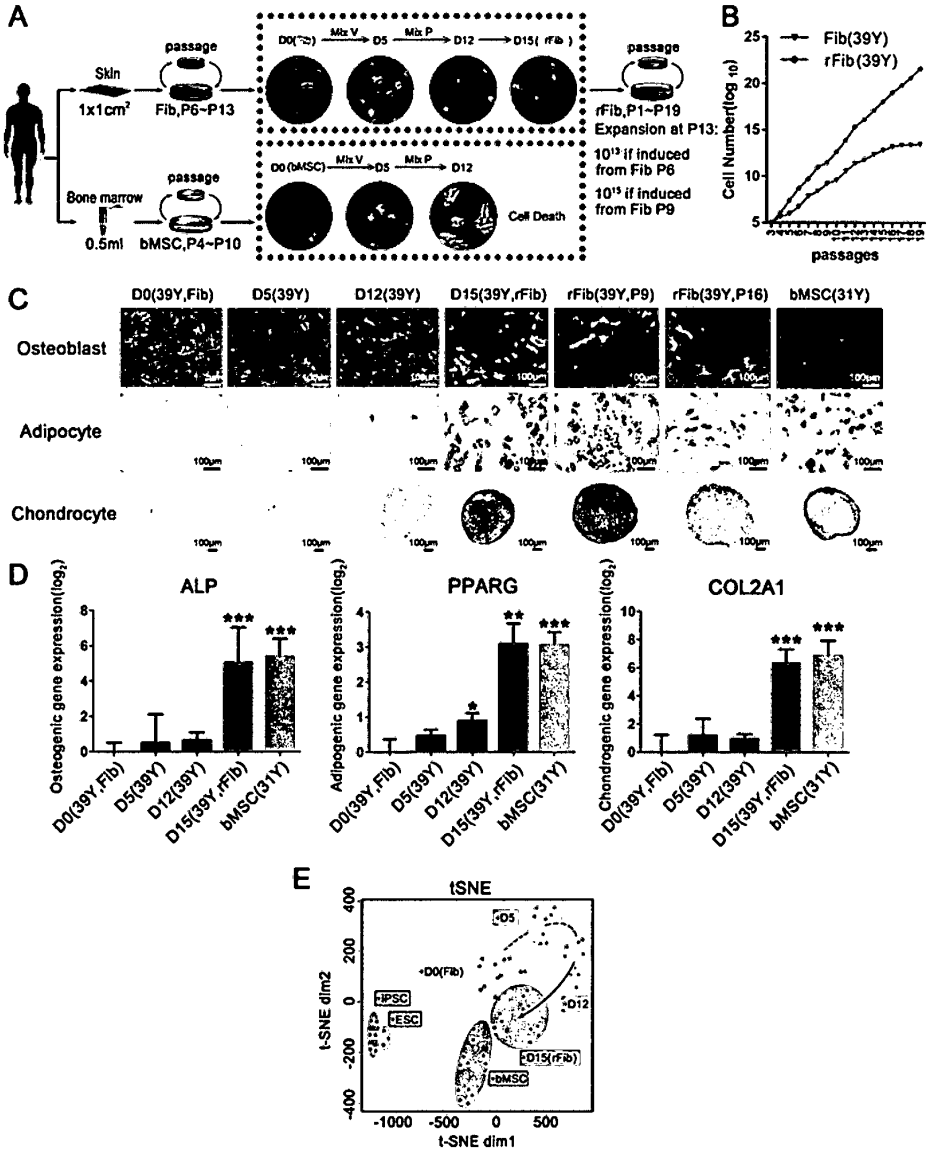

A
Skin
1x1cm²
passage
Fib,P6~P13
Bone marrow
0.5ml
passage
bMSC,P4~P10
Mix V
Mix P
D5
D12
D15(rFib)
D0(bMSC)
Cell Death
passage
rFib,P1~P19
Expansion at P13:
10¹³ if induced from Fib P6
10¹⁵ if induced from Fib P9
B
Fib(39Y)
rFib(39Y)
Cell Number(log 10)
passages
C
D0(39Y,Fib)
D5(39Y)
D12(39Y)
D15(39Y,rFib)
rFib(39Y,P9)
rFib(39Y,P16)
bMSC(31Y)
Osteoblast
Adipocyte
Chondrocyte
D
ALP
PPARG
COL2A1
Osteogenic gene expression(log2)
Adipogenic gene expression(log2)
Chondrogenic gene expression(log2)
D0(39Y,Fib)
D5(39Y)
D12(39Y)
D15(39Y,rFib)
bMSC(31Y)
E
tSNE
D5
D0(Fib)
D12
iPSC
ESC
D15(rFib)
bMSC
t-SNE dim2
t-SNE dim1

图 1

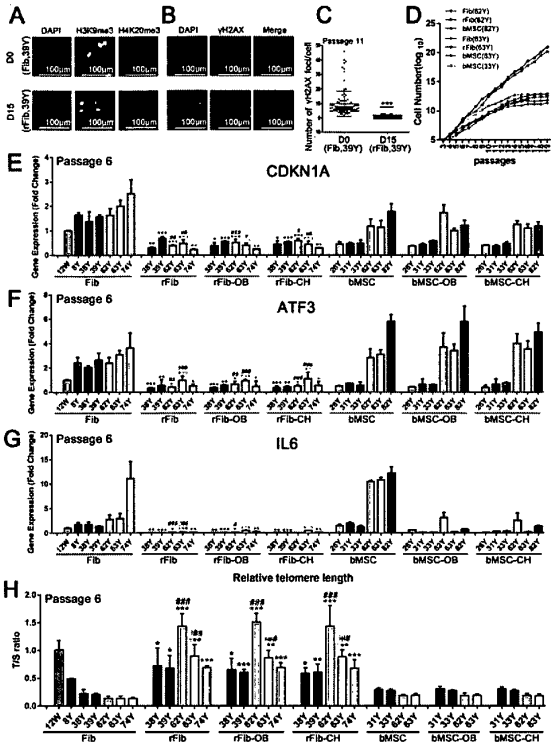

A
B
C
D
E
CDKN1A
F
ATF3
G
IL6
Relative telomere length
H
Passage 6
Fib
rFib
rFib-OB
rFib-CH
bMSC
bMSC-OB
bMSC-CH
passages

图 2

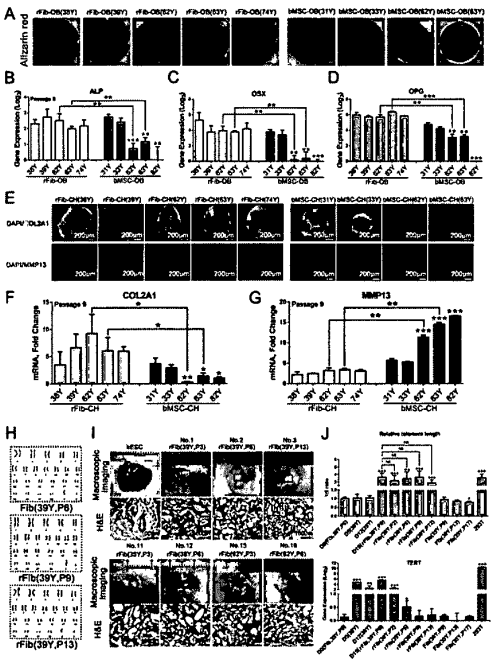

A
Alizarin red
B
ALP
C
OSX
D
OPG
E
F
COL2A1
G
MMP13
H
I
J
Macroscopic imaging
H&E

图 3

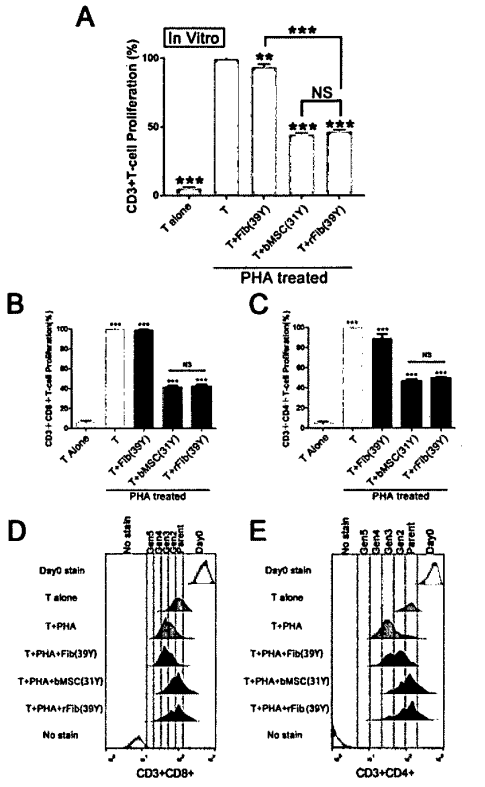

A
In Vitro
CD3+T-cell Proliferation (%)
T alone
T
T+Fib(39Y)
T+bMSC(31Y)
T+rFib(39Y)
PHA treated
B
C
D
E
Day0 stain
T alone
T+PHA
T+PHA+Fib(39Y)
T+PHA+bMSC(31Y)
T+PHA+rFib(39Y)
No stain
CD3+CD8+
CD3+CD4+

图 4

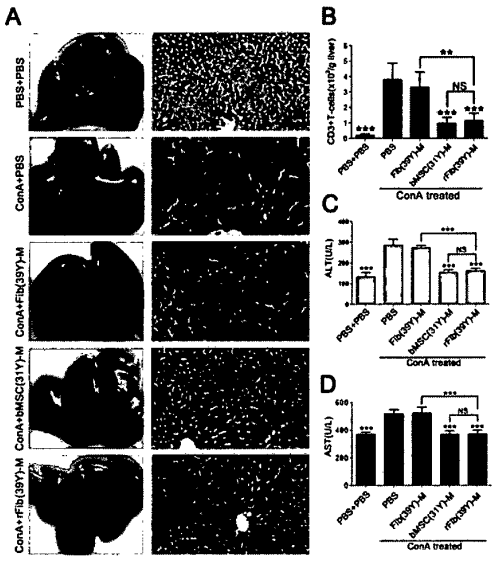

A
PBS+PBS
ConA+PBS
ConA+Fib(39Y)-M
ConA+bMSC(31Y)-M
ConA+rFib(39Y)-M
B
C
D
ALT(U/L)
AST(U/L)
ConA treated

图 5

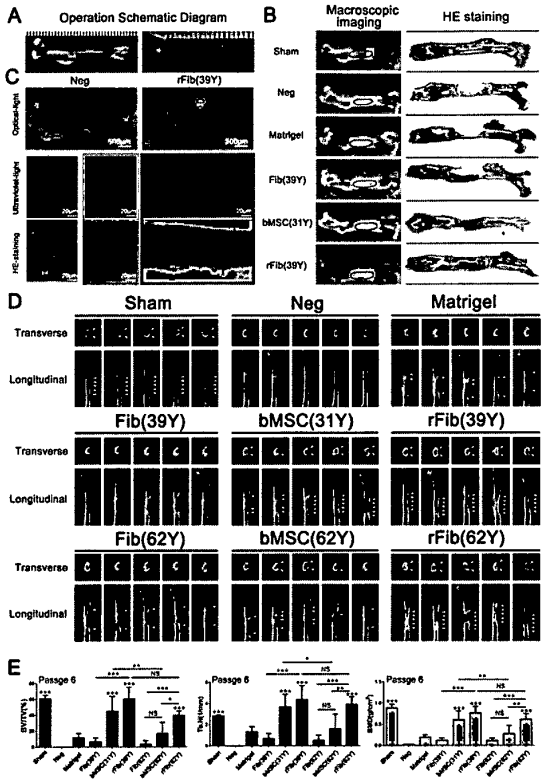

A
Operation Schematic Diagram
B
Macroscopic imaging
HE staining
Sham
Neg
Matrigel
Fib(39Y)
bMSC(31Y)
rFib(39Y)
C
Neg
rFib(39Y)
Optical-light
Ultraviolet-light
HE-staining
D
Sham
Neg
Matrigel
Transverse
Longitudinal
Fib(39Y)
bMSC(31Y)
rFib(39Y)
Fib(62Y)
bMSC(62Y)
rFib(62Y)
E
Passage 6
NS

图 6

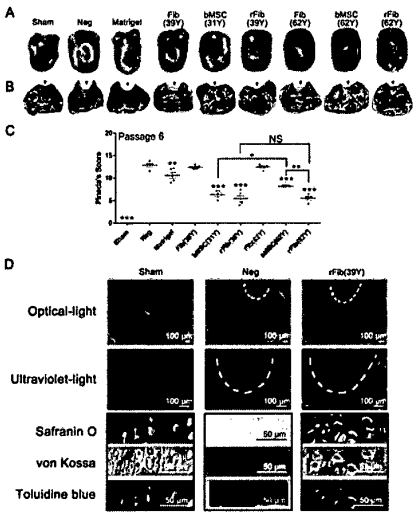

A
Sham
Neg
Matrigel
Fib (39Y)
bMSC (31Y)
rFib (39Y)
Fib (62Y)
bMSC (62Y)
rFib (62Y)
B
C
Passage 6
NS
D
Sham
Neg
rFib(39Y)
Optical-light
Ultraviolet-light
Safranin O
von Kossa
Toluidine blue

图 7

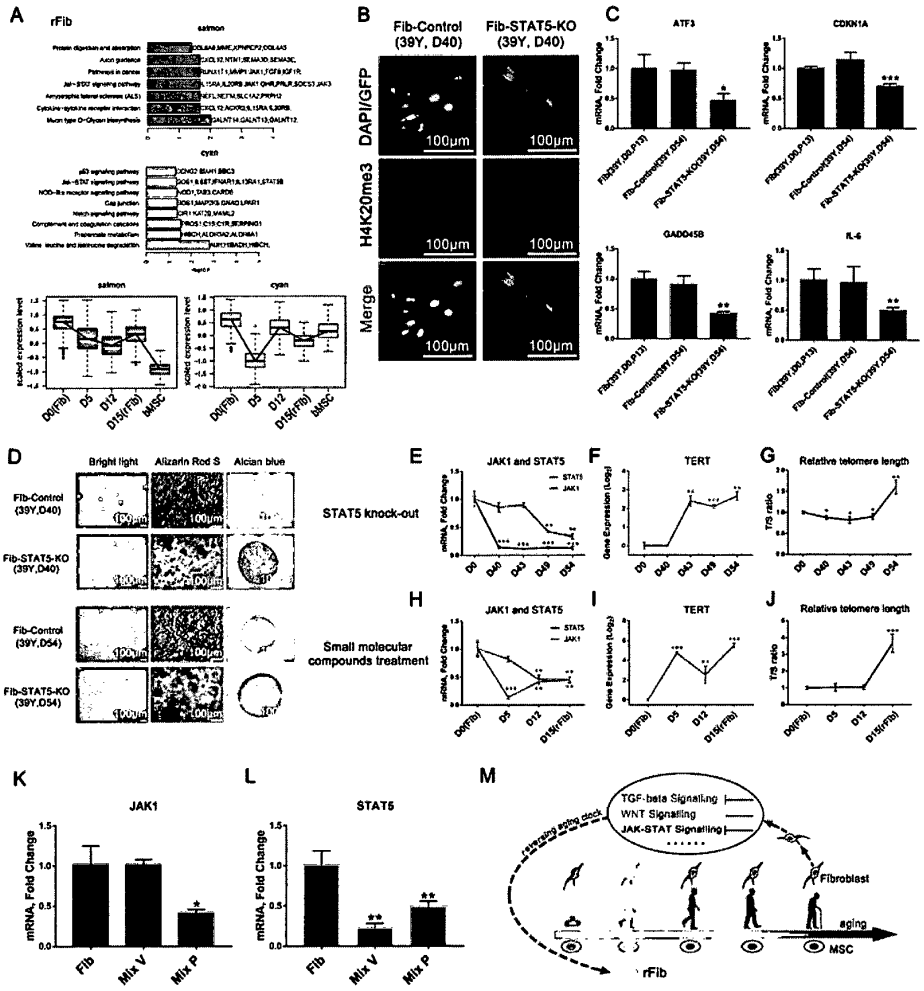

A
rFib
salmon
cyan
B
Fib-Control (39Y, D40)
Fib-STAT5-KO (39Y, D40)
DAPI/GFP
H4K20me3
Merge
100μm
C
ATF3
CDKN1A
GADD45B
IL-6
mRNA, Fold Change
D
Bright light
Alizarin Red S
Alcian blue
Fib-Control (39Y,D40)
Fib-STAT5-KO (39Y,D40)
Fib-Control (39Y,D54)
Fib-STAT5-KO (39Y,D54)
STAT5 knock-out
Small molecular compounds treatment
E
JAK1 and STAT5
F
TERT
G
Relative telomere length
H
I
J
K
JAK1
L
STAT5
Fib
Mix V
Mix P
M
TGF-beta Signalling
WNT Signalling
JAK-STAT Signalling
Fibroblast
aging
MSC
rFib

图 8

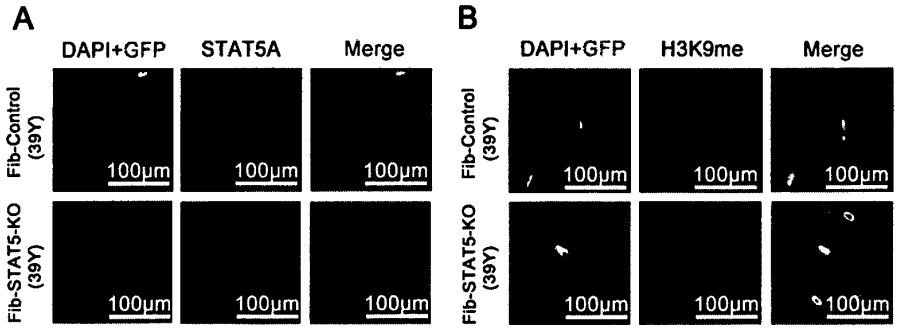

A
DAPI+GFP
STAT5A
Merge
Fib-Control (39Y)
Fib-STAT5-KO (39Y)
100μm
B
DAPI+GFP
H3K9me
Merge

图 9

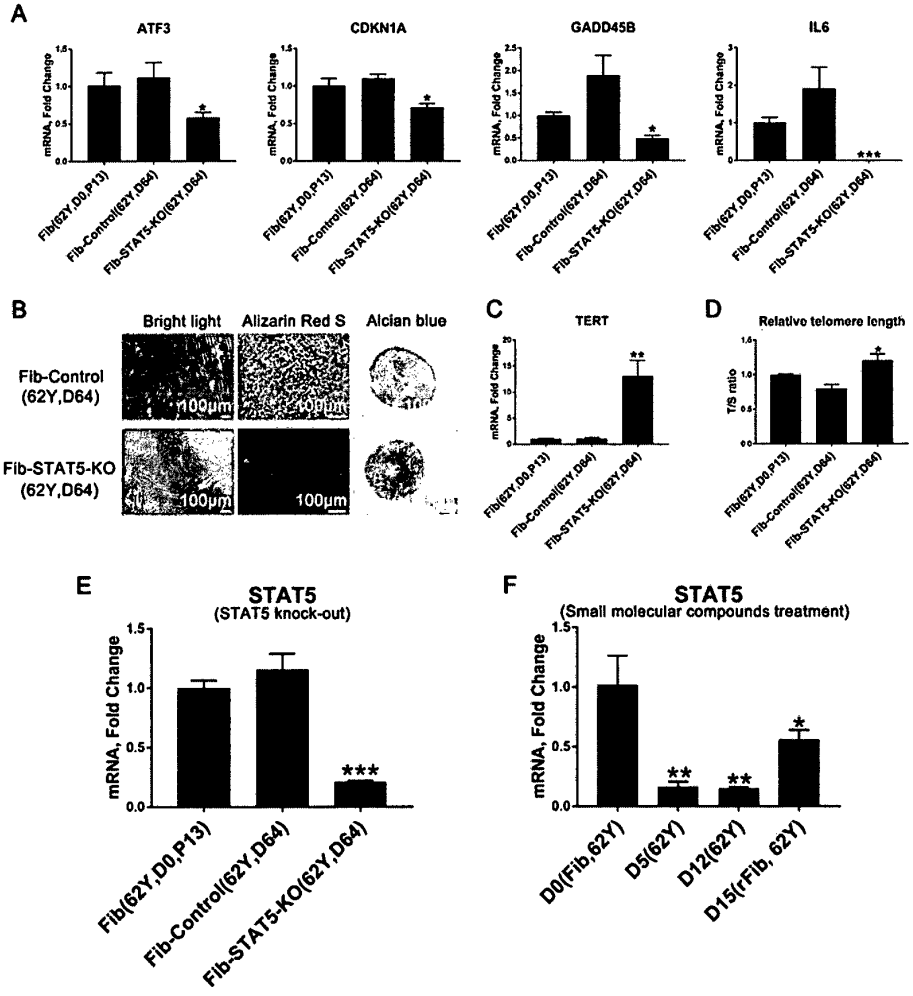

A
ATF3
CDKN1A
GADD45B
IL6
mRNA, Fold Change
Fib(62Y,D0,P13)
Fib-Control(62Y,D64)
Fib-STAT5-KO(62Y,D64)
B
Bright light
Alizarin Red S
Alcian blue
Fib-Control (62Y,D64)
Fib-STAT5-KO (62Y,D64)
100μm
C
TERT
D
Relative telomere length
T/S ratio
E
STAT5
(STAT5 knock-out)
F
STAT5
(Small molecular compounds treatment)
D0(Fib,62Y)
D5(62Y)
D12(62Y)
D15(rFib, 62Y)

图 10

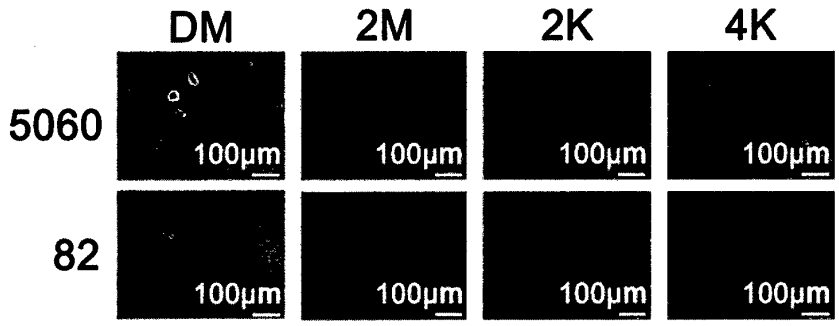

DM
2M
2K
4K
5060
82
100μm

图 11

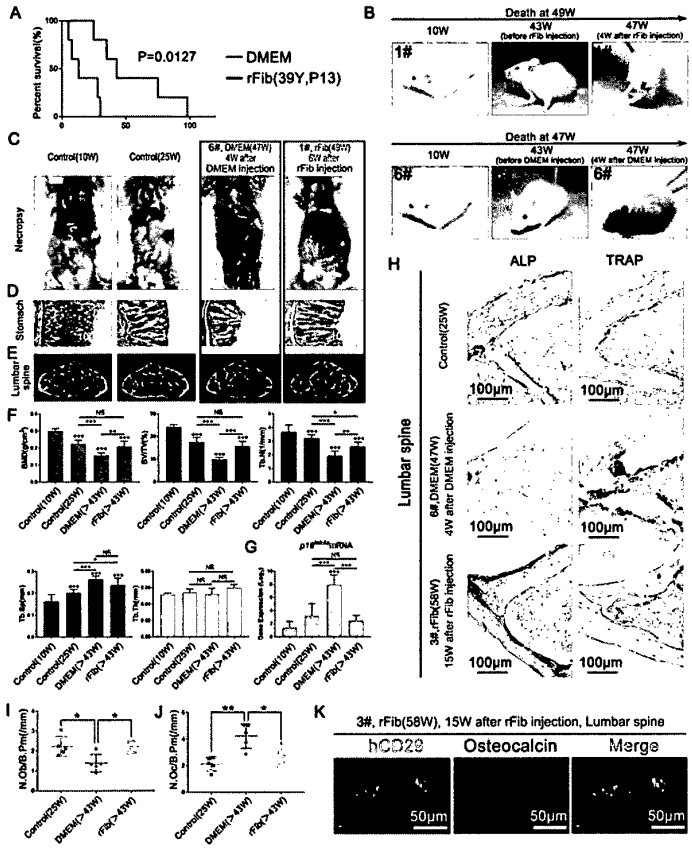

A
P=0.0127
— DMEM
— rFib(39Y,P13)
Percent survive(%)
B
Death at 49W
10W
43W
(before rFib injection)
47W
(4W after rFib injection)
1#
Death at 47W
10W
43W
(before DMEM injection)
47W
(4W after DMEM injection)
6#
C
Control(10W)
Control(25W)
6#, DMEM(47W)
4W after
DMEM injection
1#, rFib(49W)
6W after
rFib injection
Necropsy
D
Stomach
E
Lumbar spine
F
G
H
ALP
TRAP
Lumbar spine
Control(25W)
6#,DMEM(47W)
4W after DMEM injection
3#,rFib(58W)
15W after rFib injection
100μm
I
J
K
3#, rFib(58W), 15W after rFib injection, Lumbar spine
hCD29
Osteocalcin
Merge
50μm

图 12

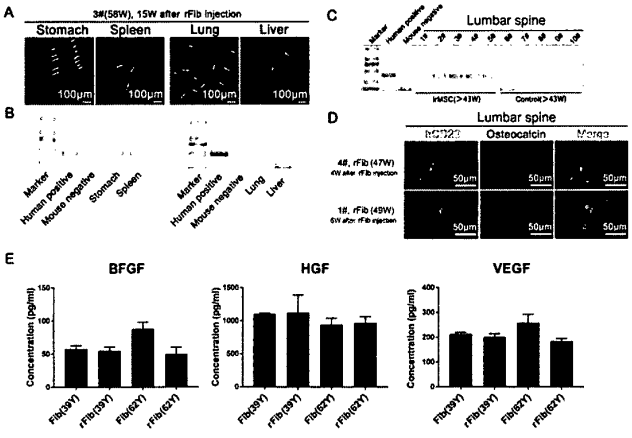

A
3#(58W), 15W after rFib injection
Stomach
Spleen
Lung
Liver
100μm
B
Marker
Human positive
Mouse negative
Stomach
Spleen
Lung
Liver
C
Lumbar spine
hMSC(>43W)
Control(>43W)
D
Lumbar spine
hCD29
Osteocalcin
Merge
4#, rFib (47W)
4W after rFib injection
1#, rFib (49W)
6W after rFib injection
50μm
E
BFGF
HGF
VEGF
Concentration (pg/ml)
rFib(39Y)
rFib(58Y)
rFib(62Y)

图 13

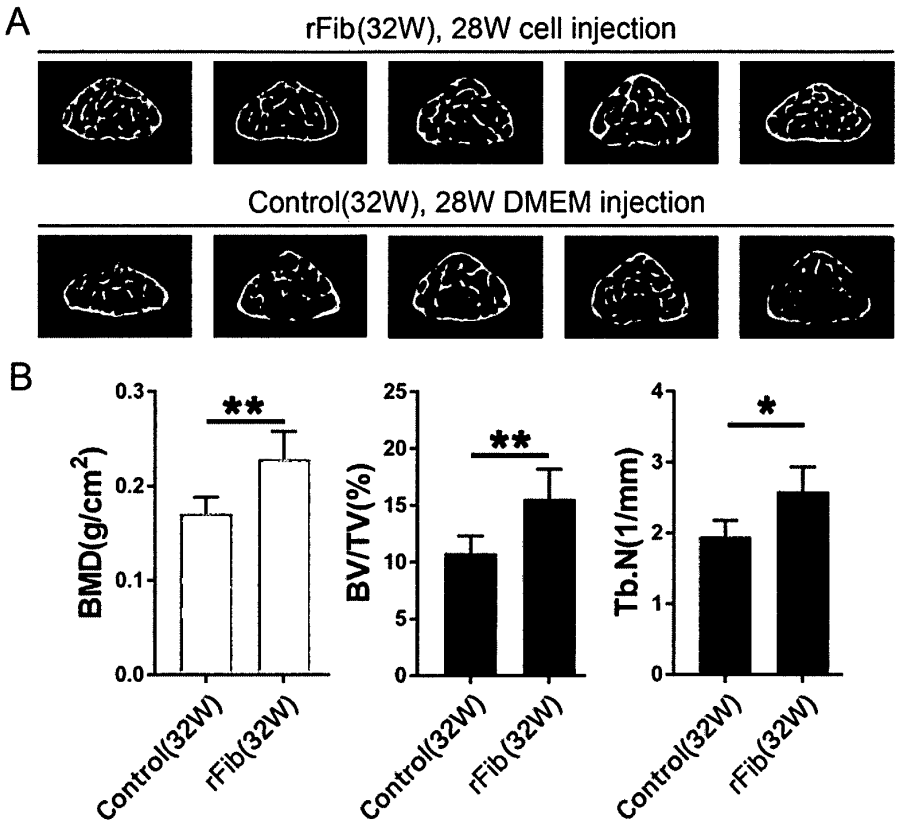

A
rFib(32W), 28W cell injection
Control(32W), 28W DMEM injection
B
BMD(g/cm²)
BV/TV(%)
Tb.N(1/mm)
**
**
*
Control(32W)
rFib(32W)

图 14

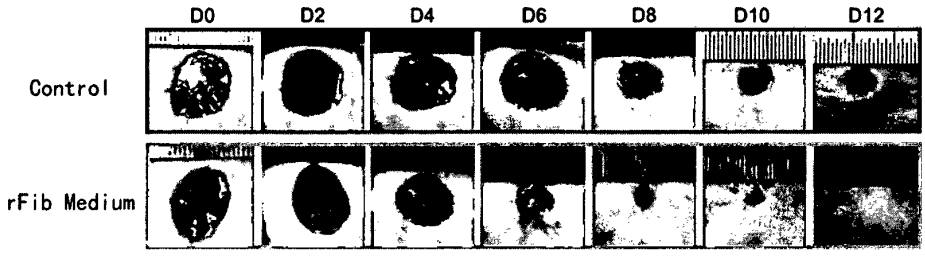

D0
D2
D4
D6
D8
D10
D12
Control
rFib Medium

图 15

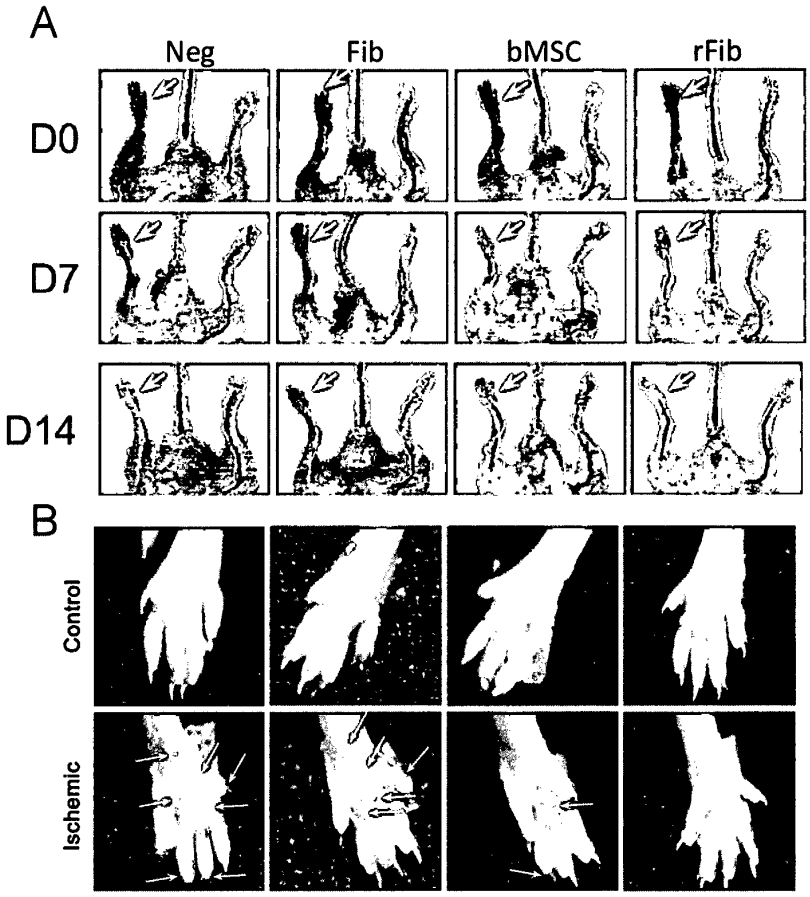

A
Neg
Fib
bMSC
rFib
D0
D7
D14
B
Control
Ischemic

图 16

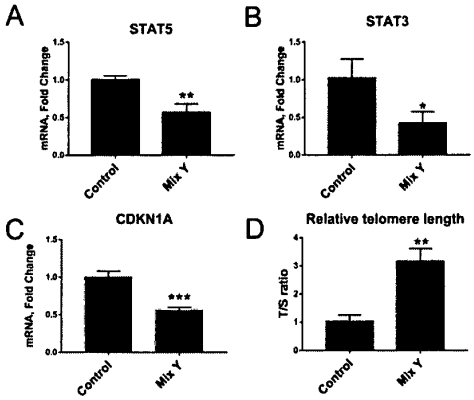

A
STAT5
mRNA, Fold Change
Control
Mix Y
B
STAT3
C
CDKN1A
D
Relative telomere length
T/S ratio

图 17

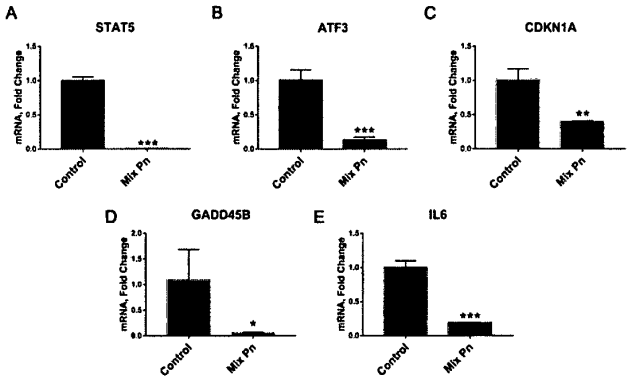


图 18

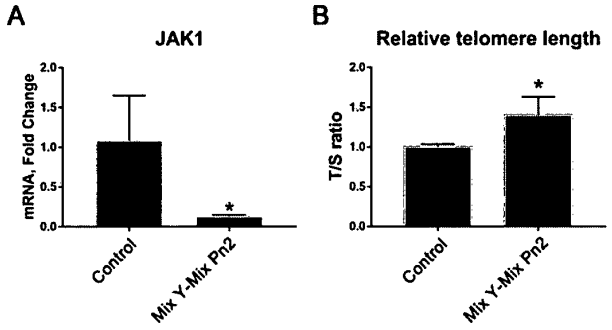


图 19

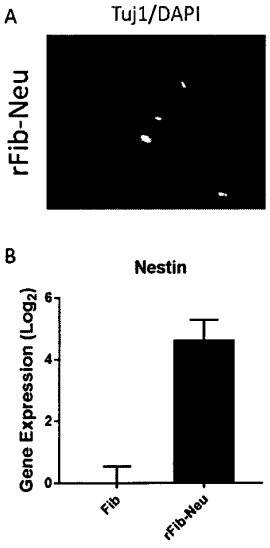


图 20

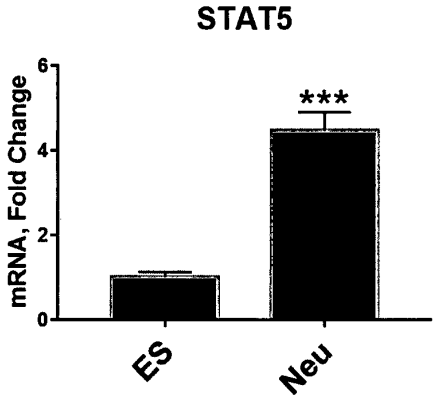


图 21

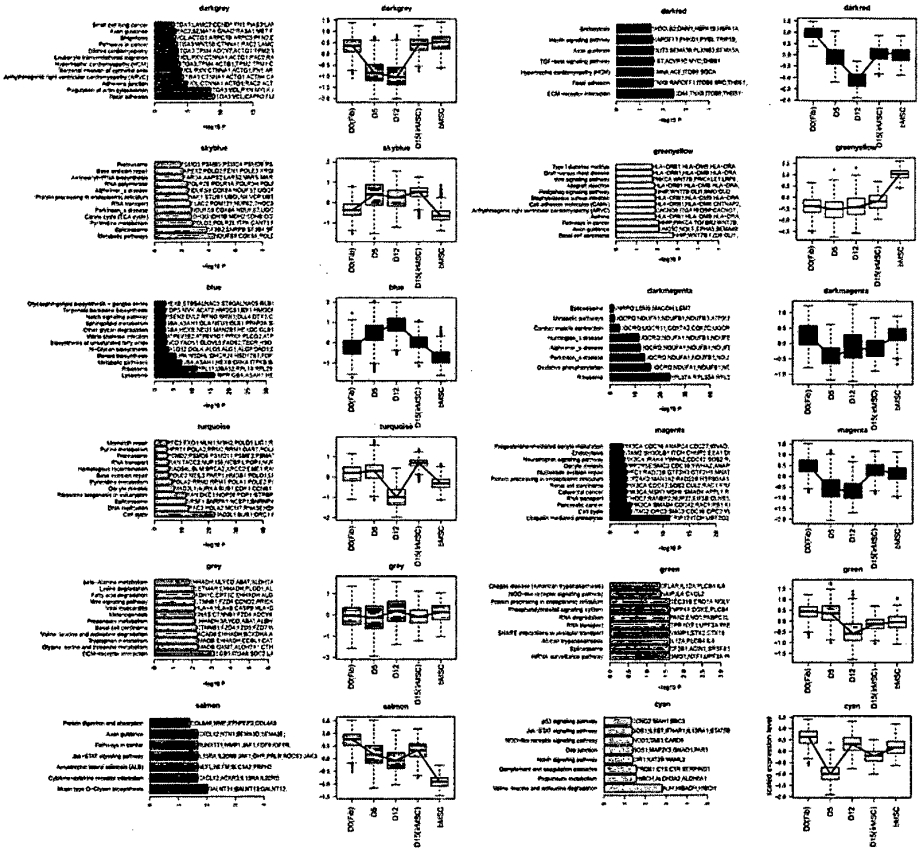


图 22