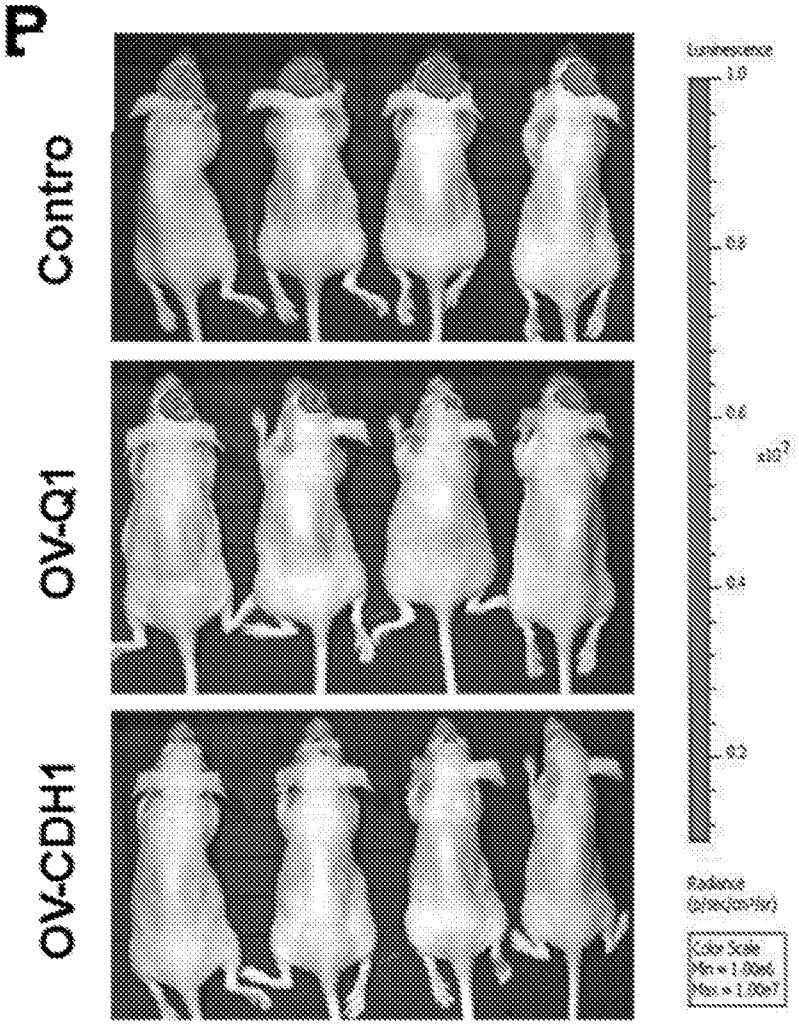

Contro
OV-Q1
OV-CDH1

FIG. 7B

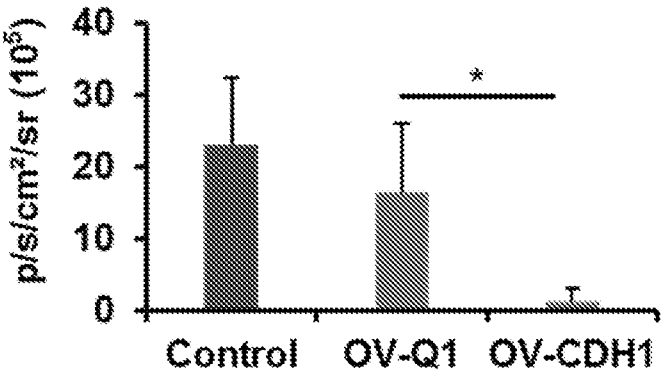

p/s/cm²/sr (10⁵)
40
30
20
10
0
*
Control
OV-Q1
OV-CDH1

FIG. 7C

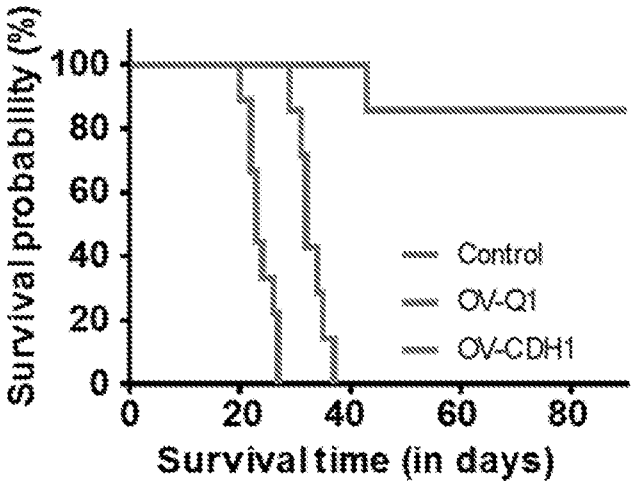

Survival probability (%)
100
80
60
40
20
0
0
20
40
60
80
Survival time (in days)
Control
OV-Q1
OV-CDH1

FIG. 7D

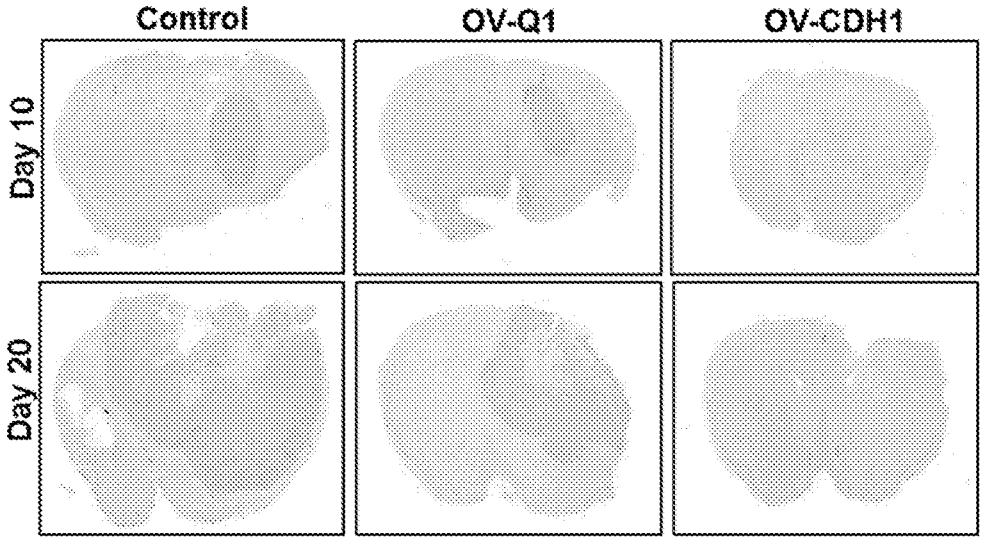

Control
OV-Q1
OV-CDH1
Day 10
Day 20

FIG. 7E

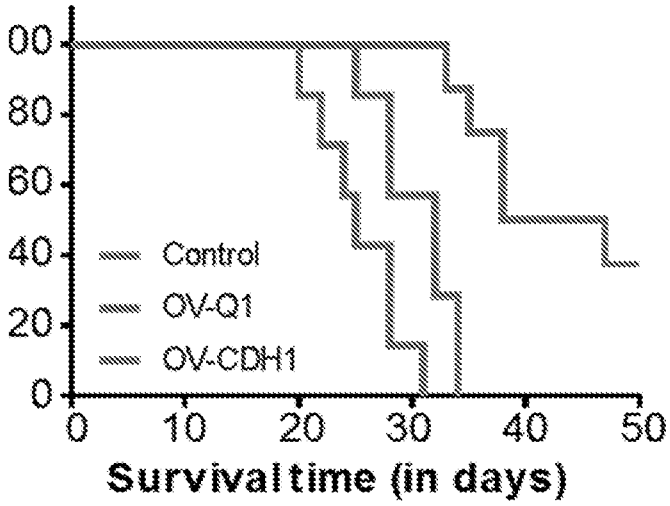

00
80
60
40
20
0
Control
OV-Q1
OV-CDH1
0
10
20
30
40
50
Survival time (in days)

FIG. 7F

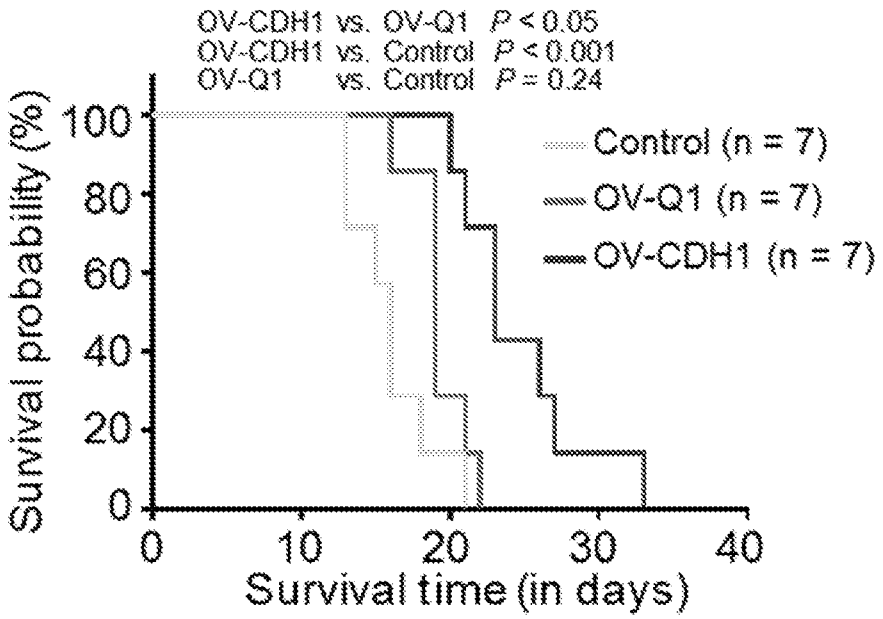

OV-CDH1 vs. OV-Q1 P < 0.05
OV-CDH1 vs. Control P < 0.001
OV-Q1 vs. Control P = 0.24
Survival probability (%)
100
80
60
40
20
0
0
10
20
30
40
Survival time (in days)
Control (n = 7)
OV-Q1 (n = 7)
OV-CDH1 (n = 7)

FIG. 7G

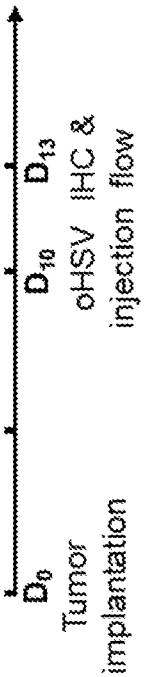


FIG. 8A

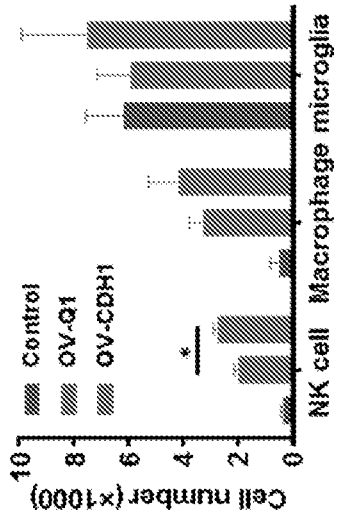


FIG. 8B

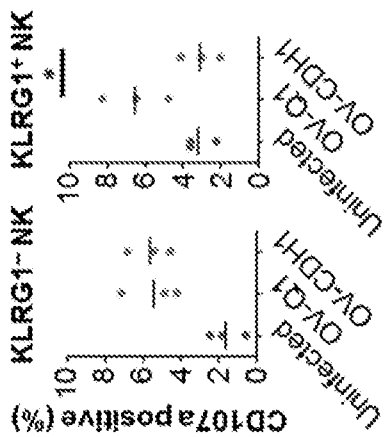


FIG. 8D

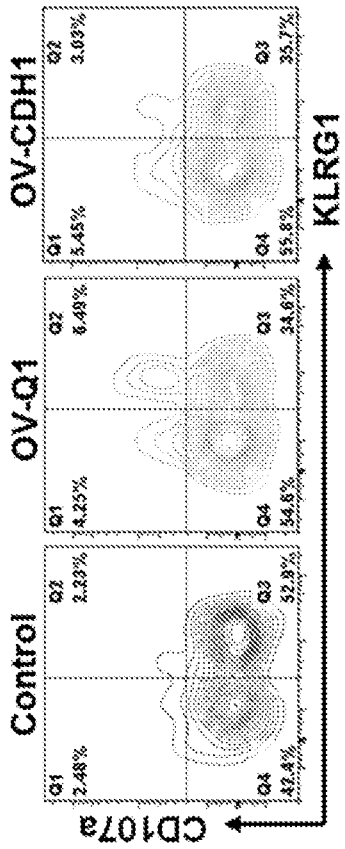


FIG. 8C

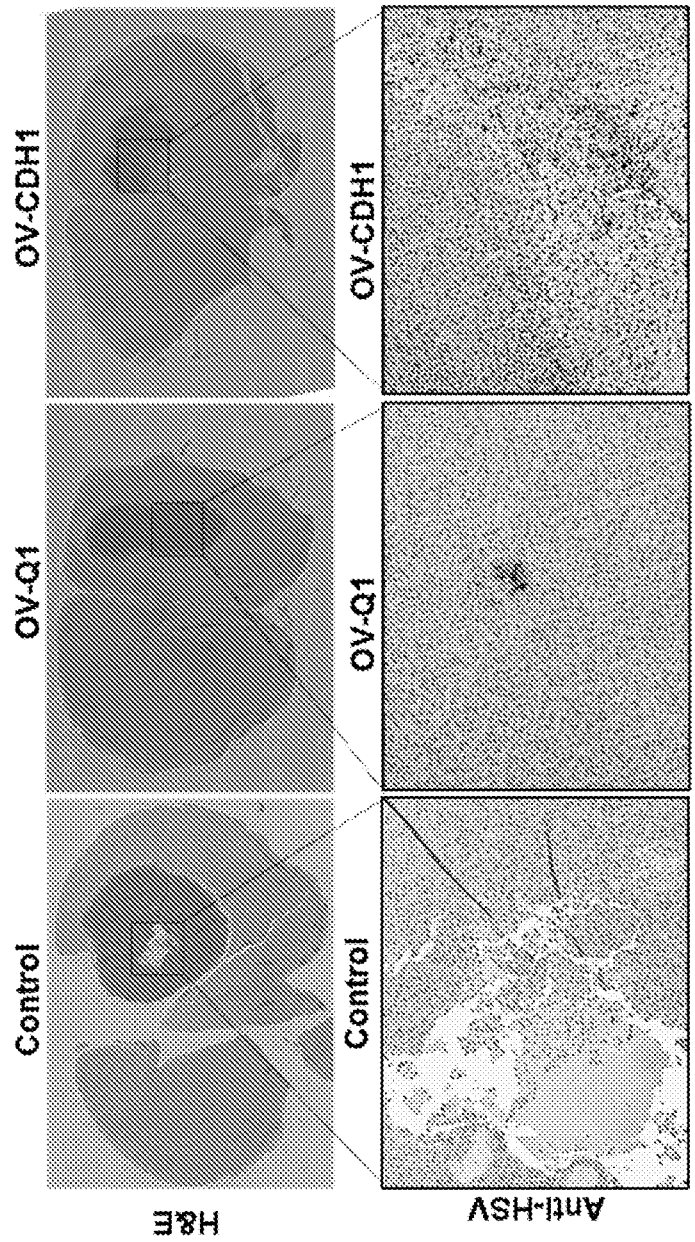


FIG. 8E

FIG. 8F

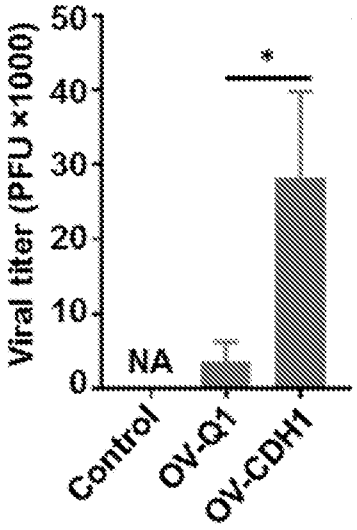


FIG. 8G

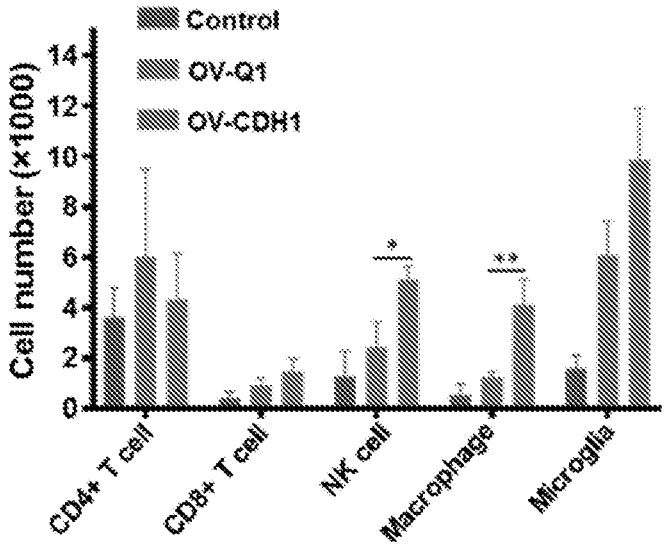


FIG. 8H

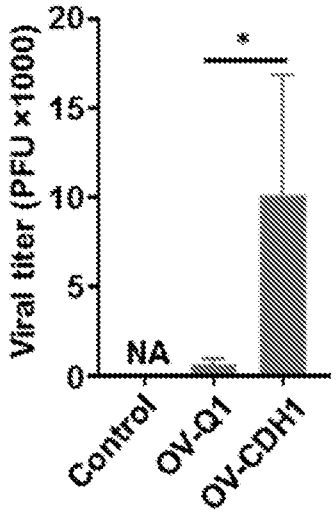


FIG. 8I

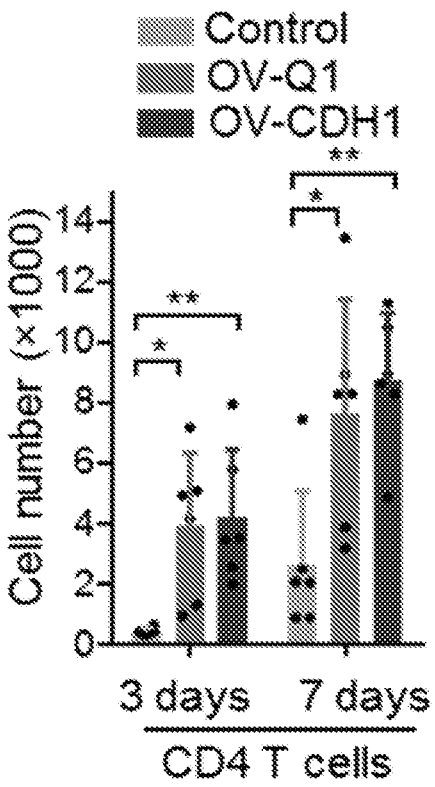

Control
OV-Q1
OV-CDH1
Cell number (×1000)
0
2
4
6
8
10
12
14
*
**
*
**
3 days
7 days
CD4 T cells

FIG. 8J

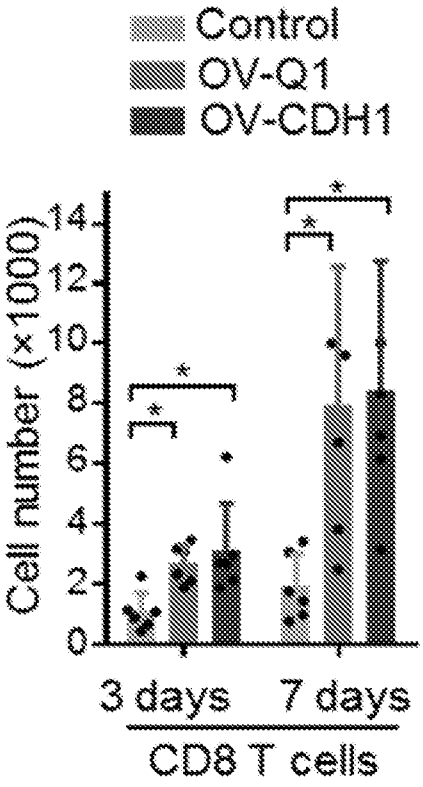

Control
OV-Q1
OV-CDH1
Cell number (×1000)
0
2
4
6
8
10
12
14
*
*
*
*
3 days
7 days
CD8 T cells

FIG. 8K

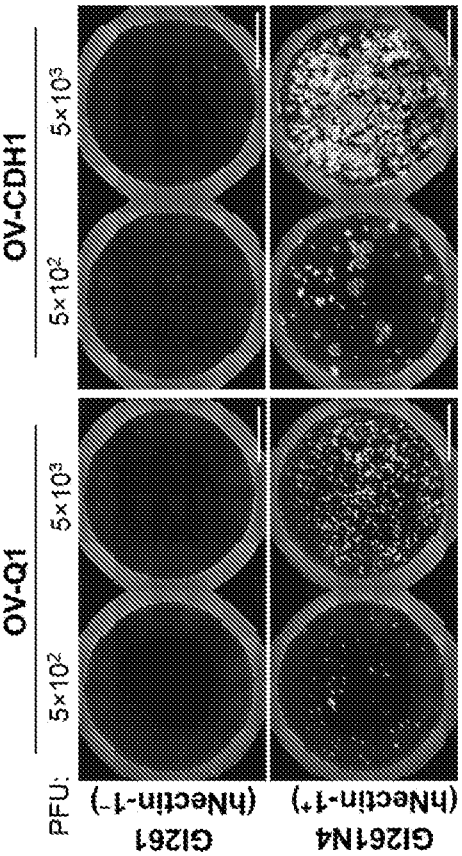

OV-Q1
OV-CDH1
PFU:
5×10²
5×10³
GI261
(hNectin-1⁻)
GI261N4
(hNectin-1⁺)

FIG. 9A

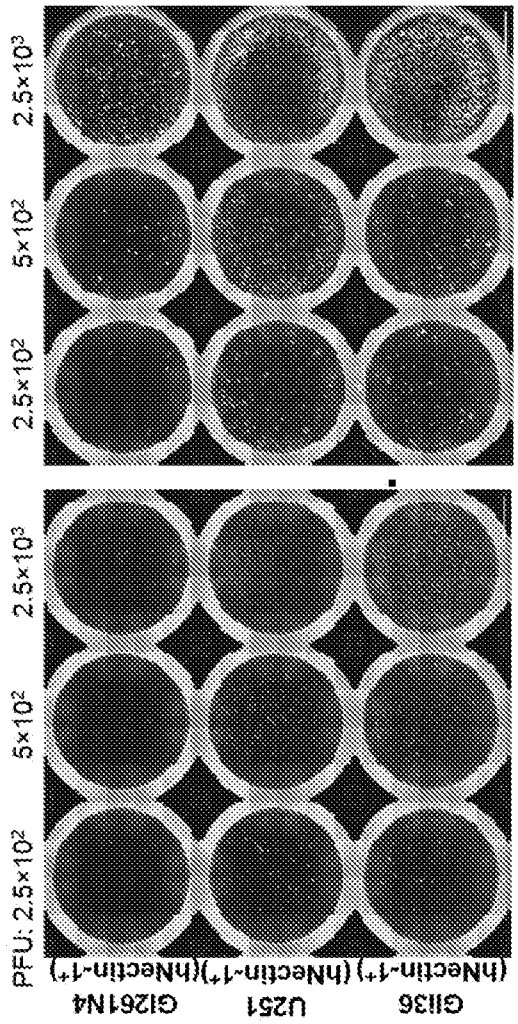

OV-Q1
OV-CDH1
PFU:
2.5×10²
5×10²
2.5×10³
GII36
(hNectin-1⁺)
U251
(hNectin-1⁺)
GI261N4
(hNectin-1⁺)

FIG. 9B

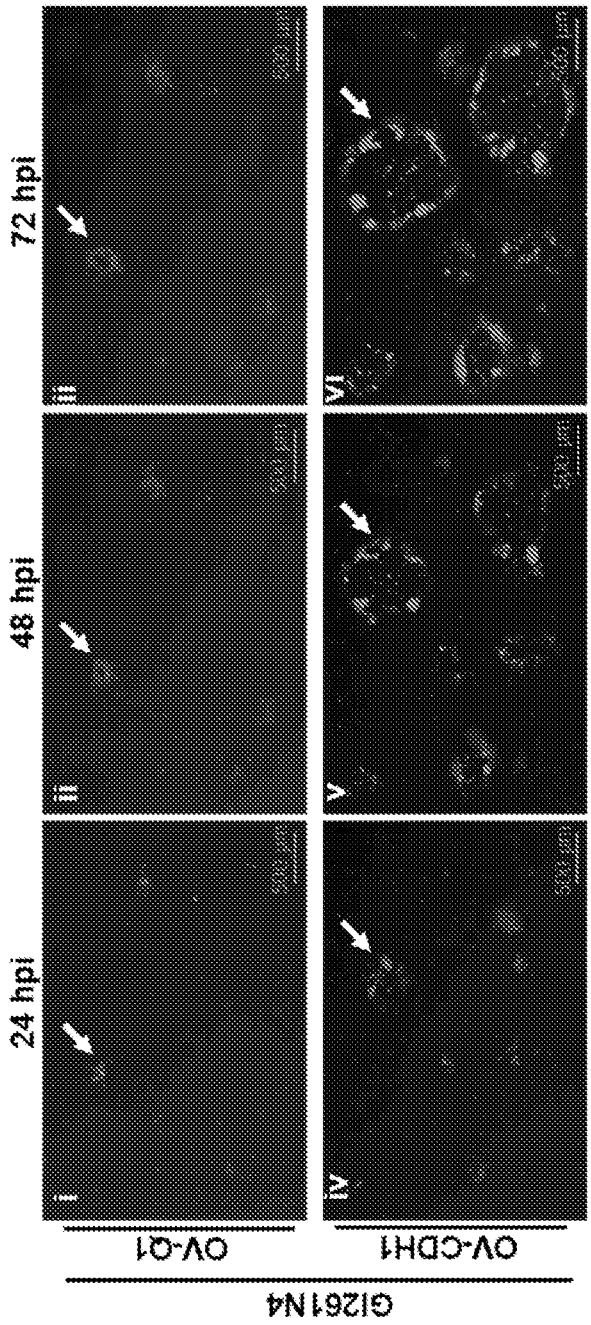


FIG. 10A

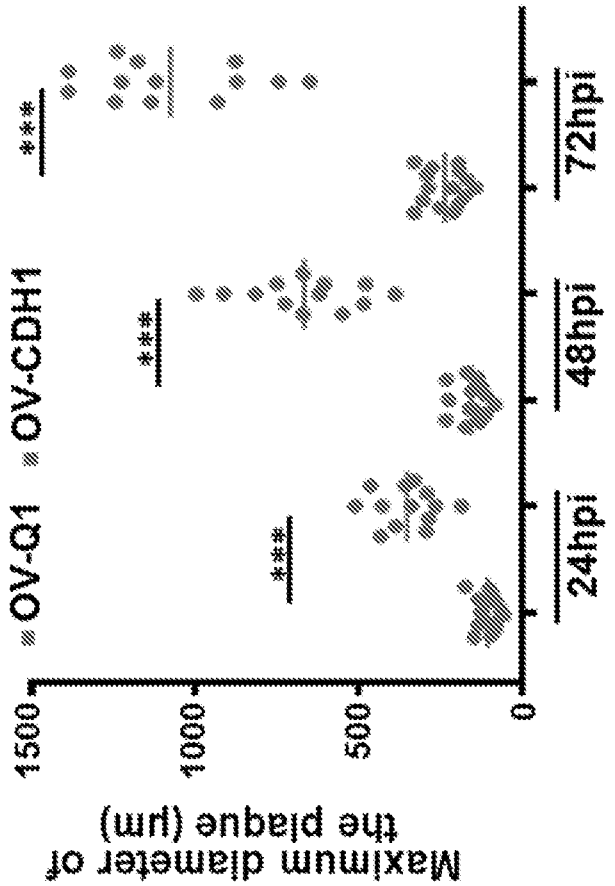

Maximum diameter of the plaque (μm)
1500
1000
500
0
OV-Q1
OV-CDH1
***
***
***
24hpi
48hpi
72hpi

FIG. 10B

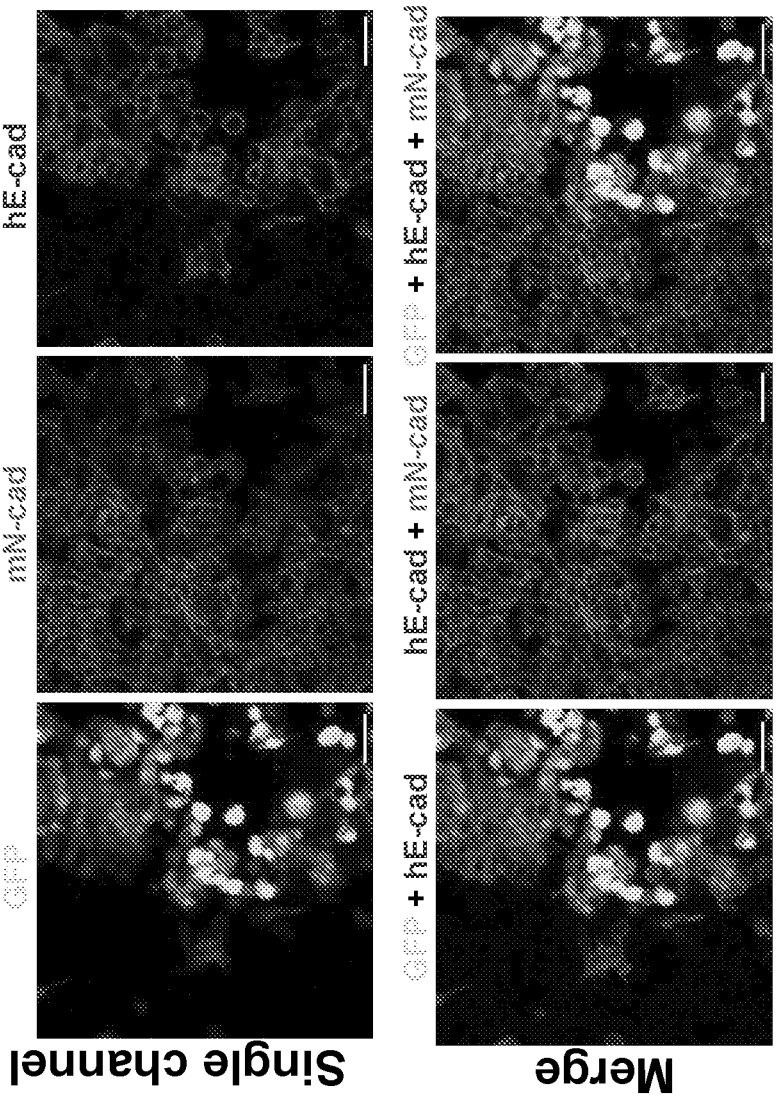

Single channel
Merge
GFP
mN-cad
hE-cad
GFP + hE-cad
hE-cad + mN-cad
GFP + hE-cad + mN-cad

FIG. 10C

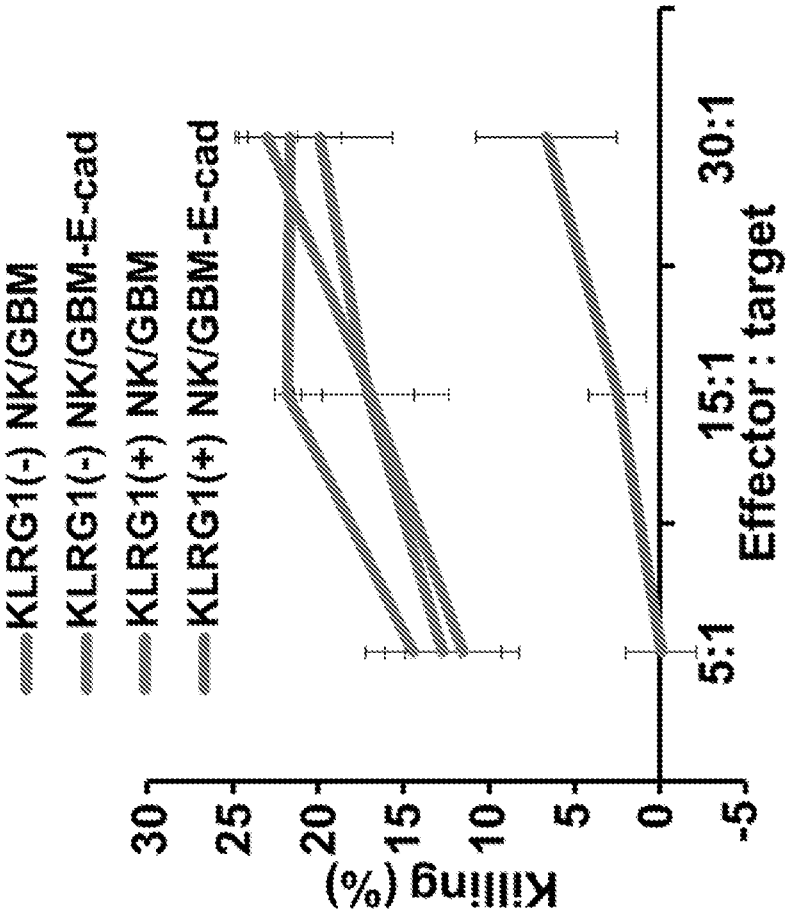

KLRG1(-) NK/GBM
KLRG1(-) NK/GBM-E-cad
KLRG1(+) NK/GBM
KLRG1(+) NK/GBM-E-cad
Killing (%)
30
25
20
15
10
5
0
-5
5:1
15:1
30:1
Effector : target

FIG. 11

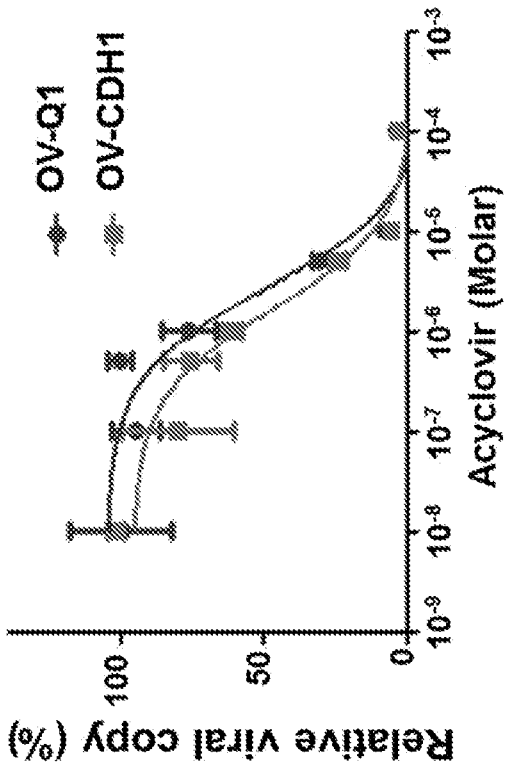


FIG. 12A

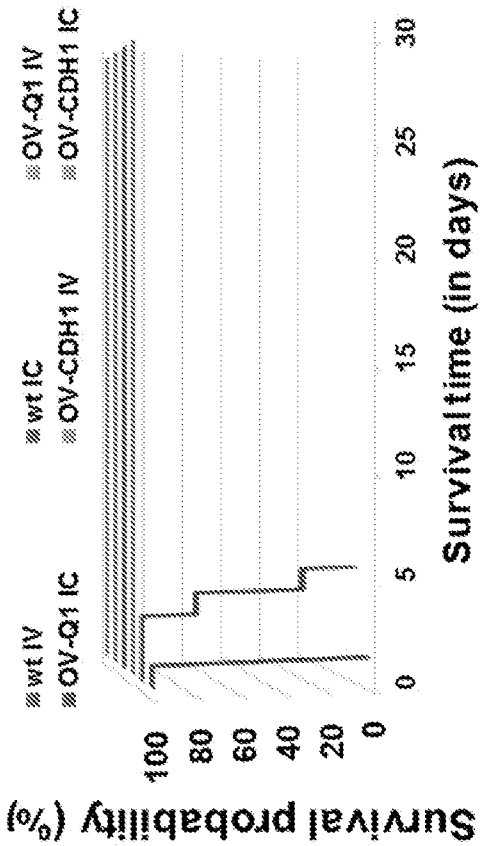


FIG. 12B

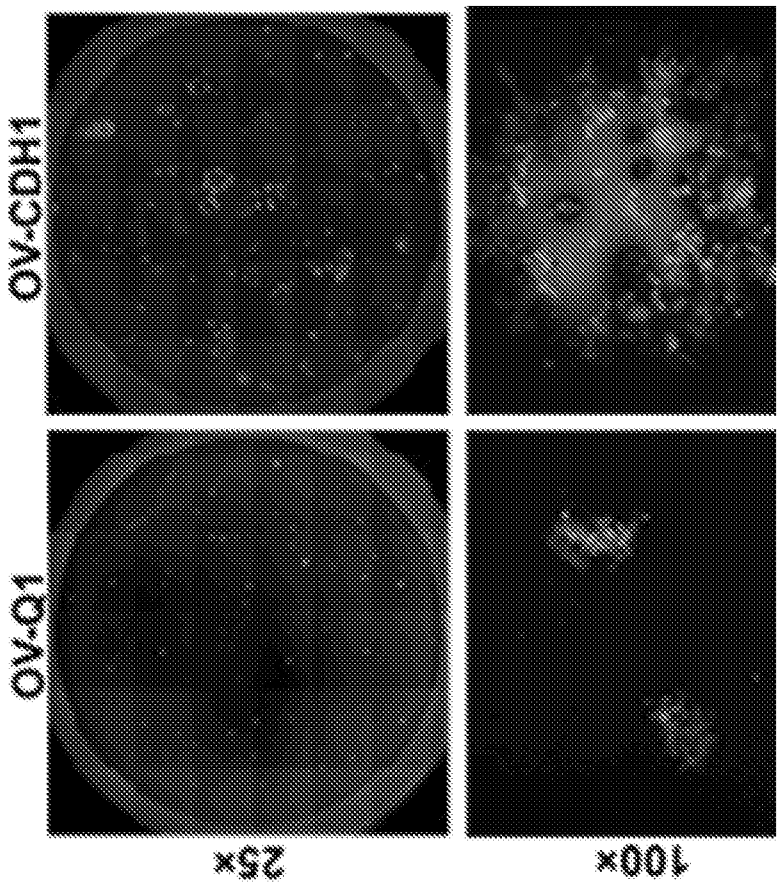


FIG. 13

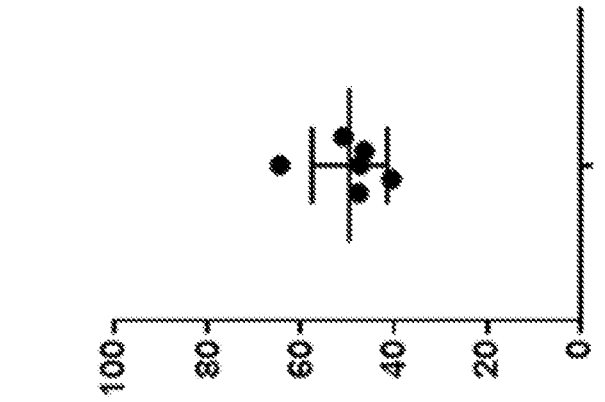


FIG. 14B

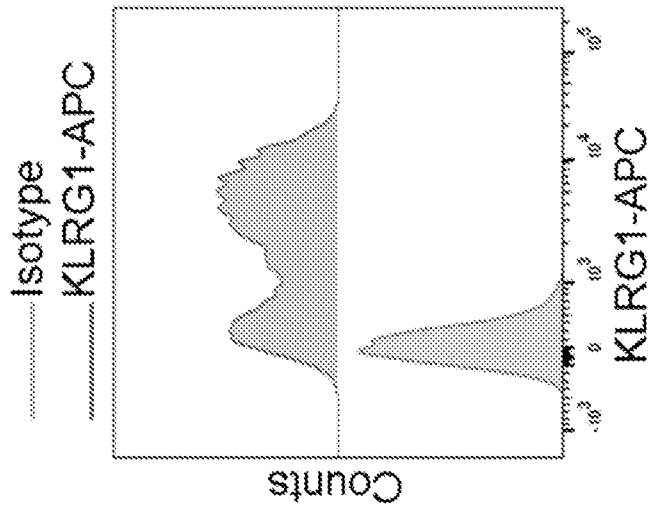


FIG. 14A

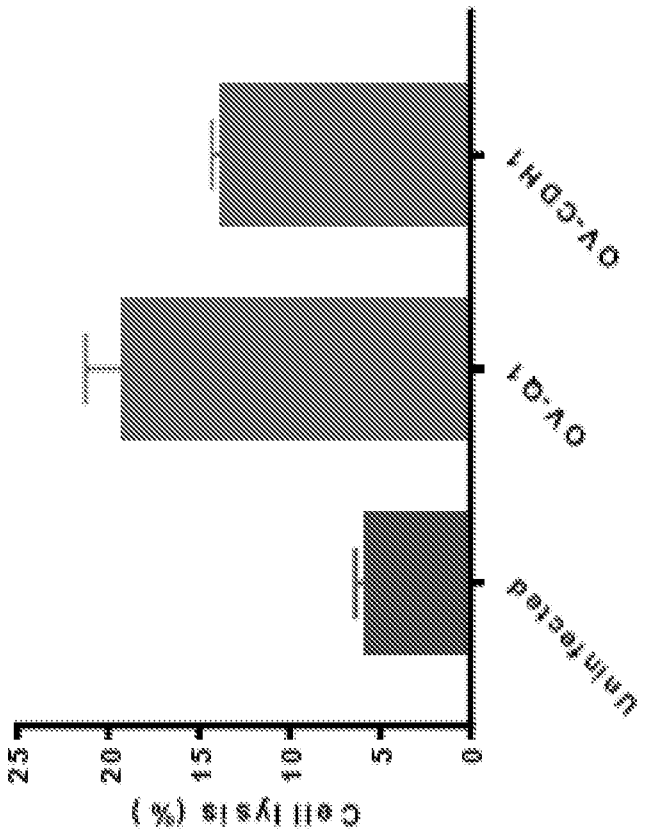


FIG. 15

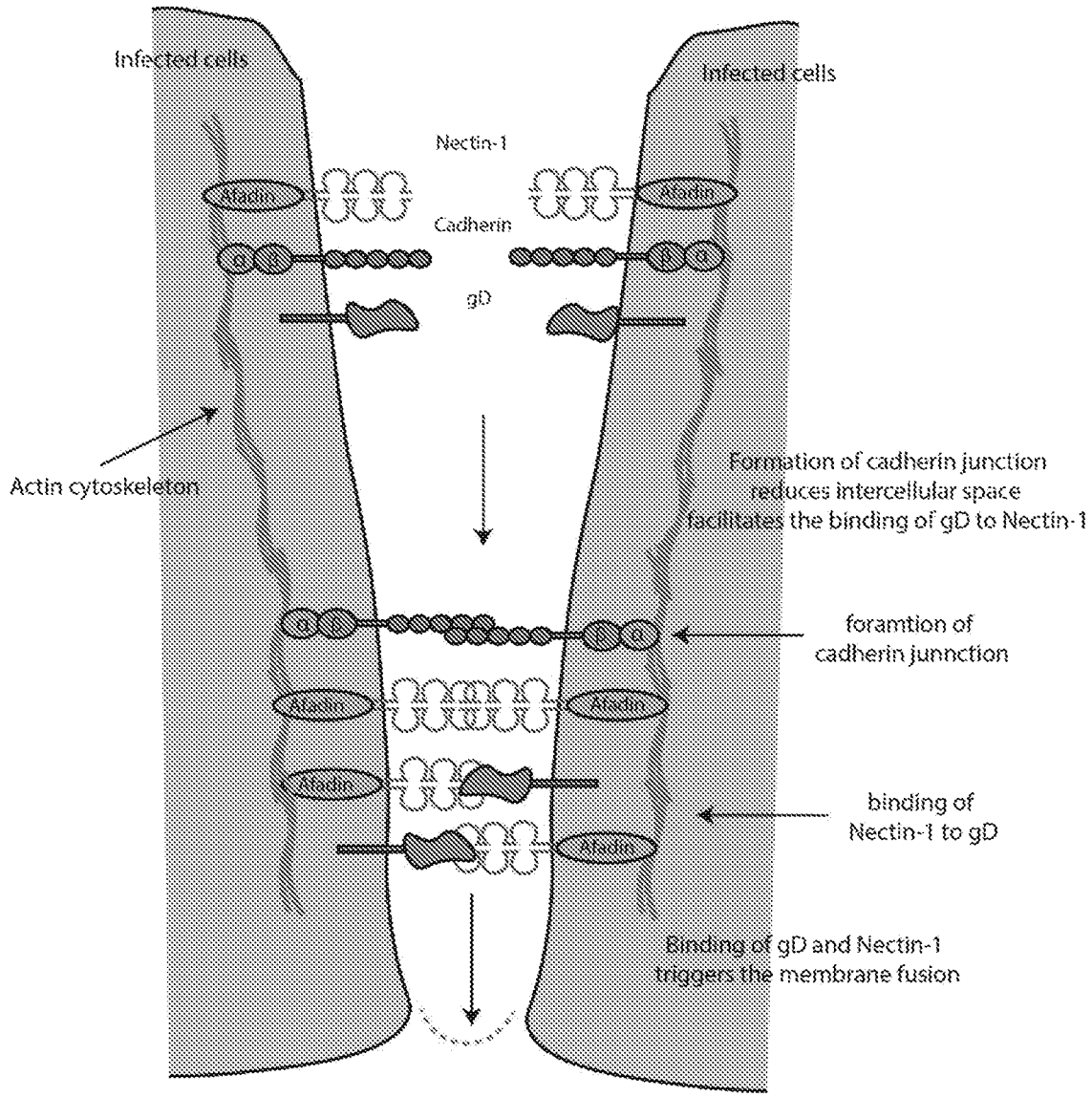

Infected cells
Infected cells
Nectin-1
Afadin
Afadin
Cadherin
gD
Actin cytoskeleton
Formation of cadherin junction
reduces intercellular space
facilitates the binding of gD to Nectin-1
foramtion of
cadherin junnction
Afadin
Afadin
Afadin
Afadin
binding of
Nectin-1 to gD
Binding of gD and Nectin-1
triggers the membrane fusion

FIG. 16

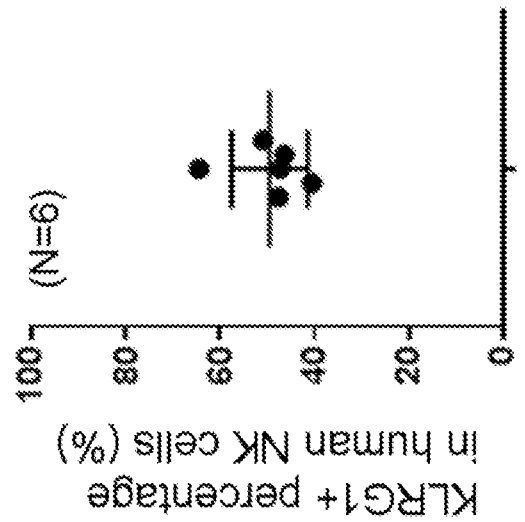


FIG. 17B

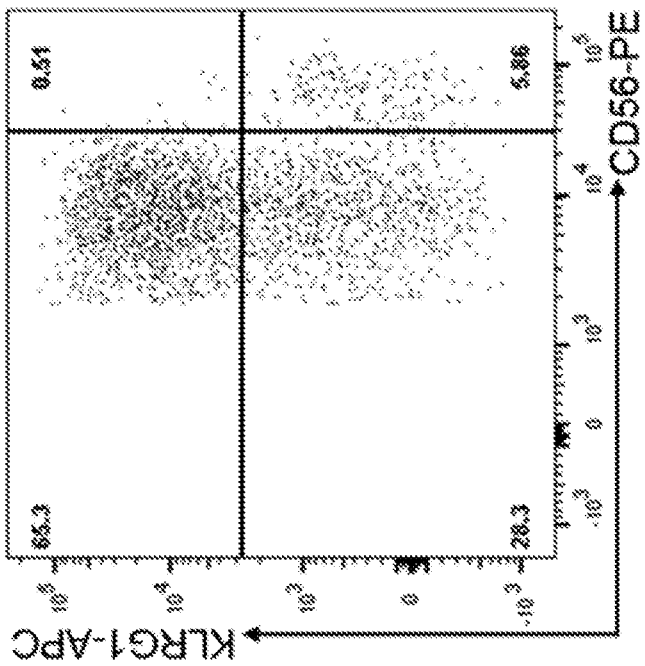


FIG. 17A

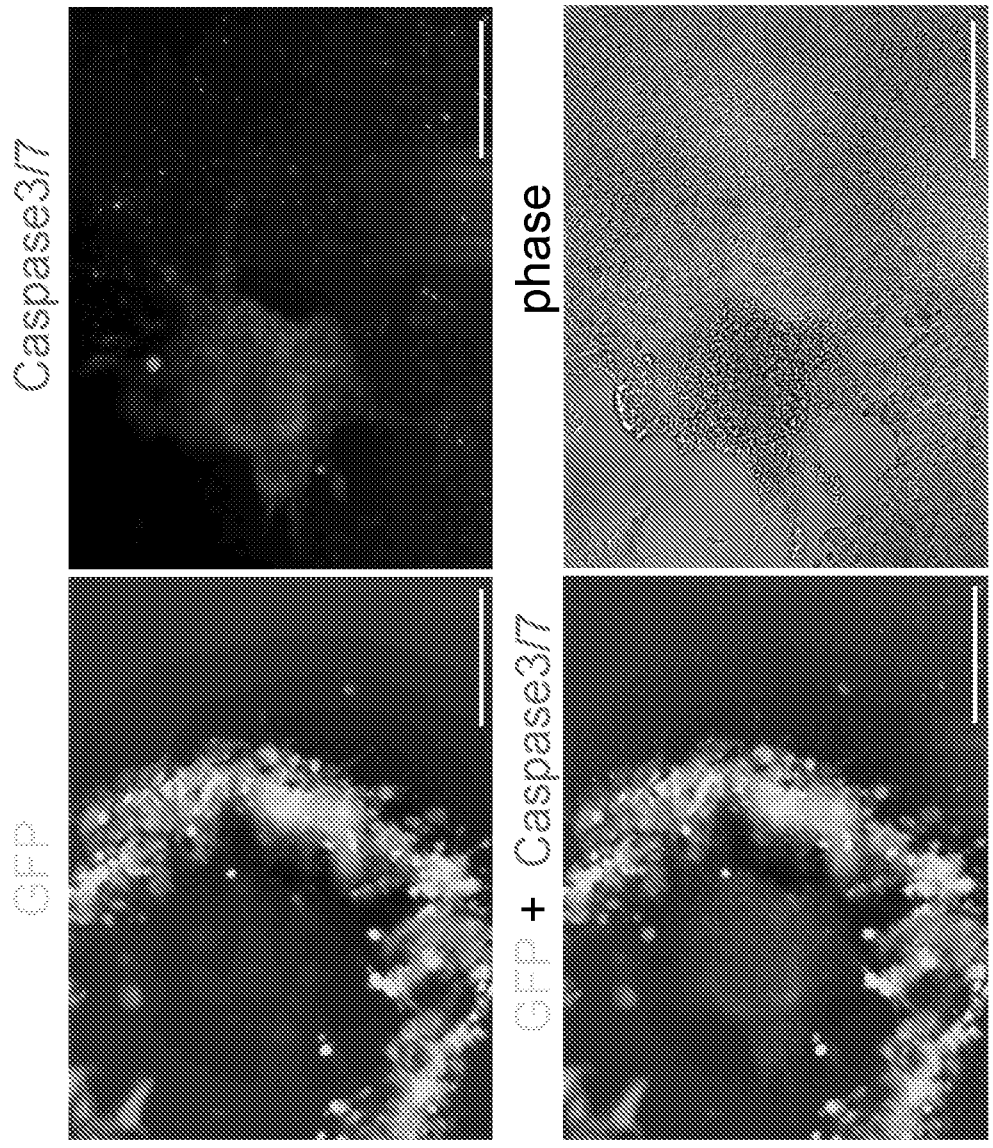


FIG. 18

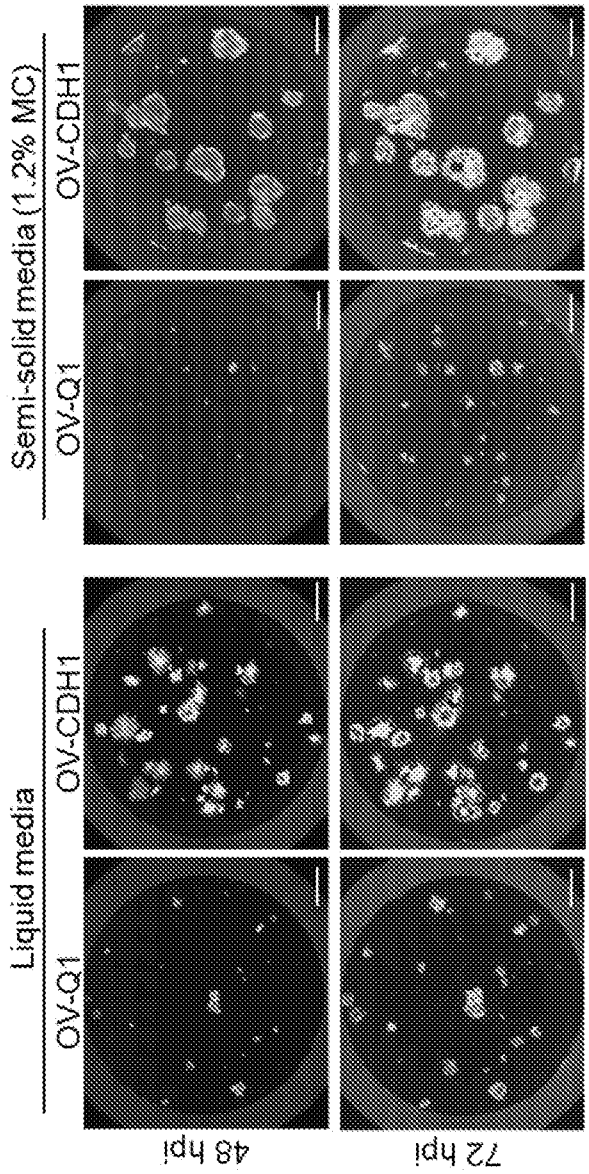

Liquid media
OV-Q1
OV-CDH1
Semi-solid media (1.2% MC)
OV-Q1
OV-CDH1
48 hpi
72 hpi

FIG. 19

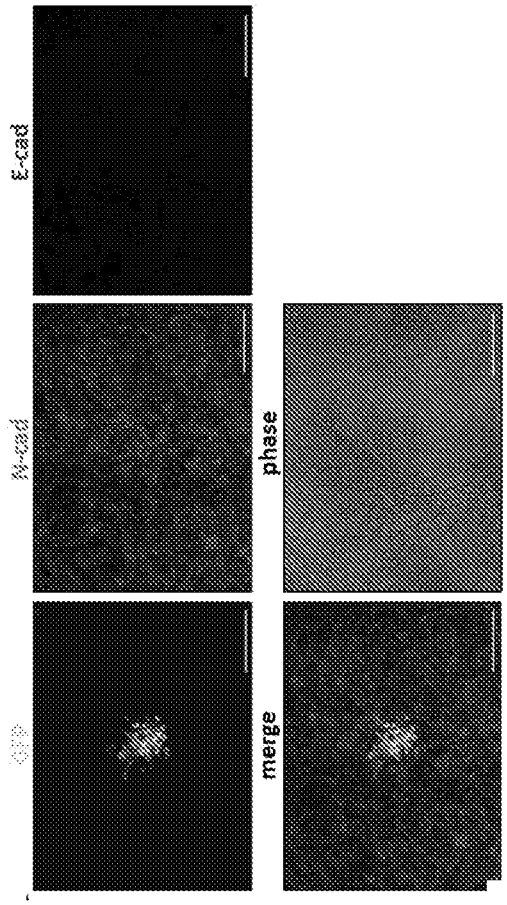


FIG. 20A

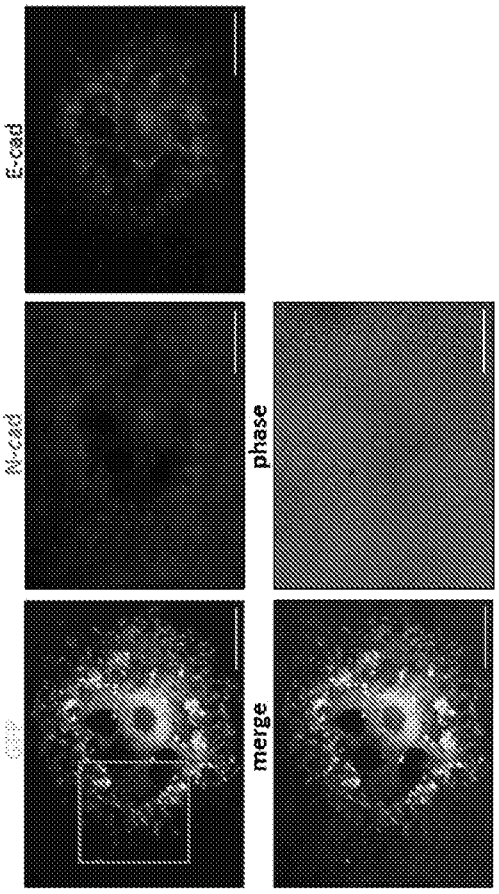


FIG. 20B

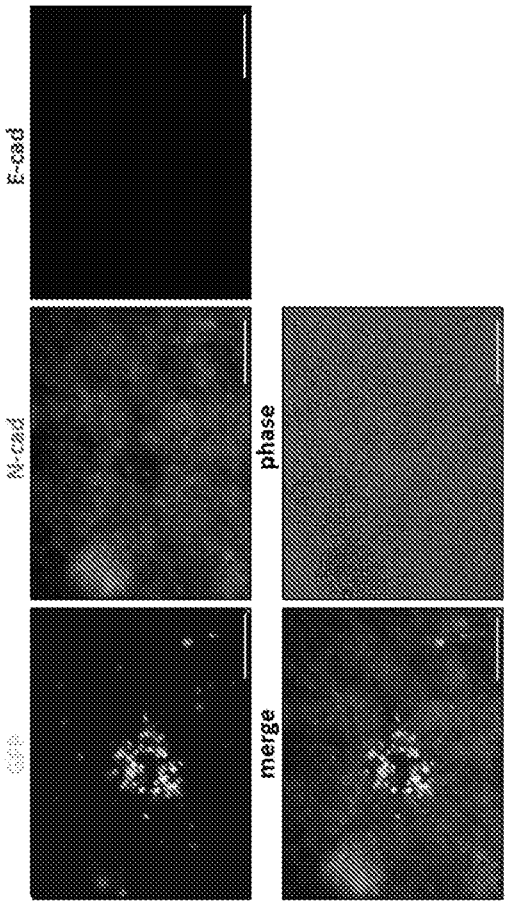


FIG. 21A

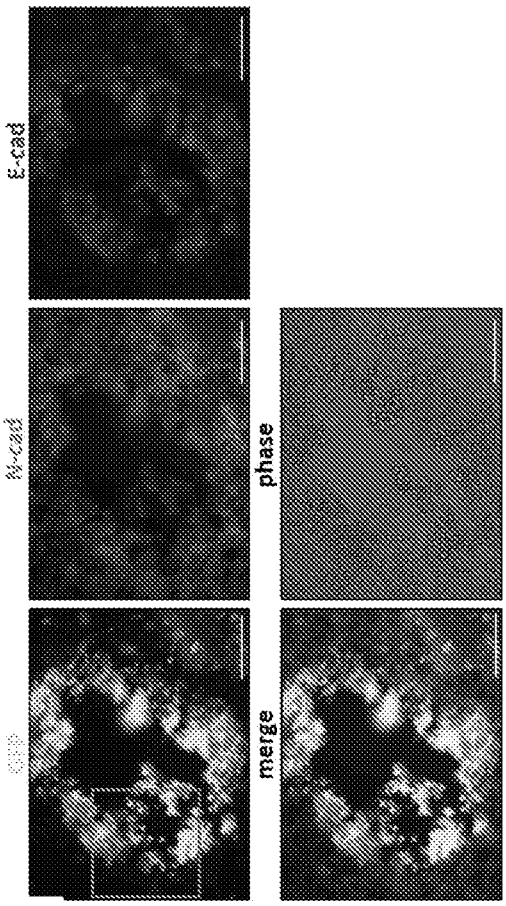


FIG. 21B

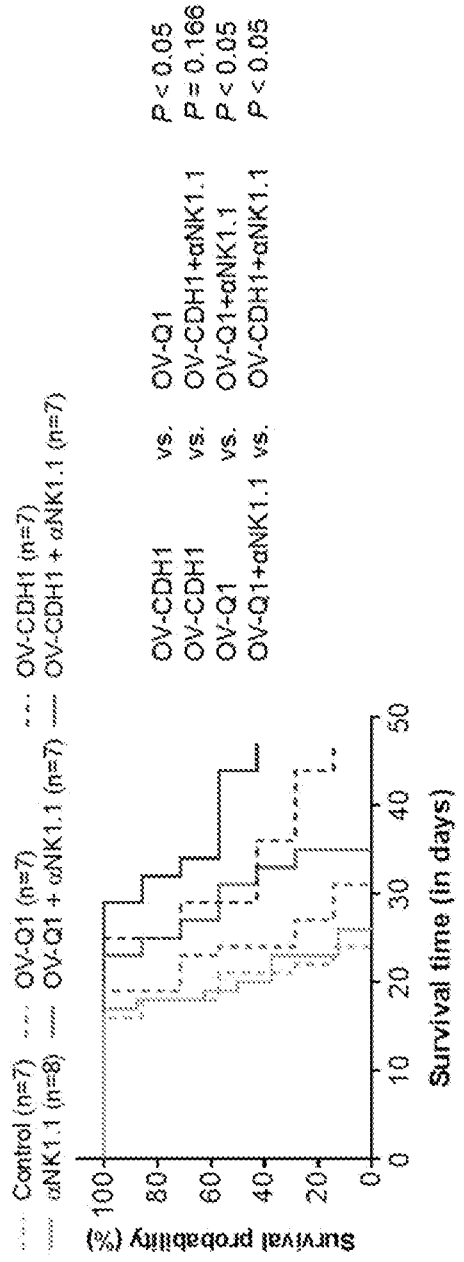


FIG. 22A

FIG. 22B

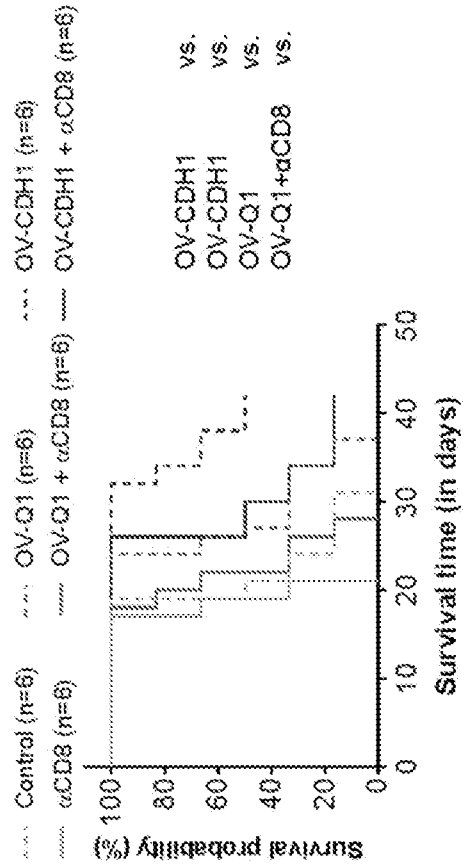


FIG. 22C

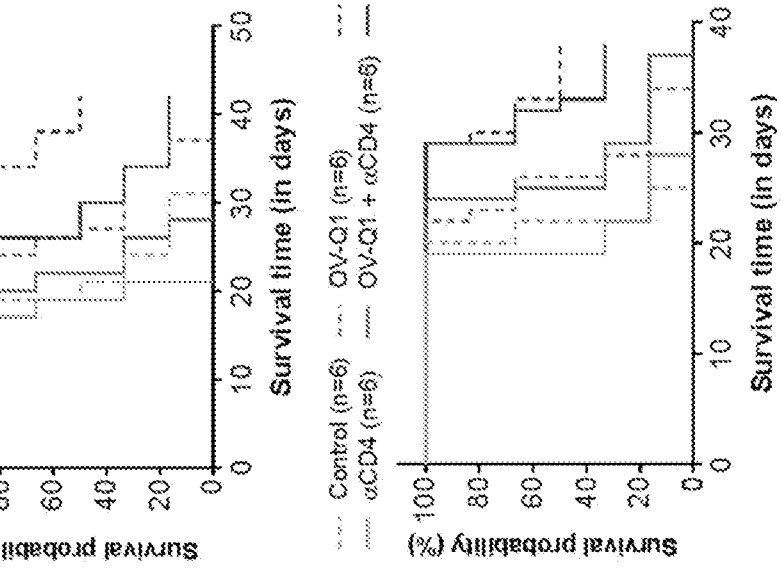


FIG. 22D

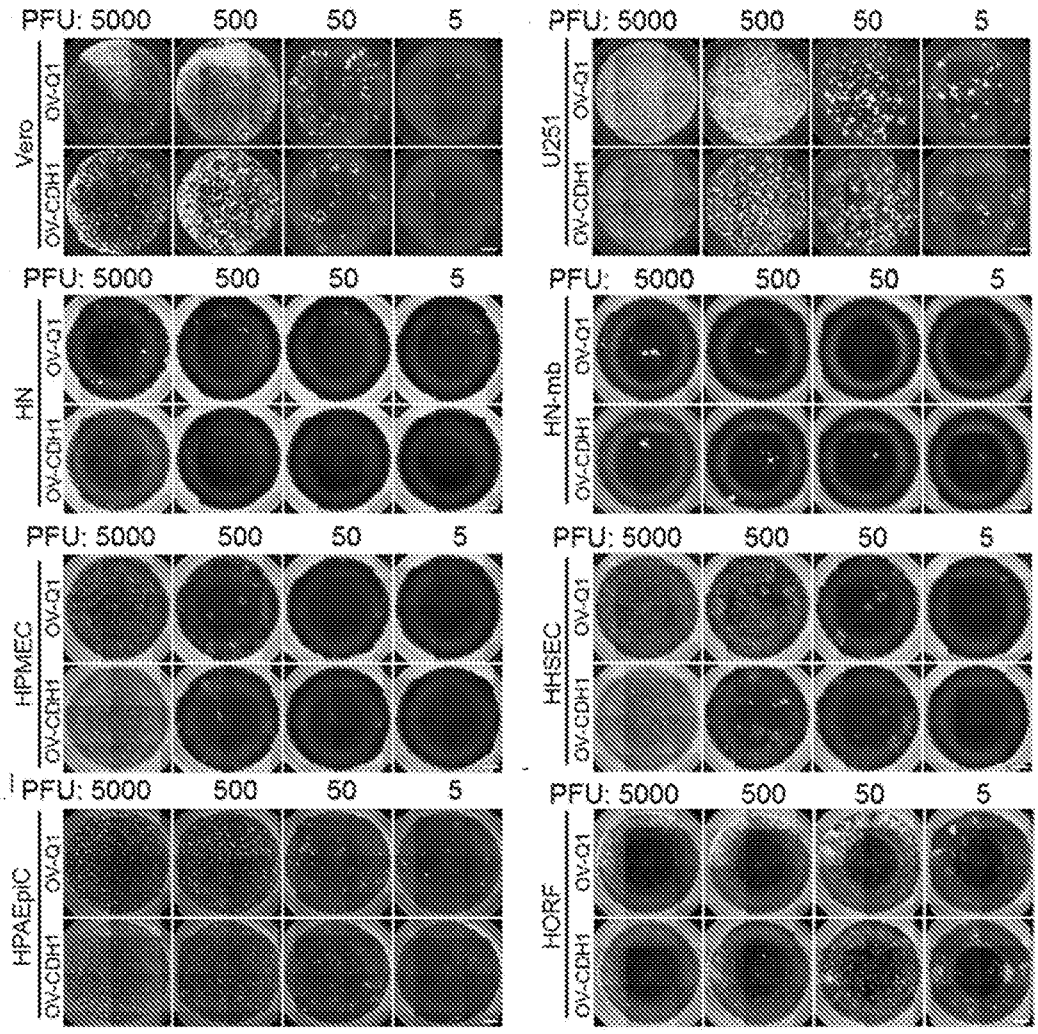

PFU: 5000
500
50
5
Vero
U251
HN
HN-mb
HPMEC
HHSEC
HPAEpiC
HORF
OV-Q1
OV-CDH1

FIG. 23

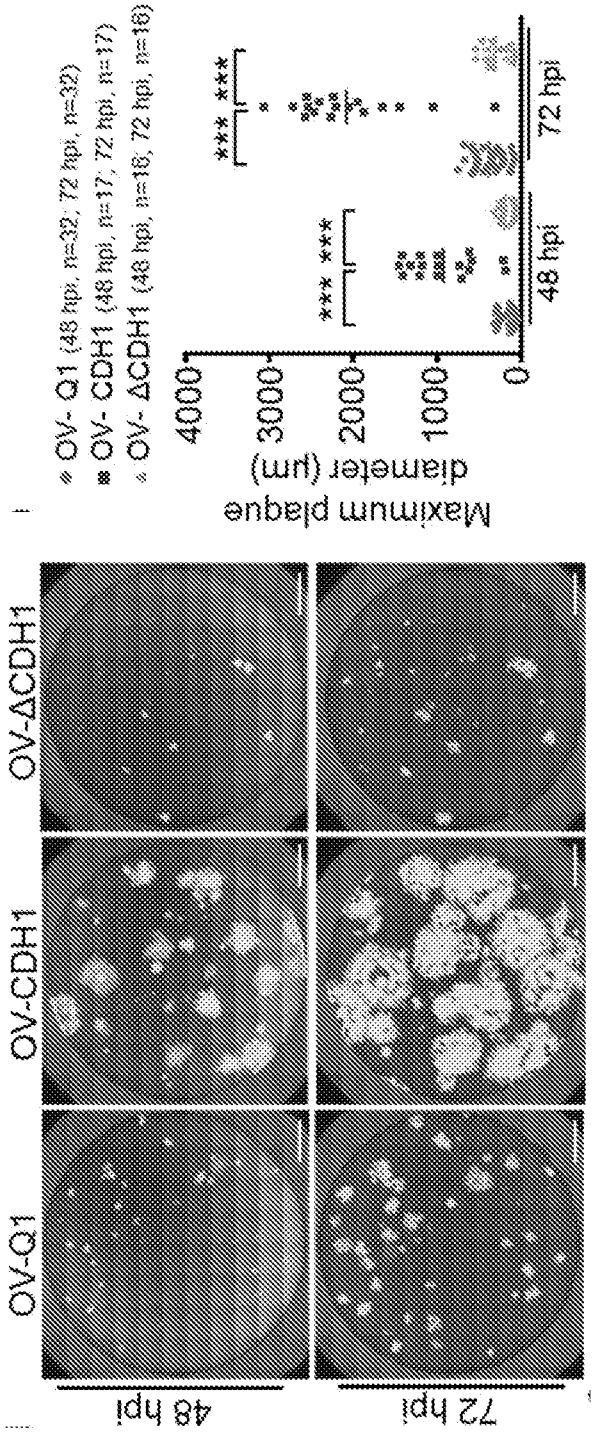


FIG. 24A

FIG. 24B

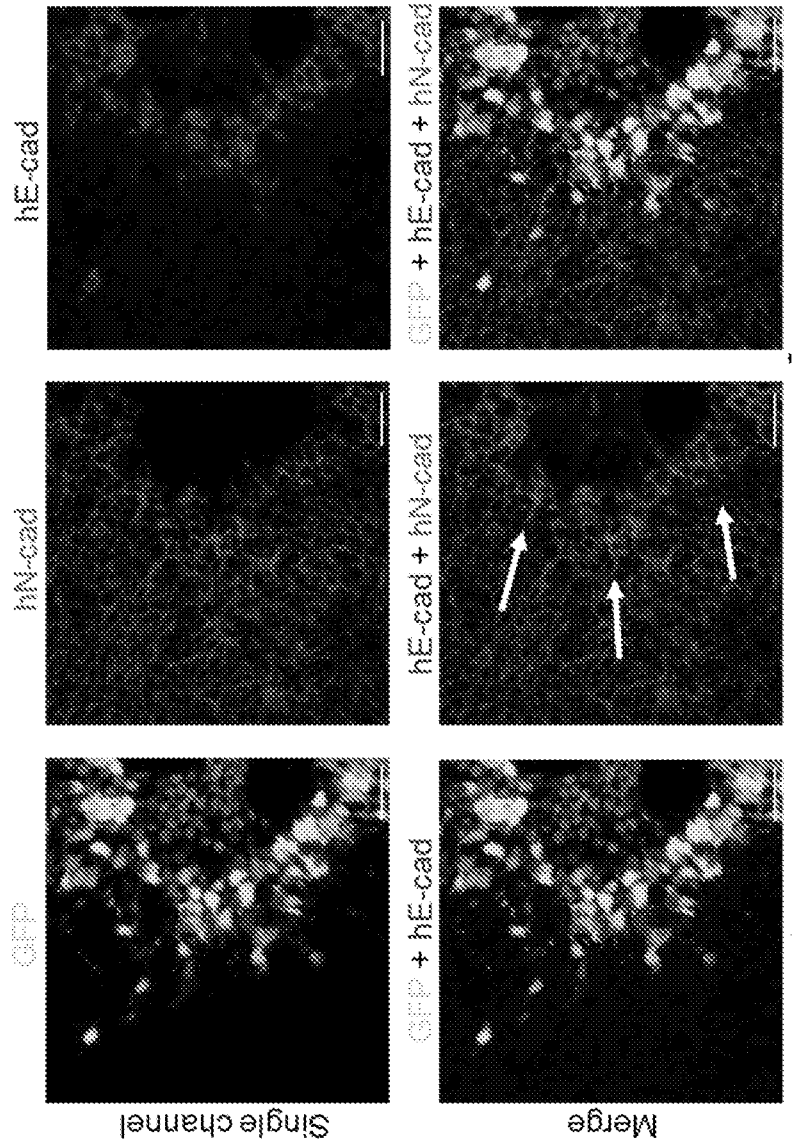

hE-cad
GFP + hE-cad + hN-cad
hN-cad
hE-cad + hN-cad
GFP
GFP + hE-cad
Single channel
Merge

FIG. 24C