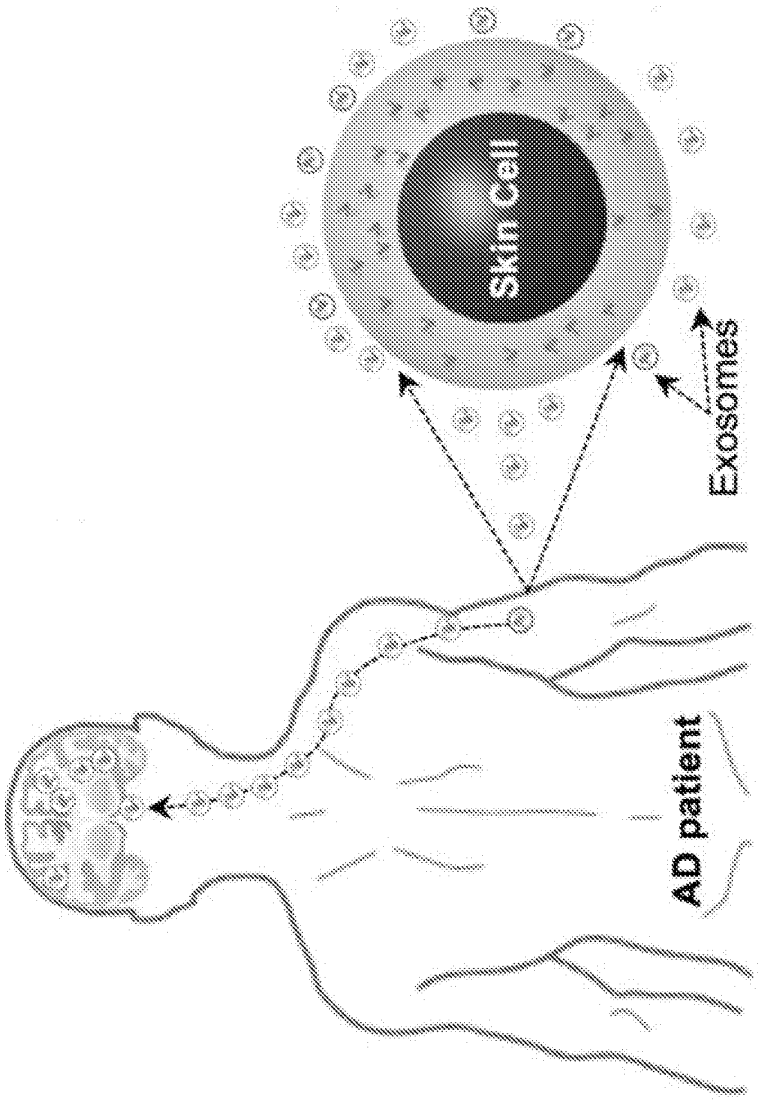


FIG. 1

FIG. 2A

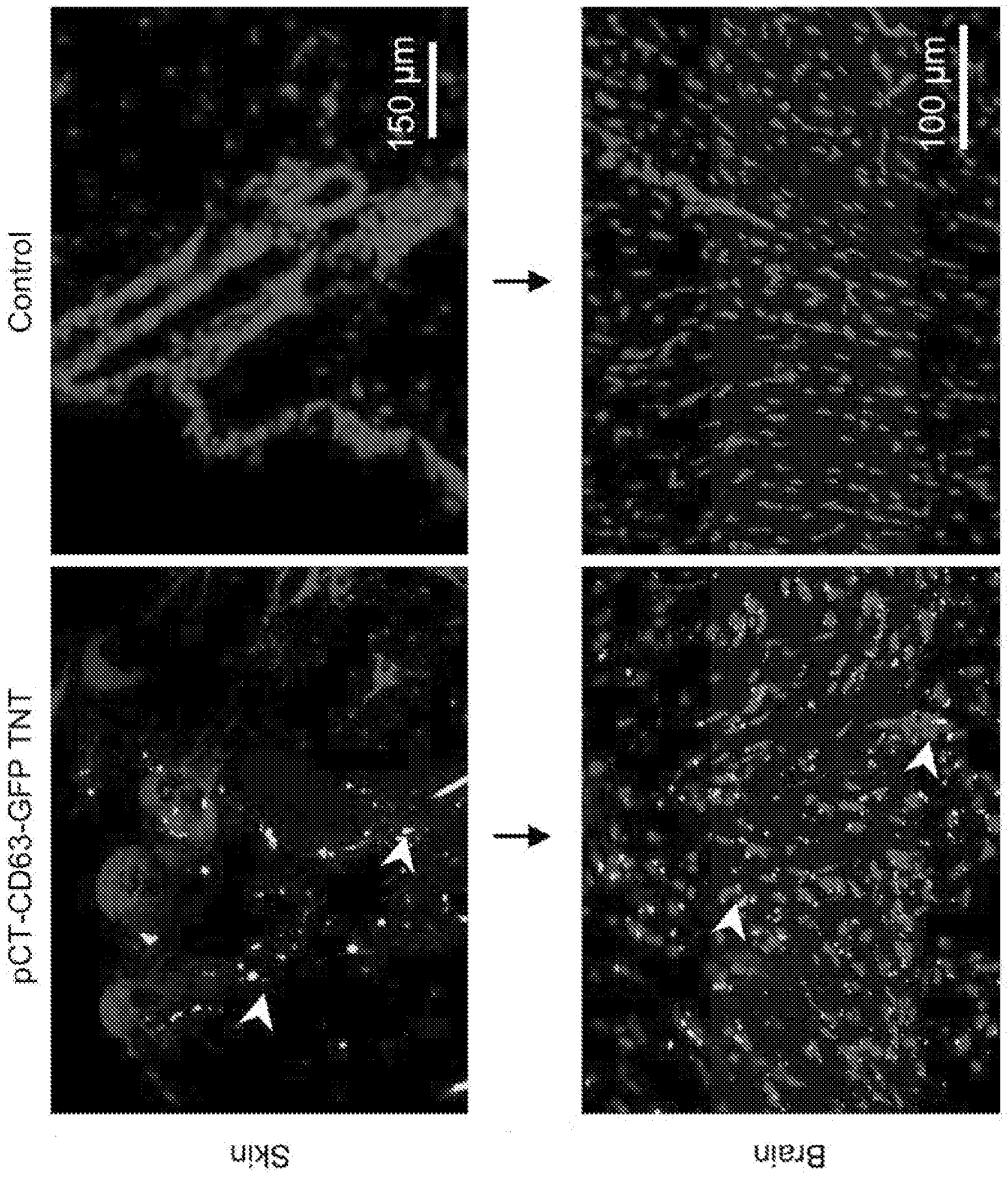


FIG. 2B

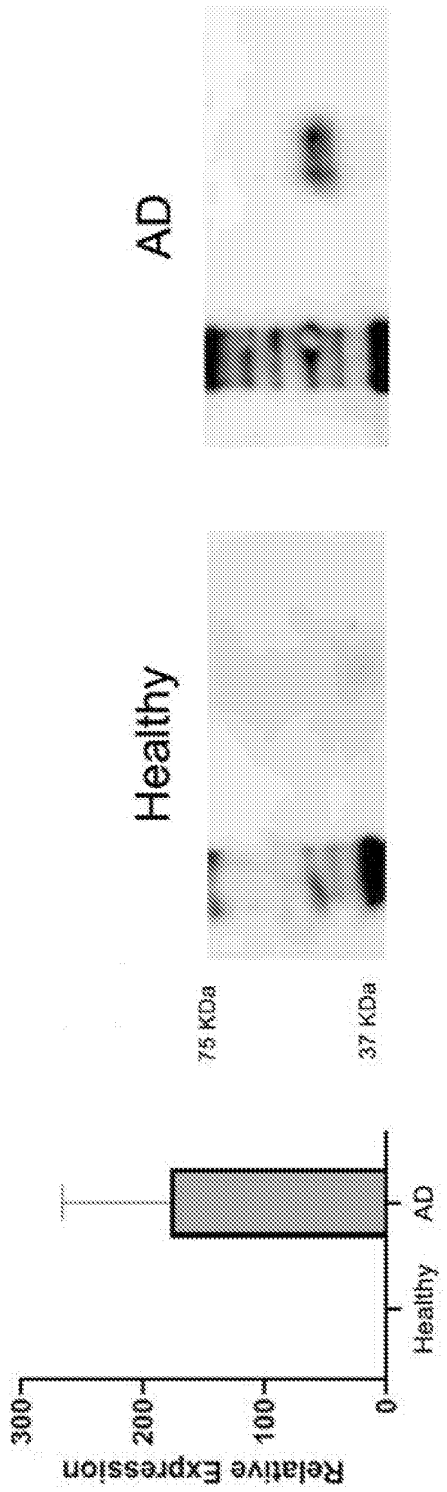

Relative Expression
300
200
100
0
Healthy
AD

FIG. 3A

75 KDa
37 KDa
Healthy
AD

FIG. 3B

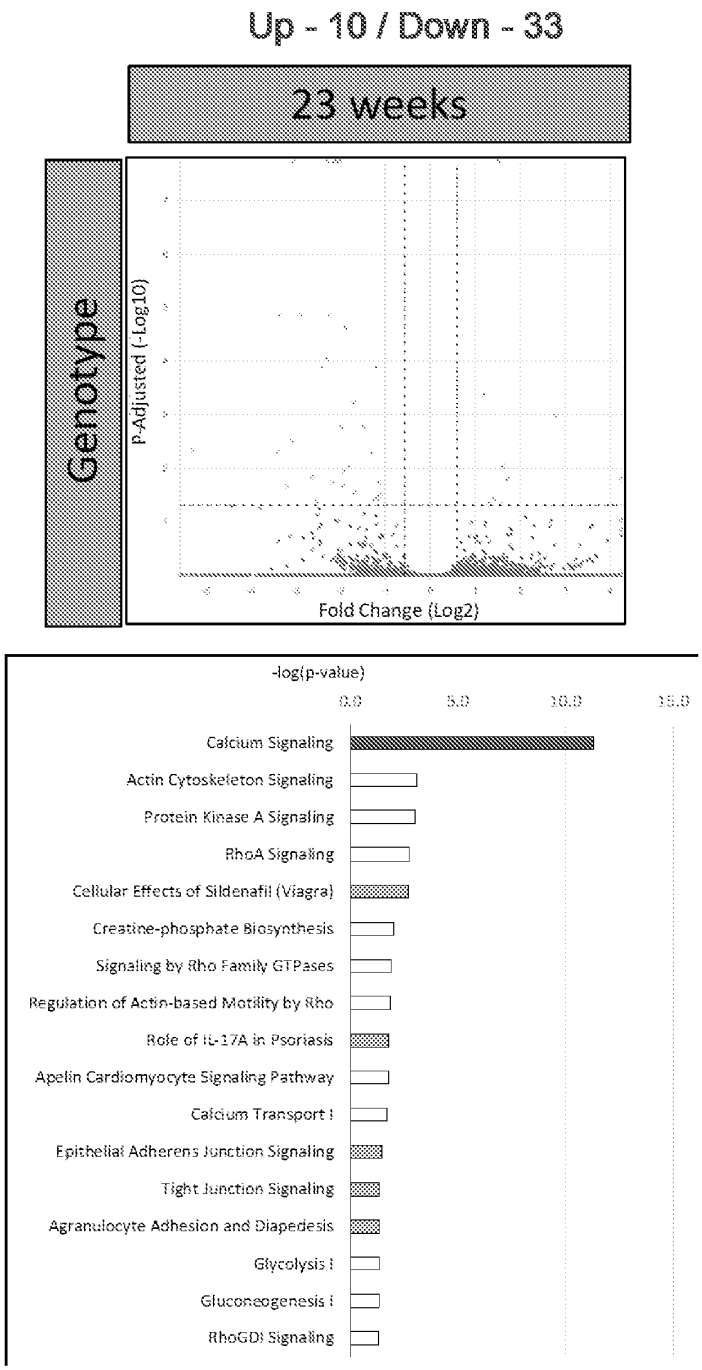

Up - 10 / Down - 33
23 weeks
Genotype
P-Adjusted (-Log10)
Fold Change (Log2)
-log(p-value)
0.0
5.0
10.0
15.0
Calcium Signaling
Actin Cytoskeleton Signaling
Protein Kinase A Signaling
RhoA Signaling
Cellular Effects of Sildenafil (Viagra)
Creatine-phosphate Biosynthesis
Signaling by Rho Family GTPases
Regulation of Actin-based Motility by Rho
Role of IL-17A in Psoriasis
Apelin Cardiomyocyte Signaling Pathway
Calcium Transport I
Epithelial Adherens Junction Signaling
Tight Junction Signaling
Agranulocyte Adhesion and Diapedesis
Glycolysis I
Gluconeogenesis I
RhoGDI Signaling

FIG. 4A

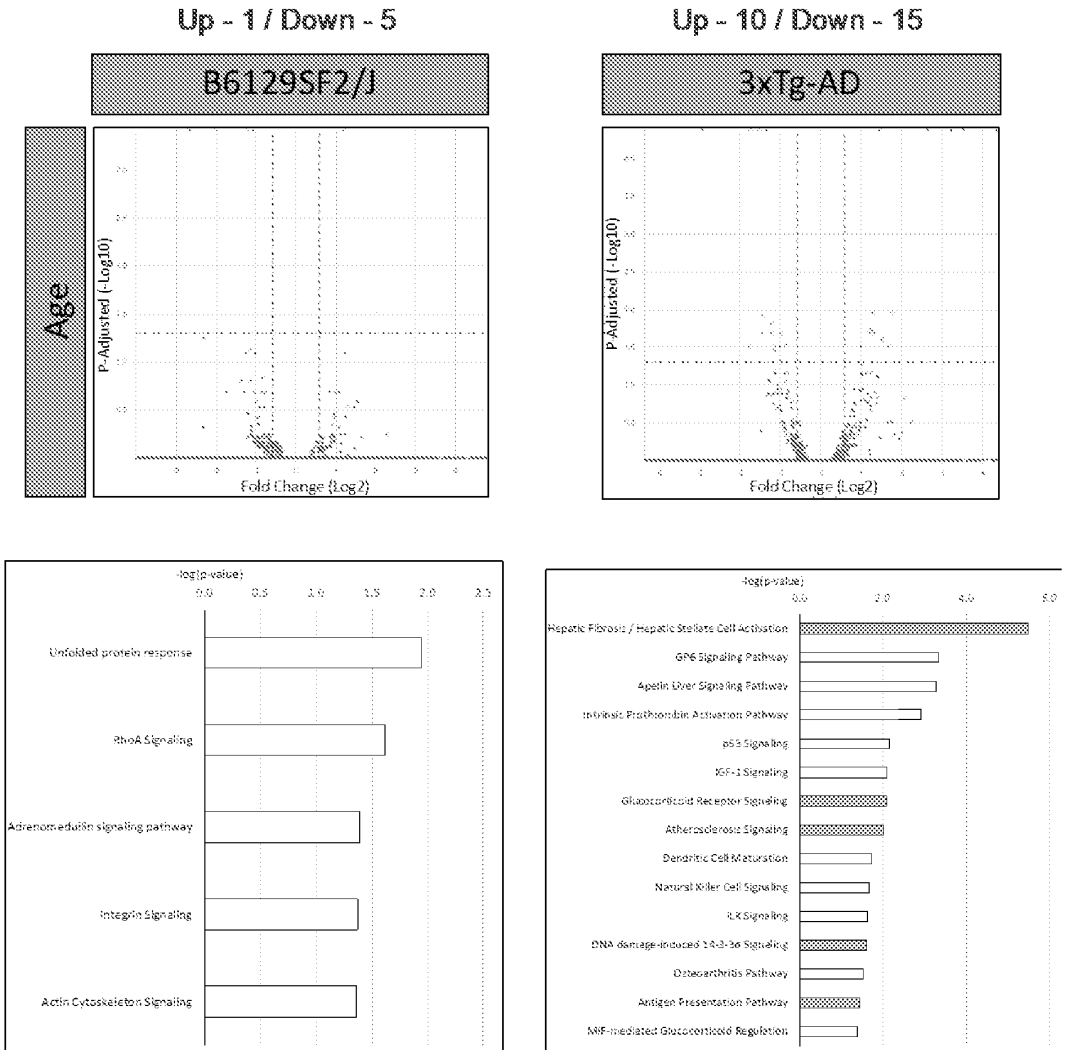

Up - 1 / Down - 5
Up - 10 / Down - 15
B6129SF2/J
3xTg-AD
Age
P-Adjusted (-Log10)
Fold Change (Log2)
-log(p-value)
Unfolded protein response
RhoA Signaling
Adrenomedullin signaling pathway
Integrin Signaling
Actin Cytoskeleton Signaling
Hepatic Fibrosis / Hepatic Stellate Cell Activation
GP6 Signaling Pathway
Apelin Liver Signaling Pathway
Intrinsic Prothrombin Activation Pathway
p53 Signaling
IGF-1 Signaling
Glucocorticoid Receptor Signaling
Atherosclerosis Signaling
Dendritic Cell Maturation
Natural Killer Cell Signaling
ILK Signaling
DNA damage-induced 14-3-3σ Signaling
Osteoarthritis Pathway
Antigen Presentation Pathway
NRF-mediated Glucocorticoid Regulation

FIG. 4B

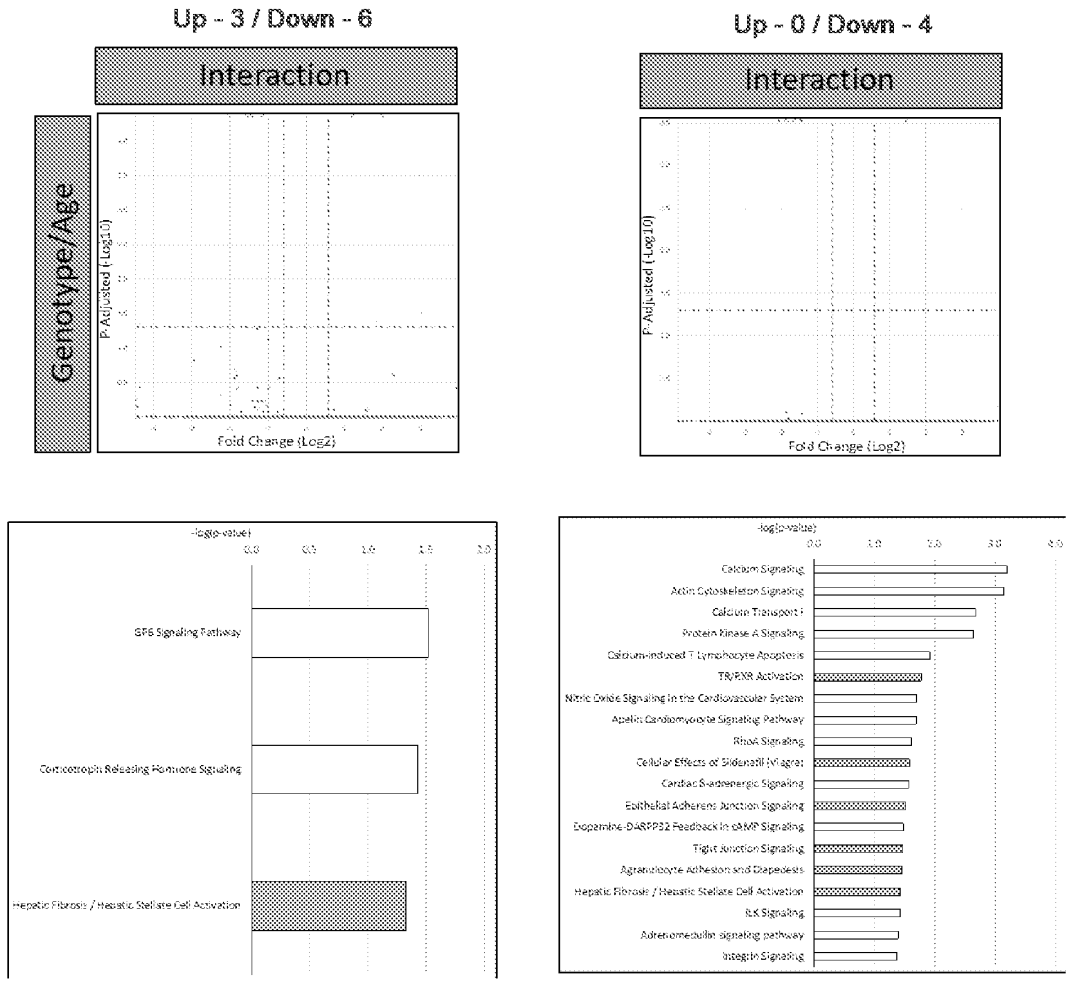

Up - 3 / Down - 6
Interaction
Genotype/Age
P Adjusted (-Log10)
Fold Change (Log2)
Up - 0 / Down - 4
Interaction
P Adjusted (-Log10)
Fold Change (Log2)
-log(p-value)
GP6 Signaling Pathway
Corticotroph Releasing Hormone Signaling
Hepatic Fibrosis / Hepatic Stellate Cell Activation
-log(p-value)
Calcium Signaling
Actin Cytoskeleton Signaling
Calcium Transport I
Protein Kinase A Signaling
Calcium-induced T Lymphocyte Apoptosis
TR/RXR Activation
Nitric Oxide Signaling in the Cardiovascular System
Apelin Cardiomyocyte Signaling Pathway
RhoA Signaling
Cellular Effects of Sildenafil (Viagra)
Cardiac β-adrenergic Signaling
Epithelial Adherens Junction Signaling
Dopamine-DARPP32 Feedback in cAMP Signaling
Tight Junction Signaling
Agranulocyte Adhesion and Diapedesis
Hepatic Fibrosis / Hepatic Stellate Cell Activation
ILK Signaling
Adrenomedullin signaling pathway
Integrin Signaling

FIG. 4C

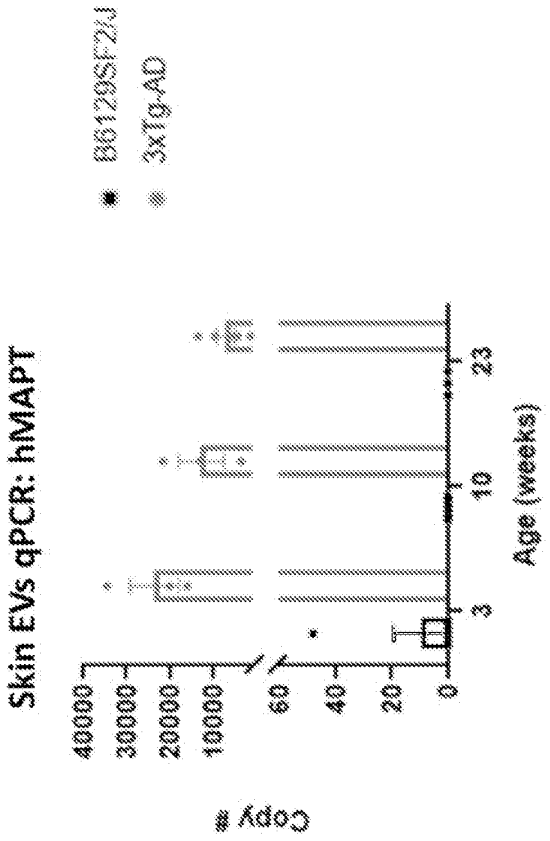

Skin EVs qPCR: hMAPT
B6129SF2/J
3xTg-AD
Copy #
40000
30000
20000
10000
60
40
20
0
3
10
23
Age (weeks)

FIG. 5B

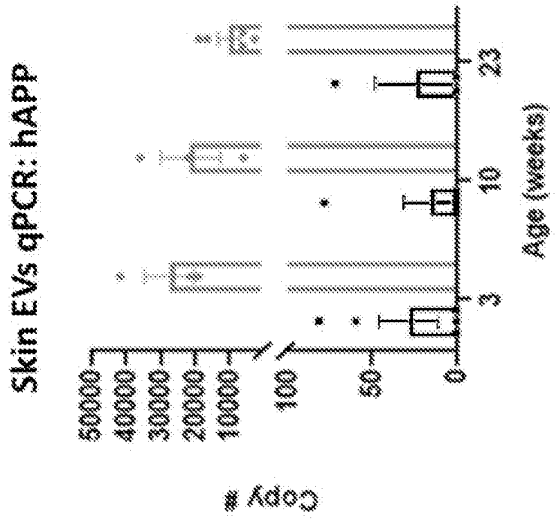

Skin EVs qPCR: hAPP
Copy #
50000
40000
30000
20000
10000
100
50
0
3
10
23
Age (weeks)

FIG. 5A

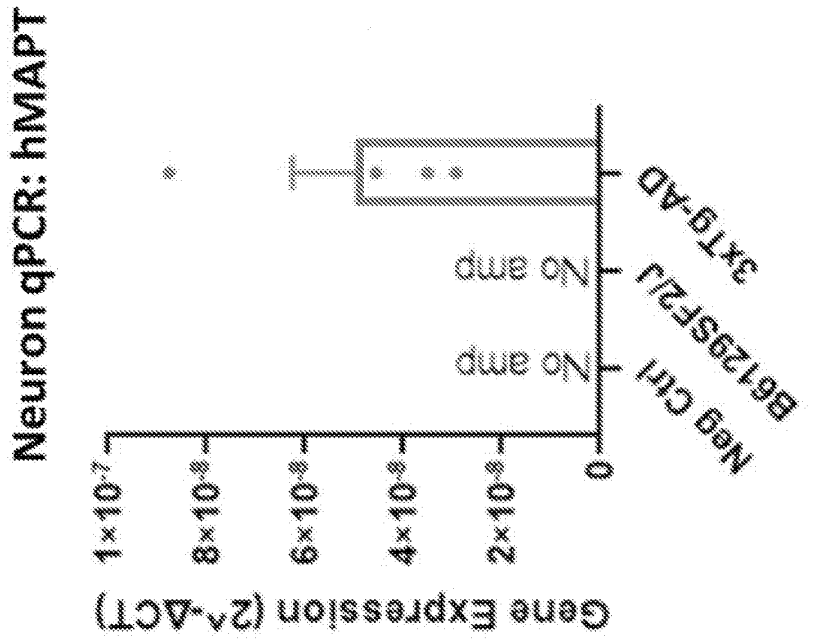

Neuron qPCR: hMAPT
Gene Expression (2^-ΔCT)
1×10⁻⁷
8×10⁻⁸
6×10⁻⁸
4×10⁻⁸
2×10⁻⁸
0
Neg Ctrl
No amp
B6.129SF2J
No amp
3xTg-AD

FIG. 6B

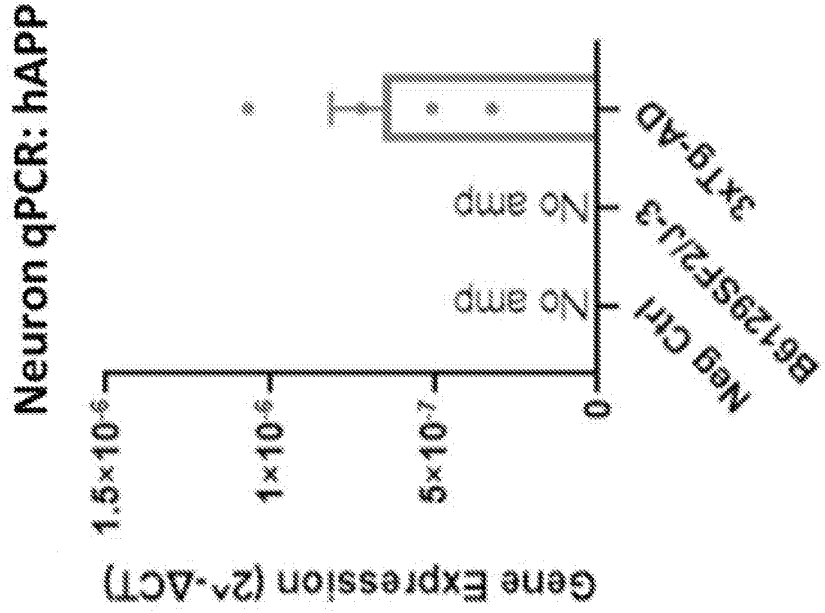

Neuron qPCR: hAPP
Gene Expression (2^-ΔCT)
1.5×10⁻⁶
1×10⁻⁶
5×10⁻⁷
0
Neg Ctrl
No amp
B6.129SF2J-3
No amp
3xTg-AD

FIG. 6A

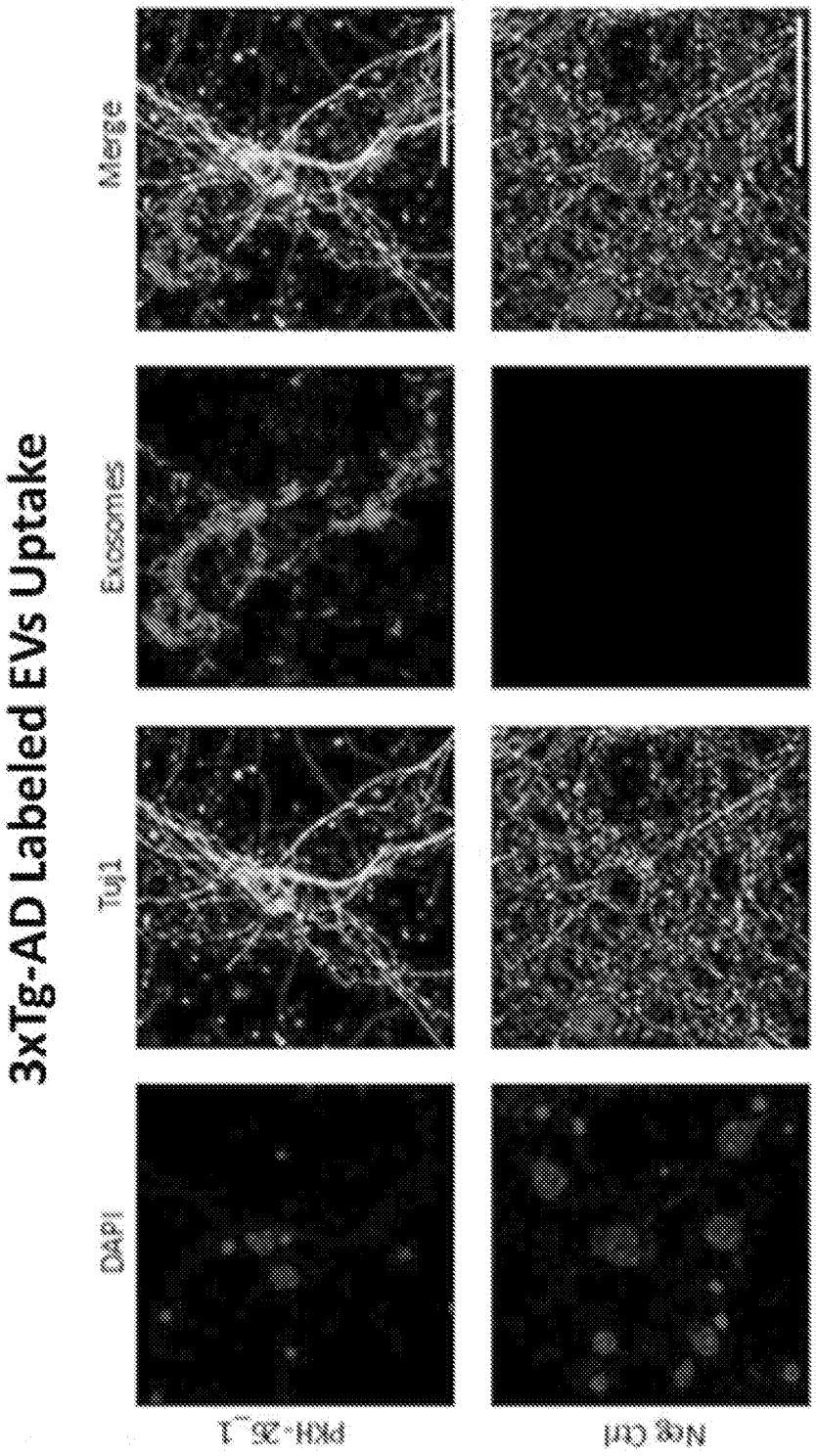

3xTg-AD Labeled EVs Uptake
DAPI
Tuj1
Exosomes
Merge
PKH-26_1
Neg Ctrl

FIG. 7A

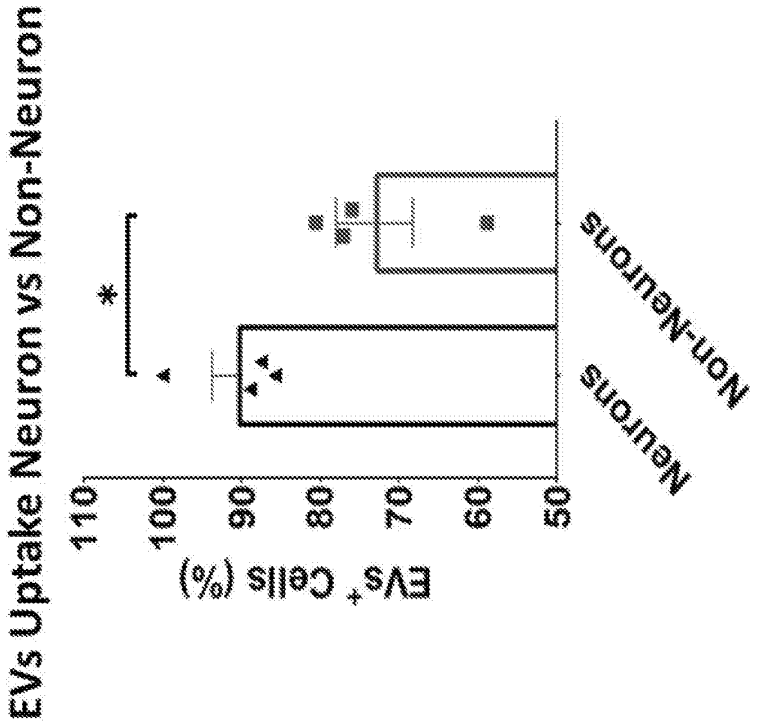

EVs Uptake Neuron vs Non-Neuron
EVs+ Cells (%)
110
100
90
80
70
60
50
Neurons
Non-Neurons
*

FIG. 7C

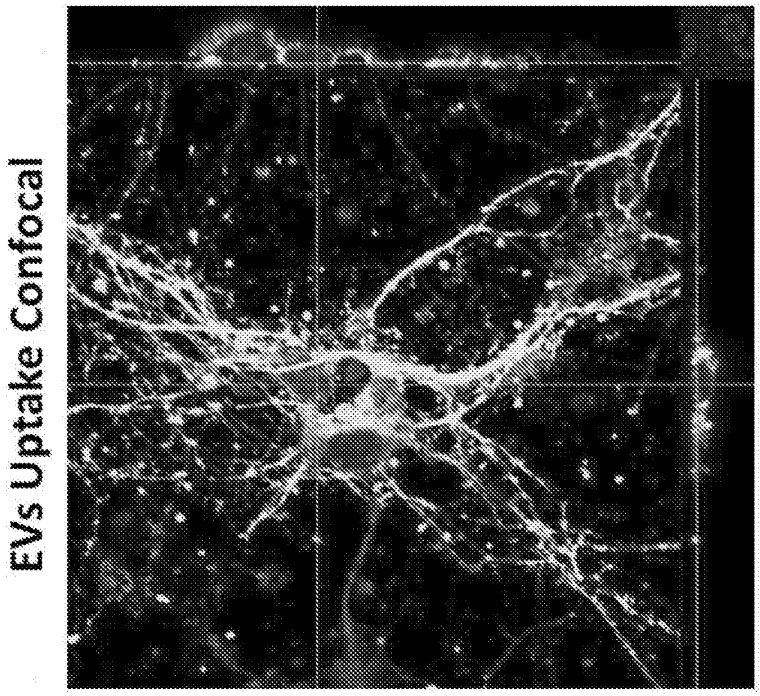

EVs Uptake Confocal

FIG. 7B

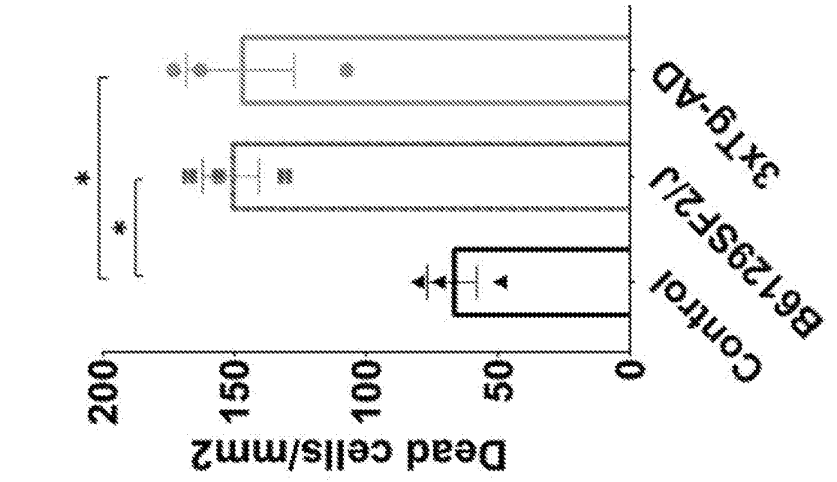

Dead cells/mm2
200
150
100
50
0
Control
B6129SF2/J
3xTg-AD
*
*

FIG. 8B

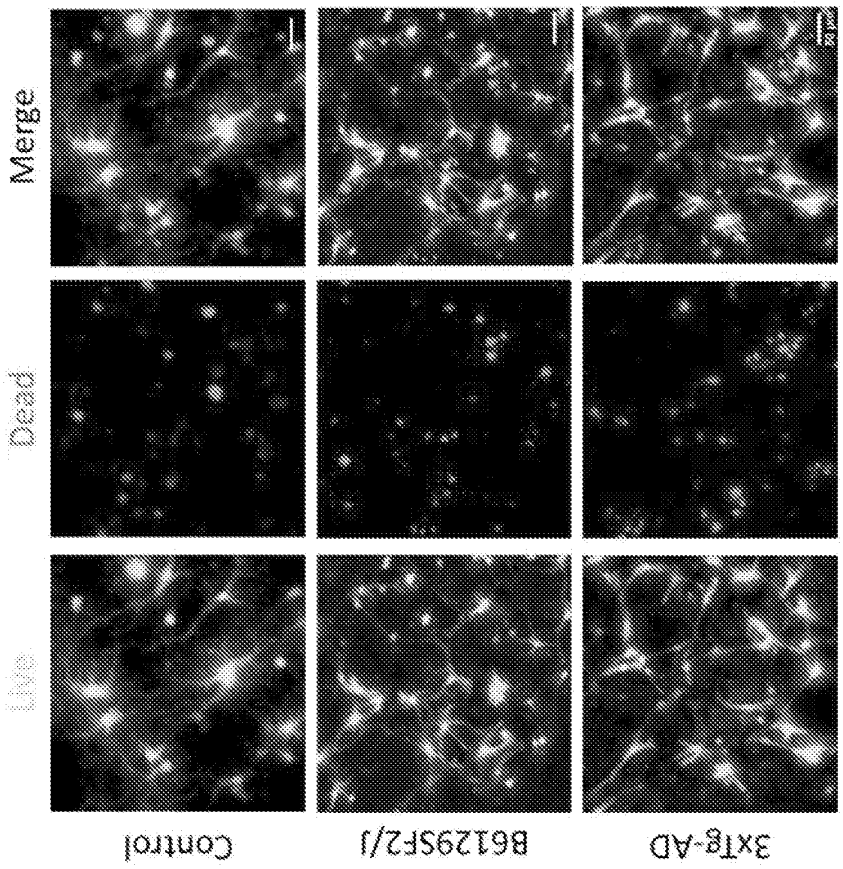

Merge
Dead
Live
Control
B6129SF2/J
3xTg-AD

FIG. 8A

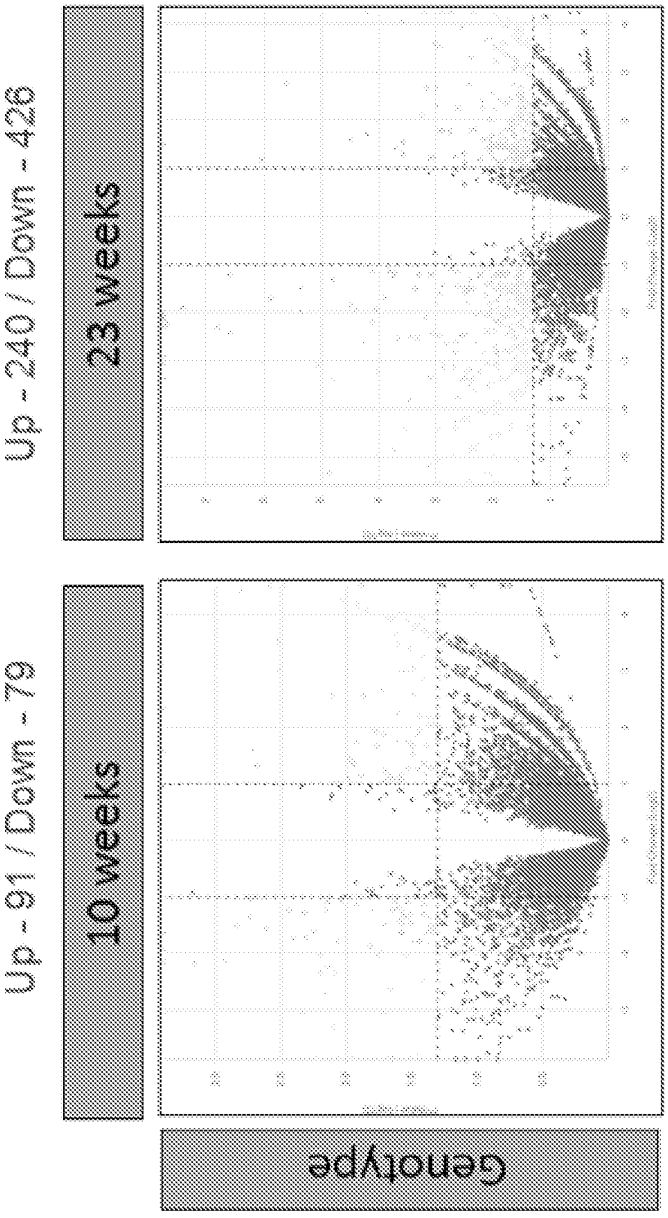


FIG. 9A

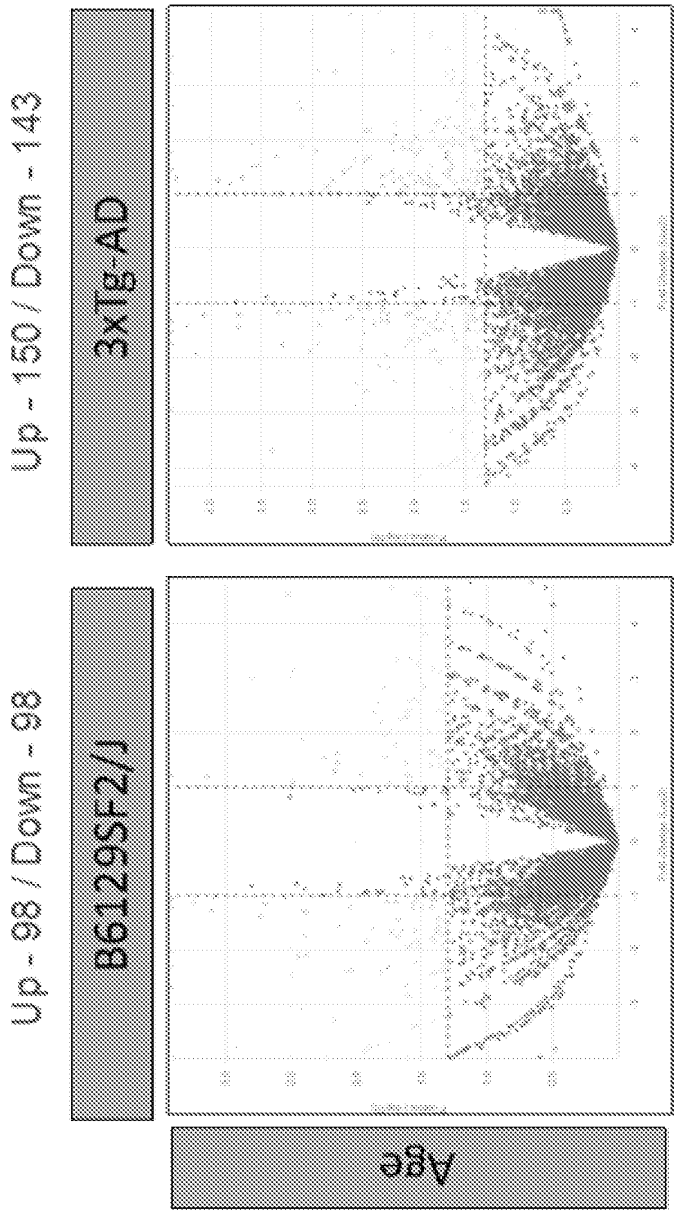


FIG. 9B

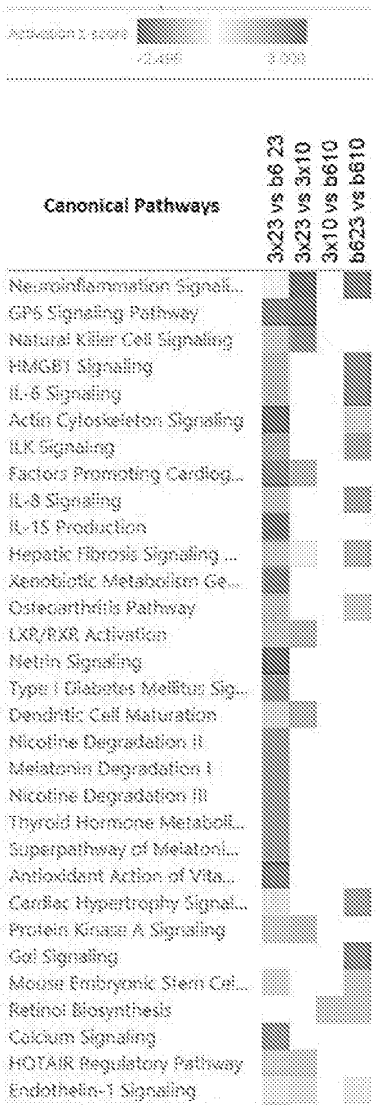


FIG. 10A

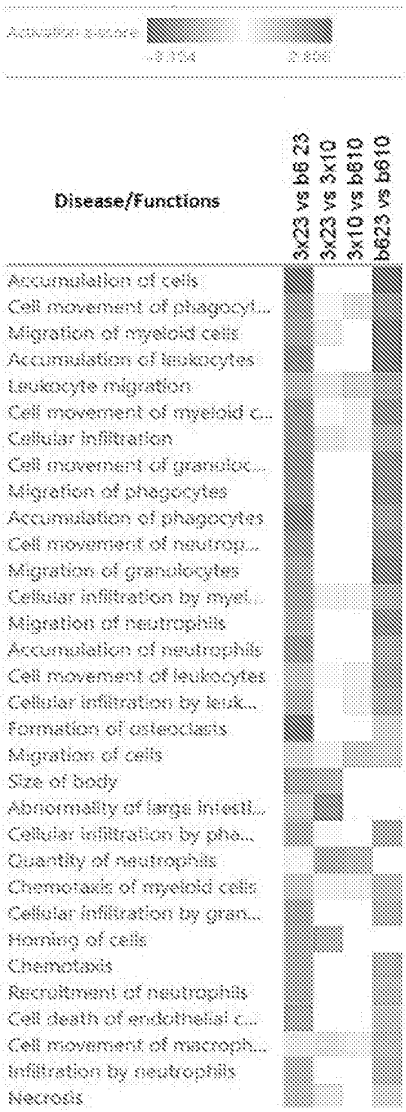


FIG. 10A