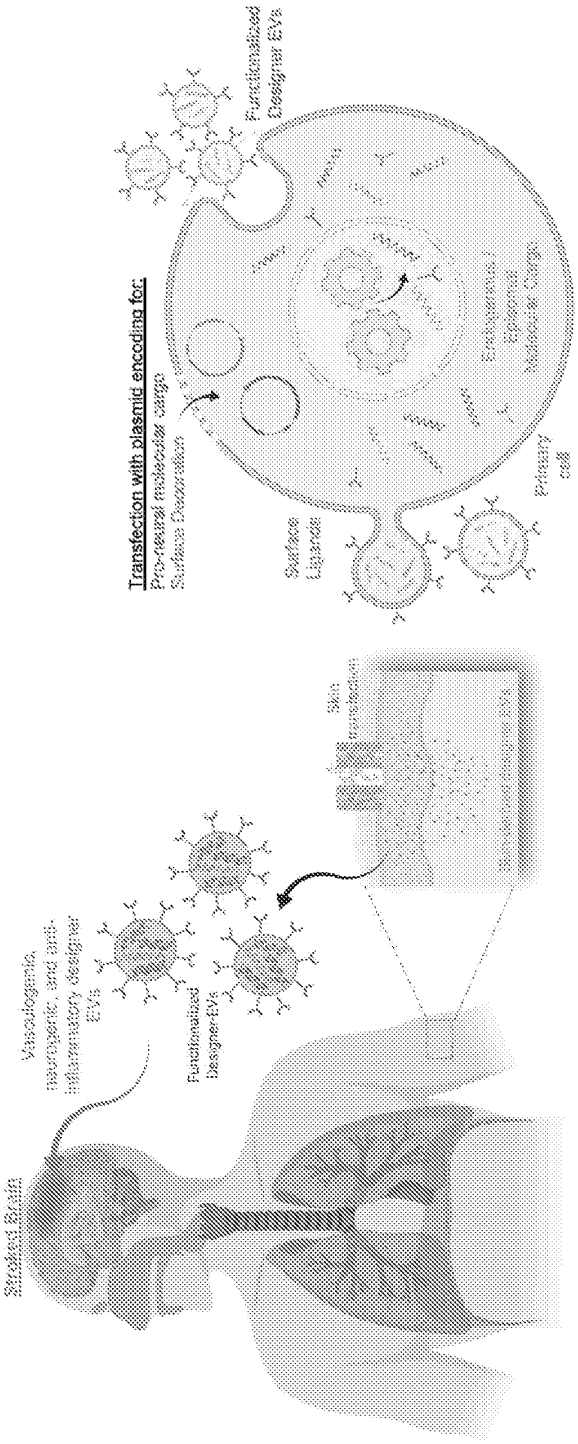

Stroked Brain
Vasculogenic, neurogenic, and anti-inflammatory designer EVs
Functionalized Designer EVs
Skin Transfection
Transfection with plasmid encoding for:
Pro-neural molecular cargo
Surface Decoration
Surface Ligands
Primary cell
Endogenous Exosomal Molecular Cargo
Functionalized Designer EVs

FIG. 1A

FIG. 1B

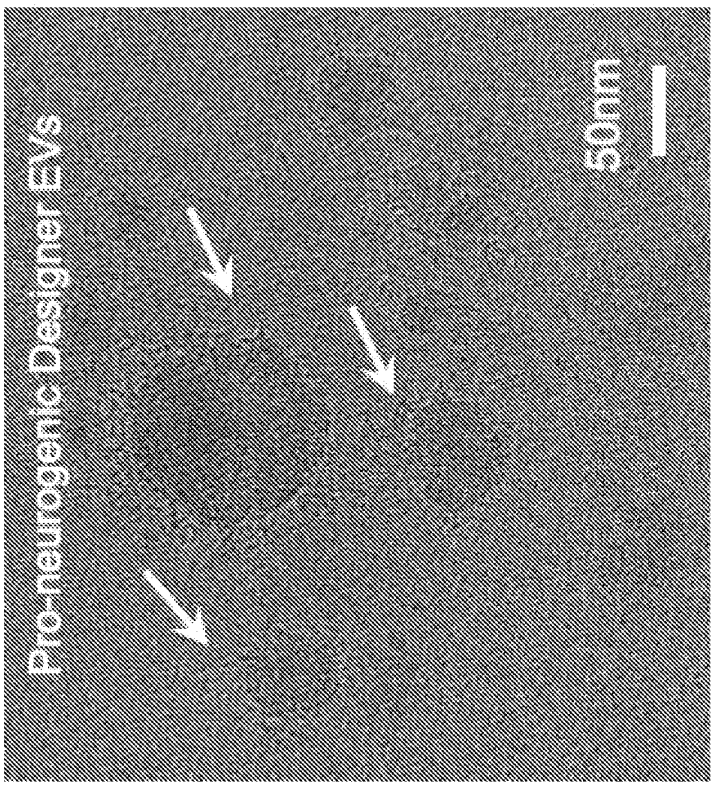

Pro-neurogenic Designer EVs
50nm

FIG. 2A

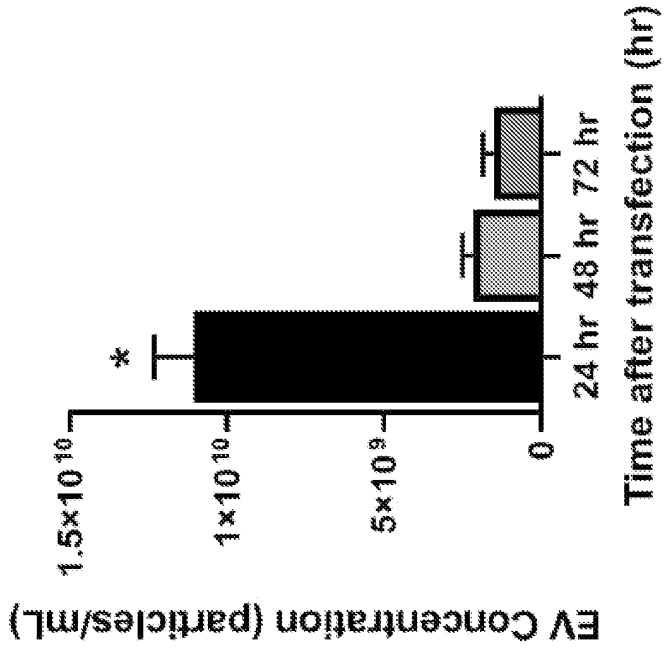

EV Concentration (particles/mL)
1.5×10^10
1×10^10
5×10^9
0
*
24 hr
48 hr
72 hr
Time after transfection (hr)

FIG. 2B

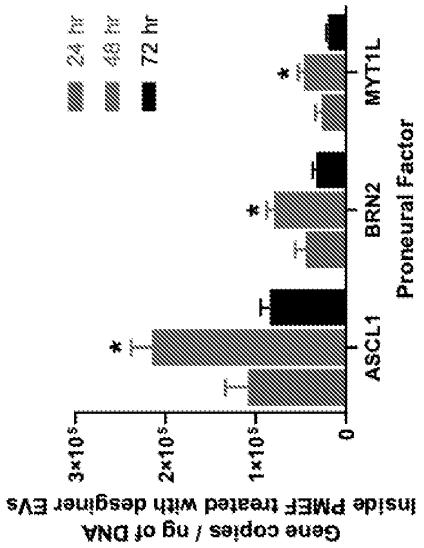

24 hr
48 hr
72 hr
Gene copies / ng of DNA
Inside PMEF treated with designer EVs
3×10^5
2×10^5
1×10^5
0
ASCL1
BRN2
MYT1L
Proneural Factor

FIG. 2D

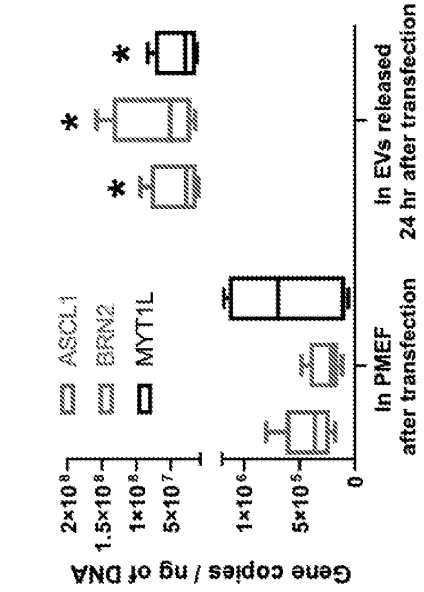

ASCL1
BRN2
MYT1L
Gene copies / ng of DNA
2×10^8
1.5×10^8
1×10^8
5×10^7
1×10^6
5×10^5
0
In PMEF
after transfection
In EVs released
24 hr after transfection

FIG. 2C

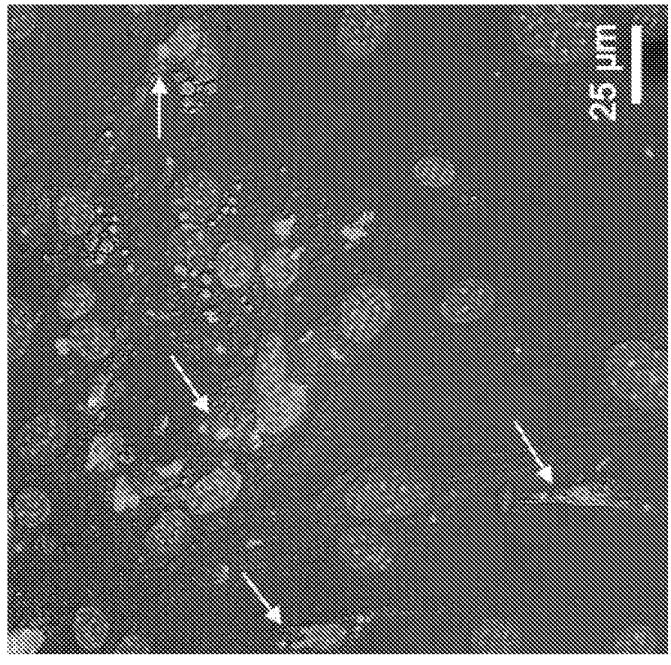


FIG. 2E

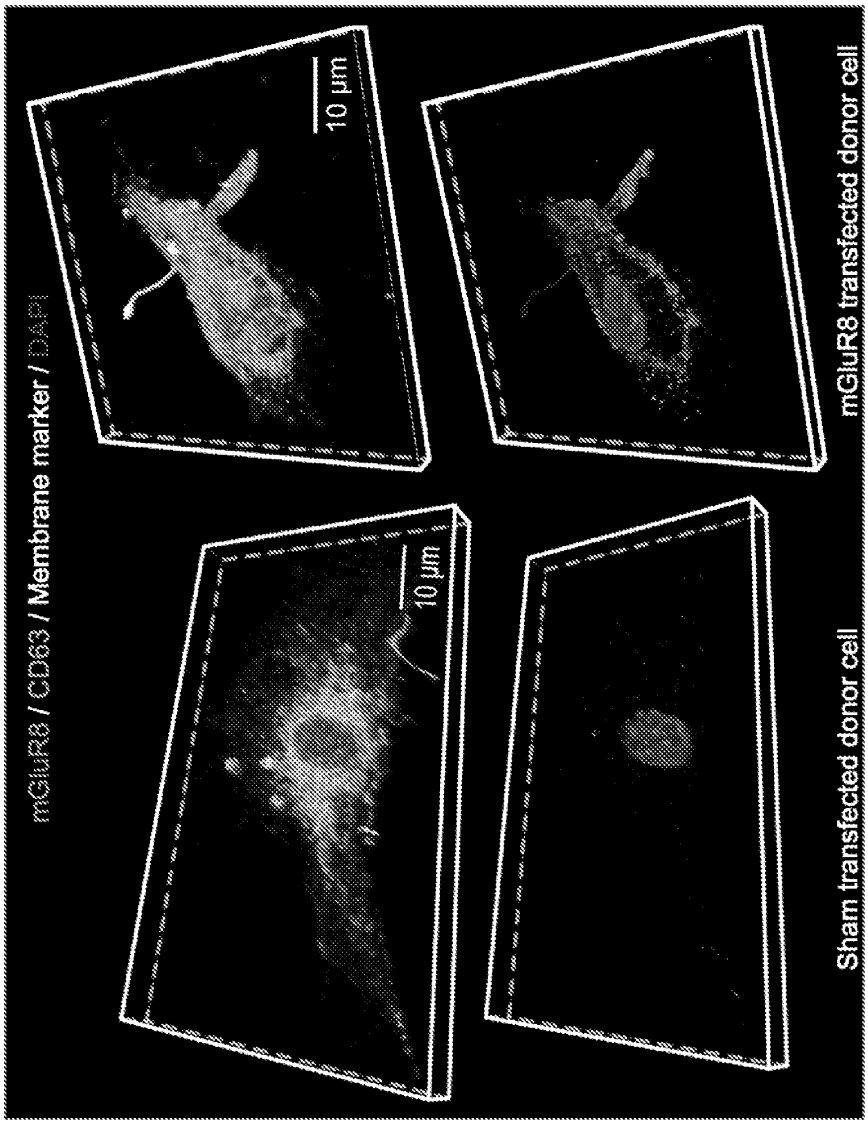

mGluR8 / CD63 / Membrane marker / DAPI
10 µm
10 µm
Sham transfected donor cell
mGluR8 transfected donor cell

FIG. 3A

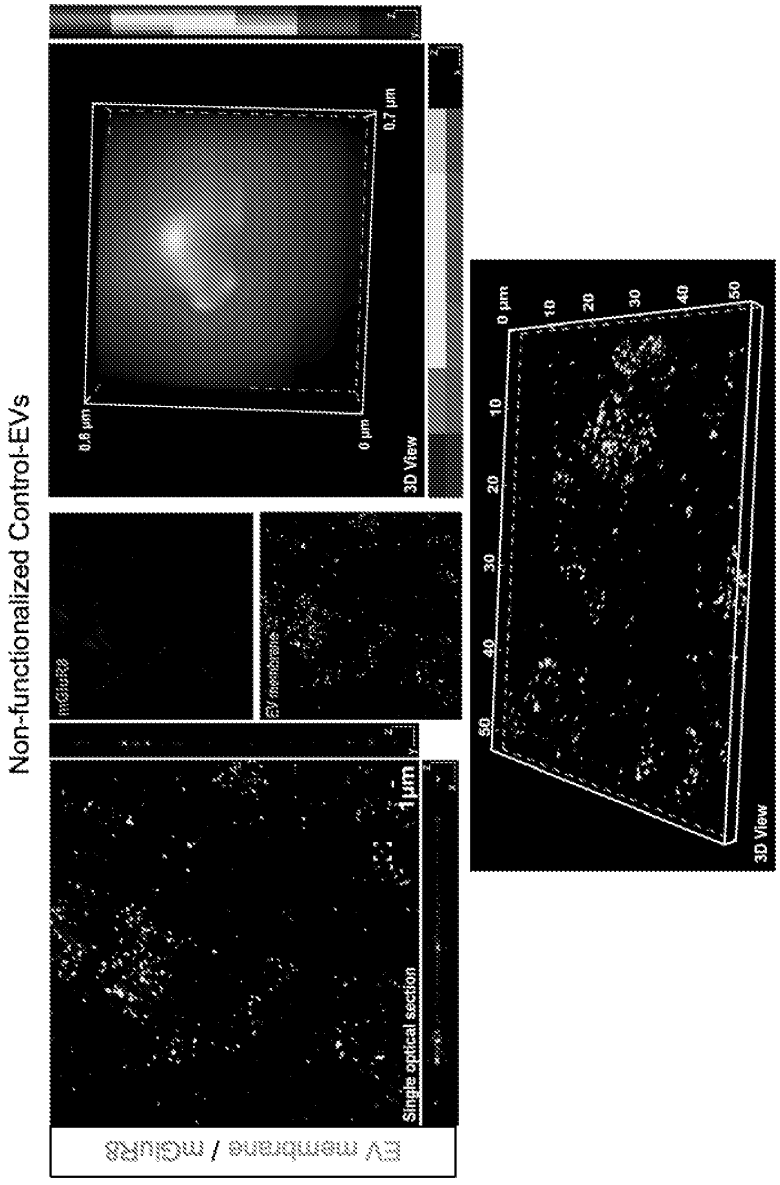

Non-functionalized Control-EVs
EV membrane / mGluR5
Single optical section
1 µm
mGluR5
EV membrane
0.8 µm
0 µm
0.7 µm
3D View
0 µm
10
20
30
40
50
3D View

FIG. 3B

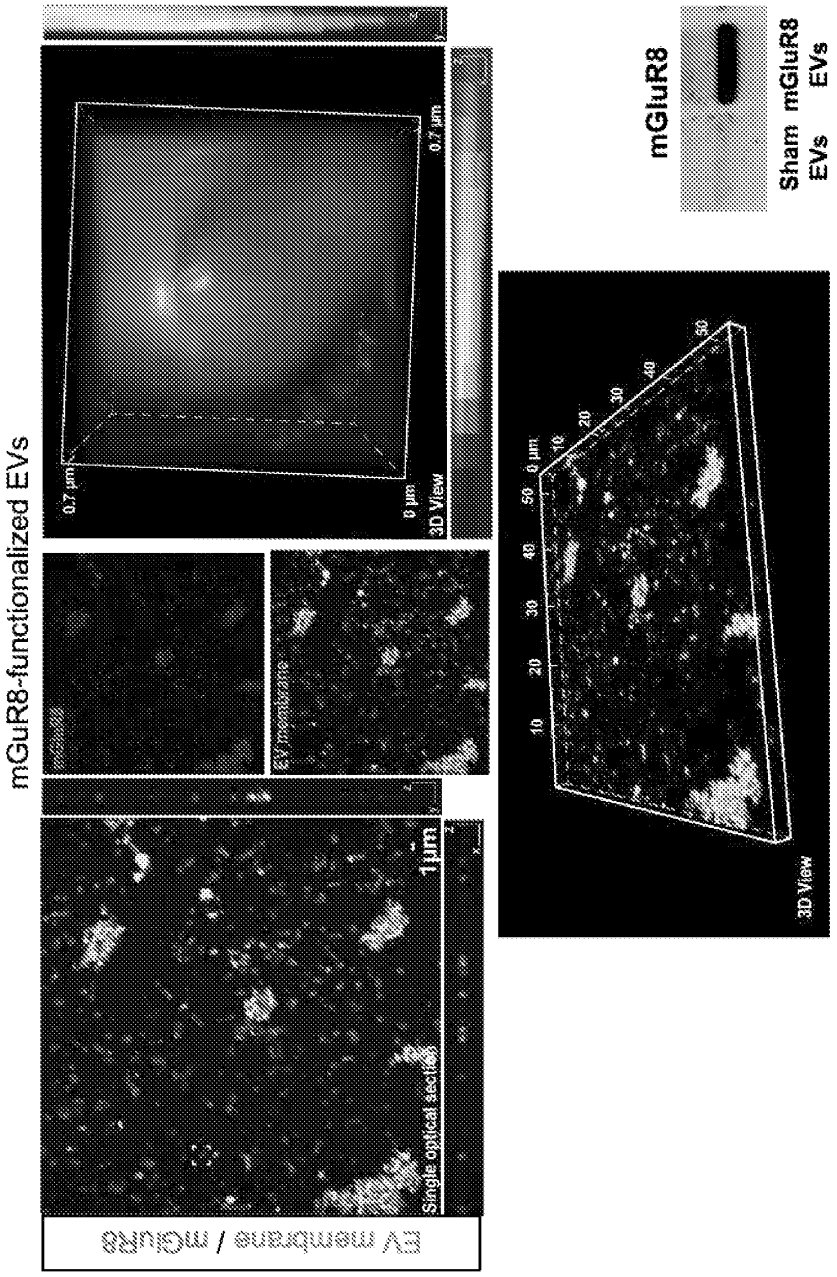

mGluR8-functionalized EVs
EV membrane / mGluR8
1μm
Single optical section
EV membrane
3D View
0.7 μm
0 μm
3D View
mGluR8
Sham EVs
mGluR8 EVs

FIG. 3C

FIG. 3D

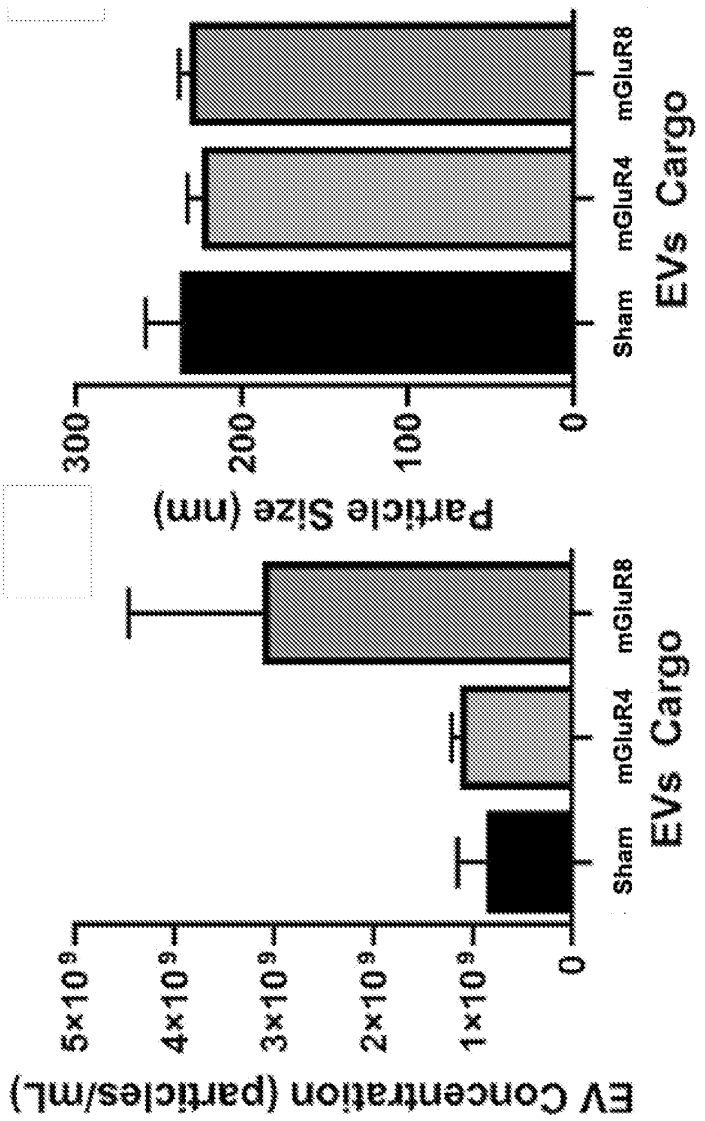

EV Concentration (particles/mL)
5×10^9
4×10^9
3×10^9
2×10^9
1×10^9
0
Sham
mGluR4
mGluR8
EVs Cargo
Particle Size (nm)
300
200
100
0
Sham
mGluR4
mGluR8
EVs Cargo

FIG. 3E

FIG. 3F

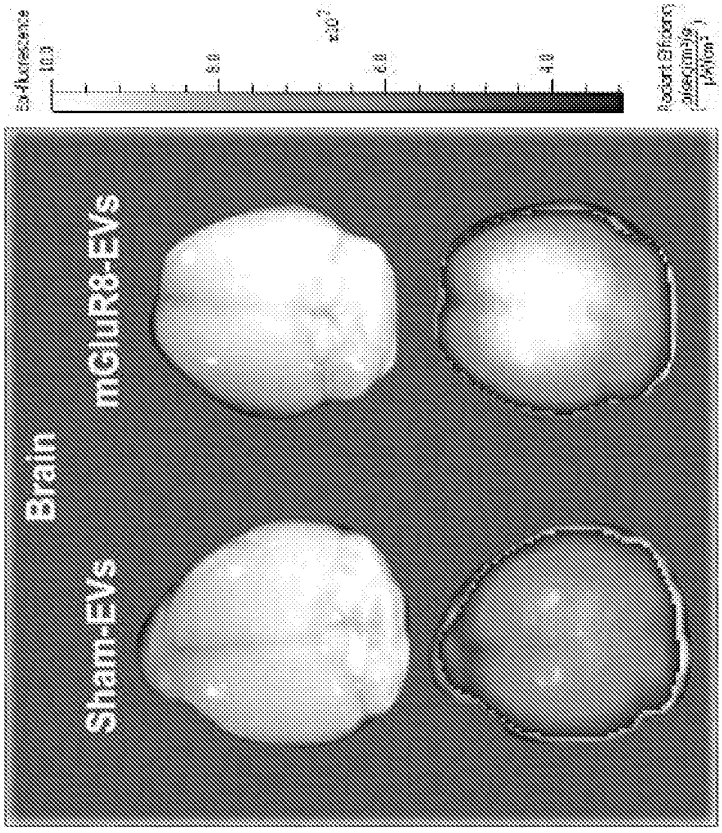


FIG. 4A

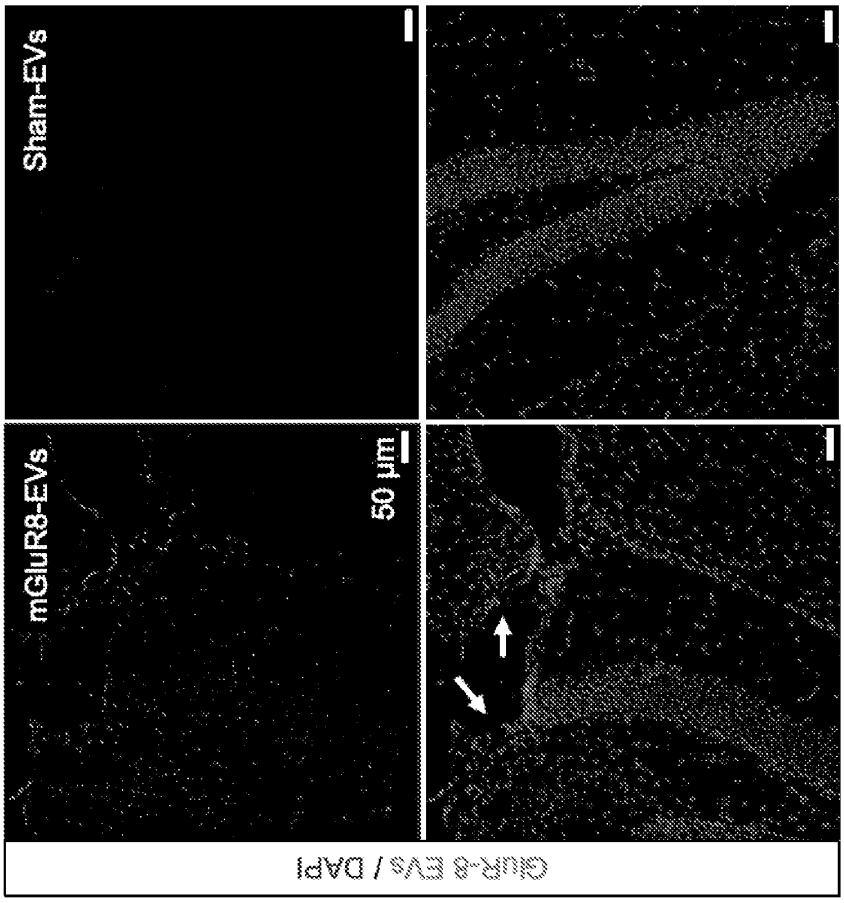

GluR-8 EVs / DAPI
mGluR8-EVs
Sham-EVs
50 µm

FIG. 4B

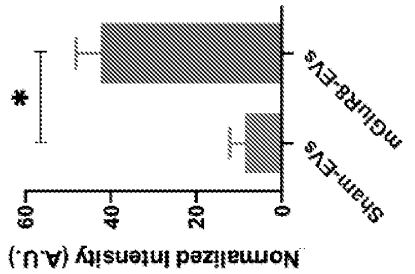

Normalized Intensity (A.U.)
0
20
40
60
Sham-EVs
mGluR8-EVs
*

FIG.4C

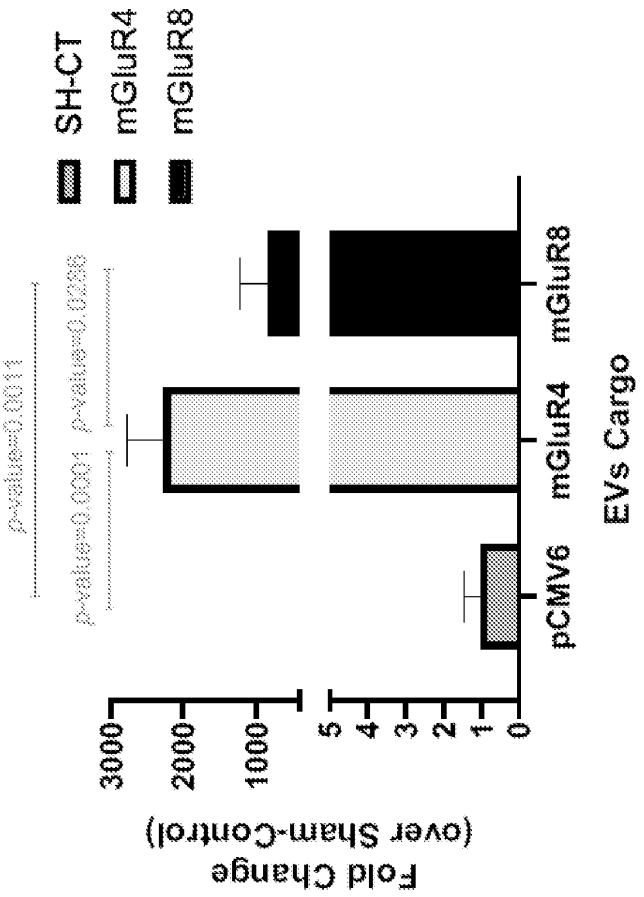

SH-CT
mGluR4
mGluR8
p-value=0.0011
p-value=0.0001
p-value=0.0206
Fold Change
(over Sham-Control)
3000
2000
1000
5
4
3
2
1
0
pCMV6
mGluR4
mGluR8
EVs Cargo

FIG. 5

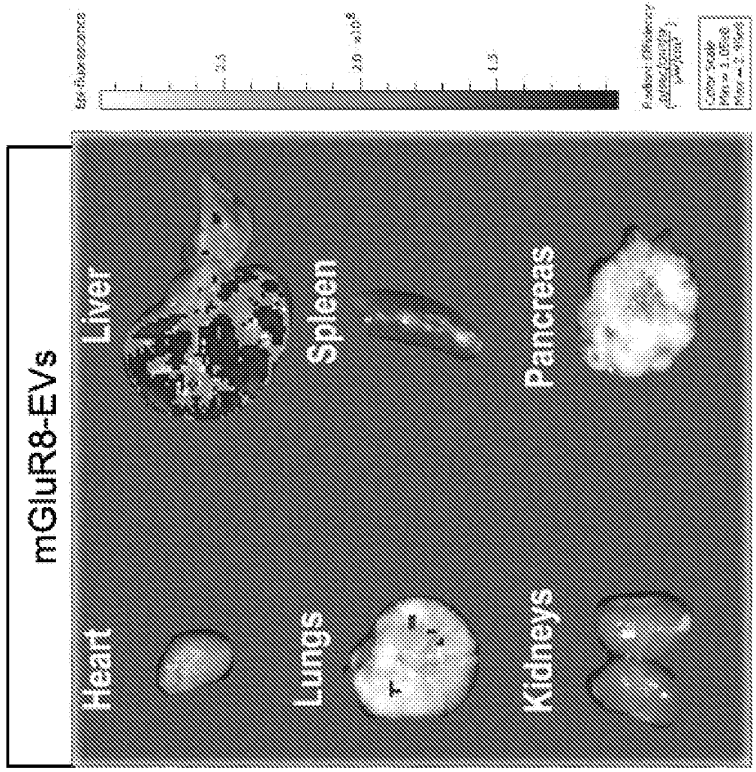

mGluR8-EVs
Heart
Liver
Lungs
Spleen
Kidneys
Pancreas

FIG. 6B

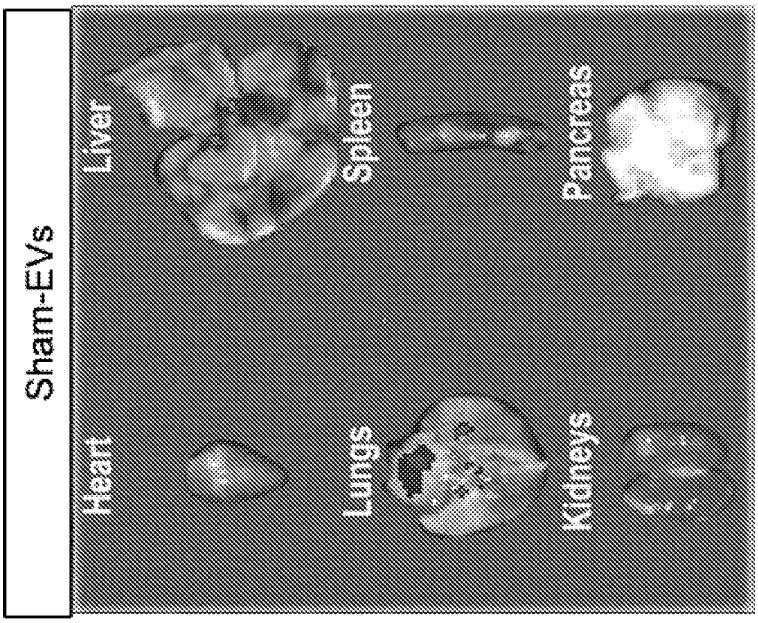

Sham-EVs
Heart
Liver
Lungs
Spleen
Kidneys
Pancreas

FIG. 6A

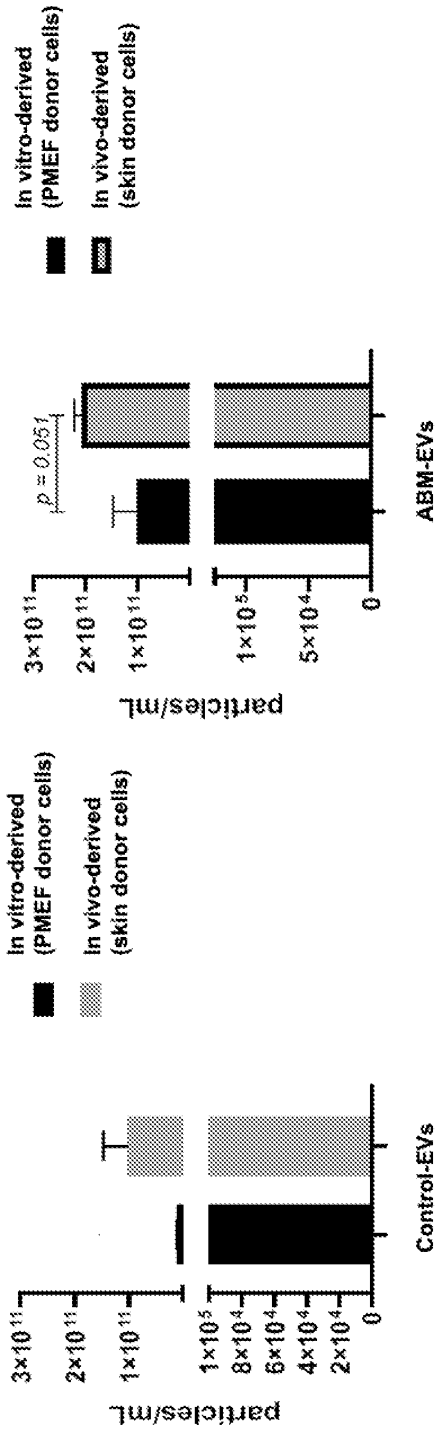

In vitro-derived
(PMEF donor cells)
In vivo-derived
(skin donor cells)
particles/mL
3×10^11
2×10^11
1×10^11
1×10^5
8×10^4
6×10^4
4×10^4
2×10^4
0
Control-EVs

FIG. 7A

In vitro-derived
(PMEF donor cells)
In vivo-derived
(skin donor cells)
p = 0.051
particles/mL
3×10^11
2×10^11
1×10^11
1×10^5
5×10^4
0
ABM-EVs

FIG. 7B

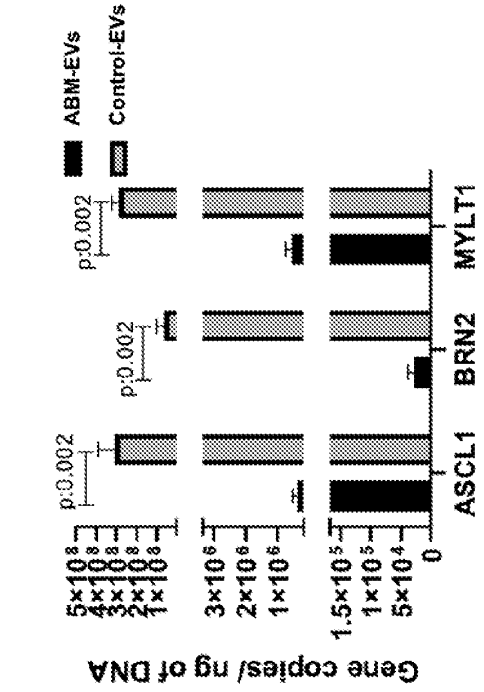

ABM-EVs
Control-EVs
p:0.002
p:0.002
p:0.002
Gene copies/ ng of DNA
ASCL1
BRN2
MYLT1

FIG. 8B

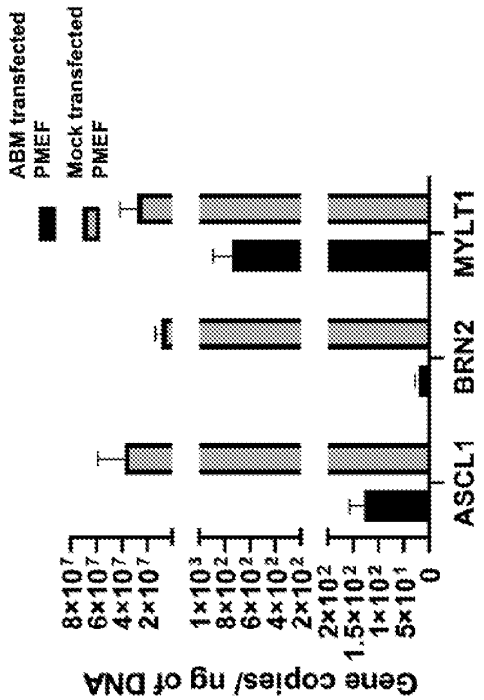

ABM transfected PMEF
Mock transfected PMEF
Gene copies/ ng of DNA
ASCL1
BRN2
MYLT1

FIG. 8A

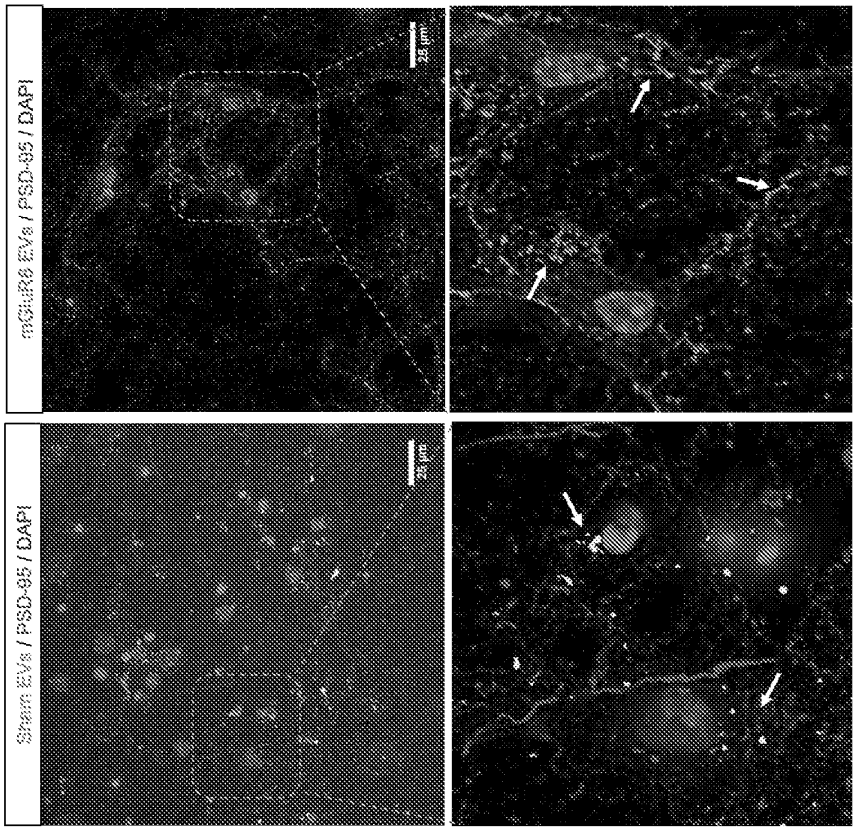


FIG. 9A

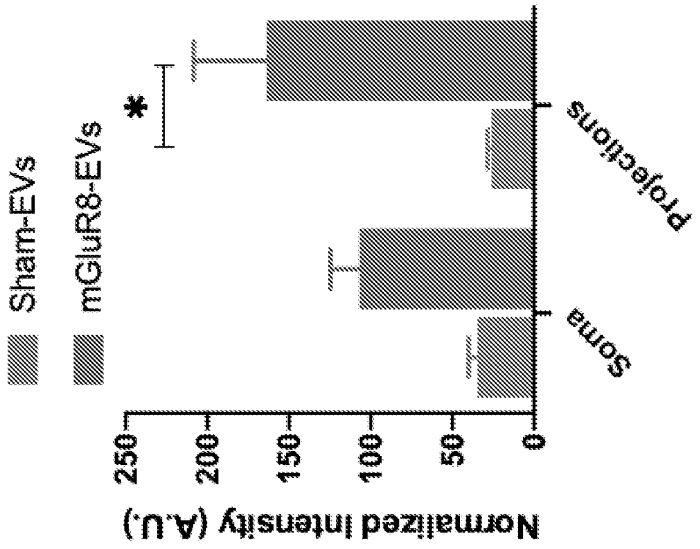

Sham-EVs
mGluR8-EVs
*
Normalized Intensity (A.U.)
250
200
150
100
50
0
Soma
Projections

FIG. 9B

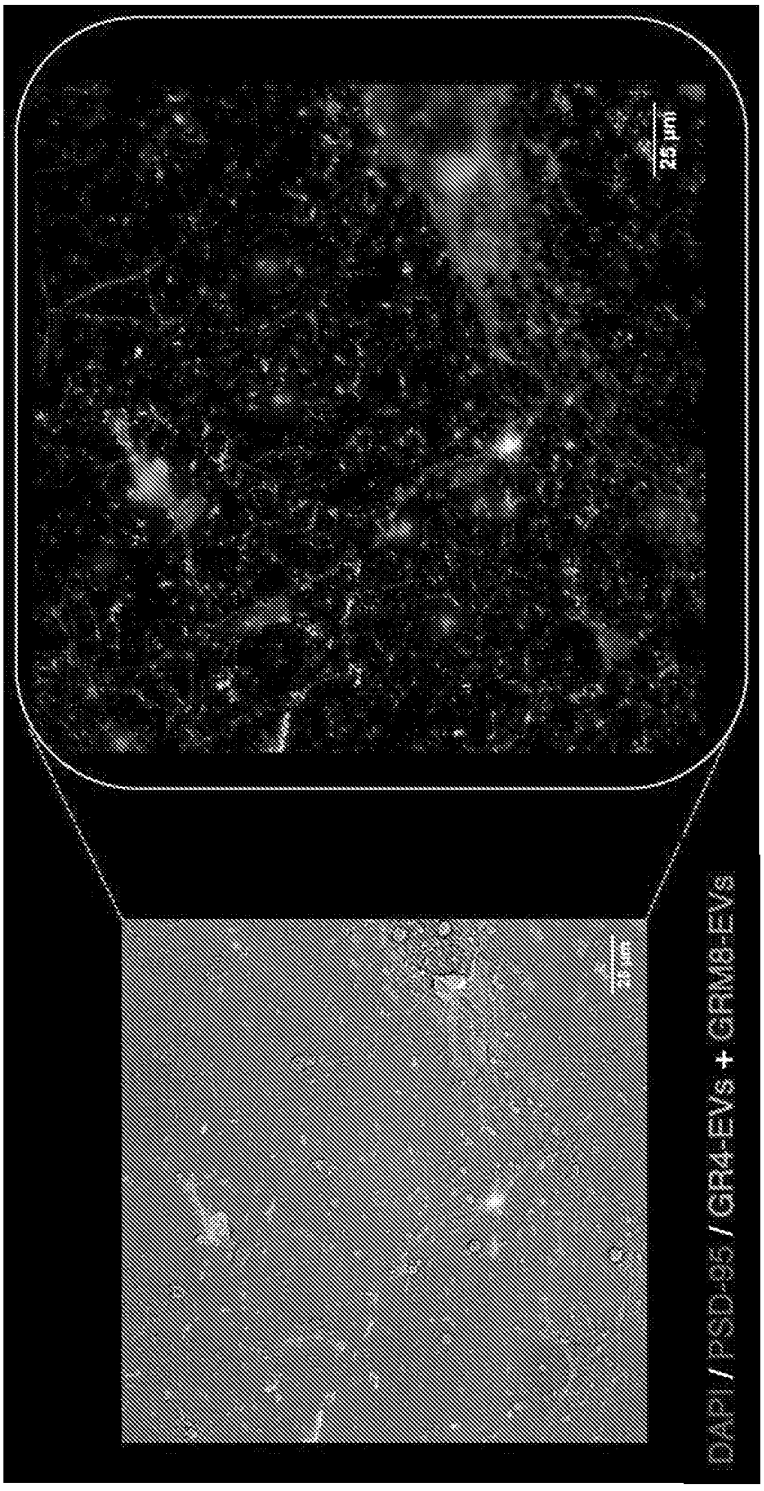


FIG. 10

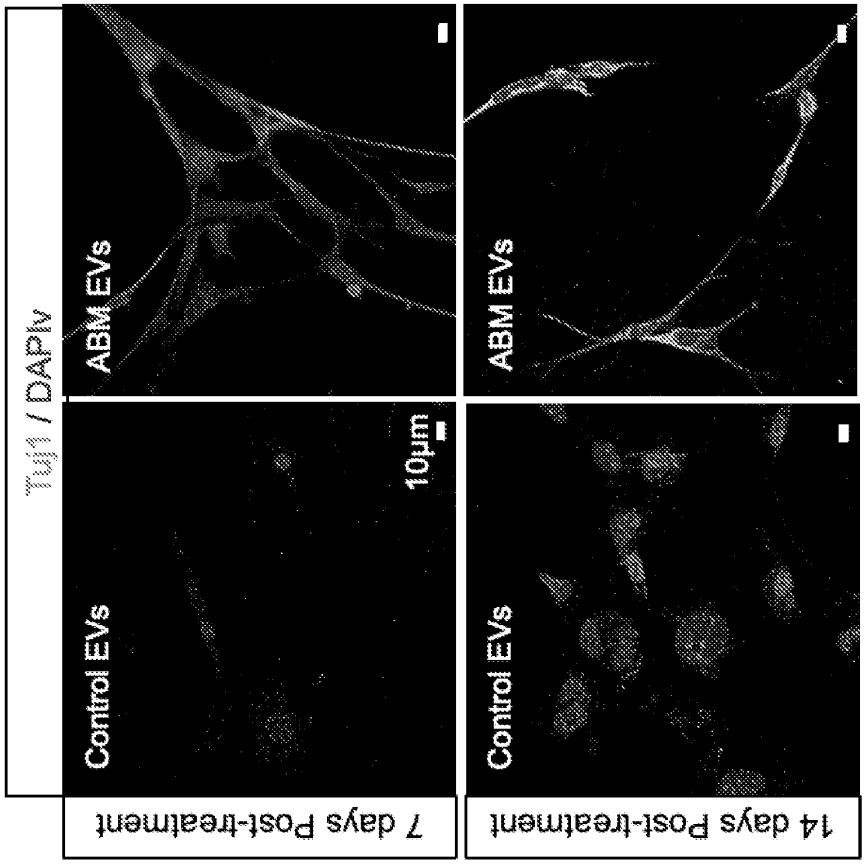


FIG. 11A

FIG.11B