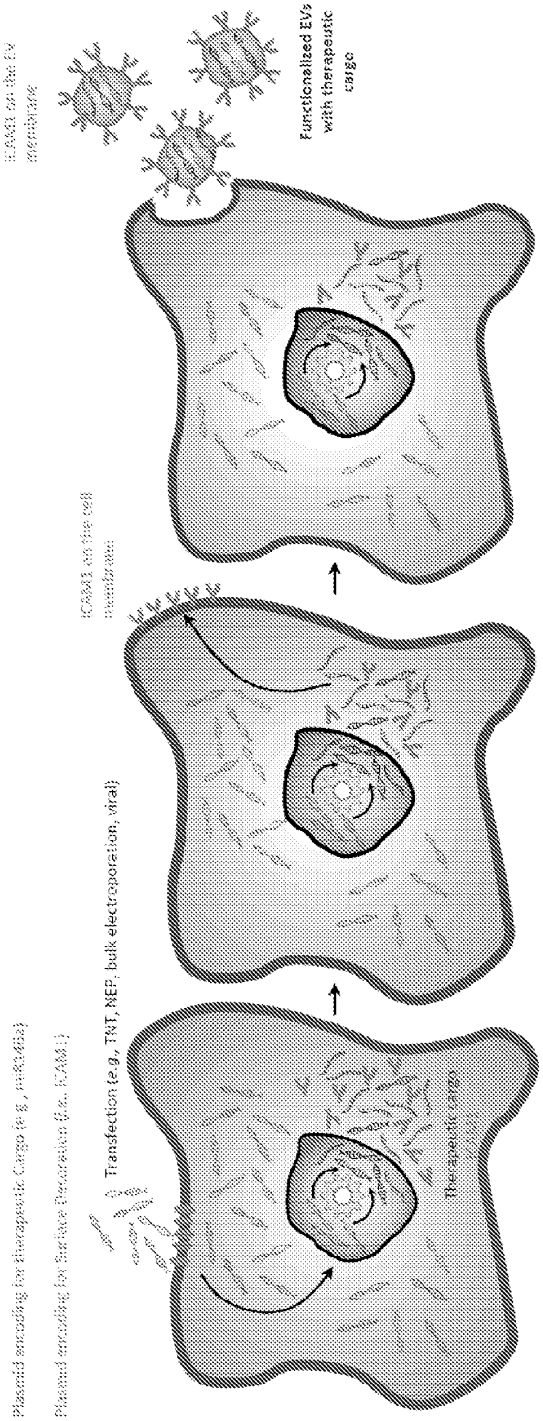

Functionalized EVs with therapeutic cargo
Transfection (e.g., TNT, MEP, bulk electroporation, viral)
Therapeutic cargo

FIG. 1

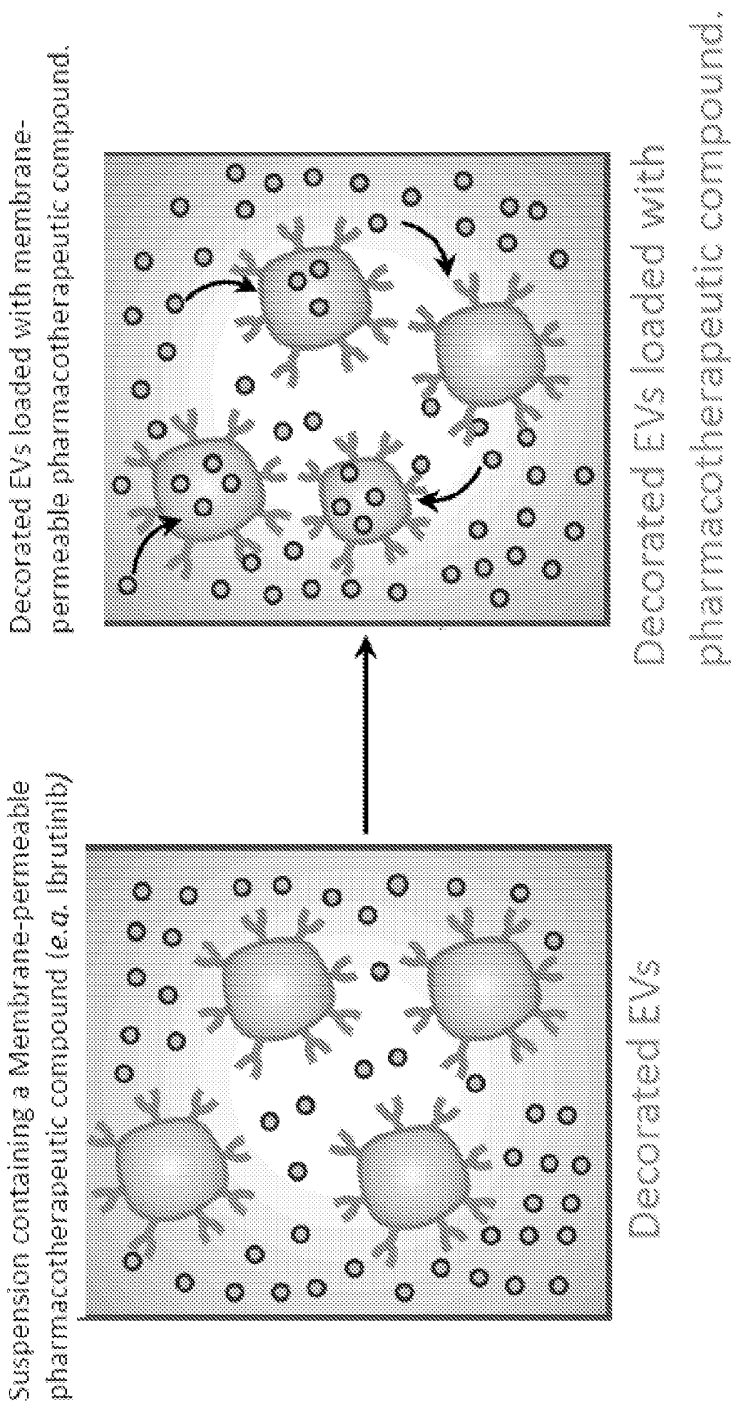

Suspension containing a Membrane-permeable pharmacotherapeutic compound (e.g. Ibrutinib)
Decorated EVs
Decorated EVs loaded with membrane-permeable pharmacotherapeutic compound.
Decorated EVs loaded with pharmacotherapeutic compound.

FIG. 2

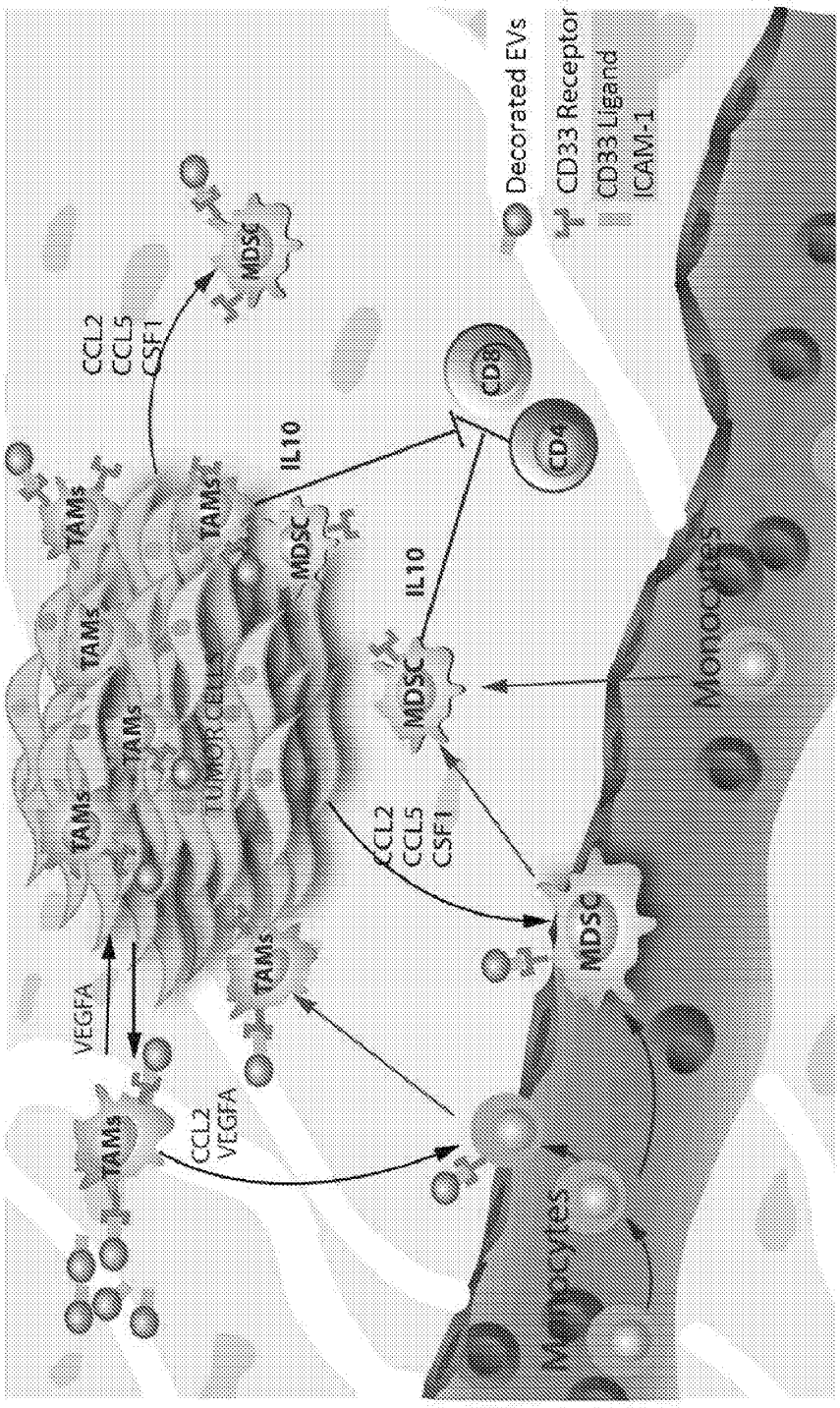

Decorated EVs
CD33 Receptor
CD33 Ligand
ICAM-1
Monocytes
Monocytes
TAMs
TAMs
TAMs
TAMs
TAMs
TAMs
TAMs
TUMOR CELL
MDSC
MDSC
MDSC
MDSC
CD8
CD4
VEGFA
CCL2
VEGFA
CCL2
CCL5
CSF1
CCL2
CCL5
CSF1
IL10
IL10

FIG. 3

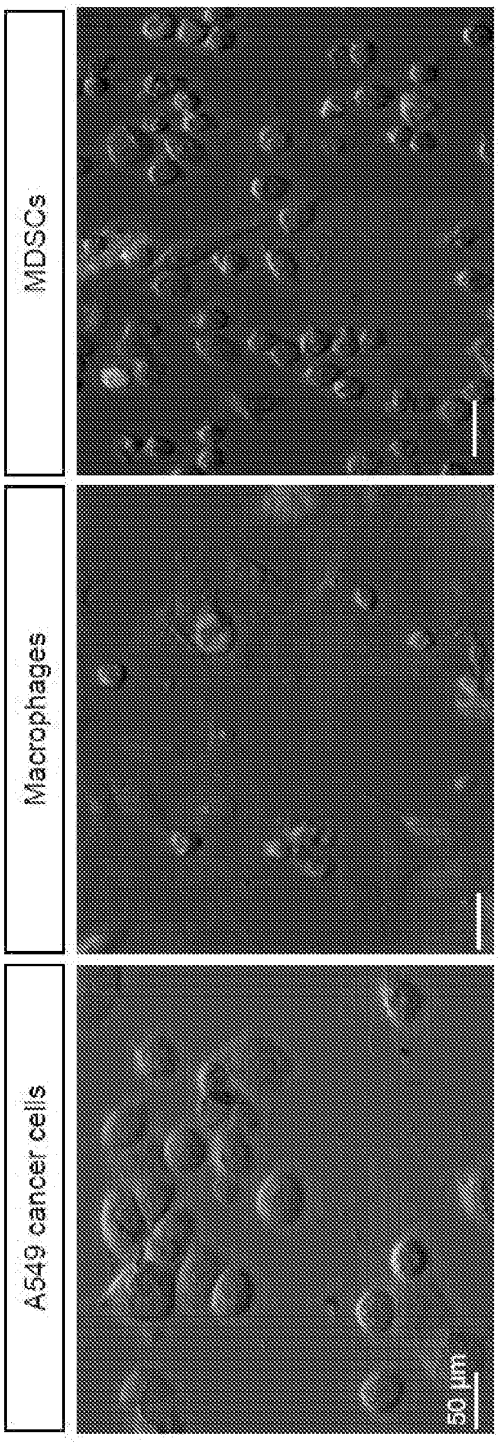


FIG. 4A

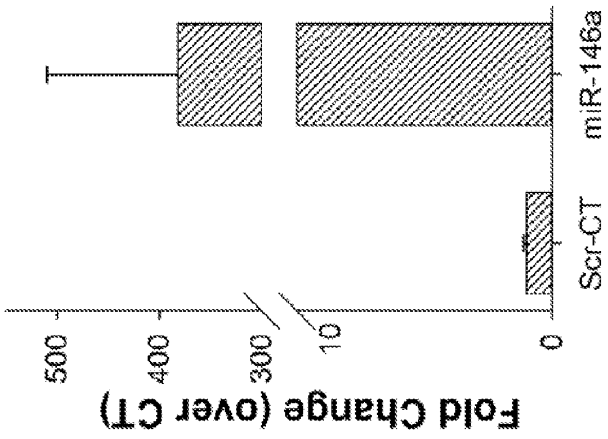


FIG. 4B

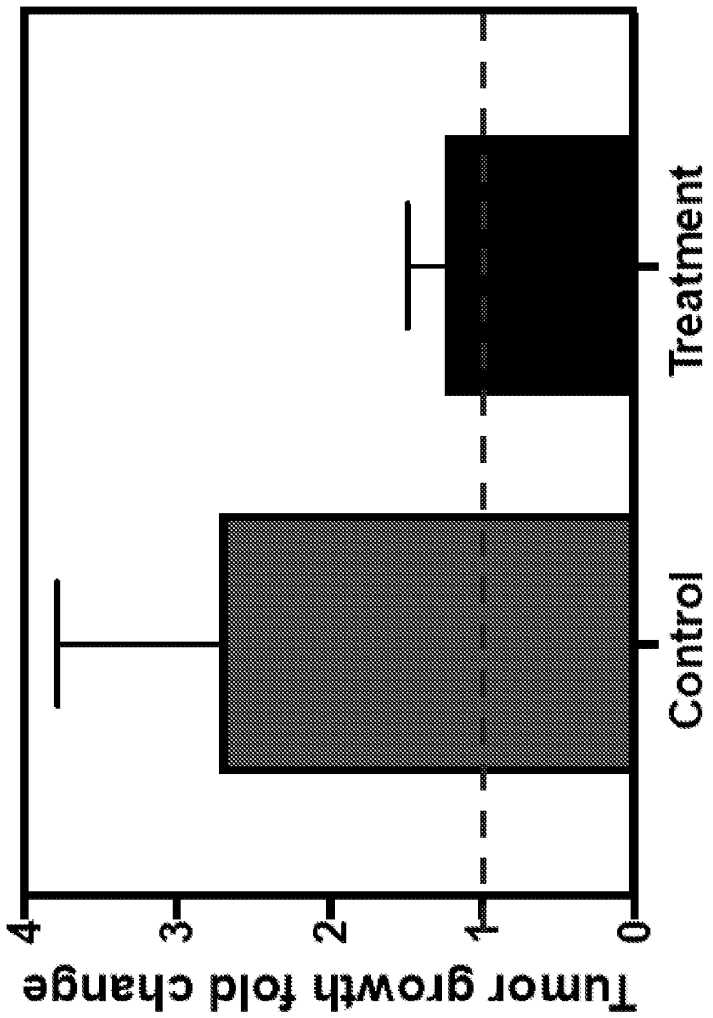


FIG. 5

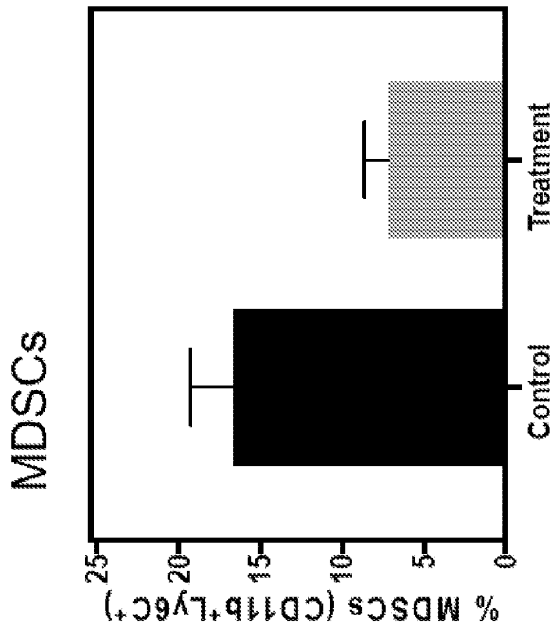

MDSCs
% MDSCs (CD11b+Ly6C+)
25
20
15
10
5
0
Control
Treatment

FIG. 6B

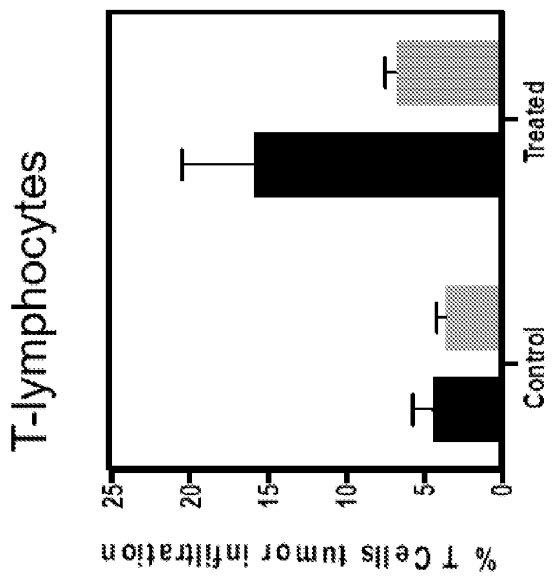

T-lymphocytes
% T Cells tumor infiltration
25
20
15
10
5
0
Control
Treated
CD4
CD8

FIG. 6A

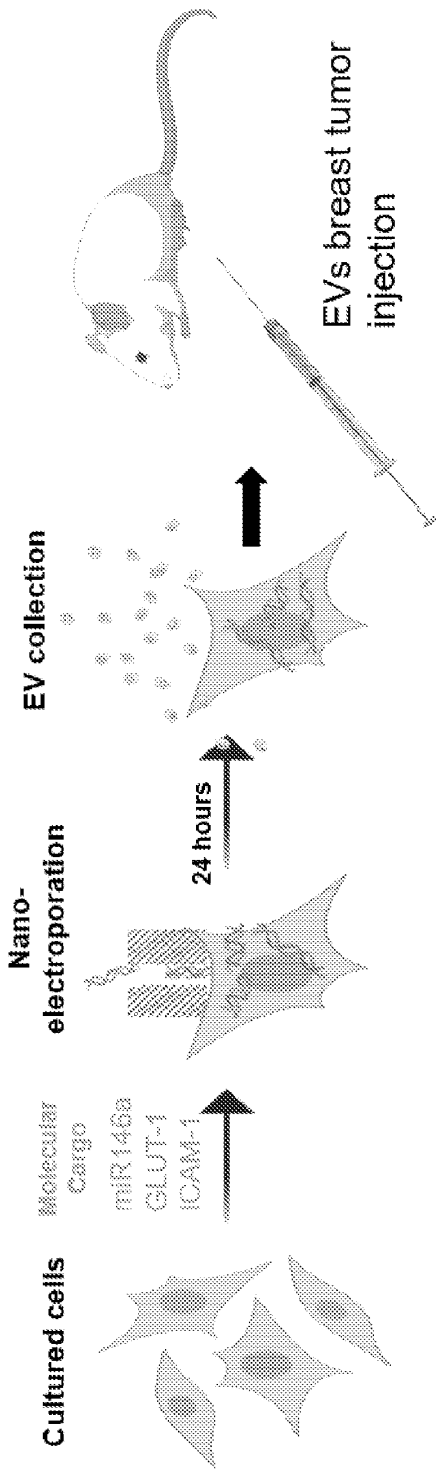

Cultured cells
Molecular Cargo
miR146a
GLUT-1
ICAM-1
Nano-electroporation
24 hours
EV collection
EVs breast tumor injection

FIG. 7

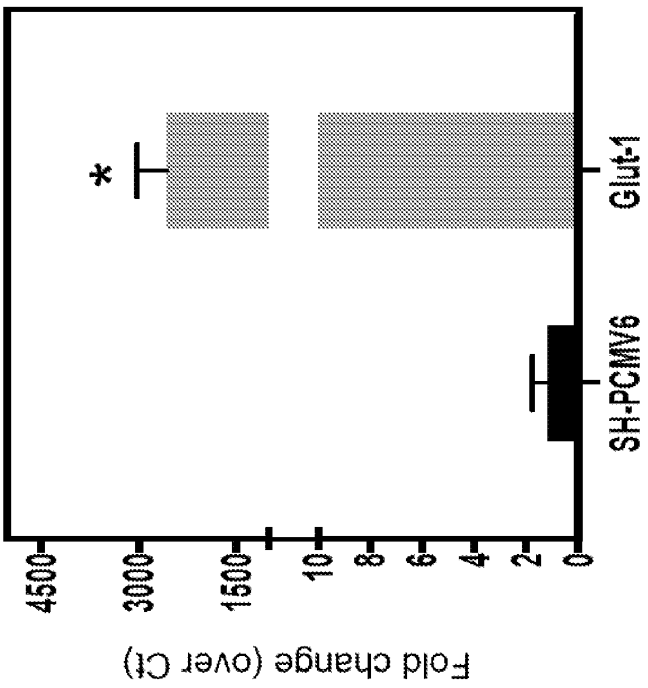

Fold change (over Ct)
4500
3000
1500
10
8
6
4
2
0
*
SH-PCMV6
Glut-1

FIG. 8B

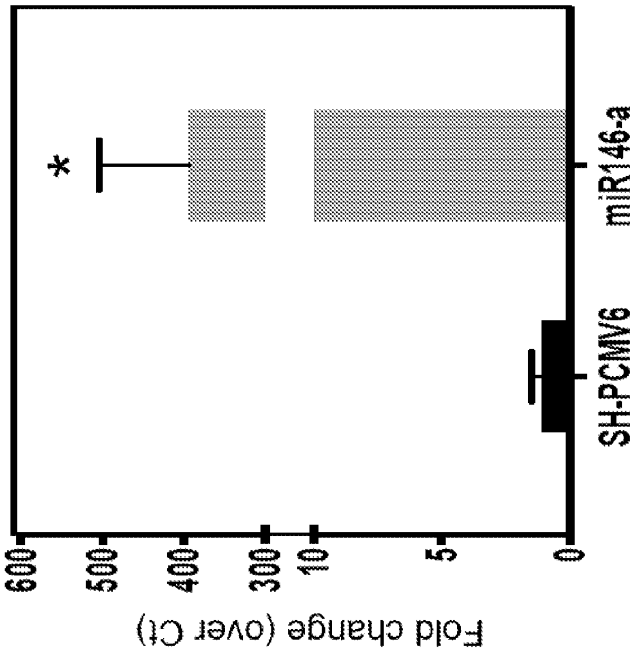

Fold change (over Ct)
600
500
400
300
10
5
0
*
SH-PCMV6
miR146-a

FIG. 8A

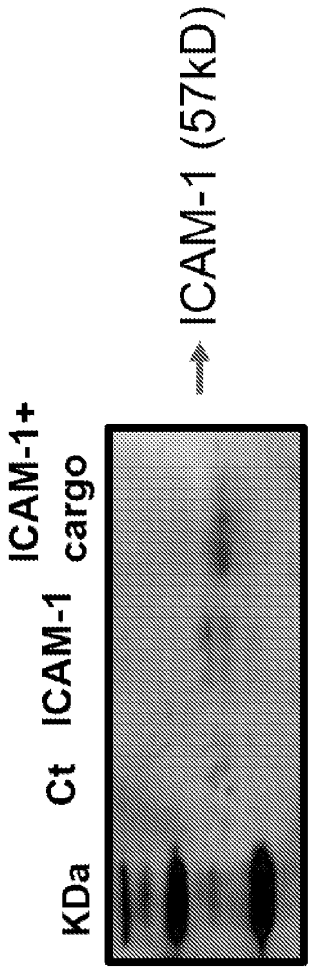


FIG. 8C

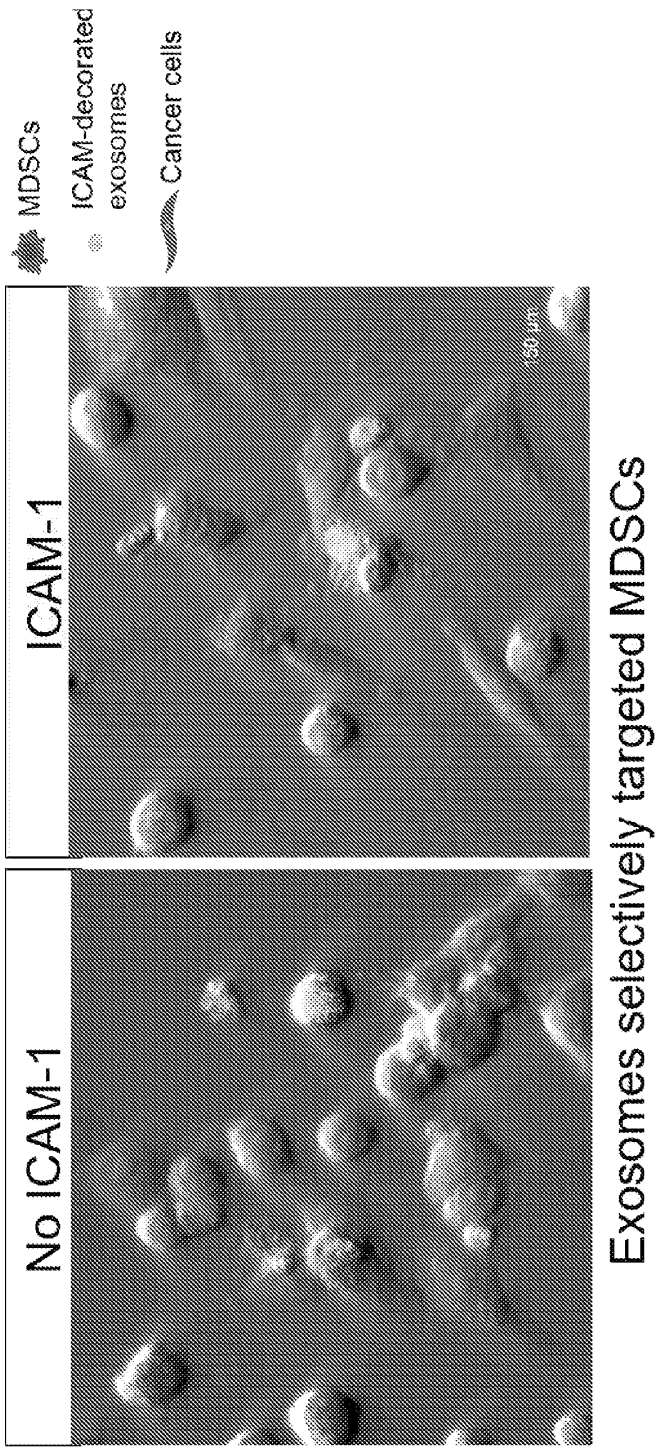

MDSCs
ICAM-decorated exosomes
Cancer cells
No ICAM-1
ICAM-1
50 μm
Exosomes selectively targeted MDSCs

FIG. 9A

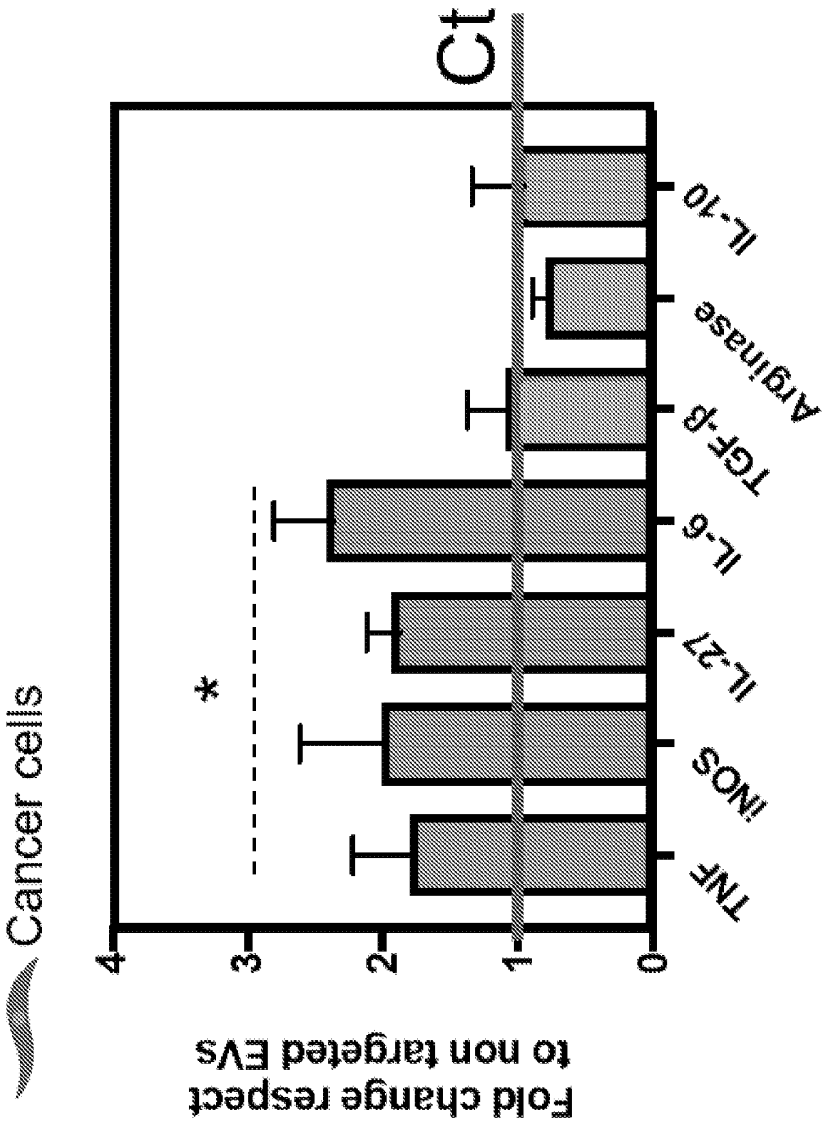

Cancer cells
Fold change respect to non targeted EVs
0
1
2
3
4
Ct
*
TNF
iNOS
IL-27
IL-6
TGF-β
Arginase
IL-10

FIG. 9B

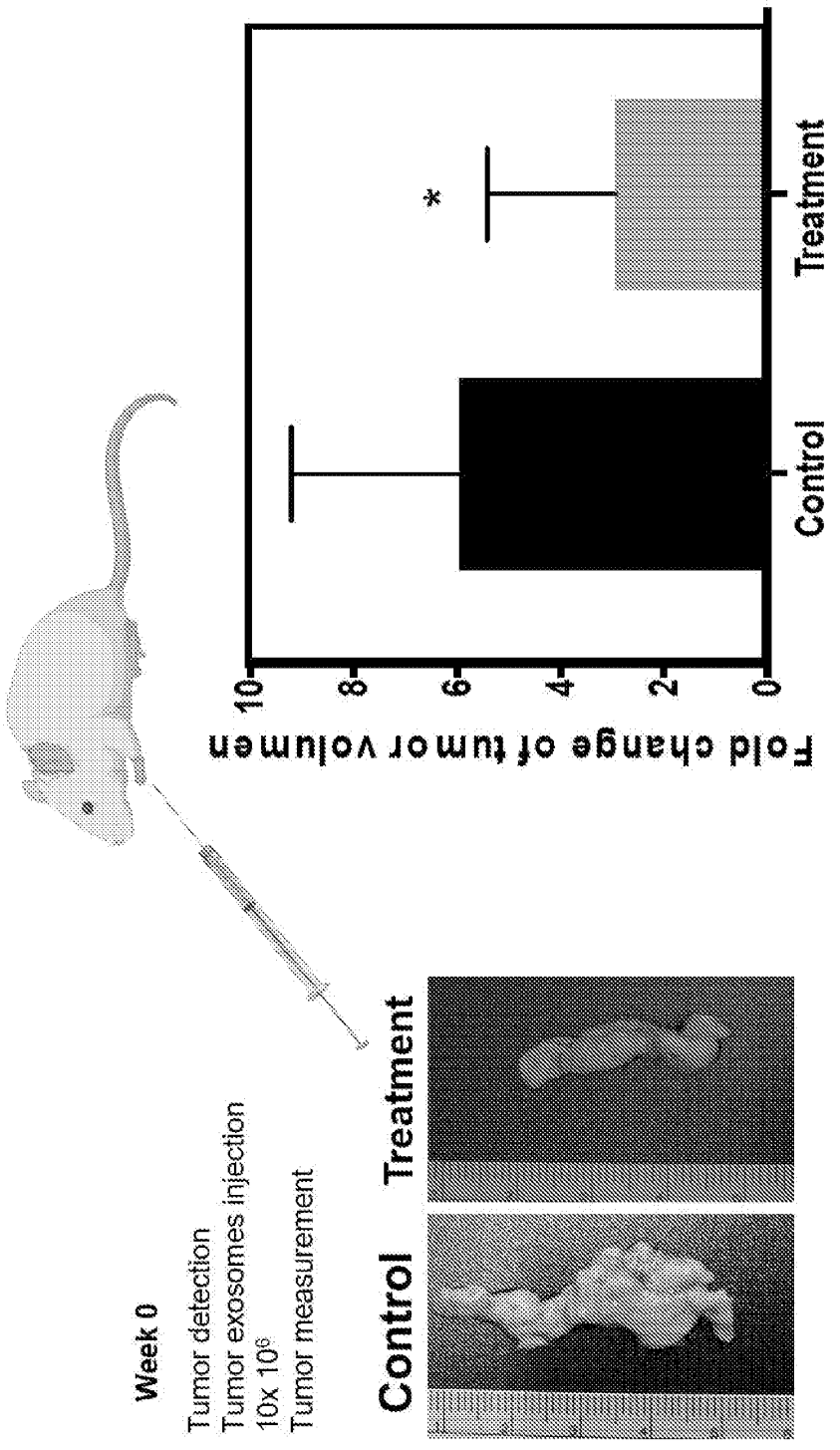

Week 0
Tumor detection
Tumor exosomes injection
10x 10^6
Tumor measurement
Control
Treatment
Fold change of tumor volumen
0
2
4
6
8
10
*
Control
Treatment

FIG. 10

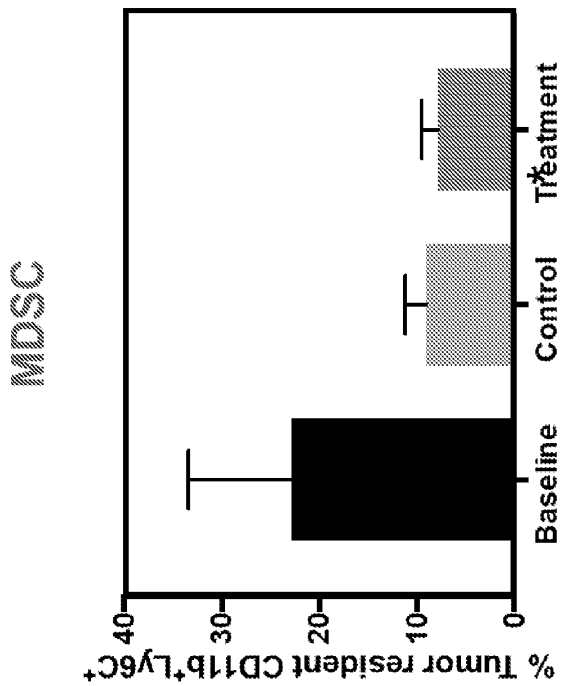


FIG. 11A

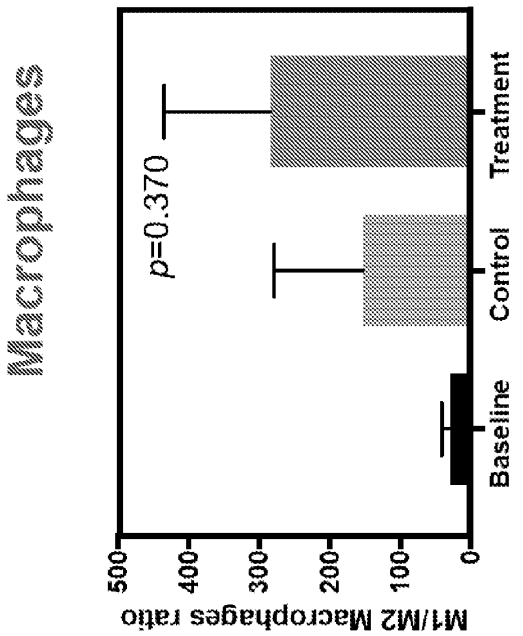


FIG. 11B

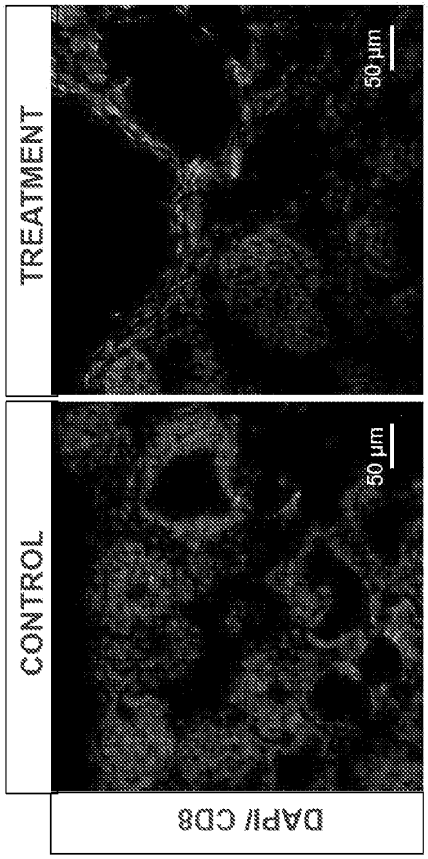


FIG. 12B

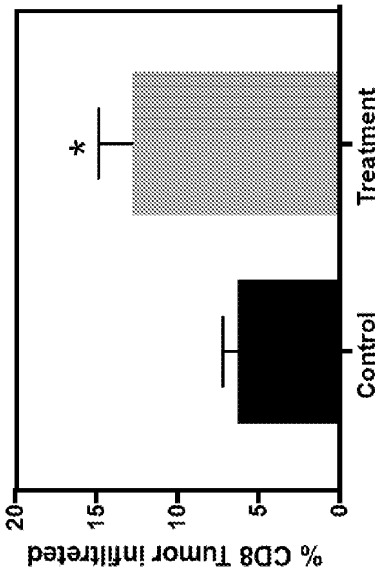


FIG. 12A