FIG. 1A

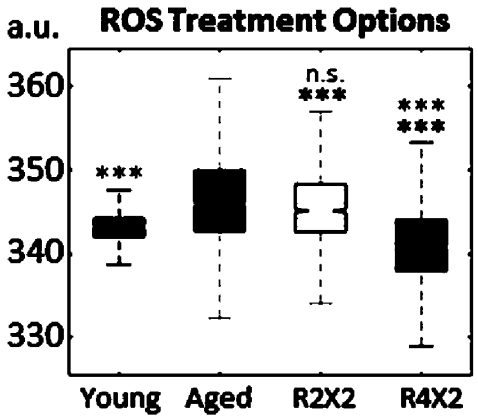
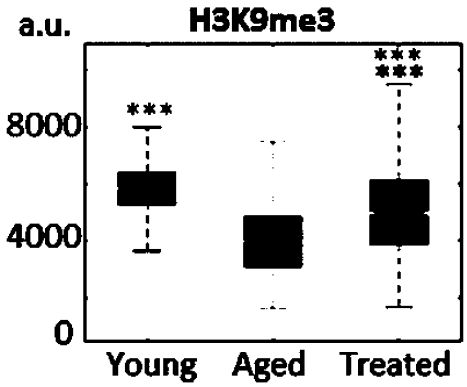

a.u.
ROS Treatment Options
360
350
340
330
***
n.s.
***
***
***
Young
Aged
R2X2
R4X2

FIG. 1B


a.u.
H3K9me3
8000
4000
0
***
***
***
Young
Aged
Treated

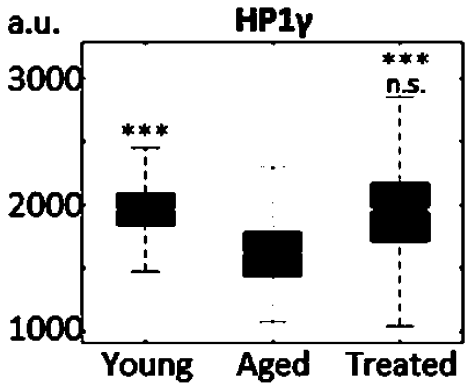
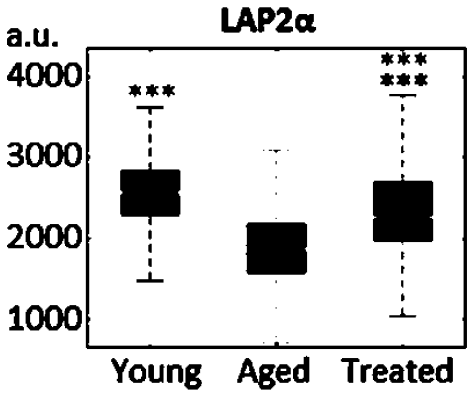

a.u.
HP1γ
3000
2000
1000
***
***
n.s.
Young
Aged
Treated

FIG. 1C



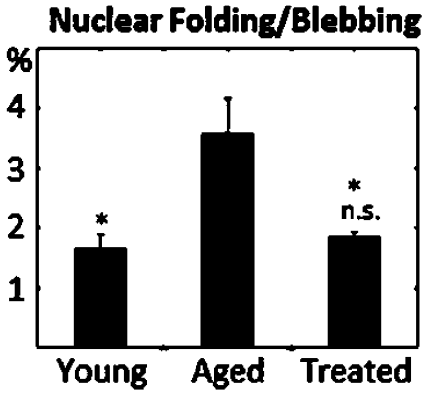
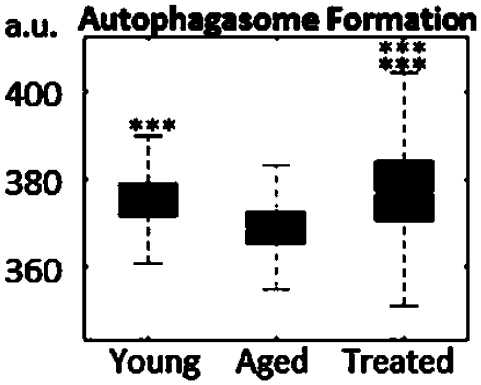


FIG. 1D



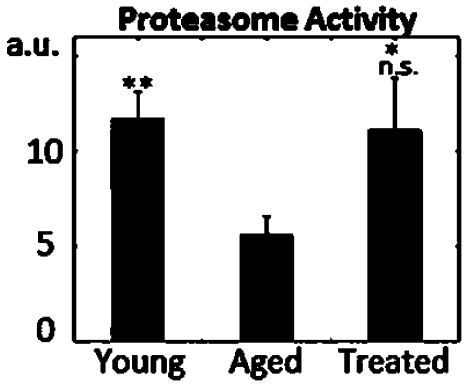
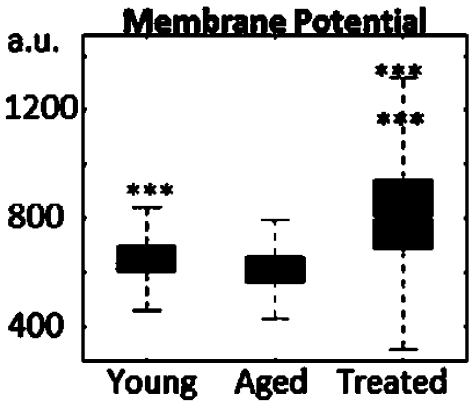


FIG. 1E



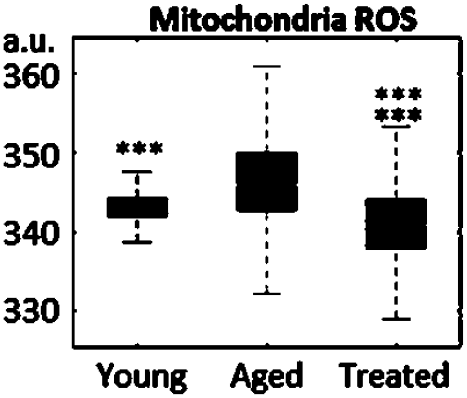


FIG. 1F



FIG. 1G

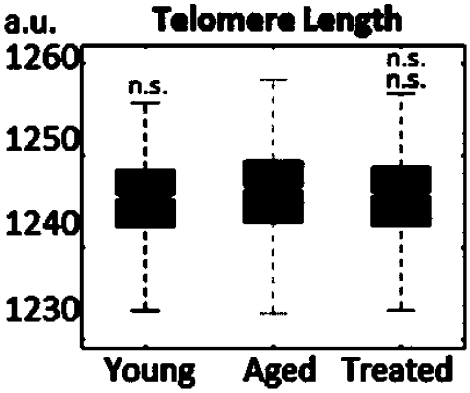


FIG. 1H



FIG. 1I

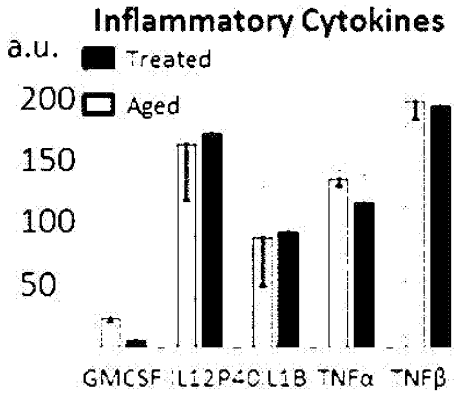


FIG. 1J

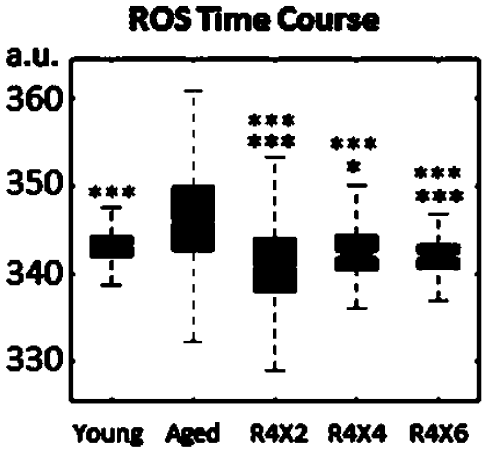


FIG. 1K

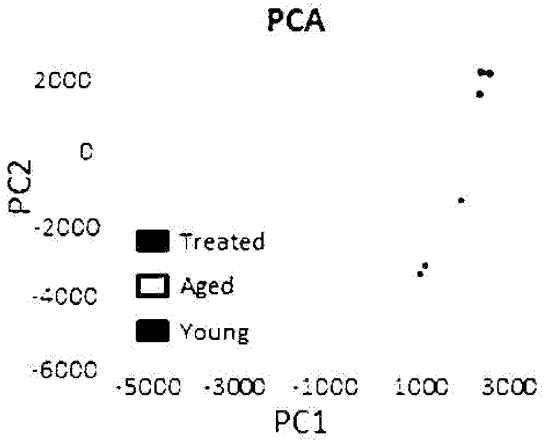


FIG. 1L

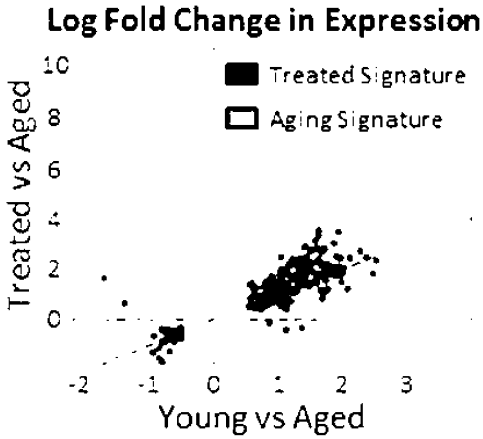


FIG. 2A

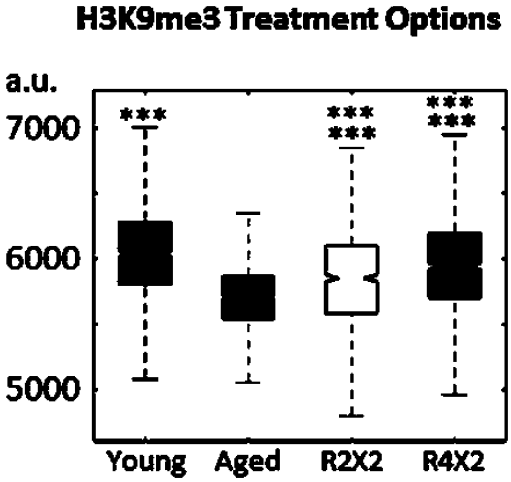
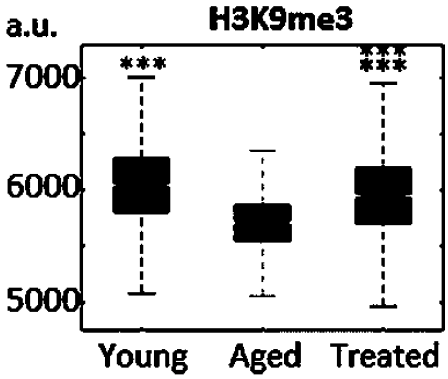


FIG. 2B



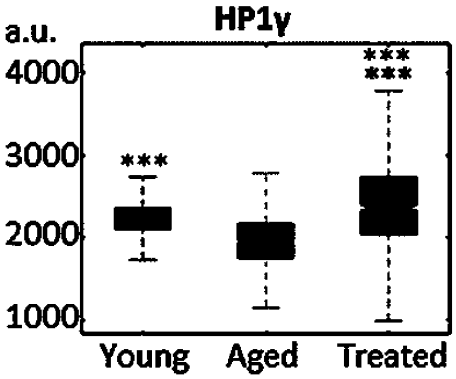
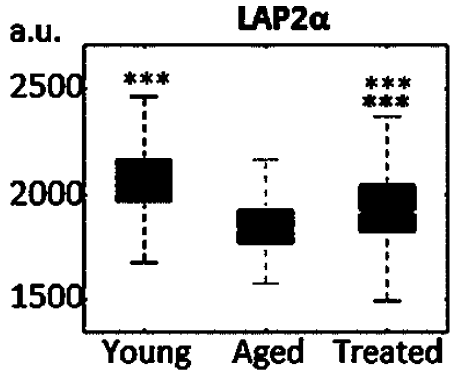


FIG. 2C



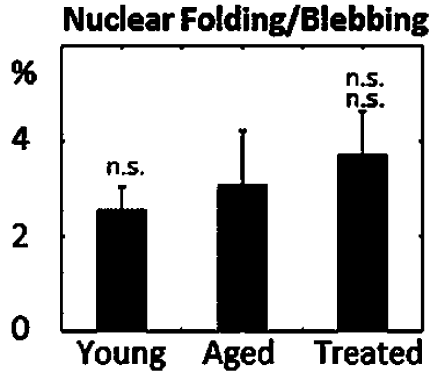
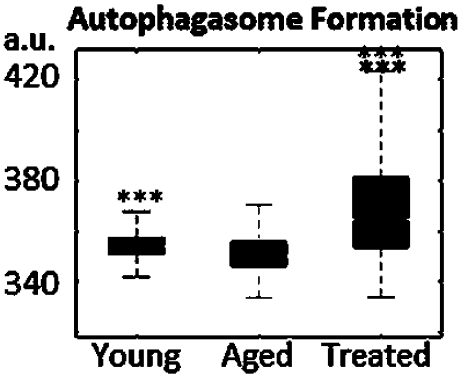


FIG. 2D



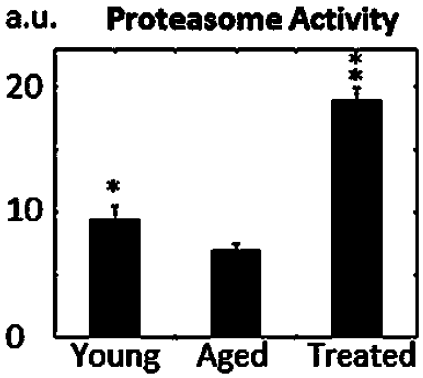
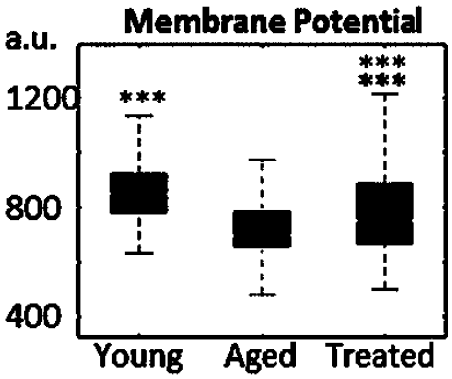


FIG. 2E



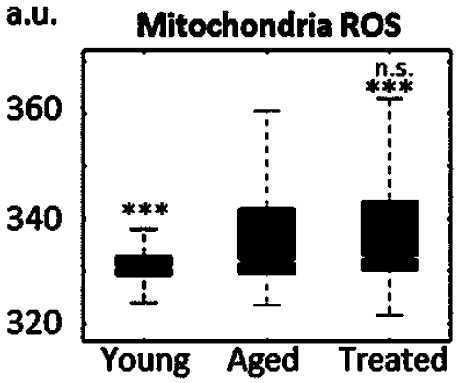


FIG. 2F

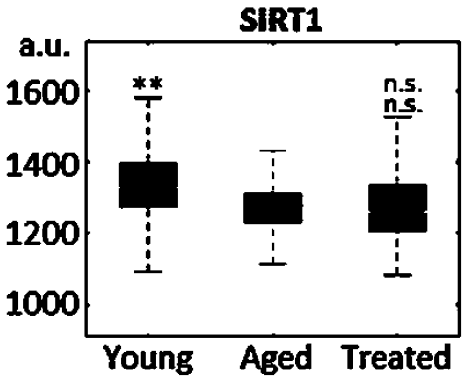


FIG. 2G

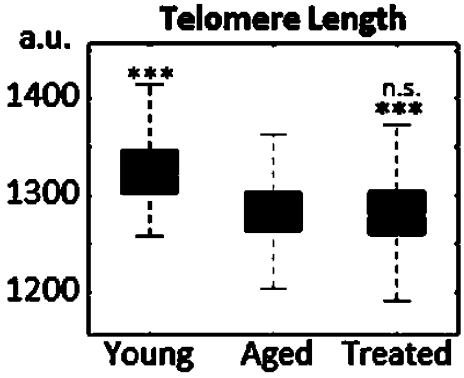


FIG. 2H

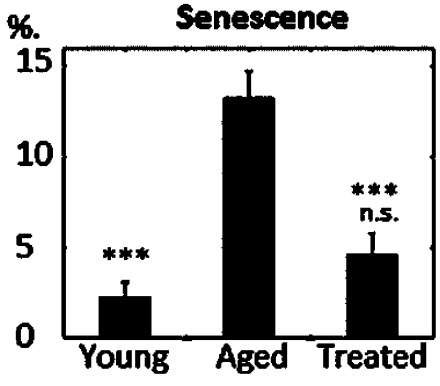


FIG. 2I

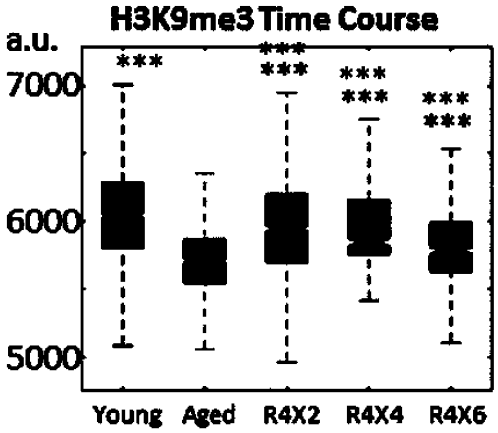


FIG. 2J

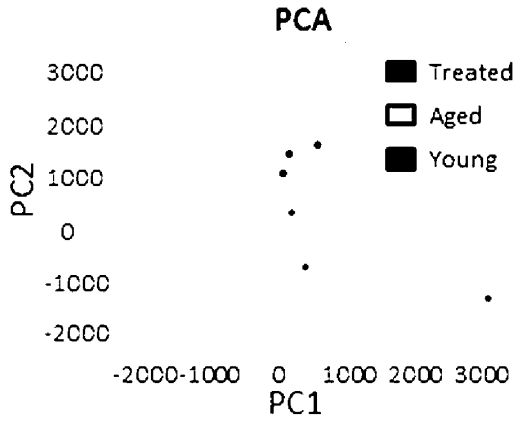


FIG. 2K

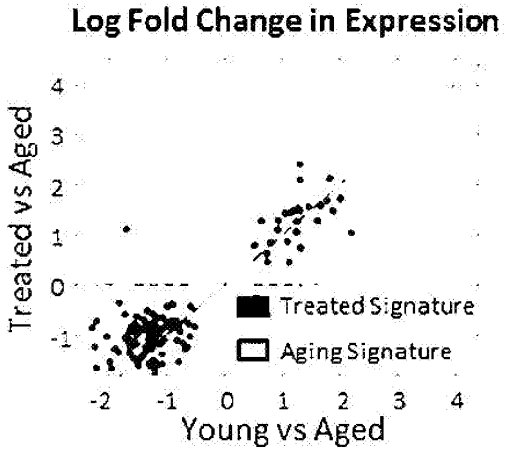


FIG. 3A

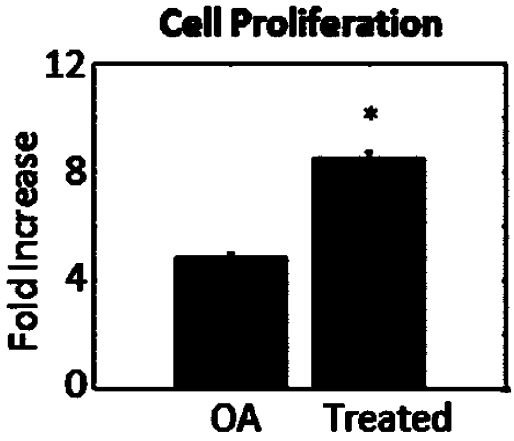


FIG. 3B

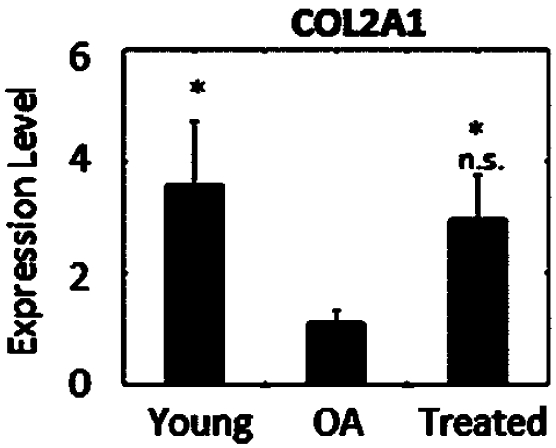


FIG. 3C

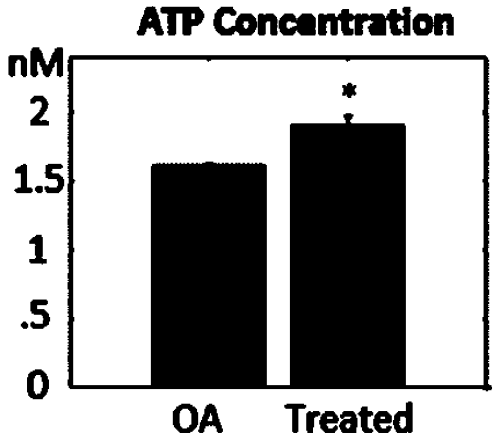


FIG. 3D

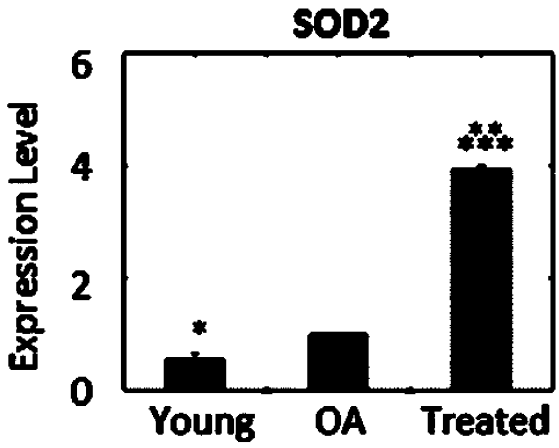


FIG. 3E

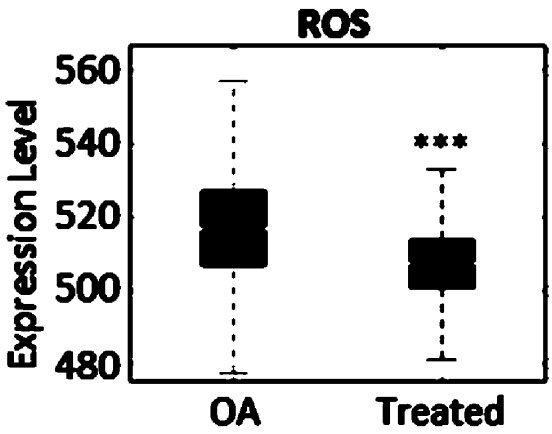


FIG. 3F

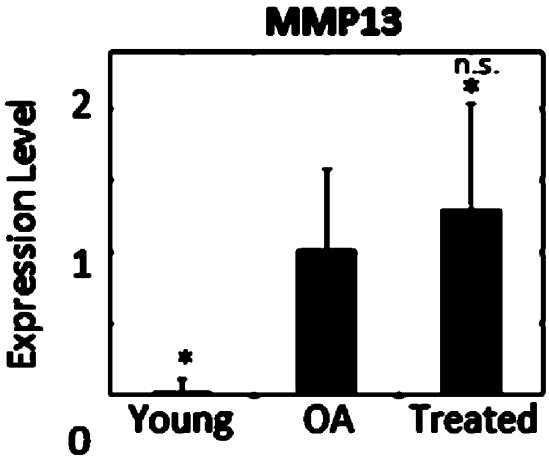


FIG. 3G

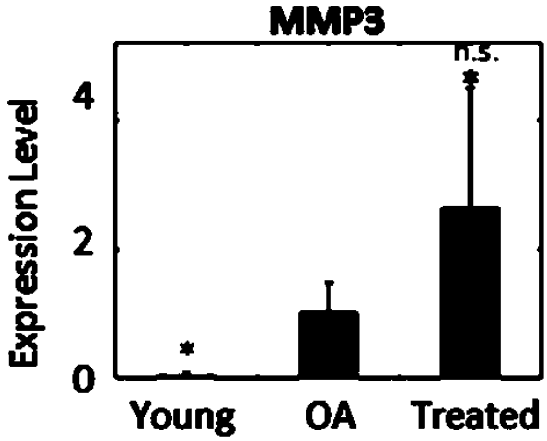


FIG. 3H

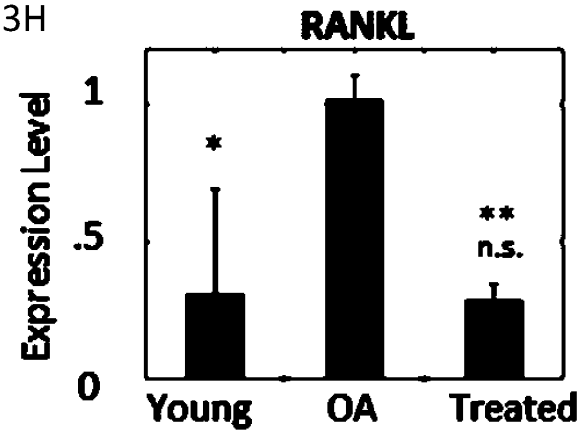


FIG. 3I

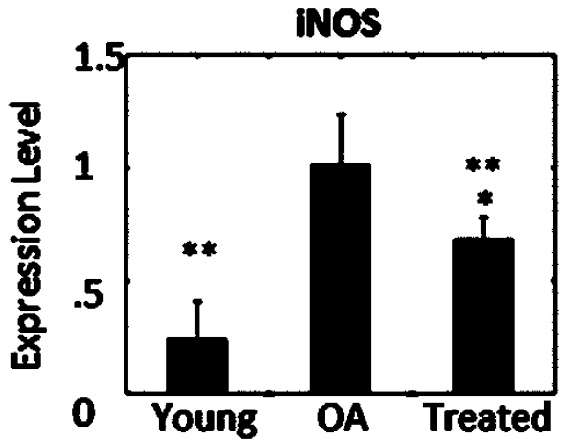


FIG. 4A

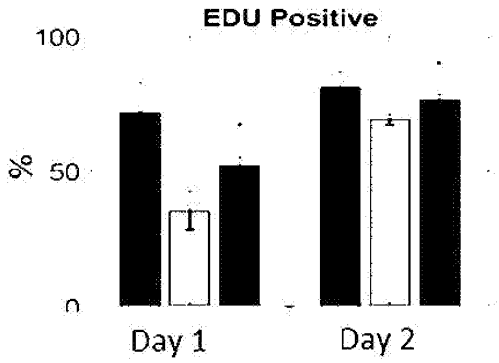


FIG. 4B

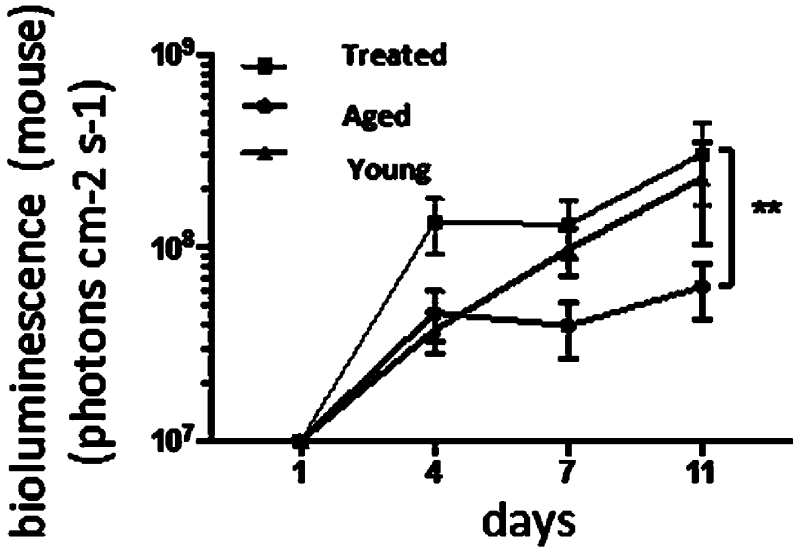

bioluminescence (mouse)
(photons cm-2 s-1)
10^9
10^8
10^7
Treated
Aged
Young
**
1
4
7
11
days

FIG. 4C

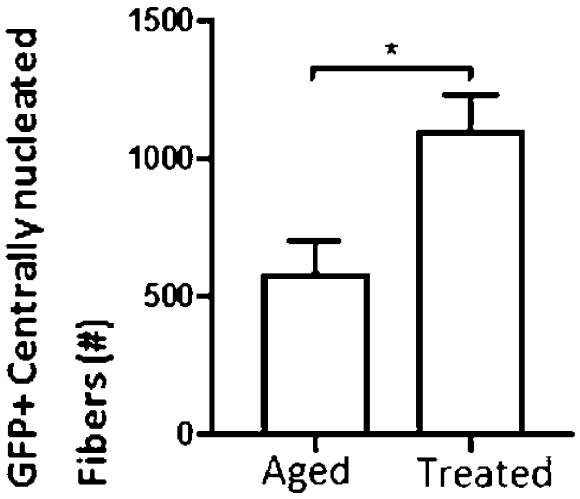

GFP+ Centrally nucleated
Fibers (#)
1500
1000
500
0
*
Aged
Treated

FIG. 4D

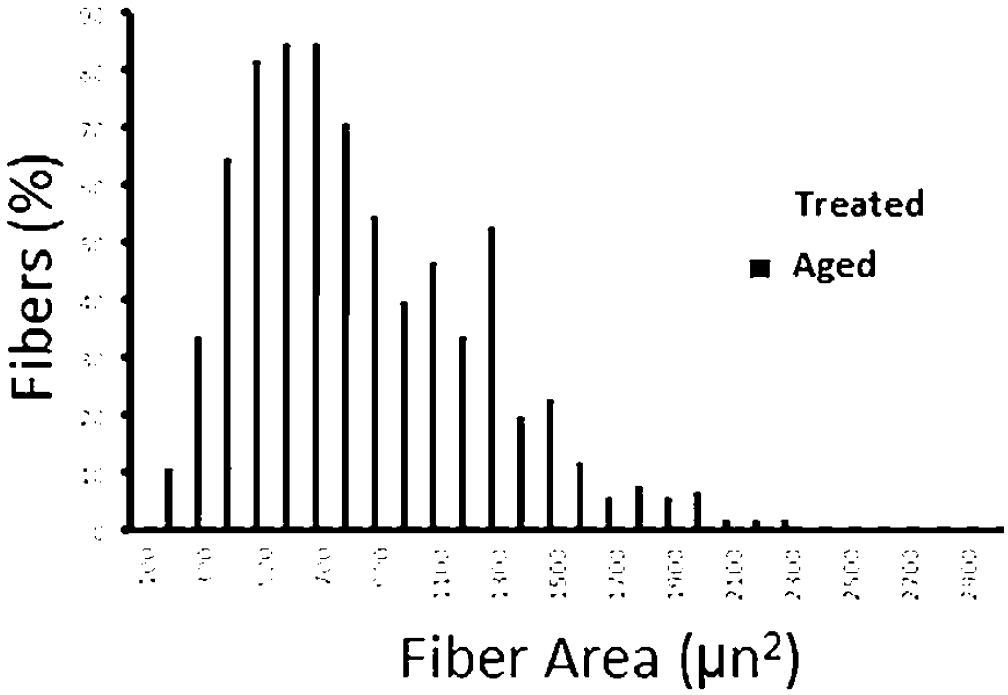

Fibers (%)
Treated
Aged
Fiber Area (μn²)

FIG. 4E

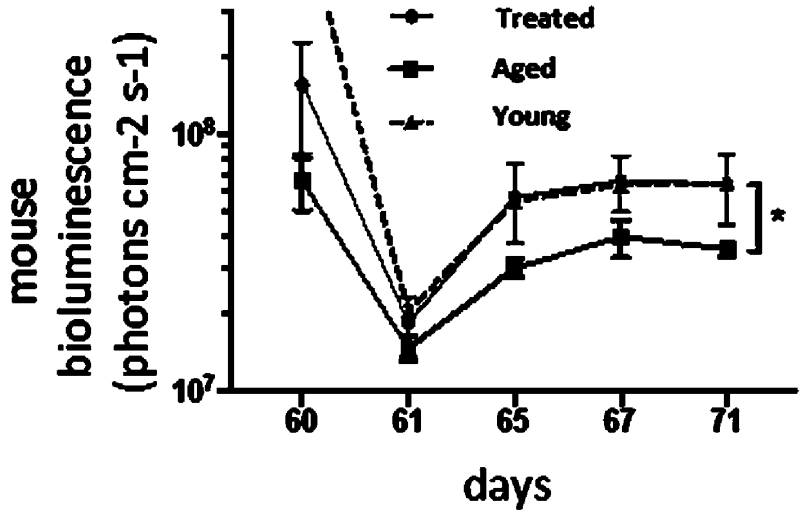

mouse bioluminescence (photons cm-2 s-1)
10⁸
10⁷
Treated
Aged
Young
*
60
61
65
67
71
days

FIG. 4F

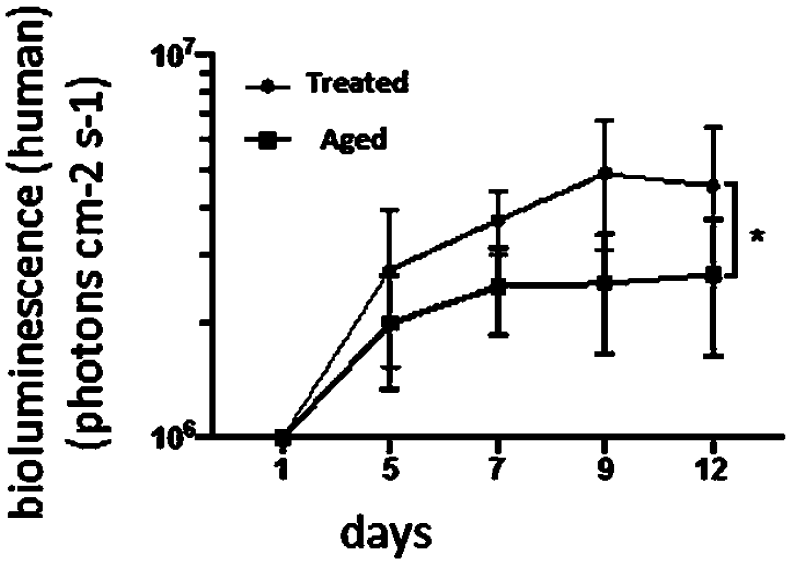

bioluminescence (human)
(photons cm-2 s-1)
10^7
10^6
Treated
Aged
*
1
5
7
9
12
days

FIG. 4G

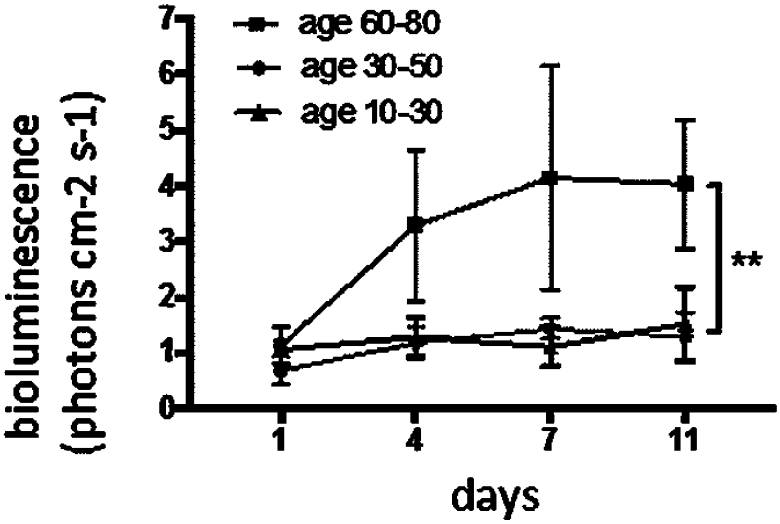

bioluminescence
(photons cm-2 s-1)
7
6
5
4
3
2
1
0
age 60-80
age 30-50
age 10-30
**
1
4
7
11
days

FIG. 5A

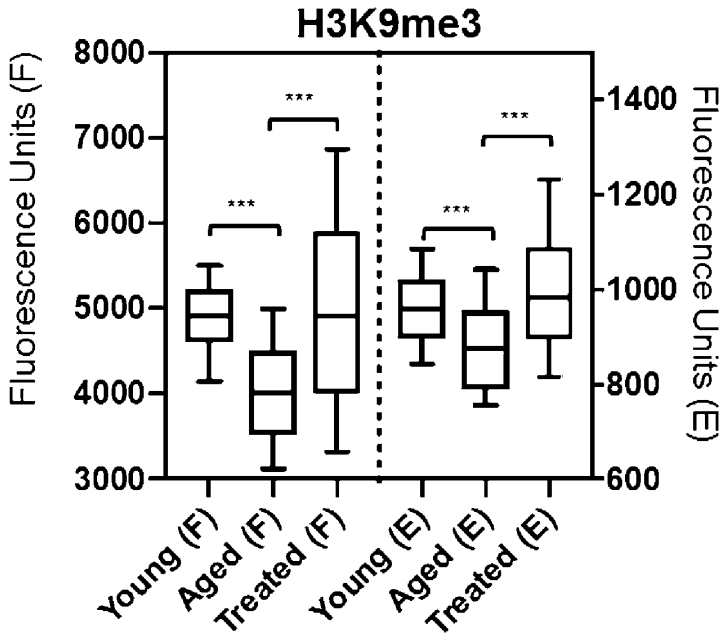

H3K9me3
Fluorescence Units (F)
Fluorescence Units (E)
8000
7000
6000
5000
4000
3000
1400
1200
1000
800
600
***
***
***
***
Young (F)
Aged (F)
Treated (F)
Young (E)
Aged (E)
Treated (E)

FIG. 5B

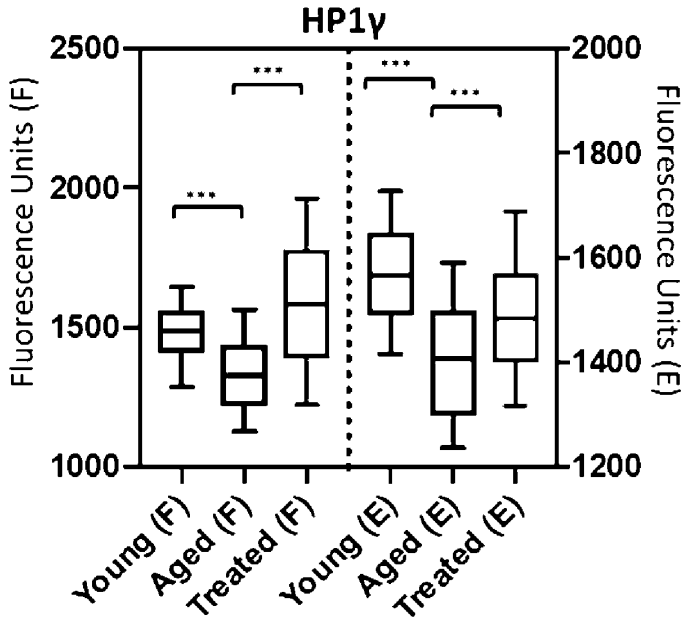

HP1γ
Fluorescence Units (F)
Fluorescence Units (E)
2500
2000
1500
1000
2000
1800
1600
1400
1200
***
***
***
***
Young (F)
Aged (F)
Treated (F)
Young (E)
Aged (E)
Treated (E)

FIG. 5C

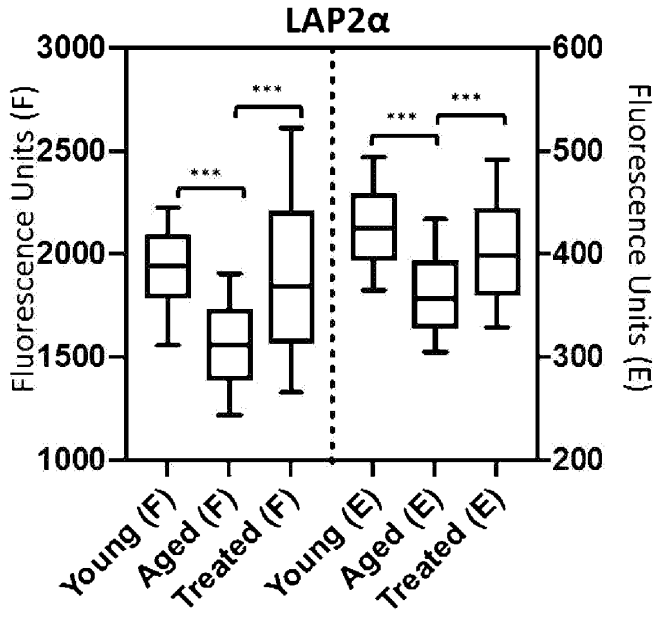

LAP2α
Fluorescence Units (F)
Fluorescence Units (E)
3000
2500
2000
1500
1000
600
500
400
300
200
***
***
***
***
Young (F)
Aged (F)
Treated (F)
Young (E)
Aged (E)
Treated (E)

FIG. 5D

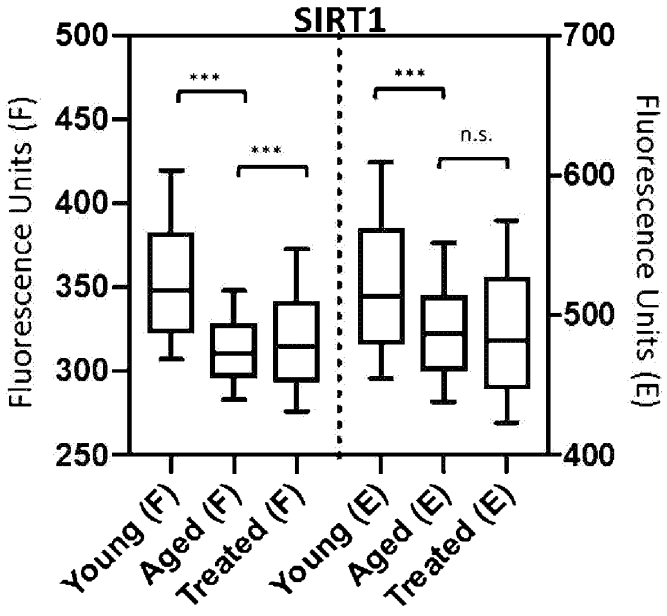

SIRT1
Fluorescence Units (F)
Fluorescence Units (E)
500
450
400
350
300
250
700
600
500
400
***
***
***
n.s.
Young (F)
Aged (F)
Treated (F)
Young (E)
Aged (E)
Treated (E)

FIG. 5E

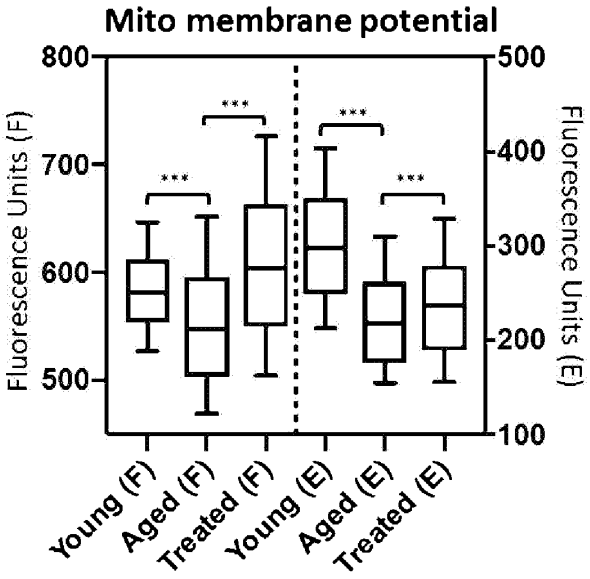

Mito membrane potential
Fluorescence Units (F)
Fluorescence Units (E)
800
700
600
500
500
400
300
200
100
***
***
***
***
Young (F)
Aged (F)
Treated (F)
Young (E)
Aged (E)
Treated (E)

FIG. 5F

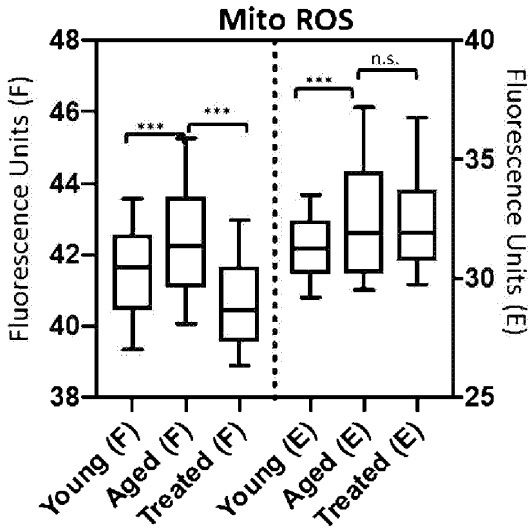

Mito ROS
Fluorescence Units (F)
Fluorescence Units (E)
48
46
44
42
40
38
40
35
30
25
***
***
***
n.s.
Young (F)
Aged (F)
Treated (F)
Young (E)
Aged (E)
Treated (E)

FIG. 5G

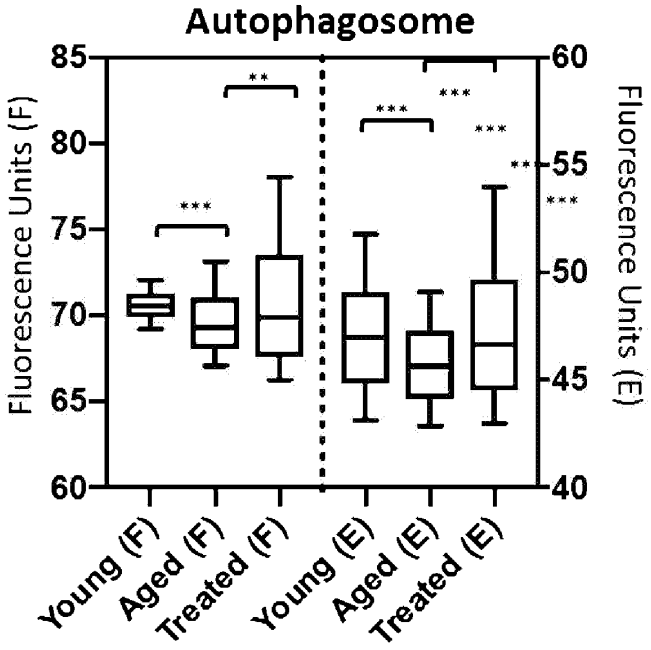

Autophagosome
Fluorescence Units (F)
Fluorescence Units (E)
85
80
75
70
65
60
60
55
50
45
40
**
***
***
***
***
***
Young (F)
Aged (F)
Treated (F)
Young (E)
Aged (E)
Treated (E)

FIG. 5H

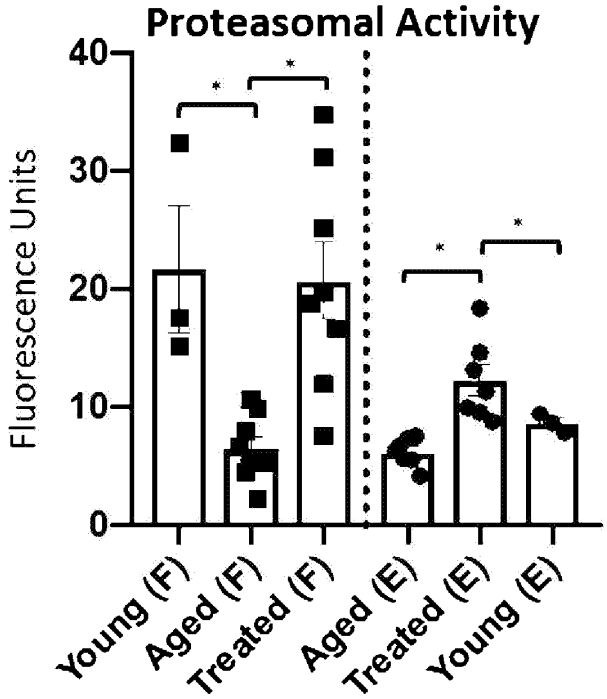

Proteasomal Activity
Fluorescence Units
40
30
20
10
0
*
*
*
*
Young (F)
Aged (F)
Treated (F)
Aged (E)
Treated (E)
Young (E)

FIG. 5I

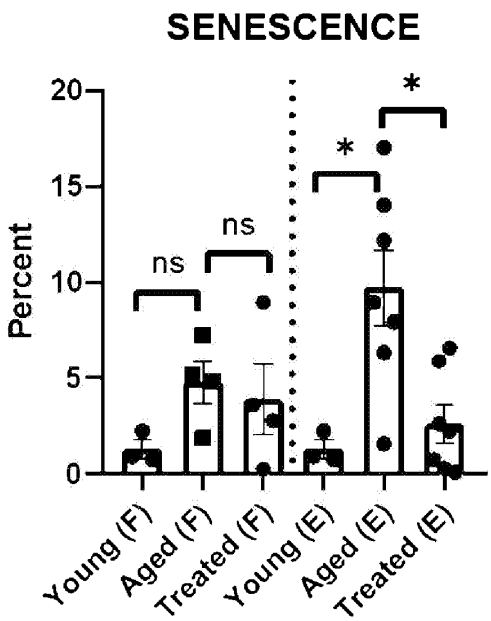

SENESCENCE
Percent
20
15
10
5
0
ns
ns
*
*
Young (F)
Aged (F)
Treated (F)
Young (E)
Aged (E)
Treated (E)

FIG. 5J

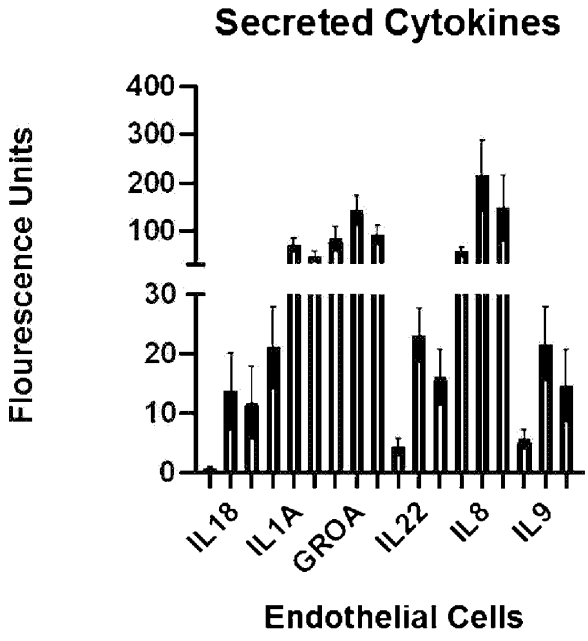

Secreted Cytokines
Flourescence Units
400
300
200
100
30
20
10
0
IL18
IL1A
GROA
IL22
IL8
IL9
Endothelial Cells

FIG. 6A

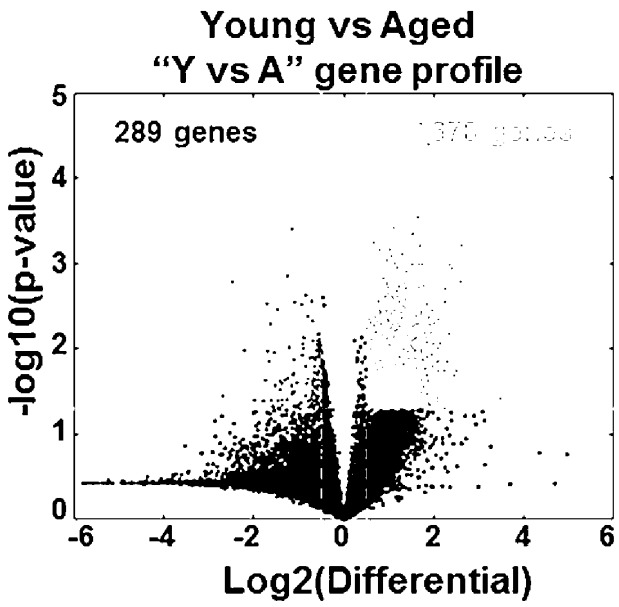

Young vs Aged
"Y vs A" gene profile
289 genes
-log10(p-value)
Log2(Differential)
5
4
3
2
1
0
-6
-4
-2
0
2
4
6

FIG. 6B

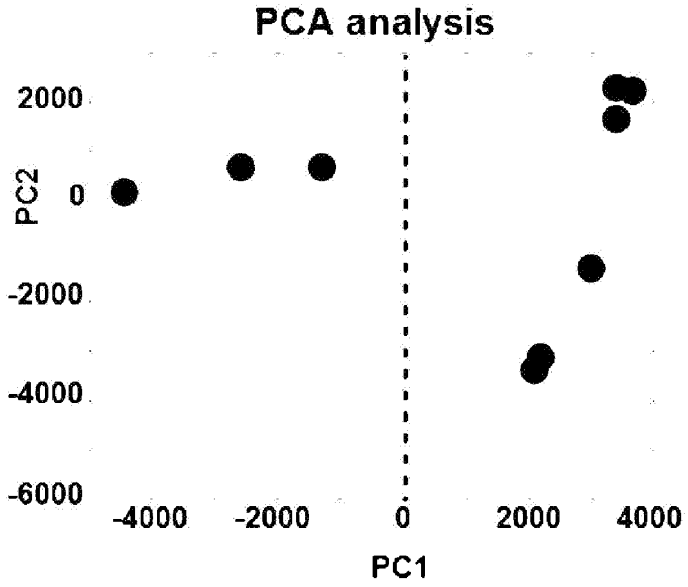

PCA analysis
PC2
PC1
2000
0
-2000
-4000
-6000
-4000
-2000
0
2000
4000

FIG. 6C

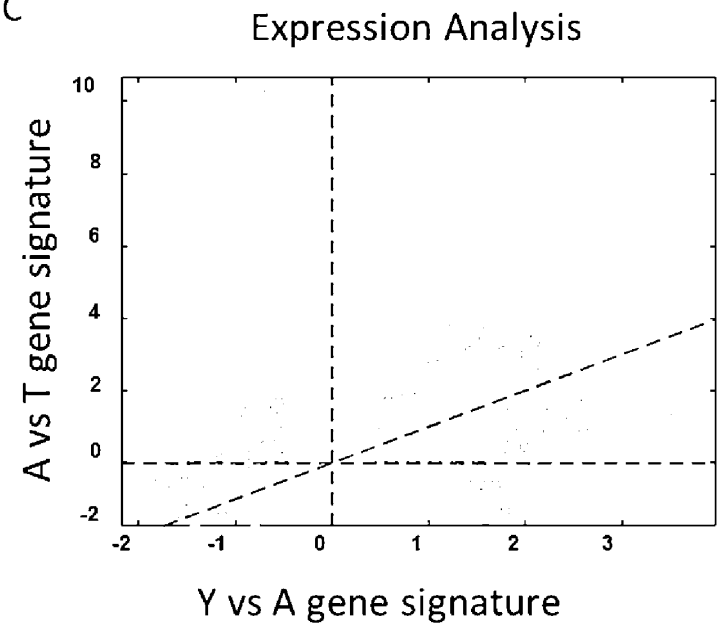

Expression Analysis
A vs T gene signature
Y vs A gene signature
10
8
6
4
2
0
-2
-2
-1
0
1
2
3

FIG. 6D

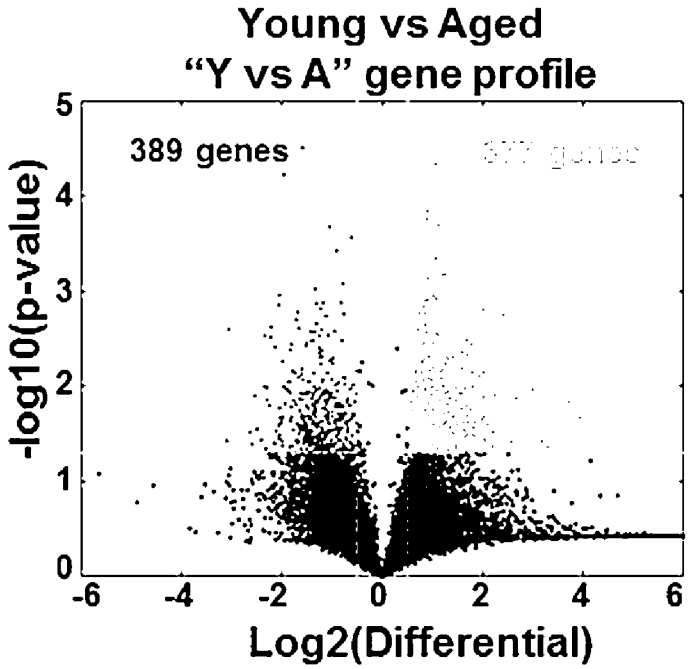

Young vs Aged
"Y vs A" gene profile
389 genes
-log10(p-value)
Log2(Differential)
5
4
3
2
1
0
-6
-4
-2
0
2
4
6

FIG. 6E

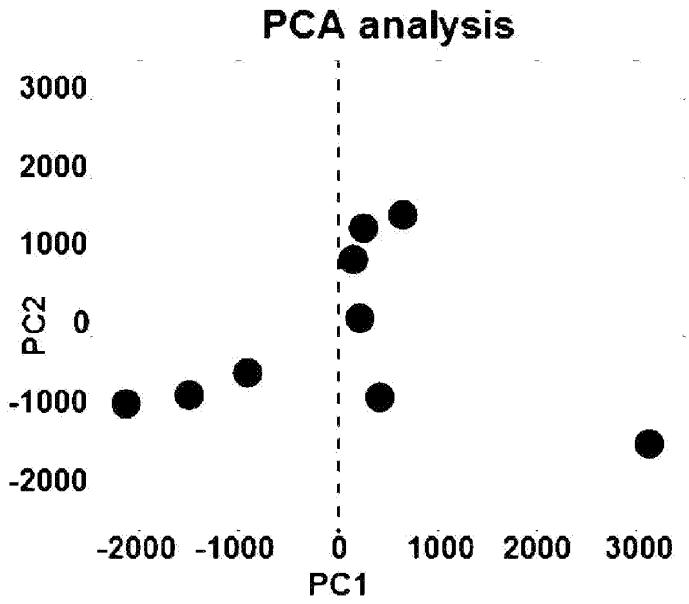

PCA analysis
3000
2000
1000
0
-1000
-2000
PC2
-2000 -1000 0 1000 2000 3000
PC1

FIG. 6F

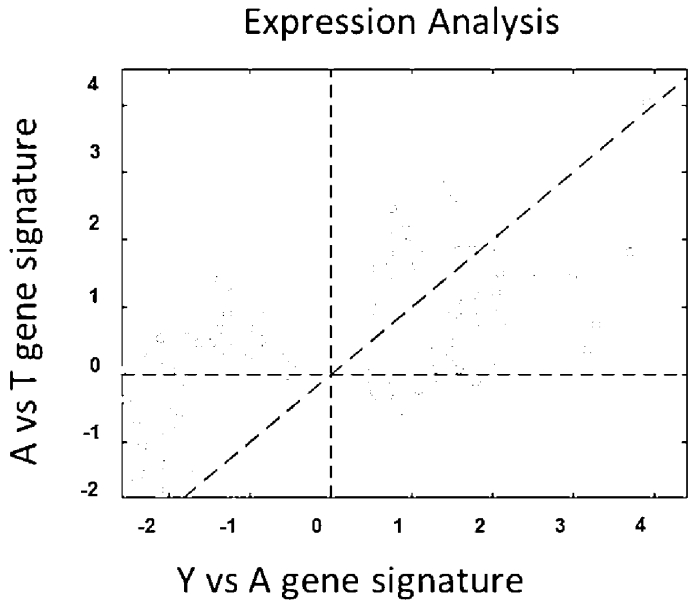

Expression Analysis
A vs T gene signature
4
3
2
1
0
-1
-2
-2 -1 0 1 2 3 4
Y vs A gene signature

FIG. 6G

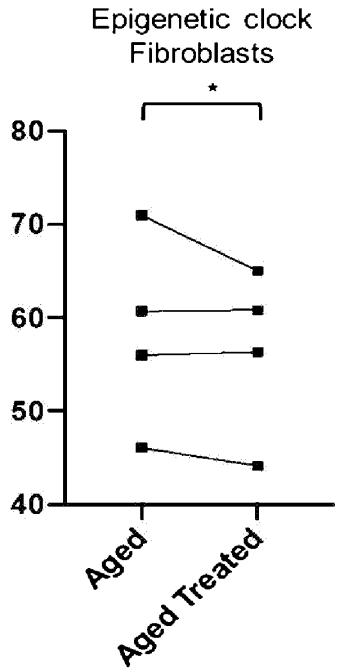

Epigenetic clock
Fibroblasts
*
80
70
60
50
40
Aged
Aged Treated

FIG. 6H

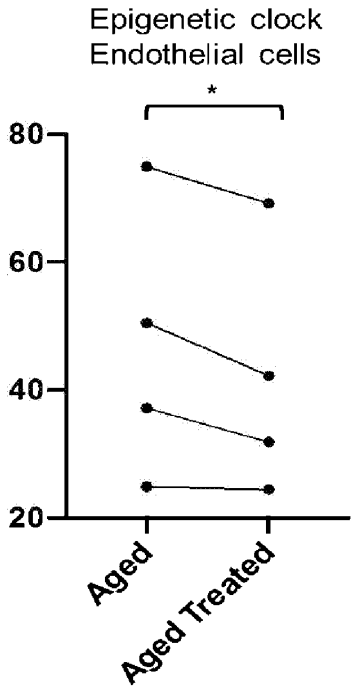

Epigenetic clock
Endothelial cells
*
80
60
40
20
Aged
Aged Treated

FIG. 6I

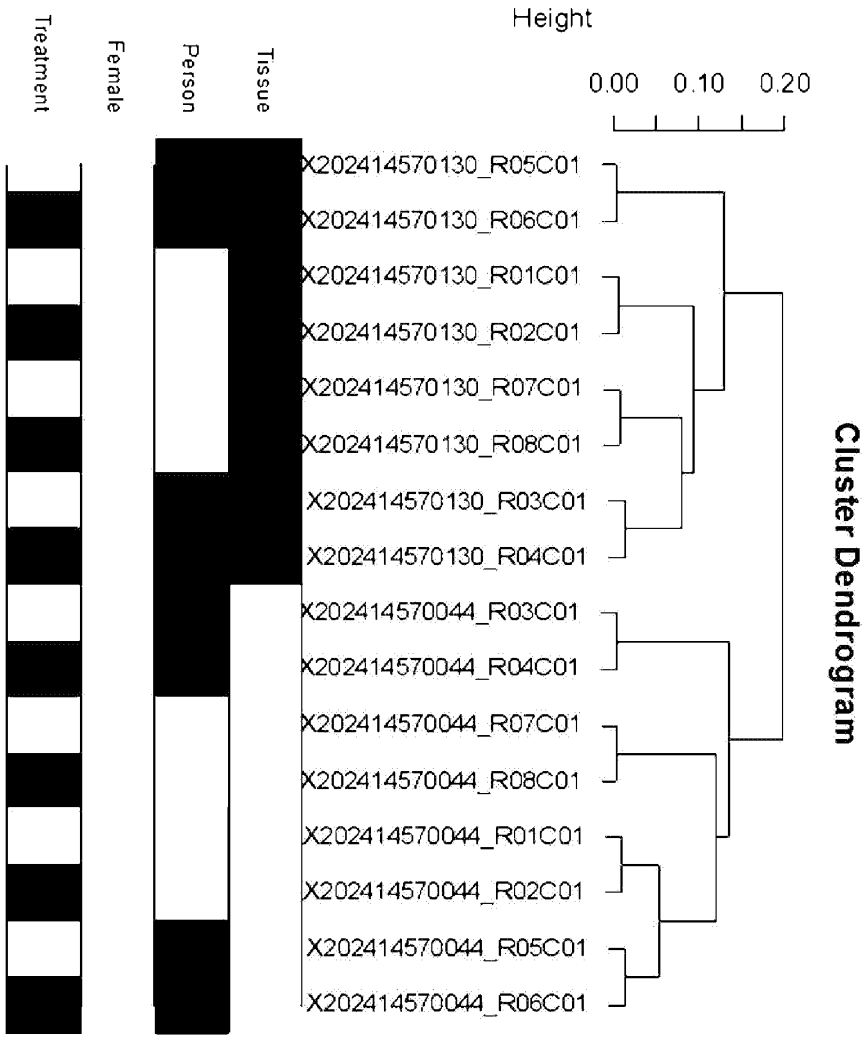

Treatment
Female
Person
Tissue
Height
0.00
0.10
0.20
X202414570130_R05C01
X202414570130_R06C01
X202414570130_R01C01
X202414570130_R02C01
X202414570130_R07C01
X202414570130_R08C01
X202414570130_R03C01
X202414570130_R04C01
X202414570044_R03C01
X202414570044_R04C01
X202414570044_R07C01
X202414570044_R08C01
X202414570044_R01C01
X202414570044_R02C01
X202414570044_R05C01
X202414570044_R06C01
Cluster Dendrogram

FIG. 7A

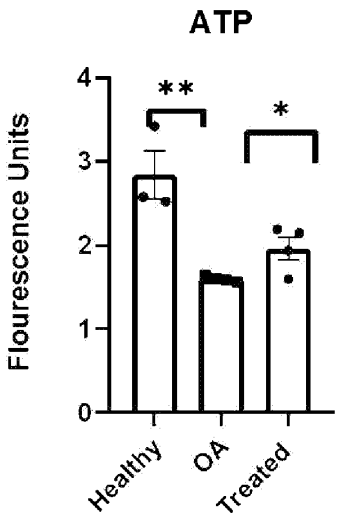


FIG. 7B

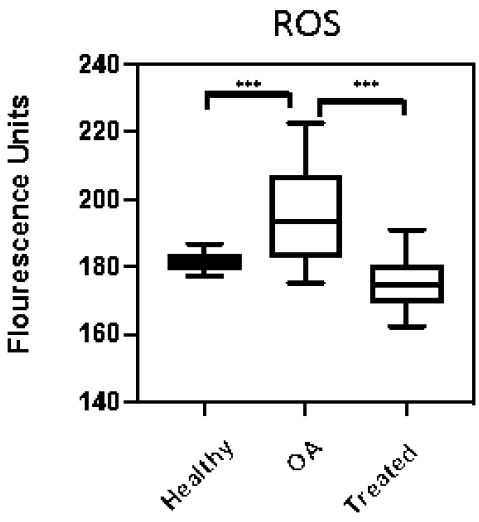


FIG. 7C

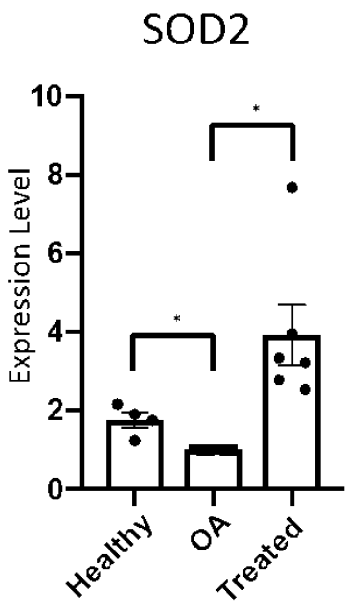


FIG. 7D

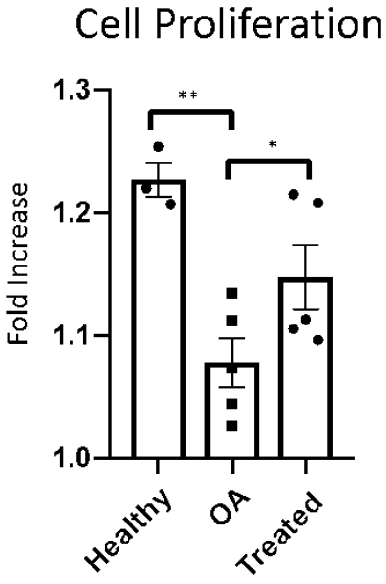


FIG. 7E

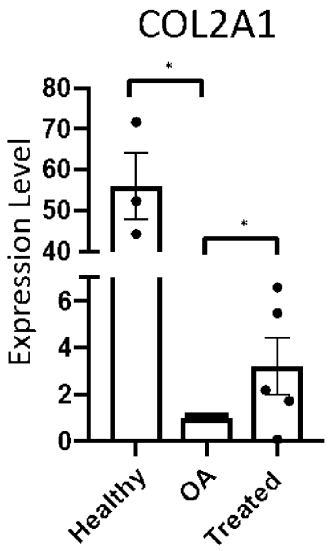


FIG. 7F

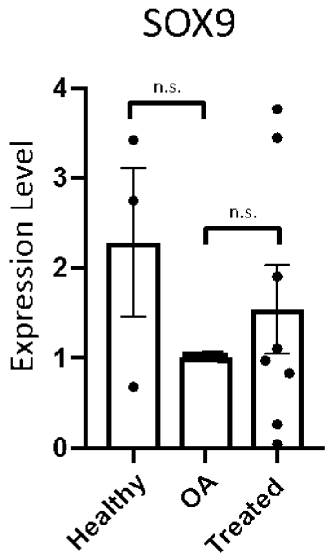


FIG. 7G

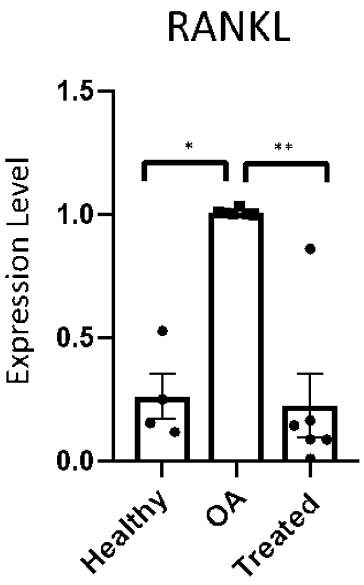


FIG. 7H

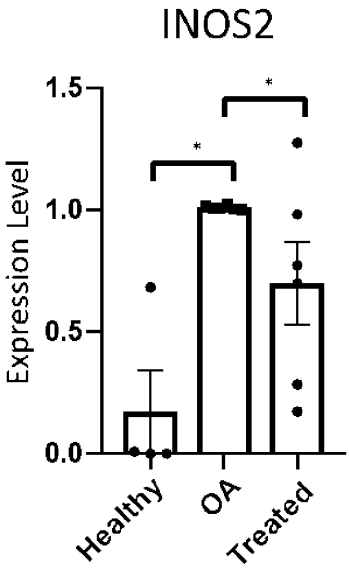


FIG. 7I

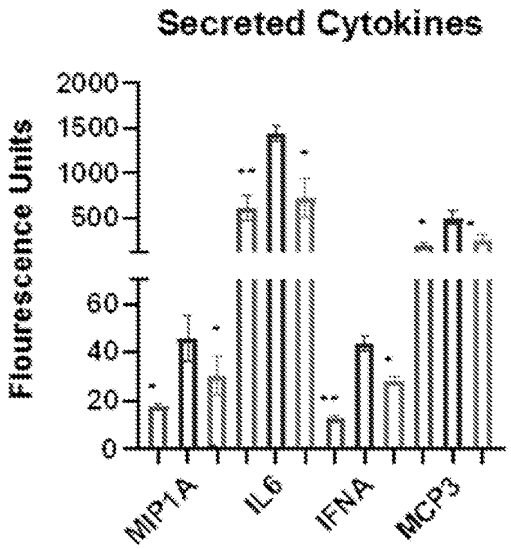


FIG. 7J

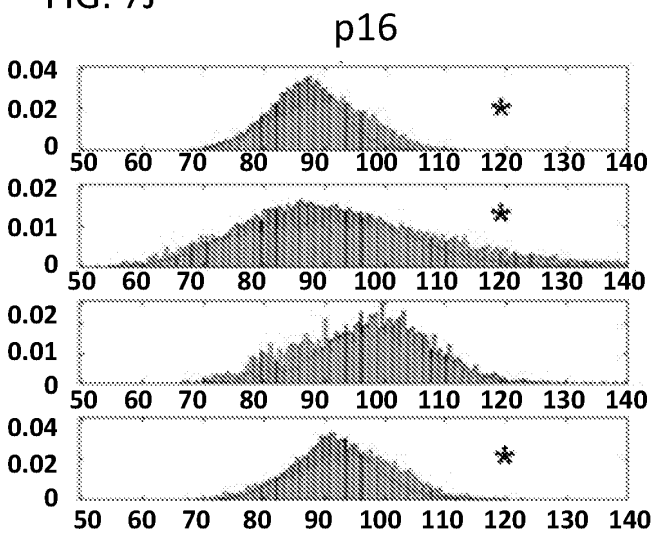


FIG. 7K

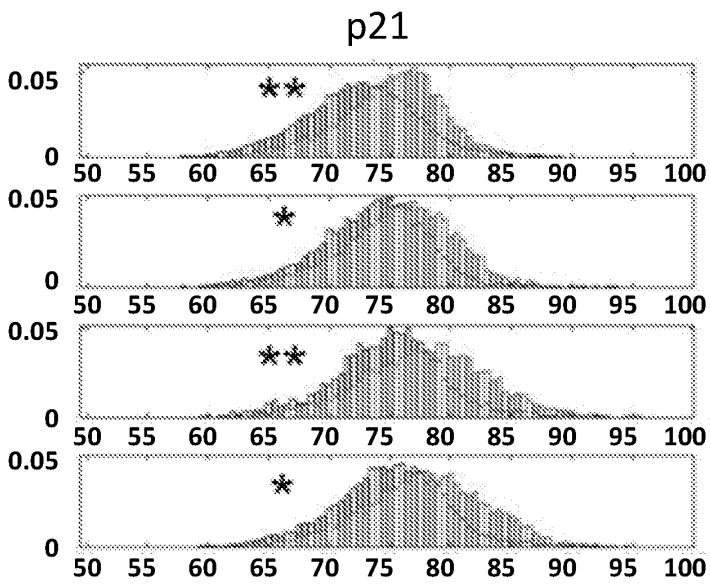


FIG. 7L

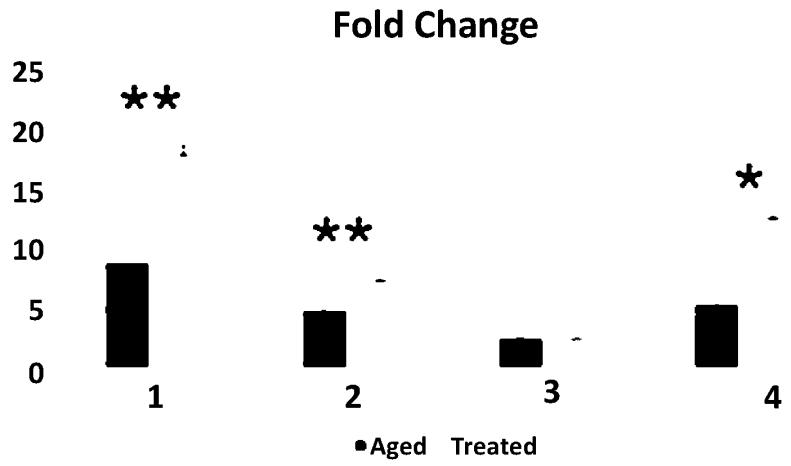

Fold Change
25
20
15
10
5
0
**
**
*
1
2
3
4
Aged
Treated

FIG. 7M

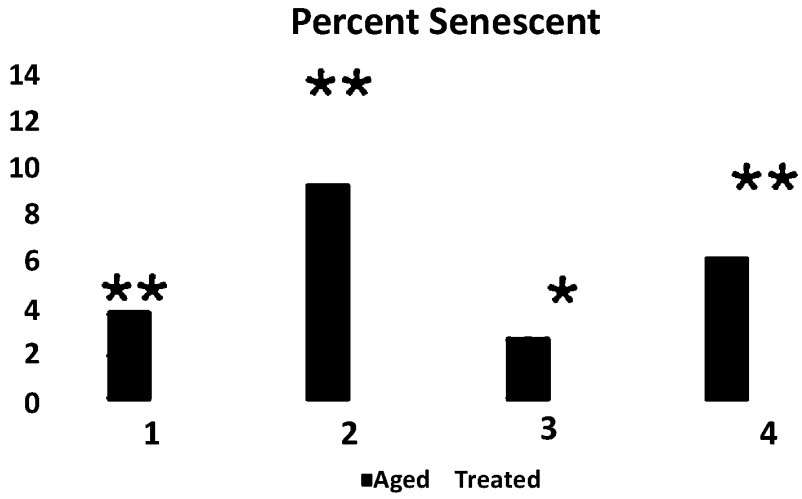

Percent Senescent
14
12
10
8
6
4
2
0
**
**
**
*
1
2
3
4
Aged
Treated

FIG. 8A

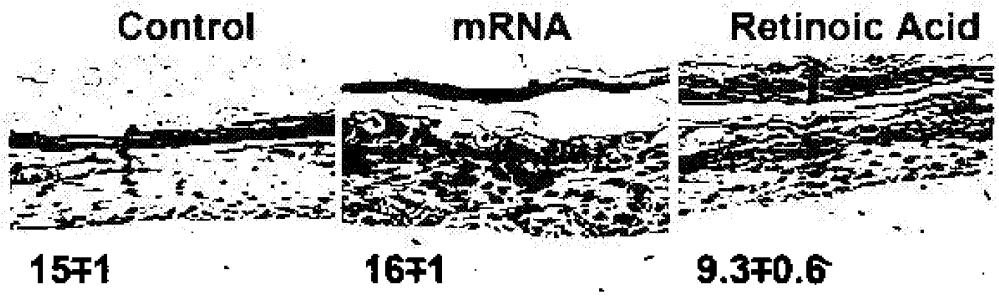


FIG. 8B

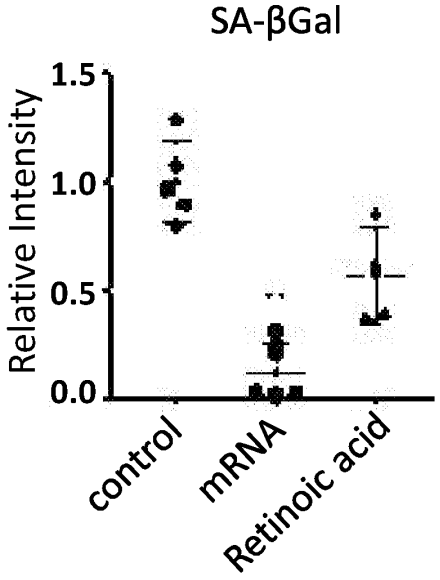


FIG. 8C

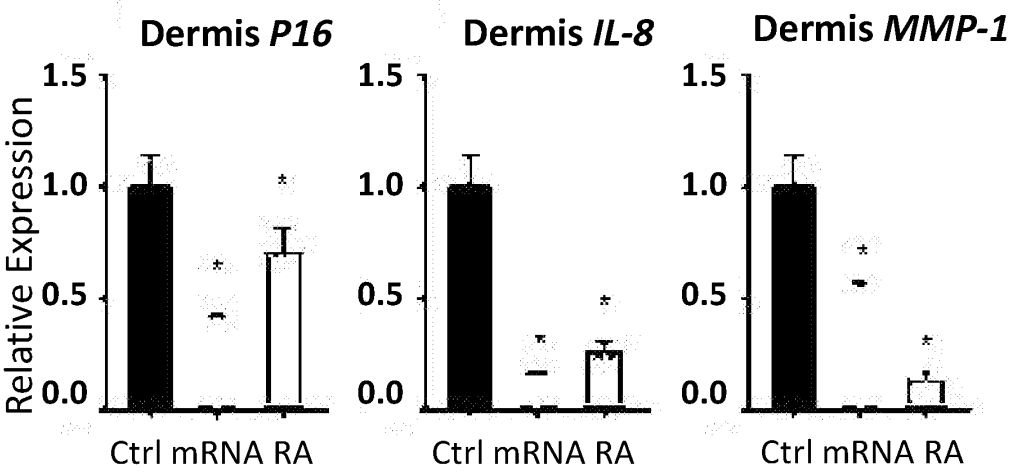


FIG. 8D

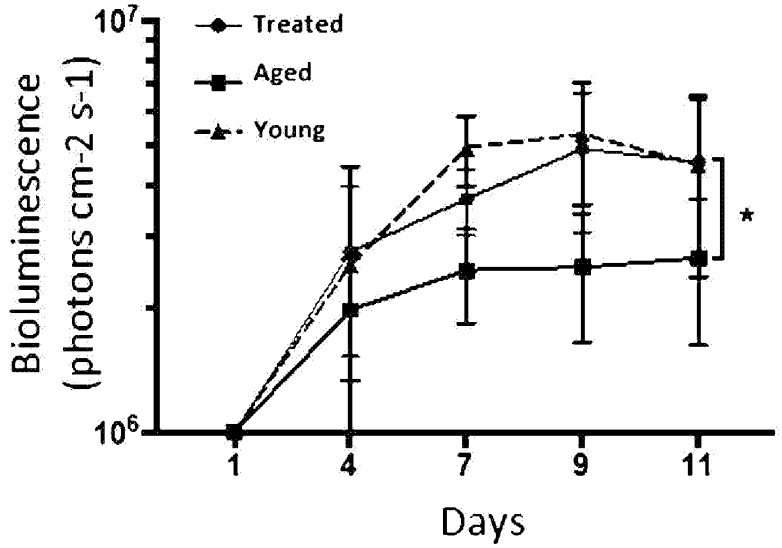

Bioluminescence (photons cm-2 s-1)
10^7
10^6
Treated
Aged
Young
*
1
4
7
9
11
Days

FIG. 8E

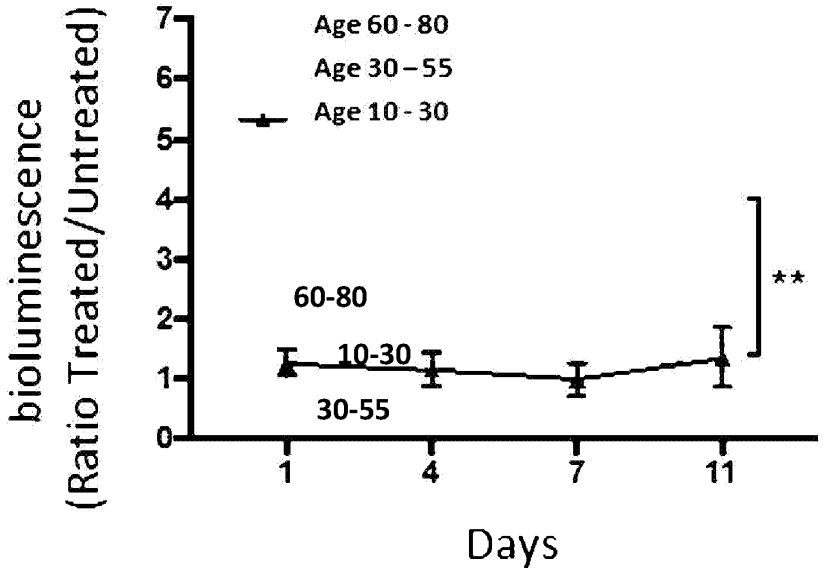

bioluminescence (Ratio Treated/Untreated)
7
6
5
4
3
2
1
0
Age 60 - 80
Age 30 – 55
Age 10 - 30
60-80
10-30
30-55
**
1
4
7
11
Days

FIG. 8F

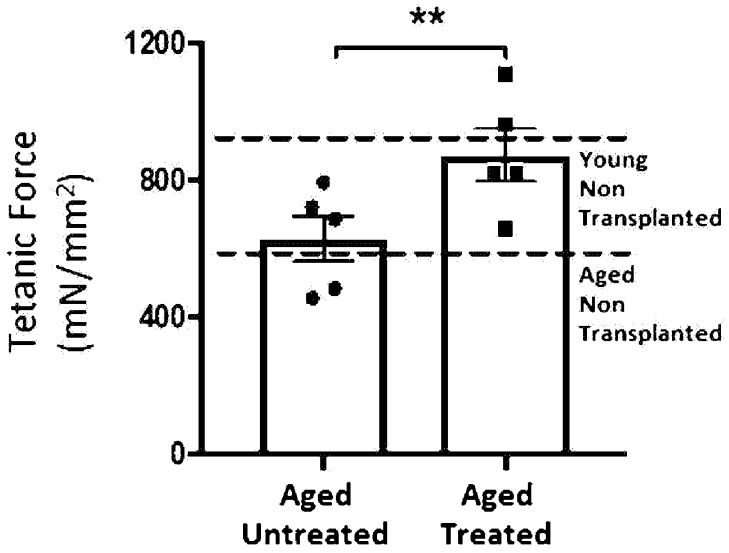

**
1200
800
400
0
Tetanic Force
(mN/mm2)
Young
Non
Transplanted
Aged
Non
Transplanted
Aged
Untreated
Aged
Treated

FIG. 8G

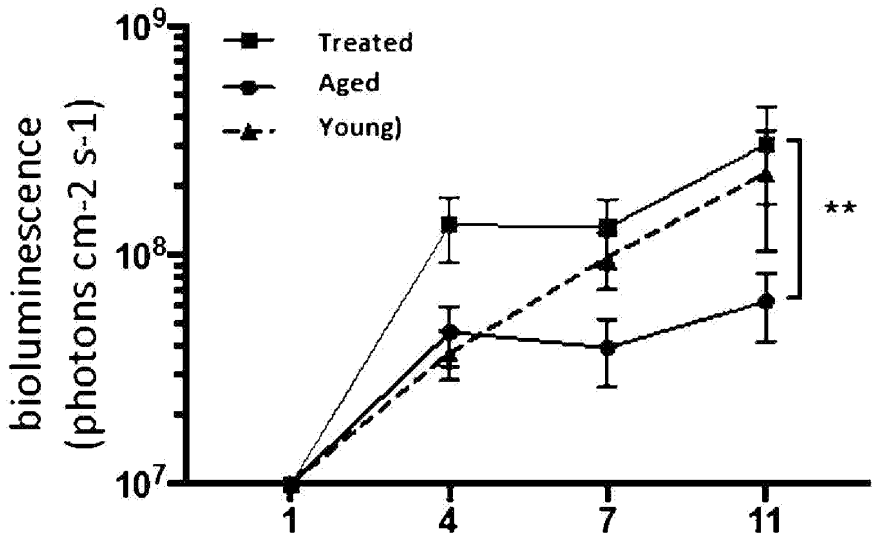

10^9
10^8
10^7
bioluminescence
(photons cm-2 s-1)
Treated
Aged
Young)
**
1
4
7
11

FIG. 8H

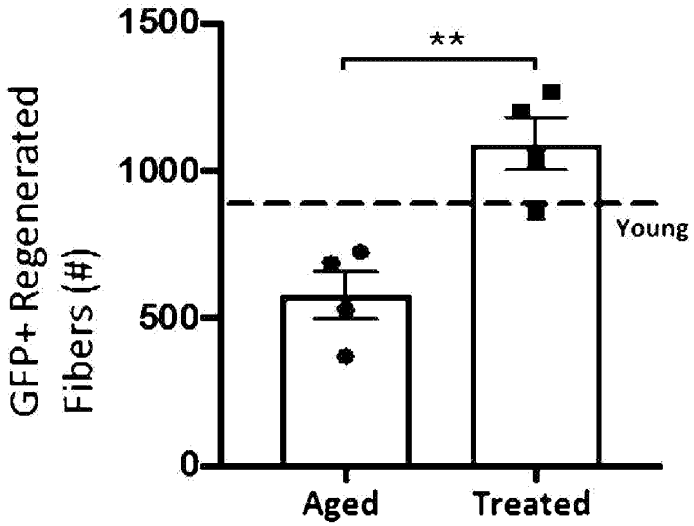

1500
1000
500
0
**
Young
GFP+ Regenerated Fibers (#)
Aged
Treated

FIG. 8I

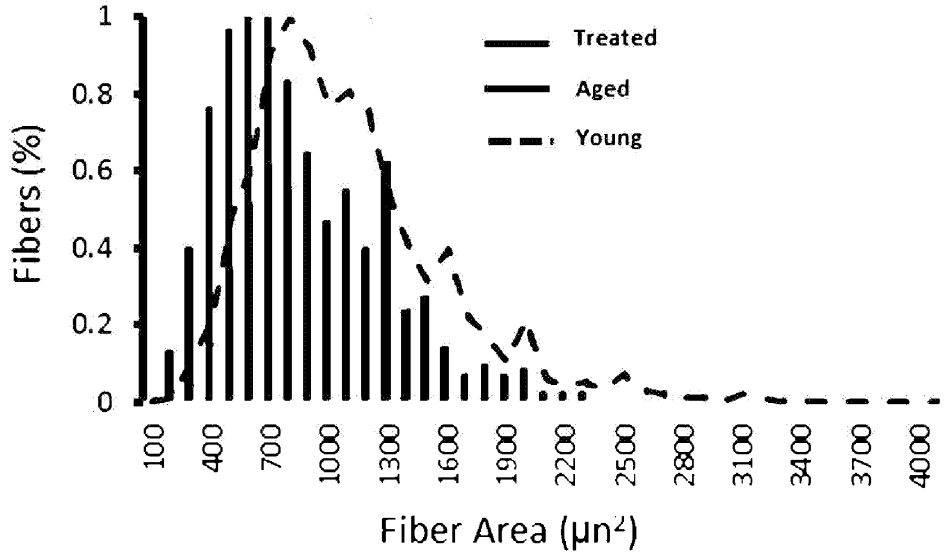

1
0.8
0.6
0.4
0.2
0
Fibers (%)
Treated
Aged
Young
100
400
700
1000
1300
1600
1900
2200
2500
2800
3100
3400
3700
4000
Fiber Area (μn²)

FIG. 8J

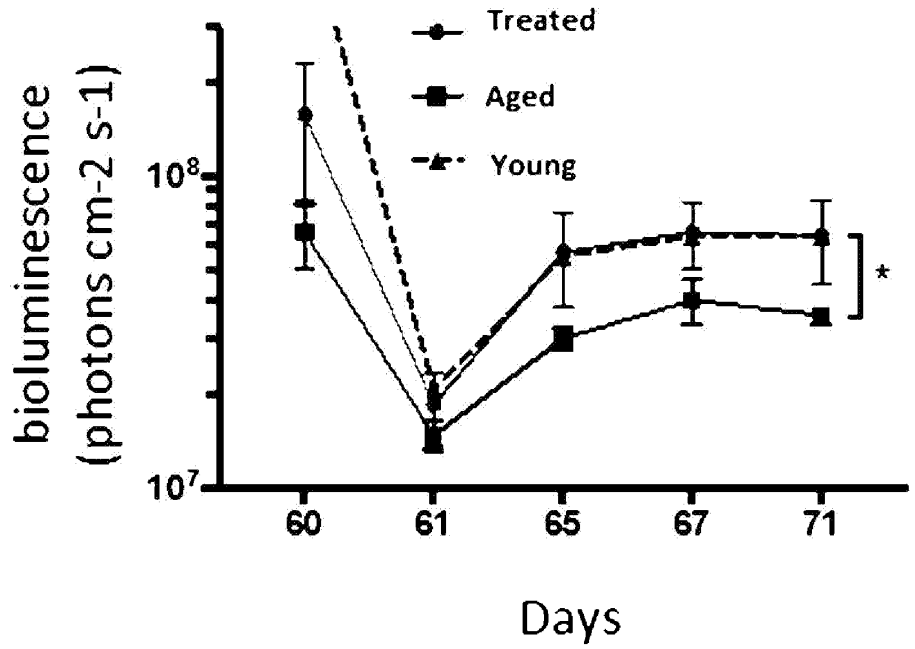

Treated
Aged
Young
bioluminescence (photons cm-2 s-1)
10^8
10^7
60
61
65
67
71
Days
*

FIG. 9A

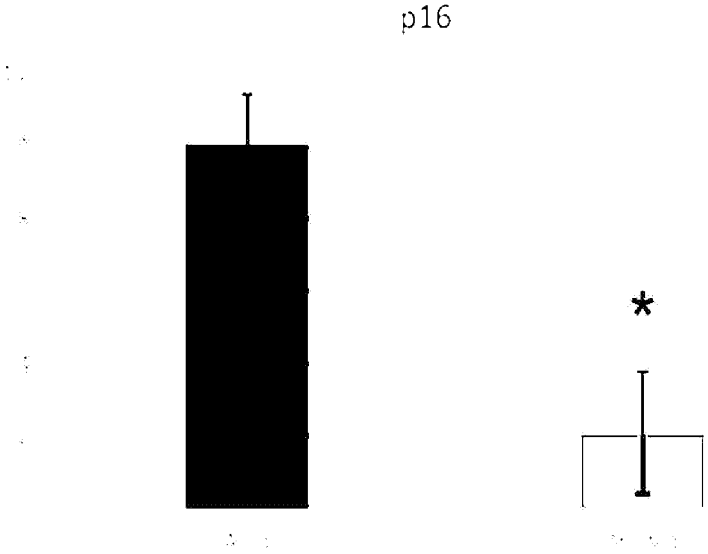

p16
*

FIG. 9B

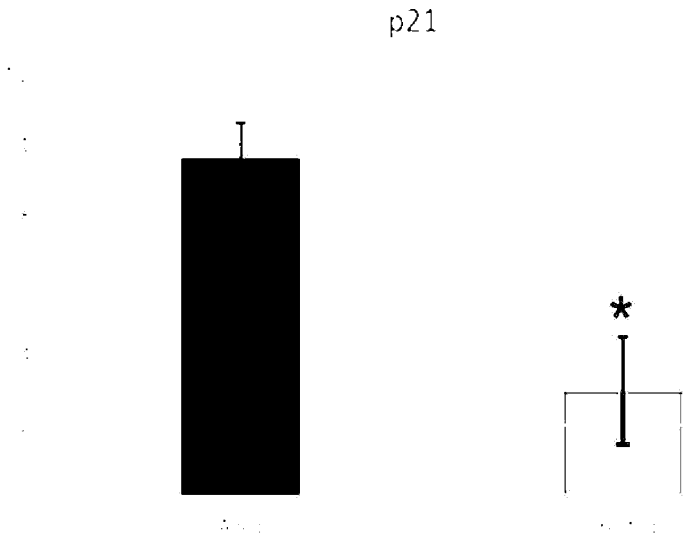


FIG. 9C

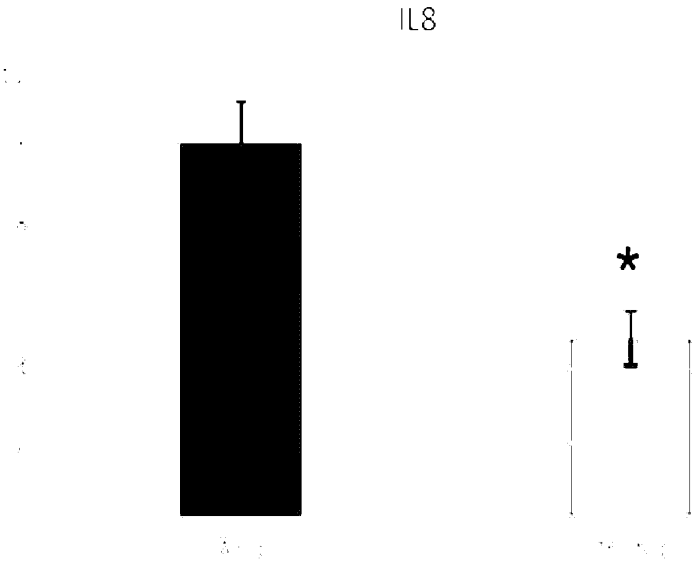


FIG. 9D

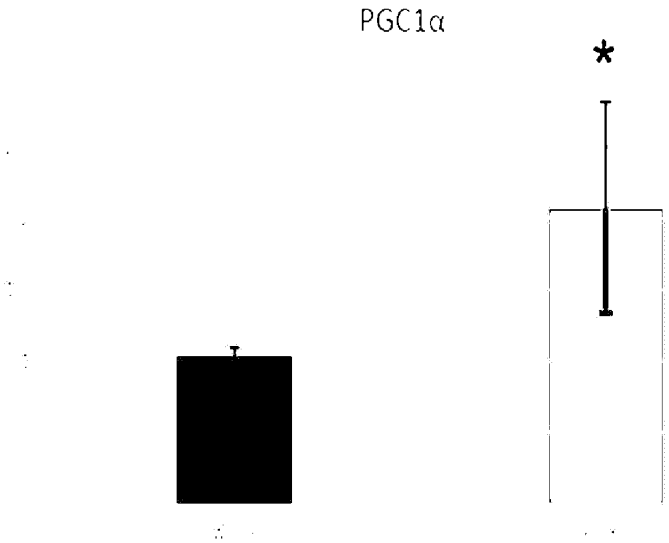


FIG. 10

Fibroblasts Markers		
Gene Name	Ratio T vs A	p Value
SERPINH1	0.671940258	0.214109899
CD34	-0.238138057	0.268448091
CD44	-0.642843806	0.23084843
COL1A2	-0.495537535	0.141297315
P4HB	-0.472032042	0.307450923
S100A4	0.280897592	0.629912708
THY1	0.884040505	0.940726389
VIM	0.221615418	0.522358401
Endothelial Cells Markers		
Gene Name	Ratio T vs A	p Value
BSG	0.491575396	0.385509369
CD34	3.394985317	0.0607054
CD151	0.49270888	0.597029569
CLK1	1.696030542	0.148605011
ACE	0.288209478	0.855311993
TYMP	-0.021805675	0.707270534
S1PR3	-0.07110968	0.562228711
FABP5	0.941584343	0.182097604
FLT1	0.904964173	0.385874061
FLT4	0.13951215	0.556669073
ICAM1	2.002445675	0.056554892
ICAM2	-0.369110936	0.330034476
ITGA4	0.685330957	0.322656645
ITGB2	-0.382927635	0.326139443
S1PR1	0.731818125	0.206905903
	0.783606486	0.147100714

FIG. 10 (cont'd)

TNFRSF10B		
MCAM	2.532381593	0.095465583
PECAM1	2.793471885	0.069559176
PODXL	1.5321432	0.15593486
PTPRC	0.595334185	0.75987991
SELE	0.984304976	0.983032351
TEK	1.106399752	0.114907237
THBD	0.598315991	0.688820613
TNFRSF1A	-0.090012076	0.652801648
SELP	0.506495926	0.136103947
VCAM1	0.678172928	0.514625848
S1PR4	0.65401203	0.661036982
TNFRSF10A	0.494643829	0.741553252
S1PR2	-0.035877036	0.706894809
CLEC4M	0.362685323	0.261411134
PROCR	-0.266074607	0.295008686
PDPN	-0.092480916	0.368066511
LYVE1	1.884638545	0.48628405
CD160	-0.035164921	0.286253573
CD93	2.836045432	0.066384409
STAB1	0.069395073	0.828062549
EGFL7	0.164693275	0.578980276
EMCN	0.107214427	0.54022725
AGGF1	-0.25317055	0.396601926
STAB2	-0.010959753	0.748665789
THSD1	0.806621332	0.923812102
CD248	0.341185795	0.43689891
COLEC12	-0.301368876	0.420367741
VWA9	-0.006983138	0.839893716
ANTXR1	-0.018729407	0.739151715
TNFRSF1B	0.758785001	0.353326732
DCBLD2	1.330405349	0.419283539
THSD7A	-	0.822024362

FIG. 10 (cont'd)

	0.024305081	
ECSCR	-0.257594317	0.524159
NECTIN2	0.281379685	0.946639419
IL1R1	0.089978493	0.958917598
Pluripotent Cells Markers		
Gene Name	Reads	
PRDM14	no reads	
SALL4	no reads	
SSEA1	no reads	
SSEA3	no reads	
SSEA4	no reads	
SSEA5	no reads	
TRA-1-60	no reads	
TRA-1-80	no reads	
UTF1	no reads	
ZFP42	no reads	

FIG. 11

Parameter	Aging Trend	Citation
HPIgamma	decrease	Miller, Justine D., et al. "Human iPSC-based modeling of late-onset disease via progerin-induced aging," Cell stem cell 13.6 (2013): 691-705.
H3K9me3	decrease	
LAP2alpha	decrease	
Nuclear Folding/Blebbing	increase	
Senescence	increase	Kang, Hyun Tae, et al. "Autophagy impairment induces premature senescence in primary human fibroblasts," PloS one 6.8 (2011): e23367.
Mitochondria Superoxide	increase	
Chymotrypsin Proteosome Activity	decrease	
Mitochondria Membrane Potential	decrease	
Autophagy	decrease	Gamerdinger, Martin et al. "Protein quality control during aging involves recruitment of the macroautophagy pathway by BAG3," The EMBO journal 28.7 (2009): 889-901.
Telomere Length	decrease	Canela, Andrés, et al. "High-throughput telomere length quantification by FISH and its application to human population studies," Proceedings of the National Academy of Sciences 104.13 (2007): 5300-5305.
SIRT1	decrease	Donato, Anthony J., et al. "SIRT-1 and vascular endothelial dysfunction with ageing in mice and humans," The journal of physiology 589.18 (2011): 4545-4554
Cytokines	increase	Leng, Sean X., et al. "ELISA and multiplex technologies for cytokine measurement in inflammation and aging research," The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 63.8 (2008): 879-884.