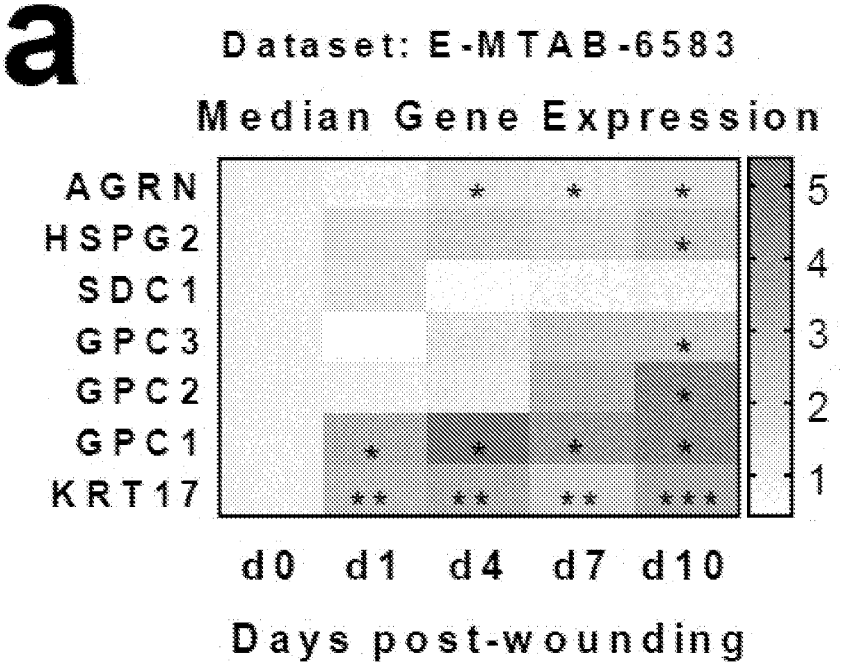
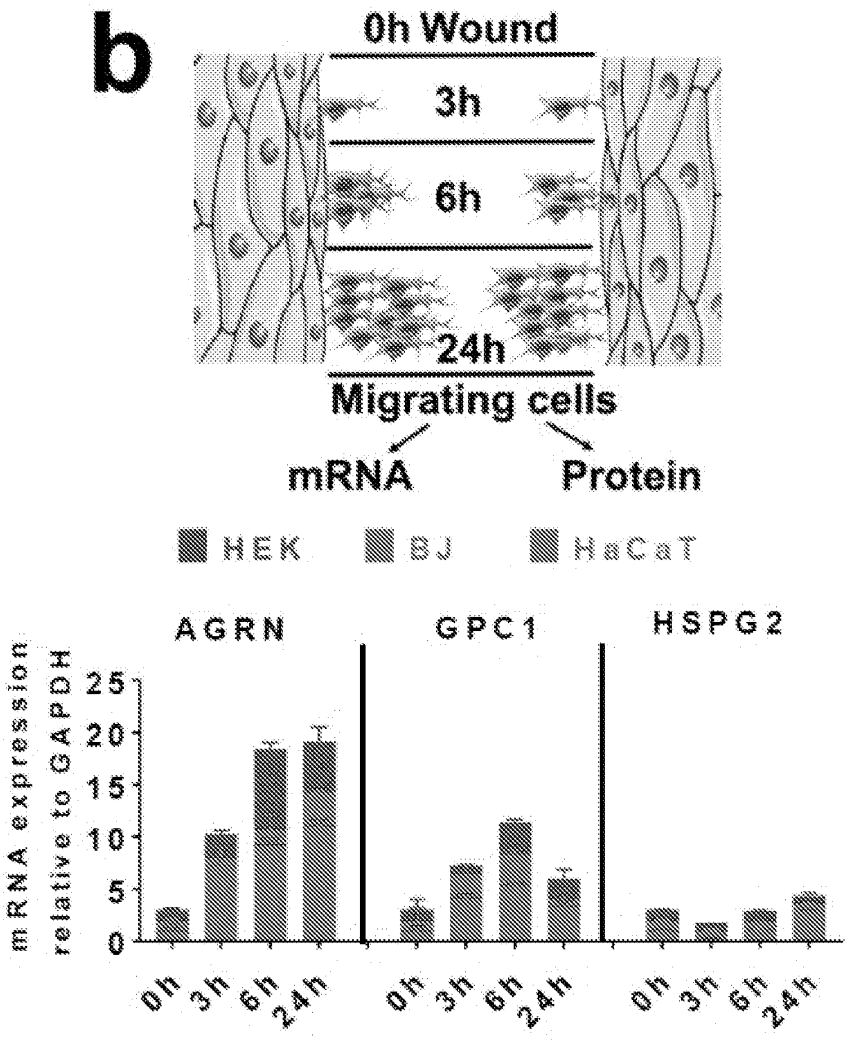

a
Dataset: E-MTAB-6583
Median Gene Expression
AGRN
HSPG2
SDC1
GPC3
GPC2
GPC1
KRT17
5
4
3
2
1
d0 d1 d4 d7 d10
Days post-wounding

Fig. 1



AGRN	0h vs 3h	0h vs 6h	0h vs 24h
HaCaT	0.00531	4.27E-05	2.16E-05
BJ	0.90778	0.545148	0.0001723
HEK	0.00576	4.77E-05	0.0092186
GPC1	**0h vs 3h**	**0h vs 6h**	**0h vs 24h**
HaCaT	0.00029	9.77E-05	0.0069739
BJ	0.20482	0.040578	0.8884021
HEK	0.75763	0.032549	0.352612
HSPG2	**0h vs 3h**	**0h vs 6h**	**0h vs 24h**
HaCaT	3.7E-05	0.15142	1.161E-06
BJ	0.25015	0.027334	0.0128924
HEK	0.00011	0.023829	0.1345741

Fig. 1 (Continued)

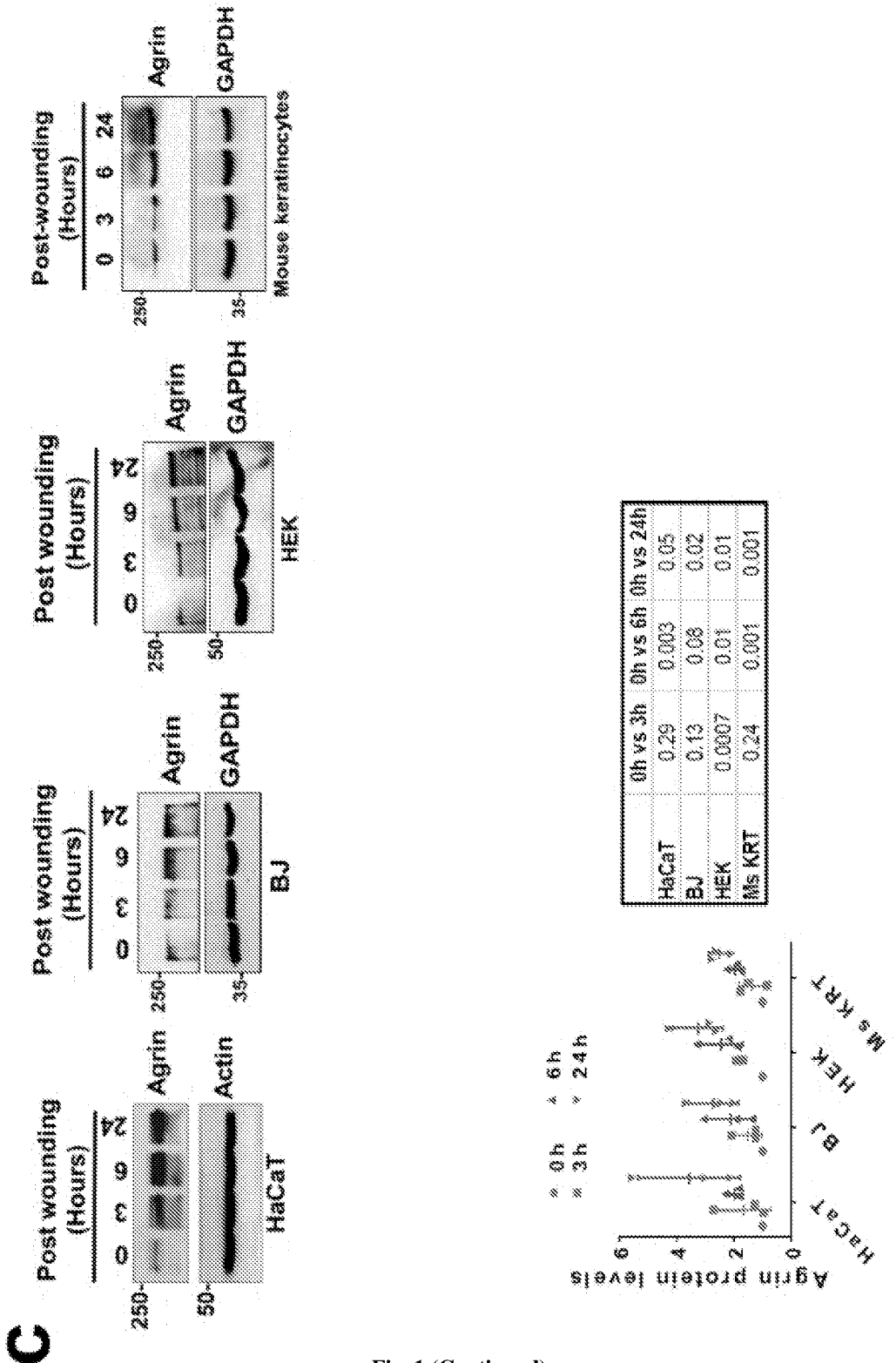


Fig. 1 (Continued)

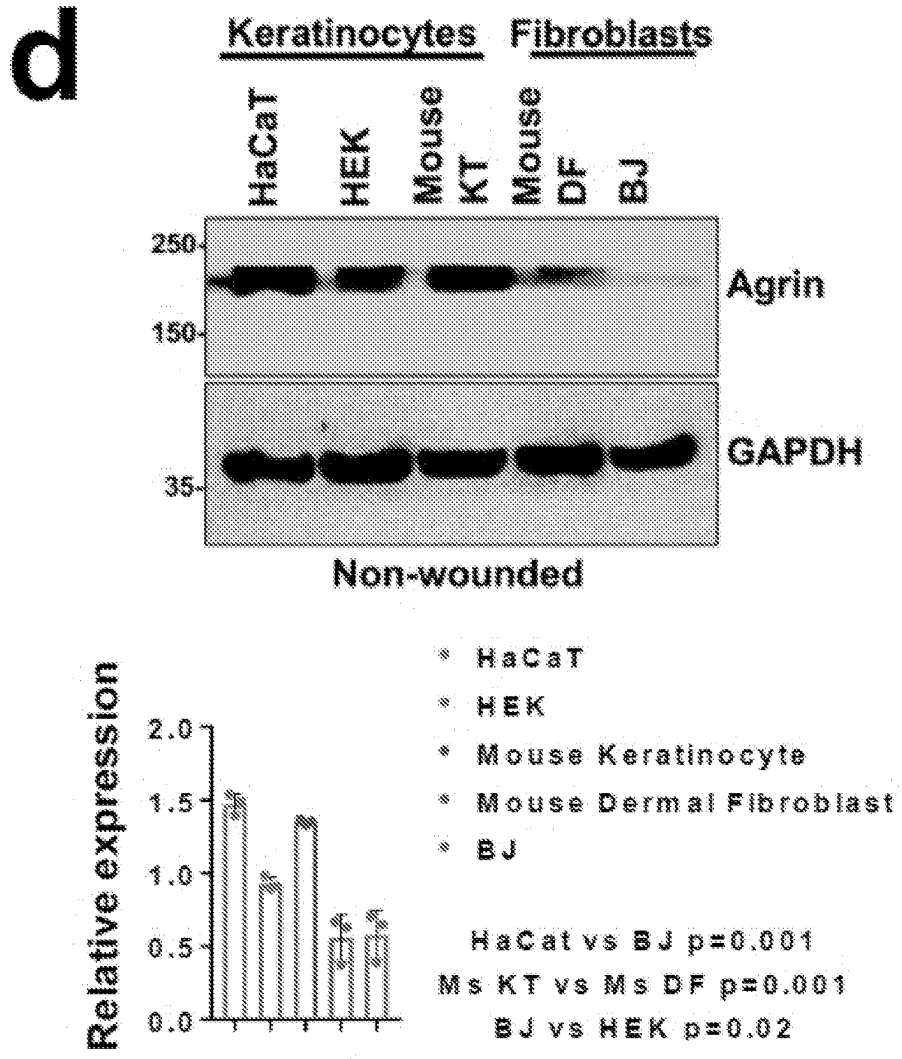


Fig. 1 (Continued)

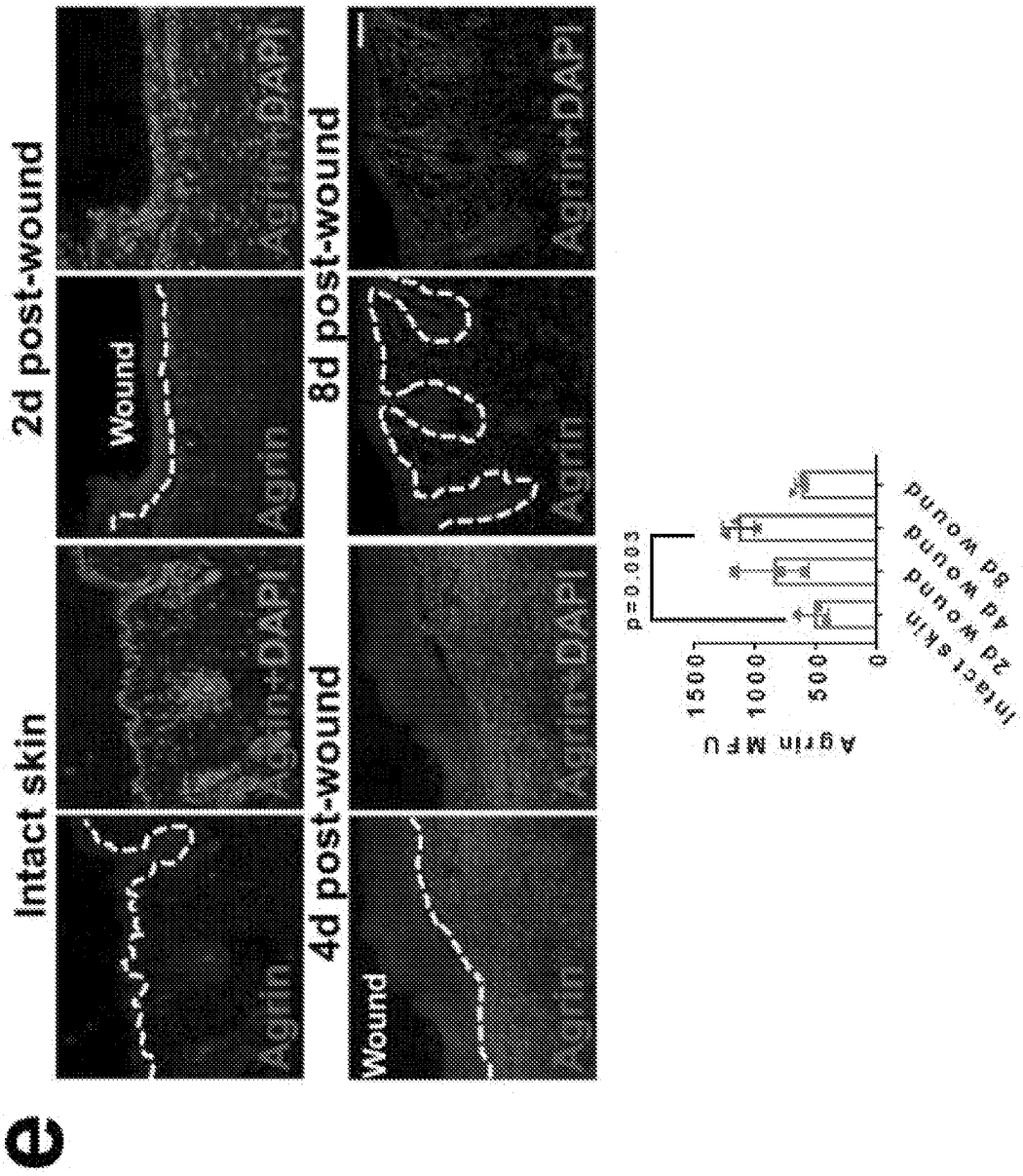
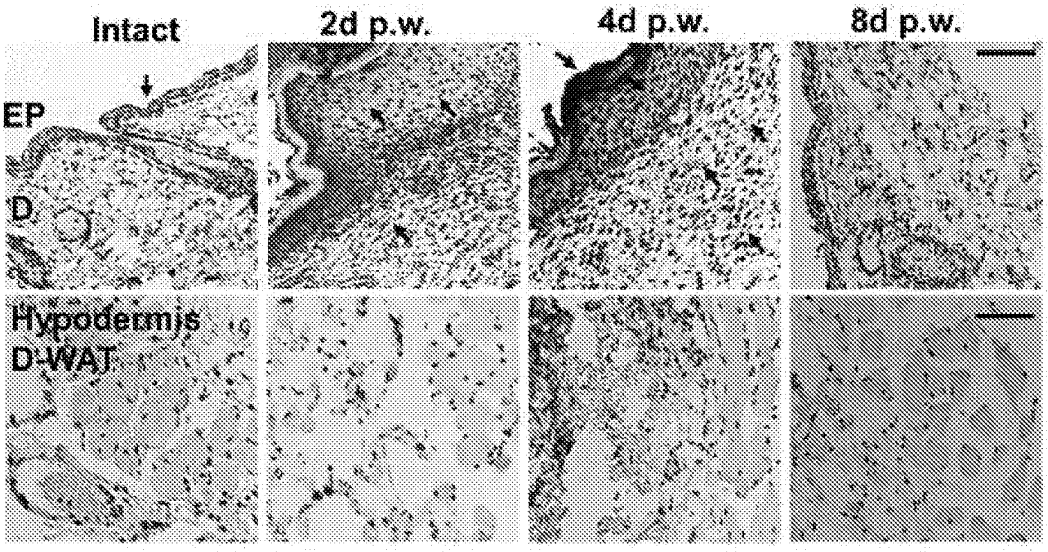
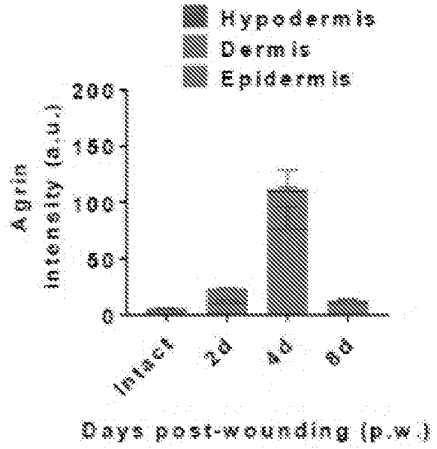


Fig. 1 (Continued)

f





EP intact vs 2d vs 4d	0.0002
D intact vs 2d vs 4d	0.04
Hypodermis intact vs 2d vs 4d	ns
EP vs D vs Hypodermis	0.0001

Fig. 1 (Continued)

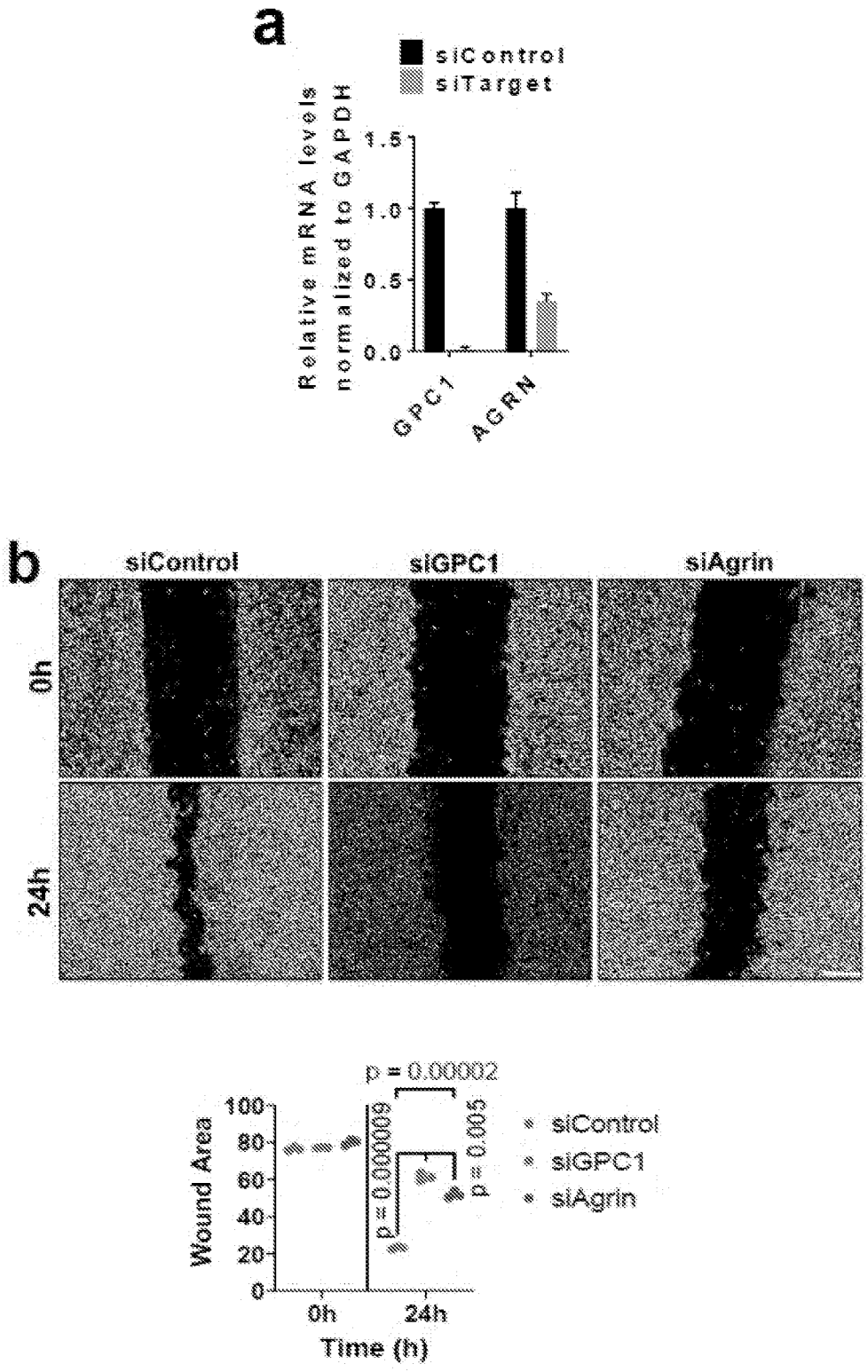

a
siControl
siTarget
Relative mRNA levels normalized to GAPDH
1.5
1.0
0.5
0.0
GPC1
AGRN
b
siControl
siGPC1
siAgrin
0h
24h
p = 0.00002
p = 0.000009
p = 0.005
Wound Area
100
80
60
40
20
0
0h
24h
Time (h)
siControl
siGPC1
siAgrin

Fig. 2

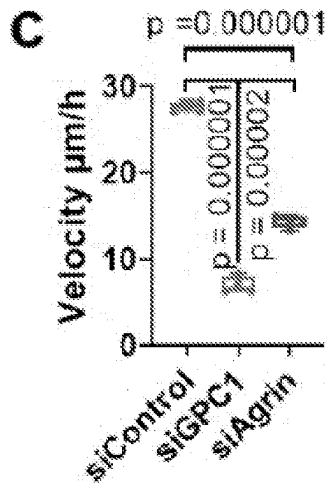


Fig. 2 (Continued)

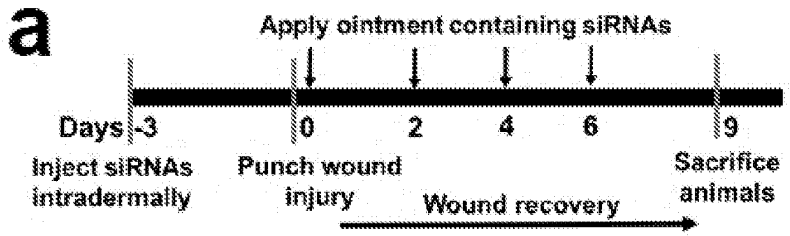


Fig. 3

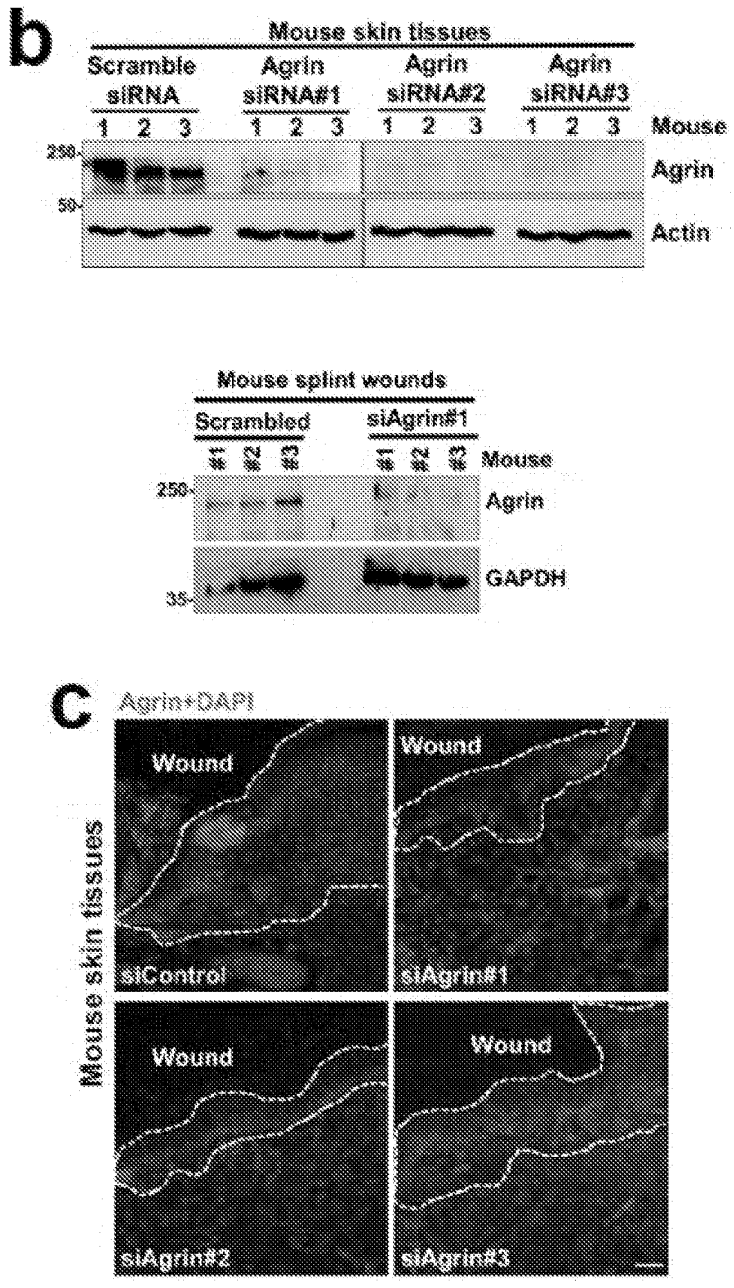


Fig. 3 (Continued)

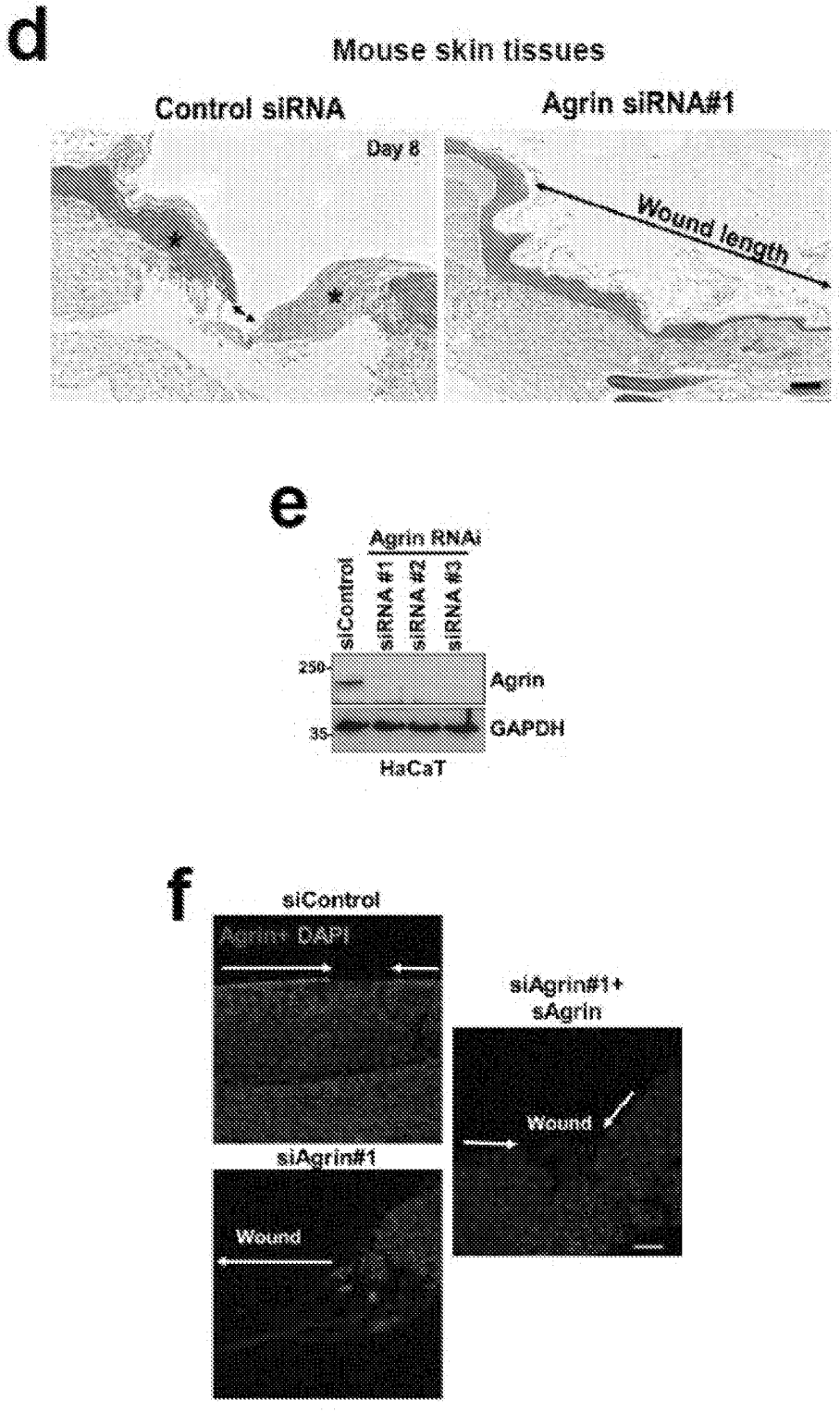


Fig. 3 (Continued)

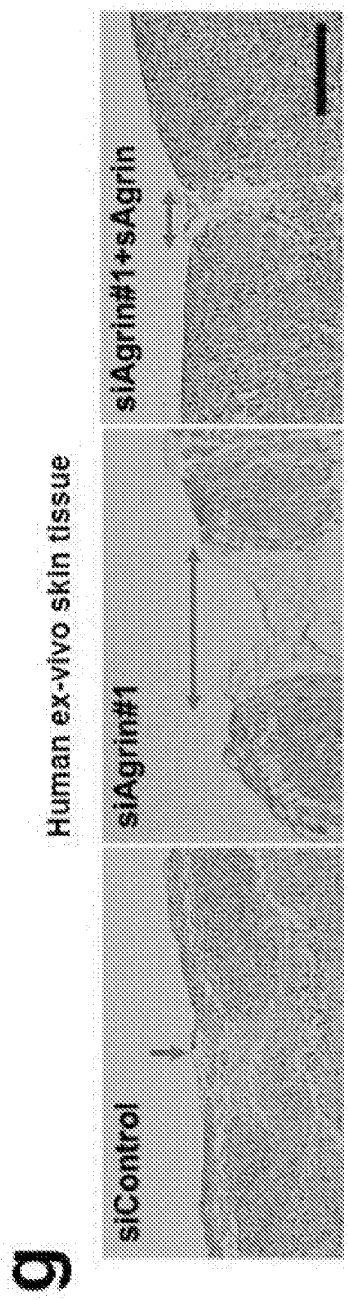
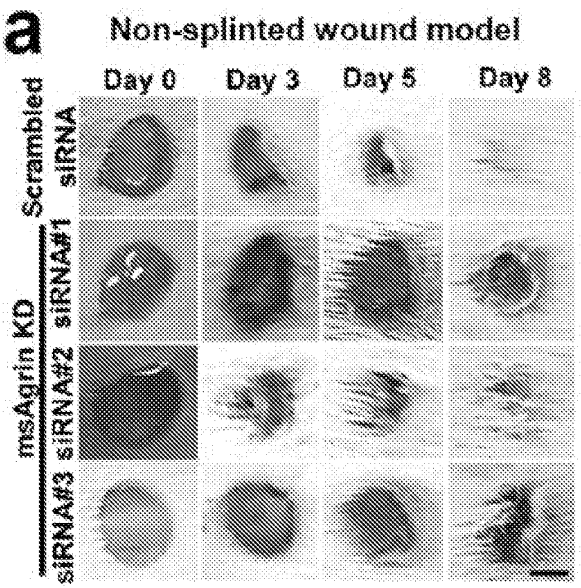


Fig. 3 (Continued)


a
Non-splinted wound model
Day 0
Day 3
Day 5
Day 8
msAgrin KD
Scrambled siRNA
siRNA#1
siRNA#2
siRNA#3

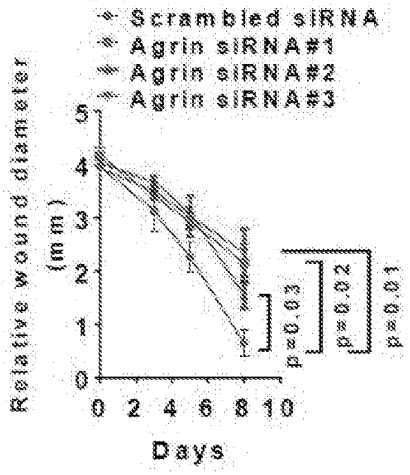

Scrambled siRNA
Agrin siRNA#1
Agrin siRNA#2
Agrin siRNA#3
Relative wound diameter (mm)
0
1
2
3
4
5
0 2 4 6 8 10
Days
p = 0.03
p = 0.02
p = 0.01

Fig. 4

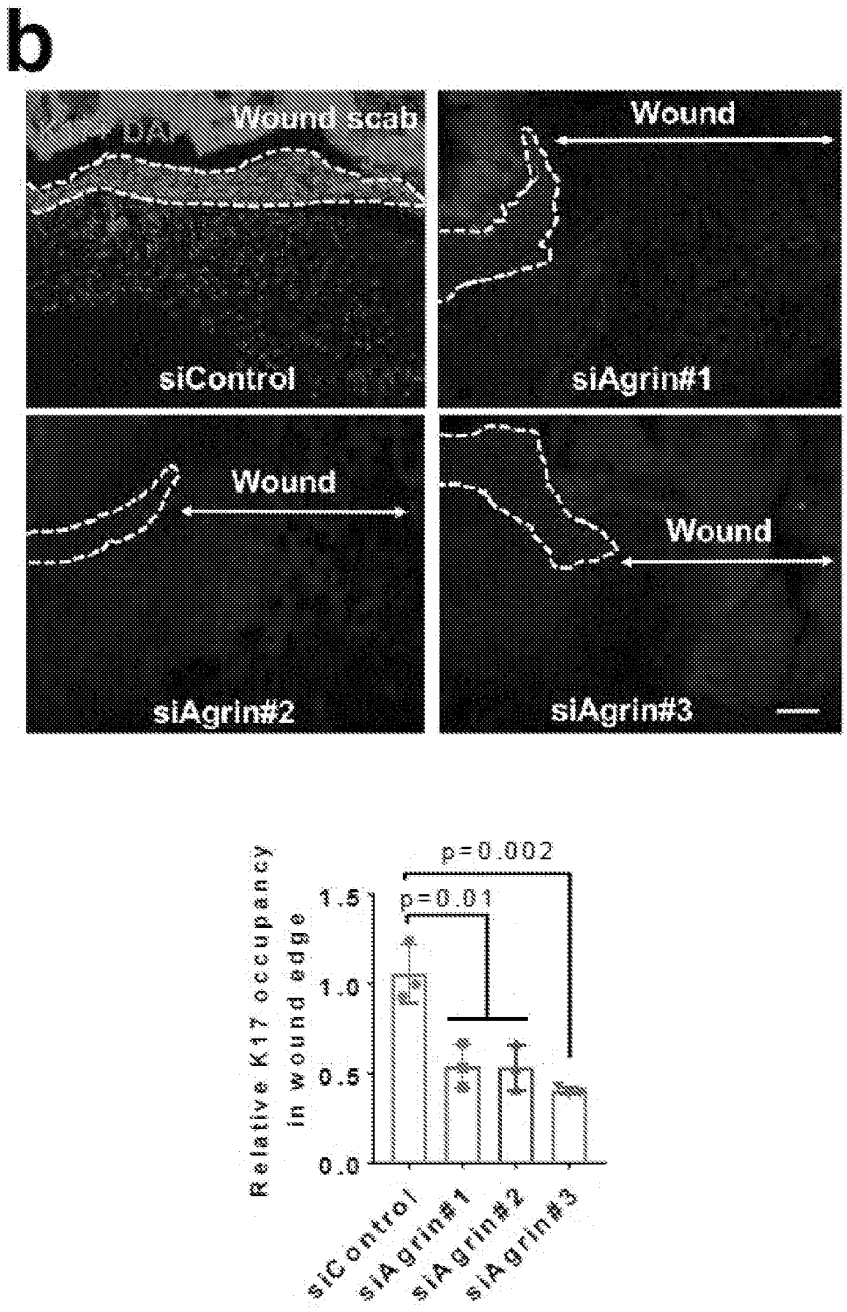


Fig. 4 (Continued)

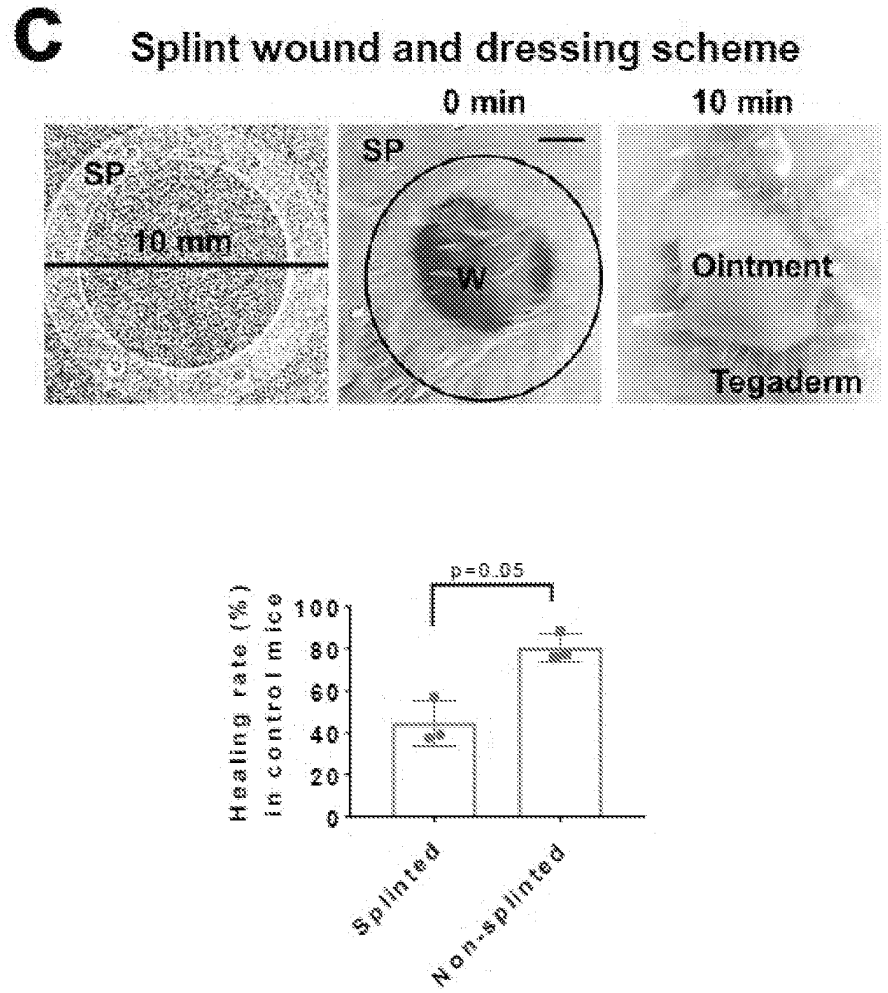


Fig. 4 (Continued)

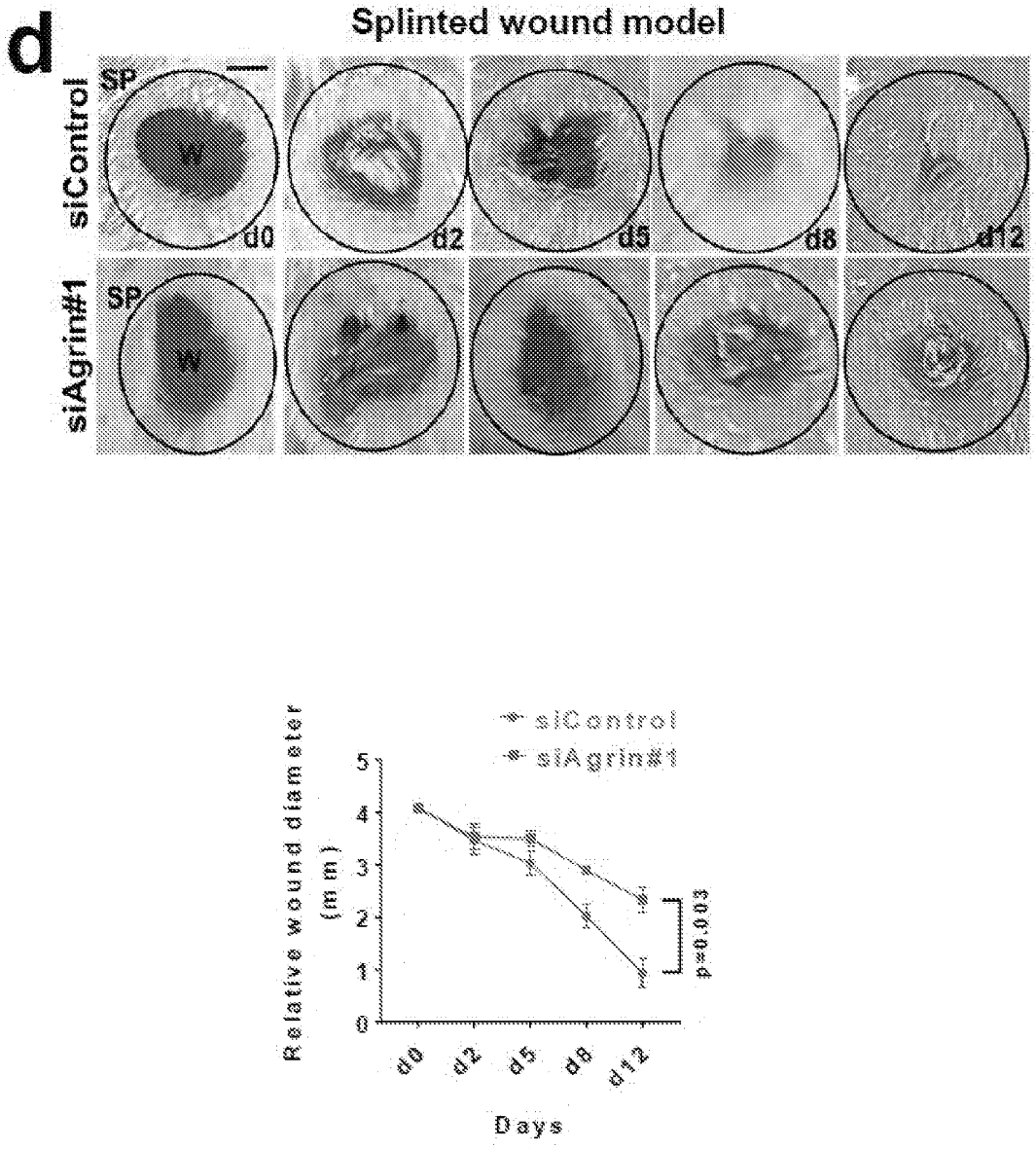


Fig. 4 (Continued)

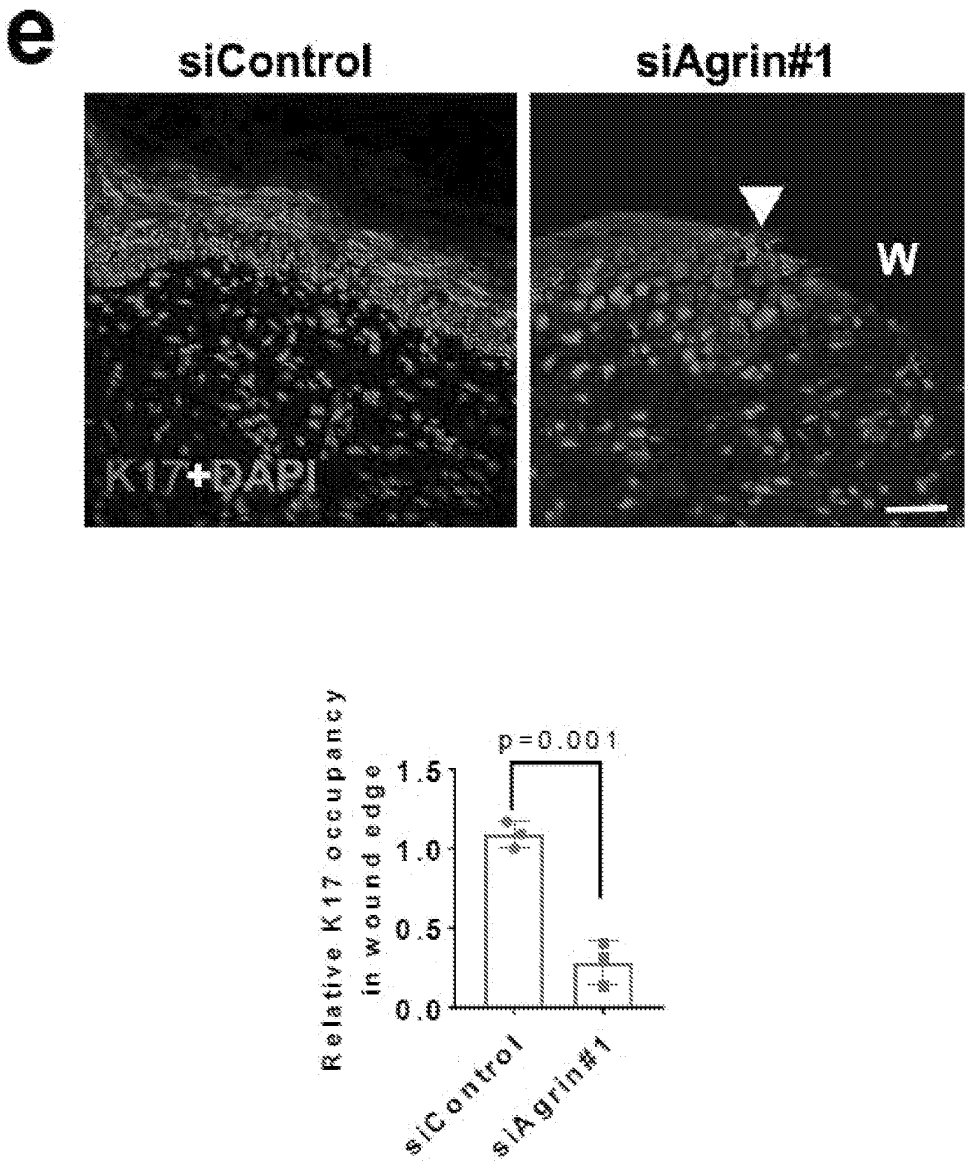


Fig. 4 (Continued)

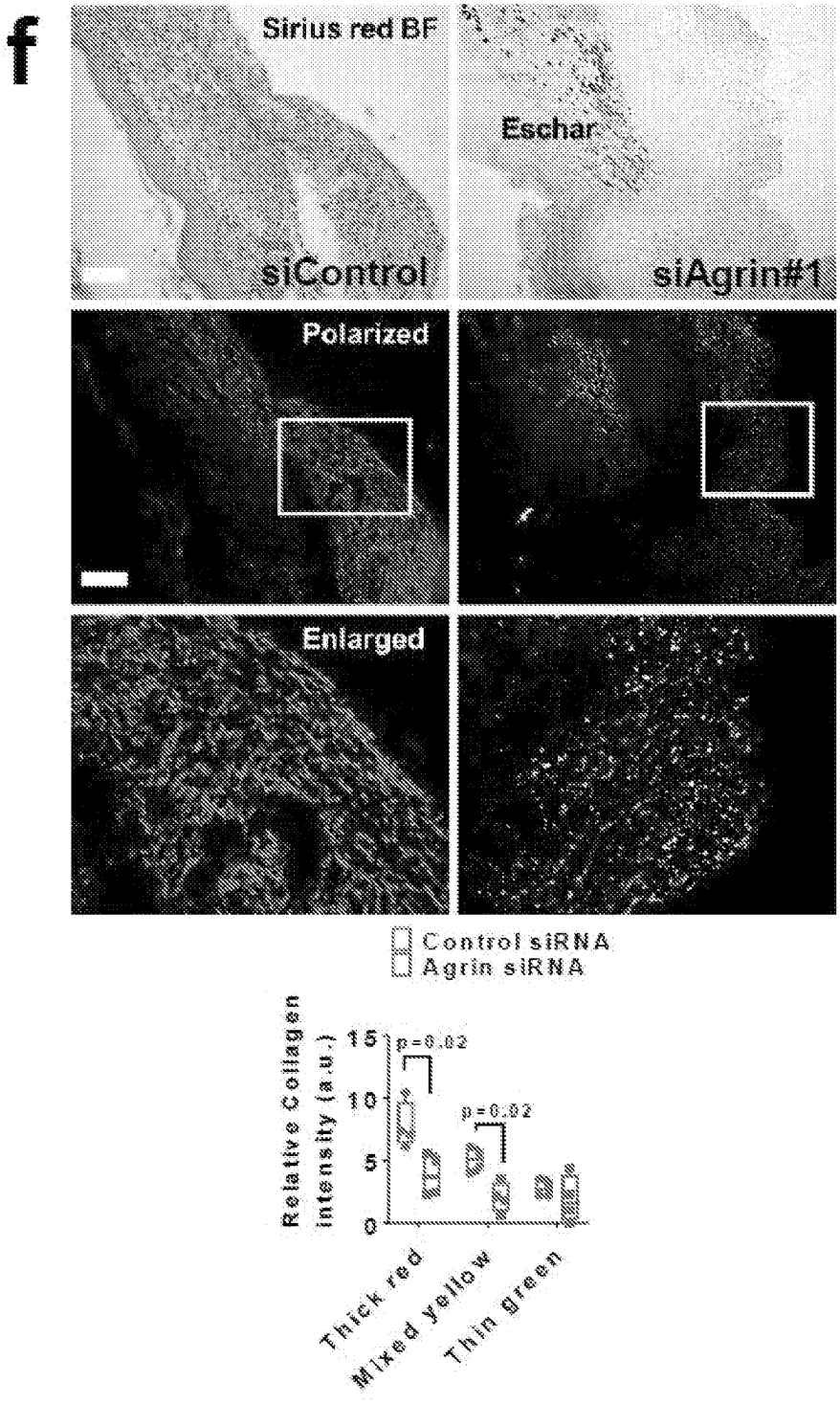


Fig. 4 (Continued)

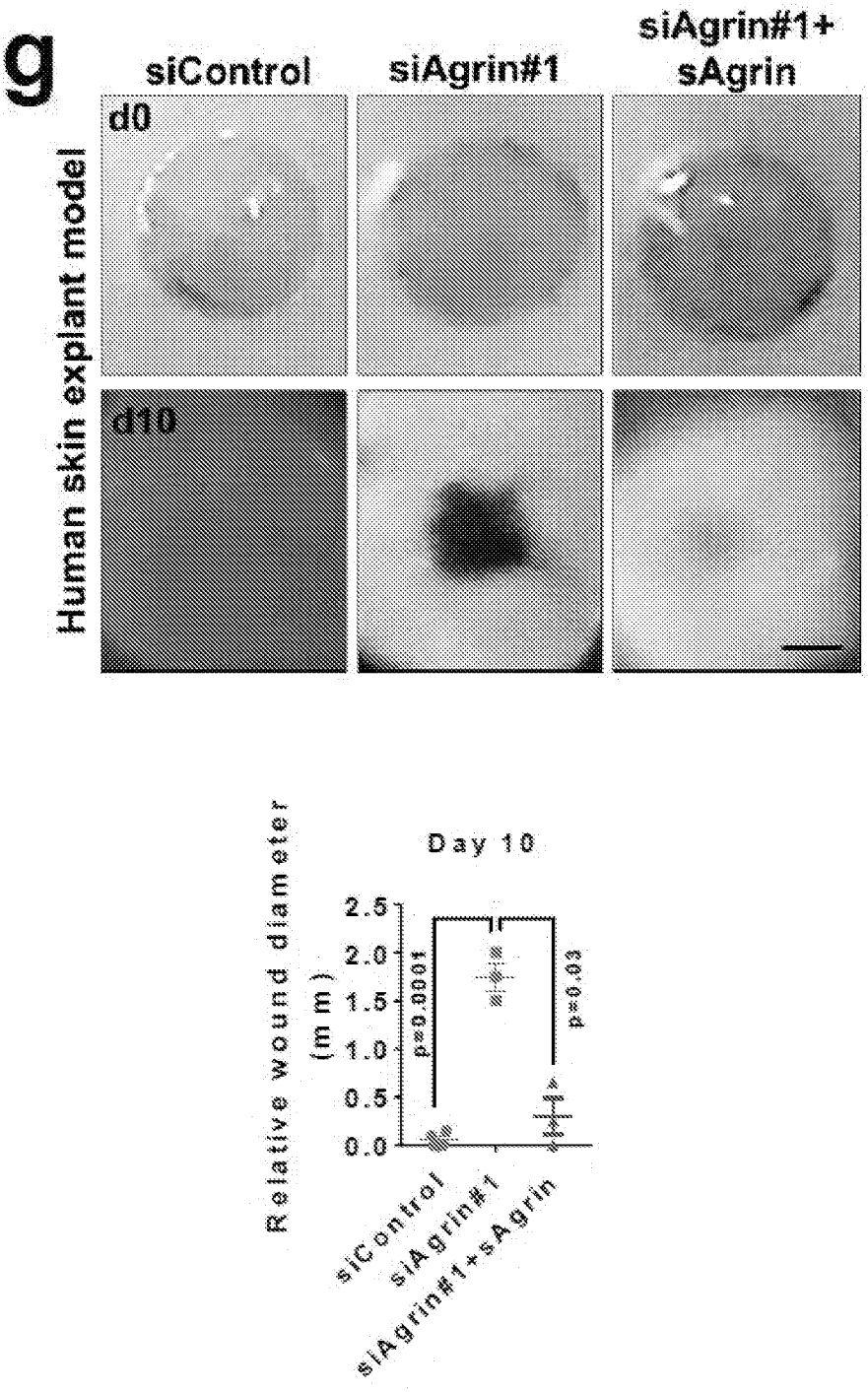


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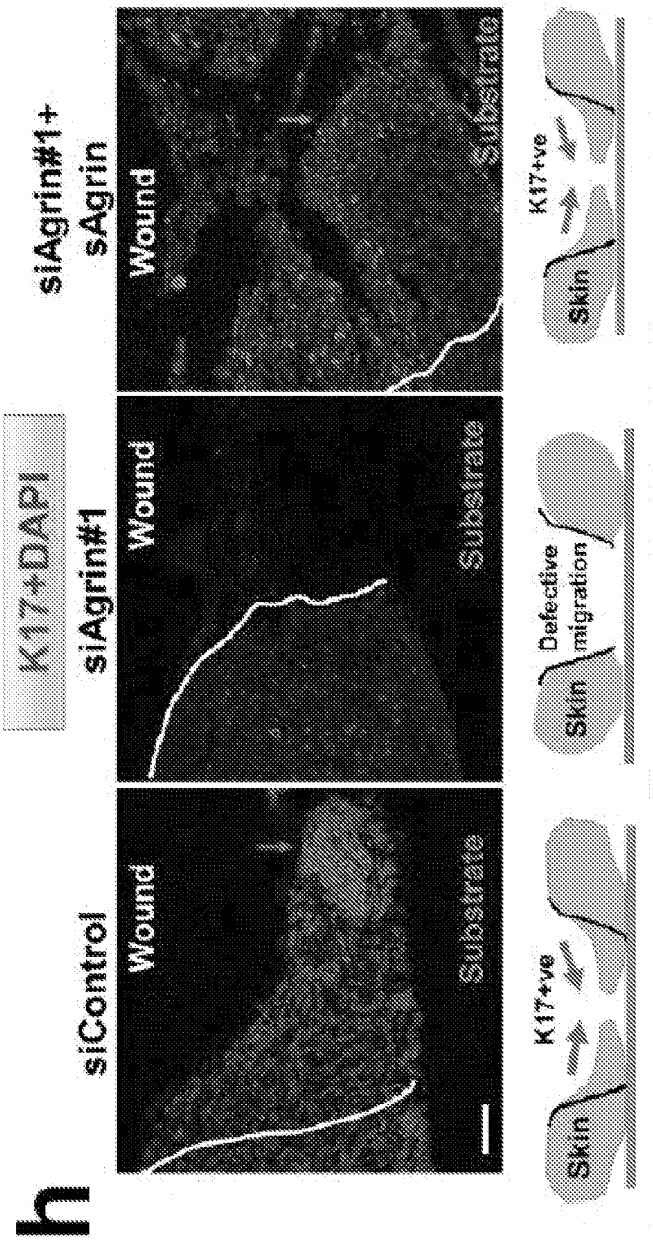


Fig. 4 (Continued)

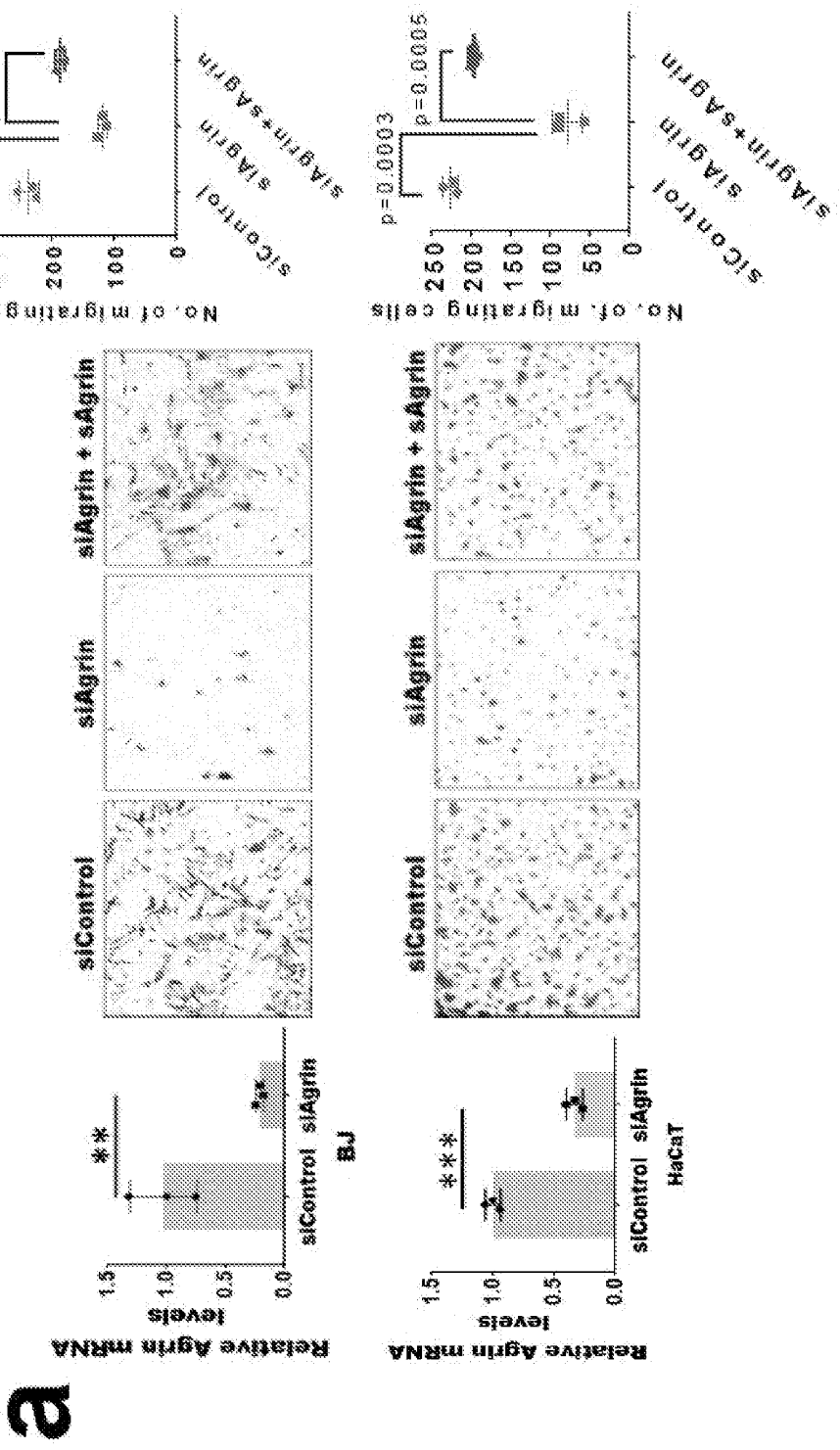
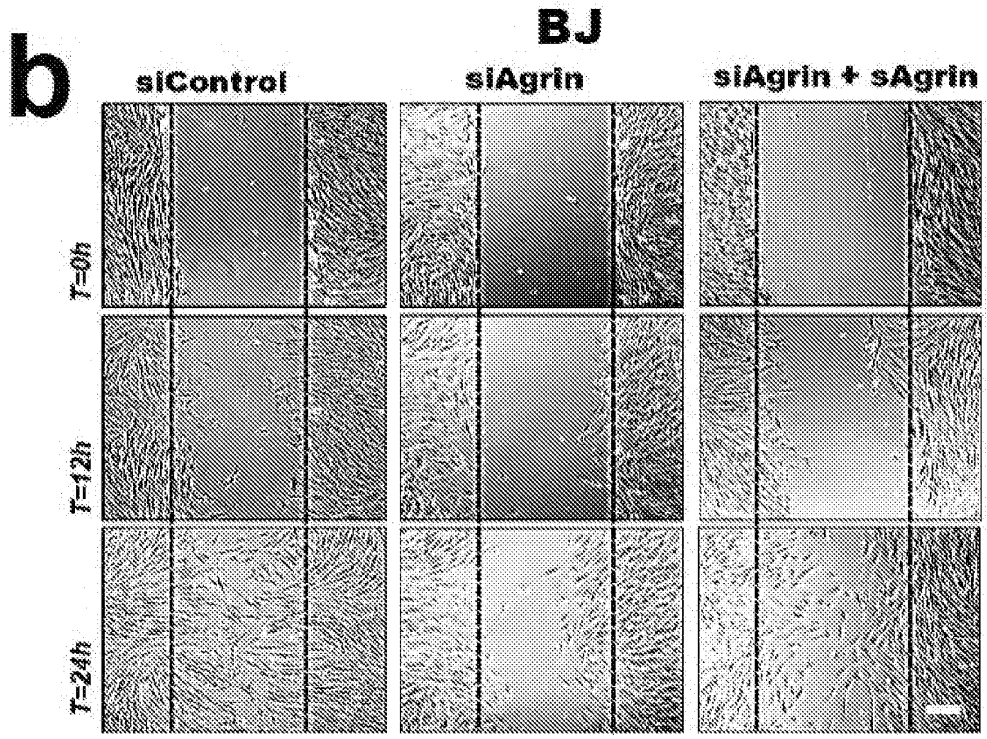

a
Relative Agrin mRNA levels
siControl
siAgrin
siAgrin + sAgrin
BJ
HaCaT
No. of migrating cells
p=0.0003
p=0.0004
p=0.0005

Fig. 5



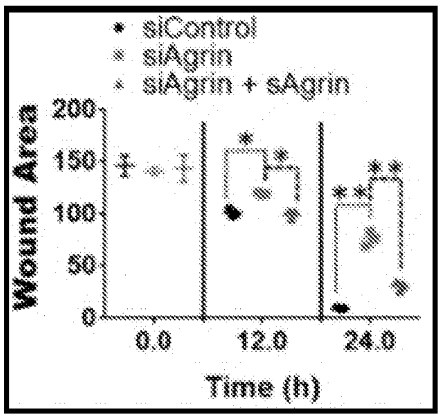


Fig. 5 (Continued)

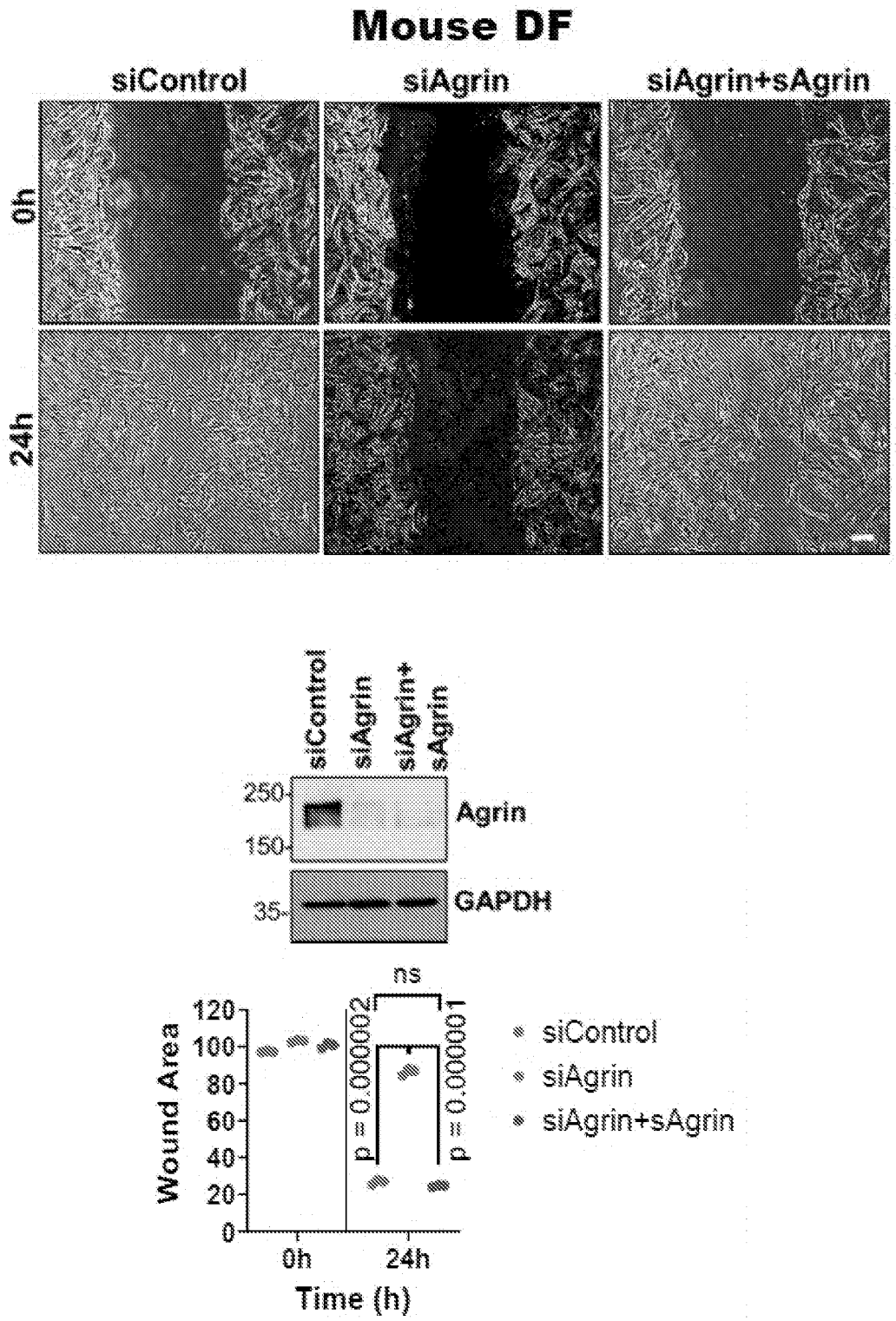


Fig. 5 (Continued)

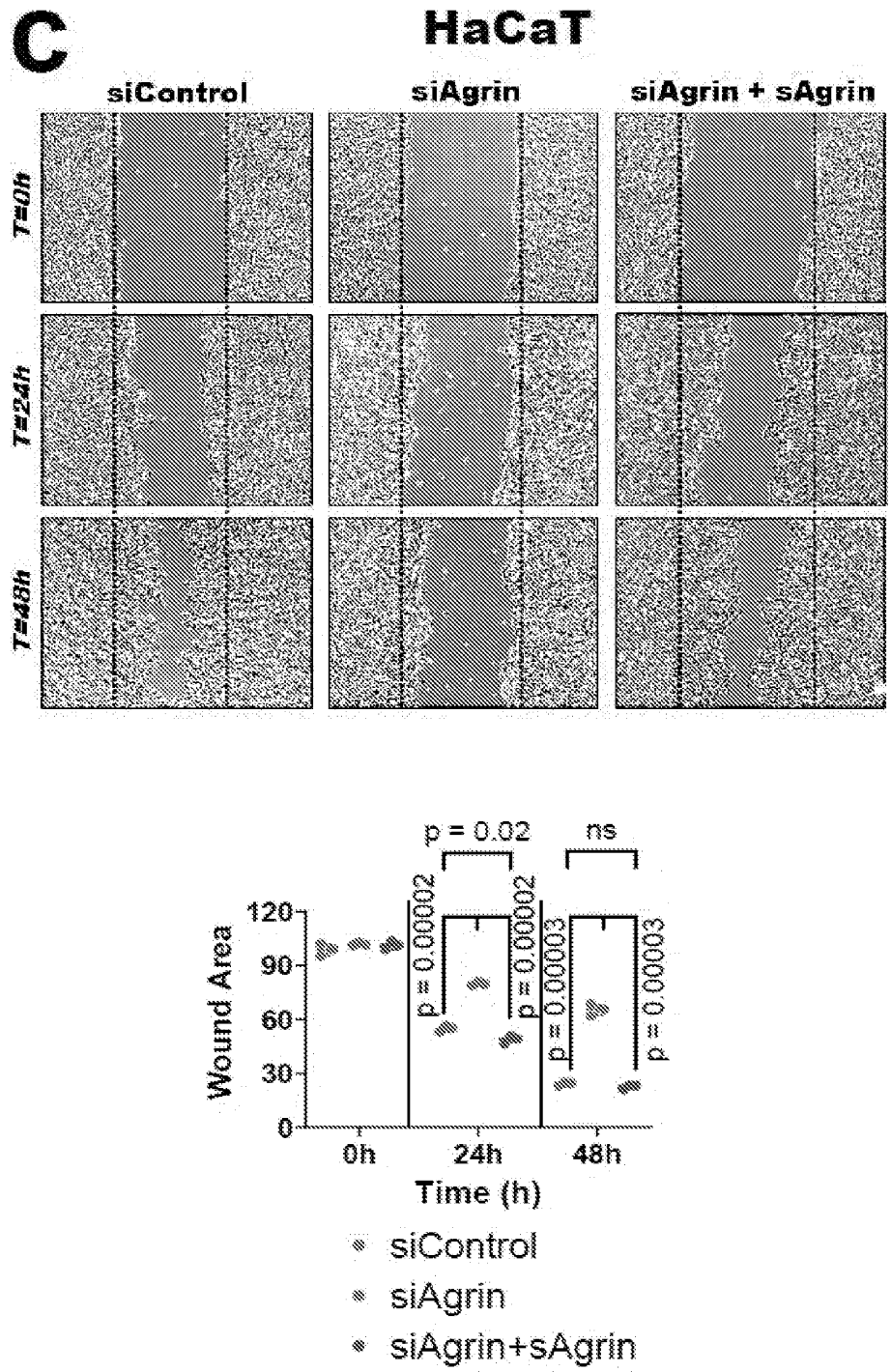


Fig. 5 (Continued)

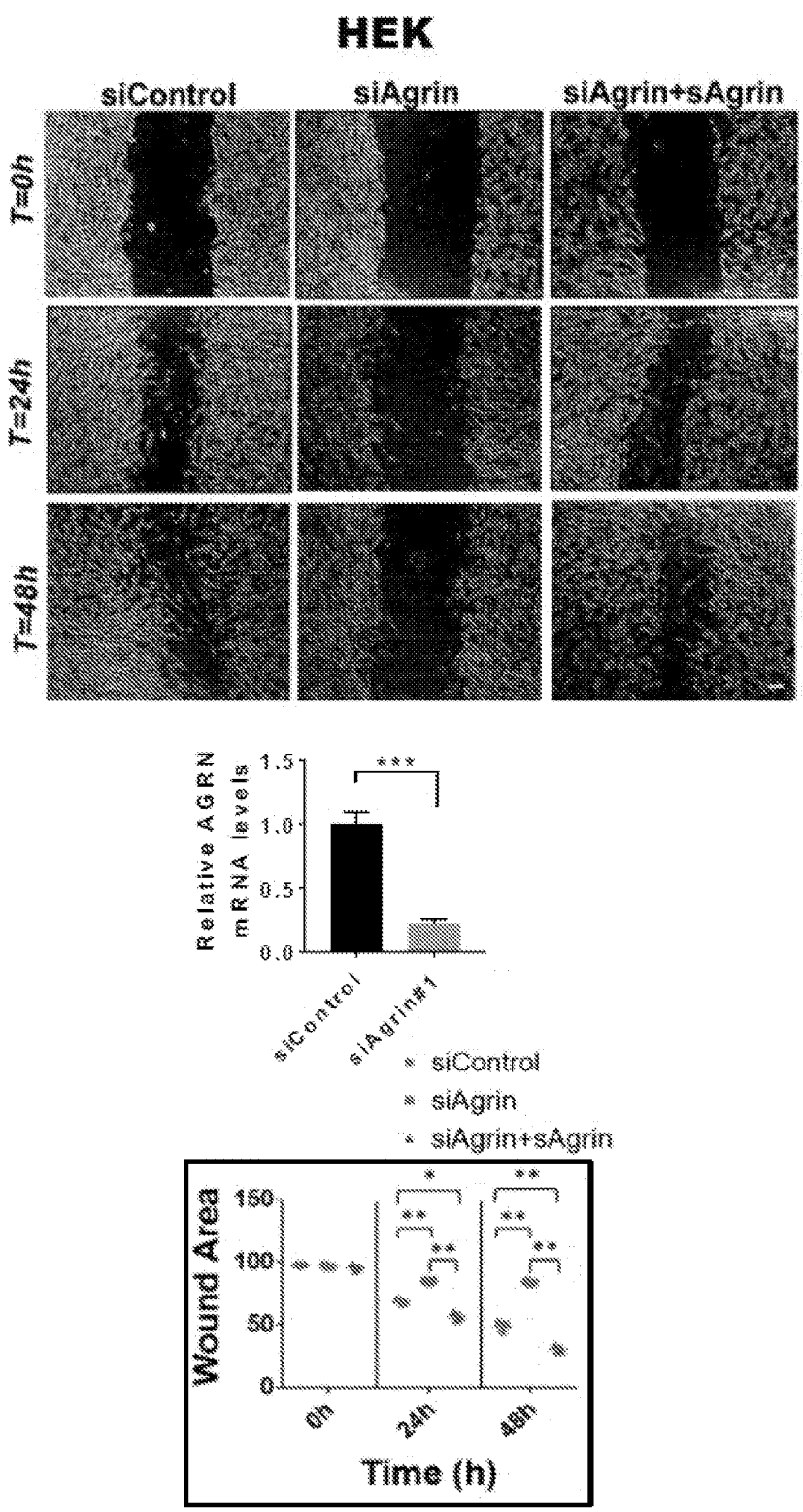


Fig. 5 (Continued)

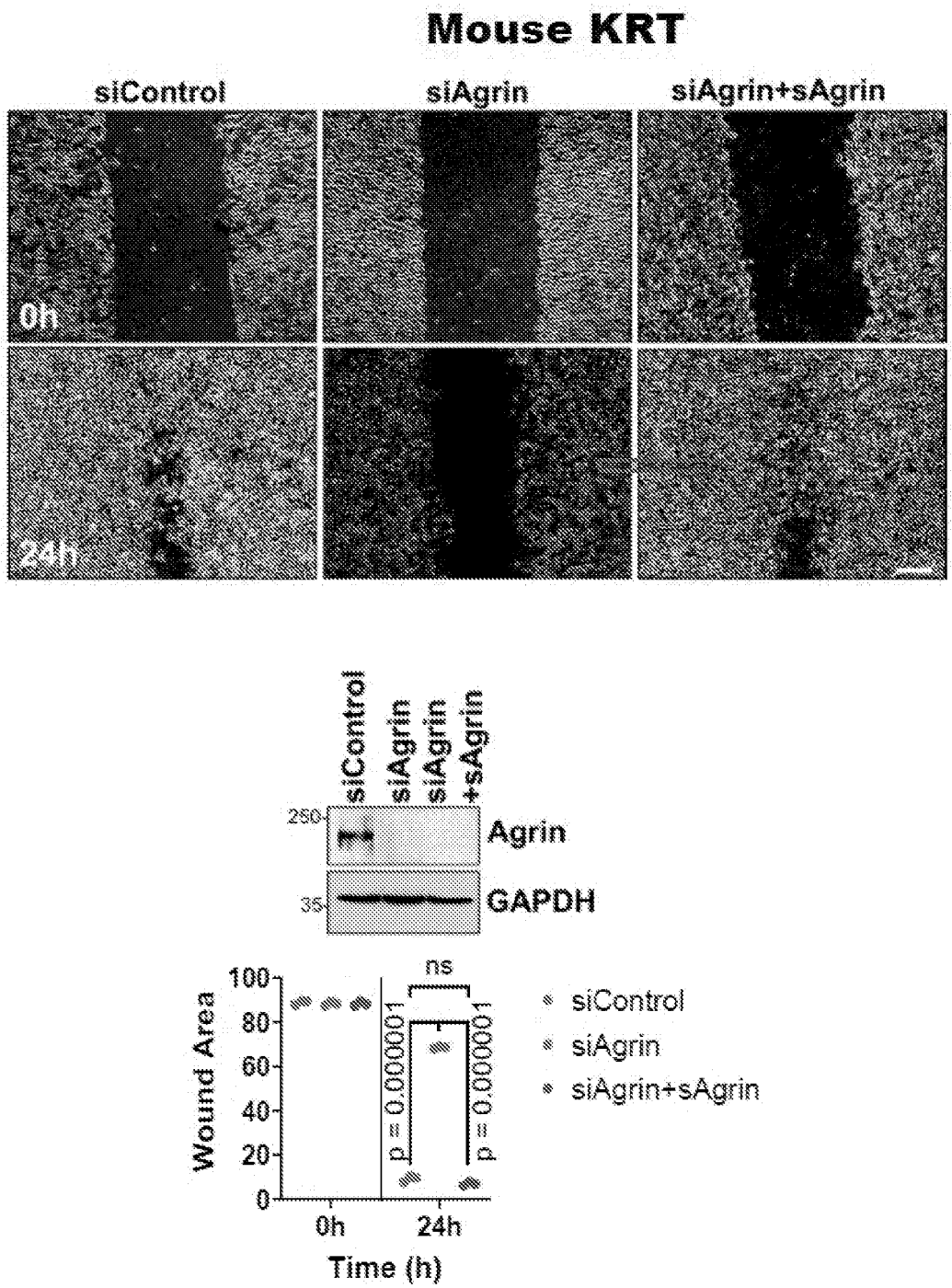


Fig. 5 (Continued)

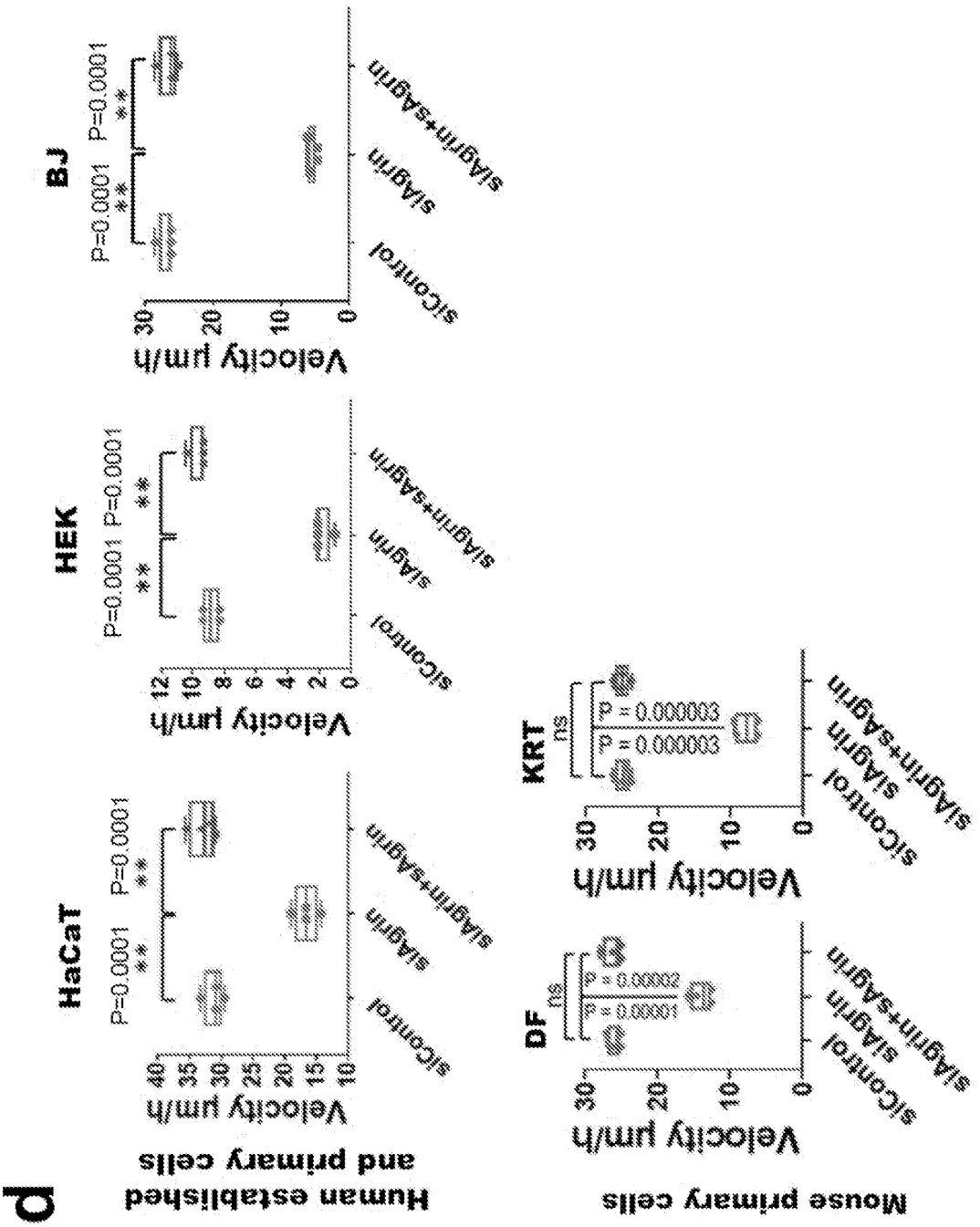


Fig. 5 (Continued)

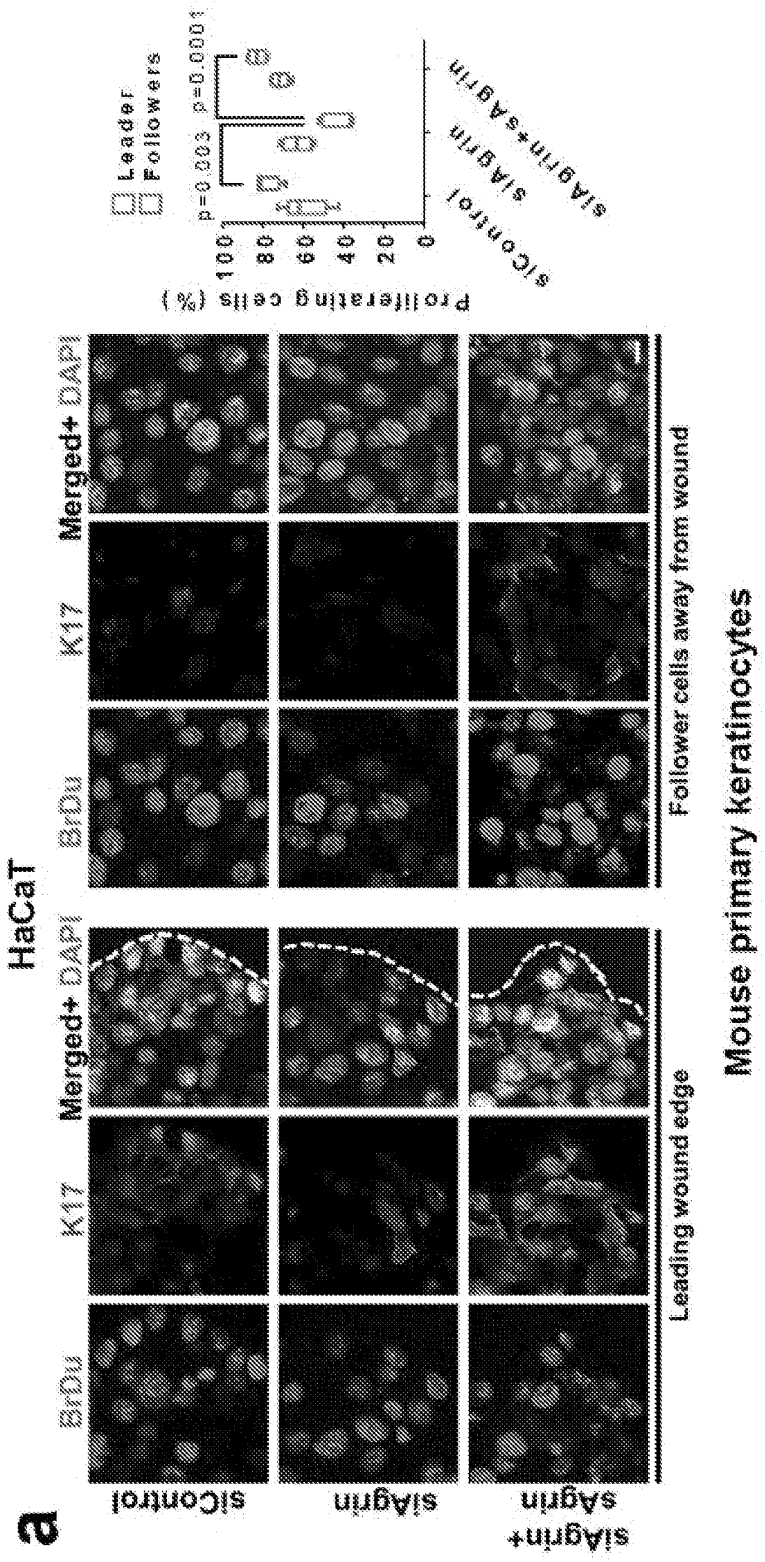

a
HaCaT
Mouse primary keratinocytes
siControl
siAgrin
siAgrin+ sAgrin
BrDu
K17
Merged+ DAPI
Leading wound edge
Follower cells away from wound
Proliferating cells (%)
100
80
60
40
20
0
p=0.003
p=0.0001
Leader
Followers
siControl
siAgrin
siAgrin+sAgrin

Fig. 6

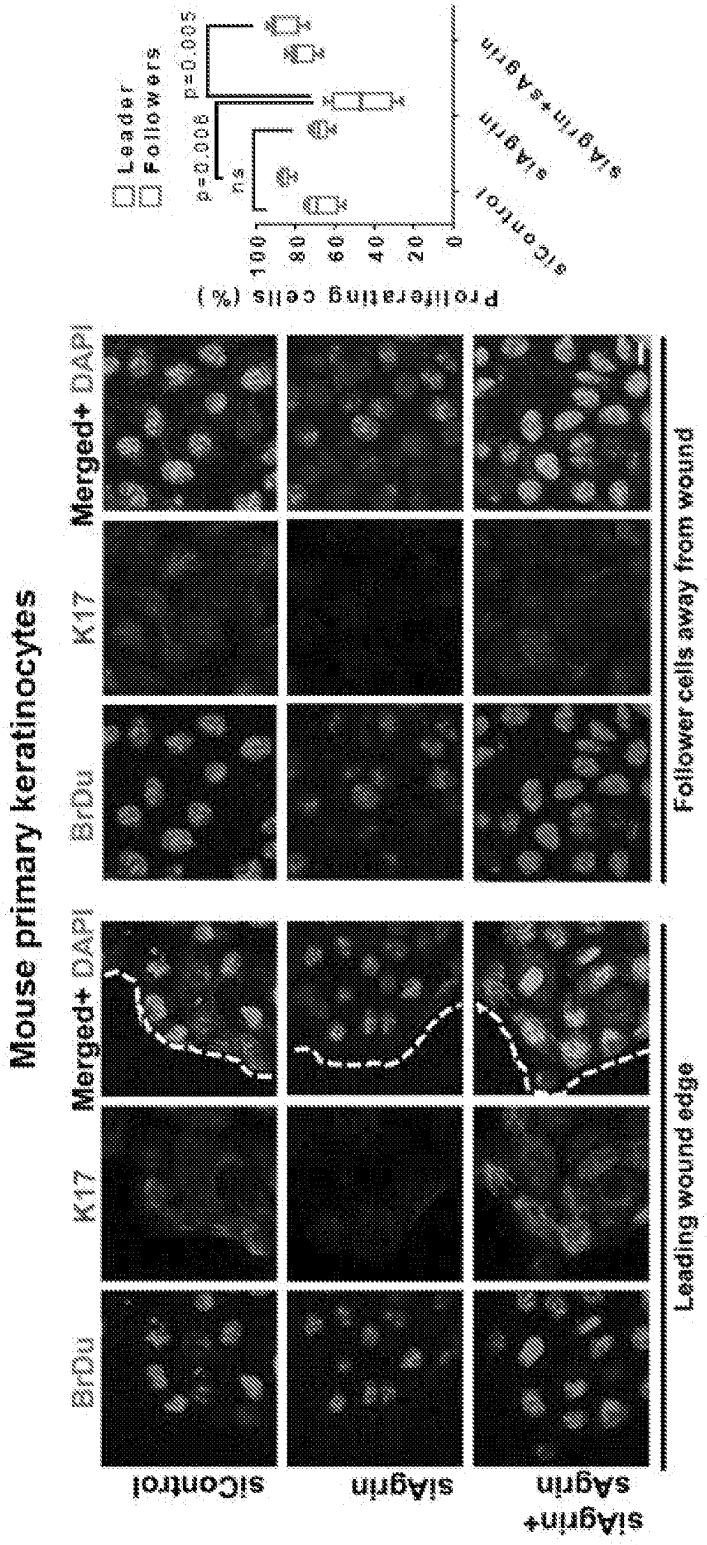


Fig. 6 (Continued)

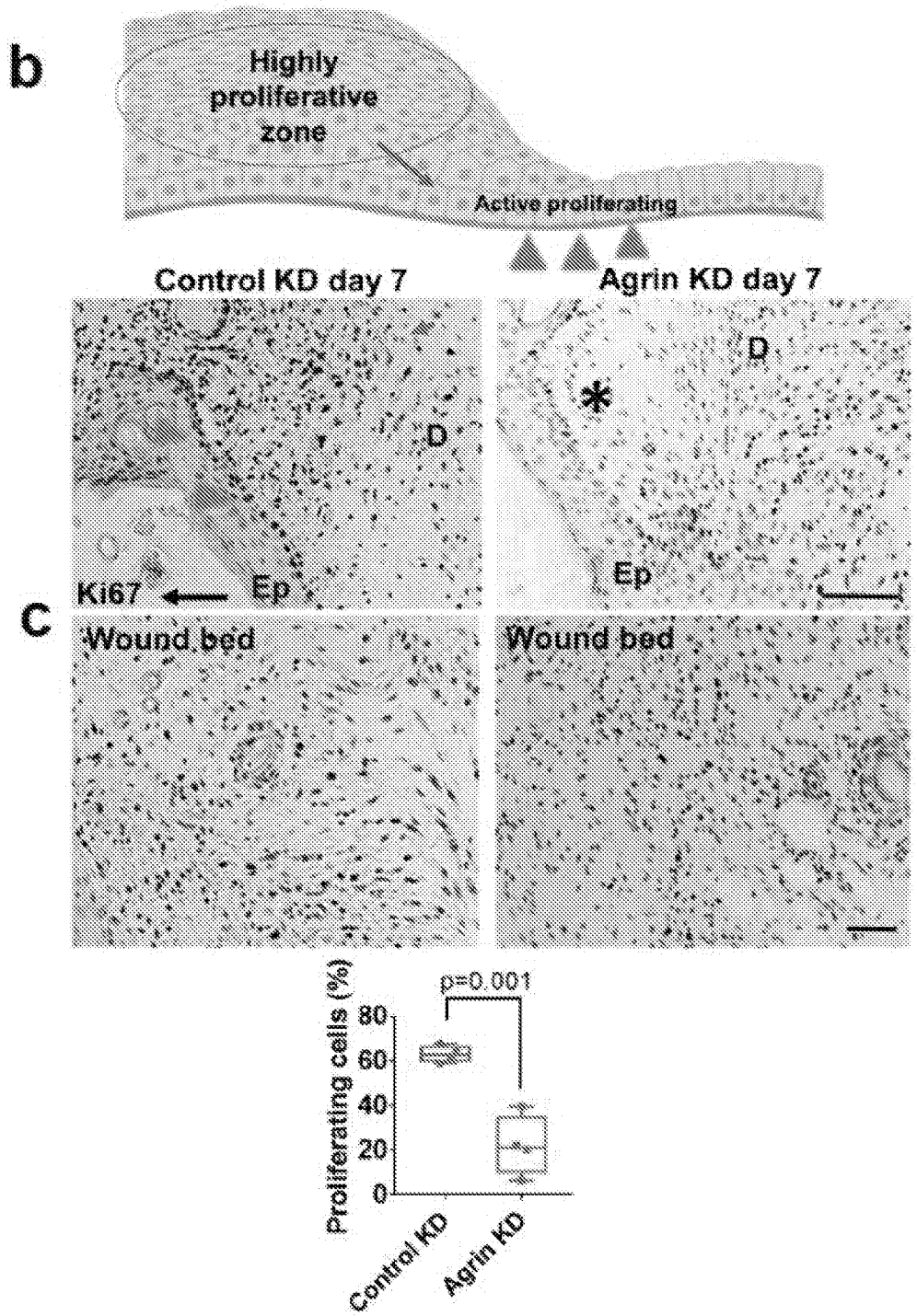


Fig. 6 (Continued)

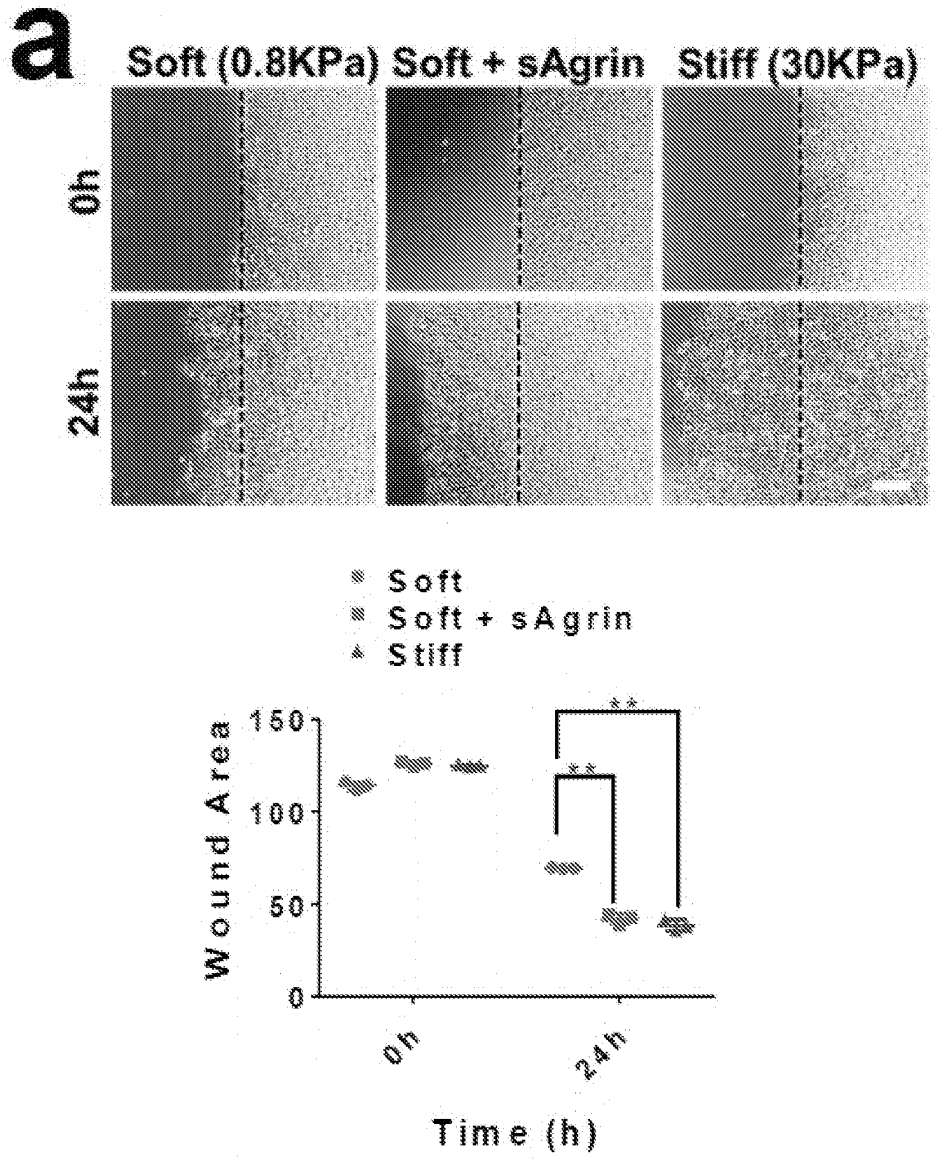

a
Soft (0.8KPa)
Soft + sAgrin
Stiff (30KPa)
0h
24h
Soft
Soft + sAgrin
Stiff
Wound Area
150
100
50
0
**
**
0h
24h
Time (h)

Fig. 7

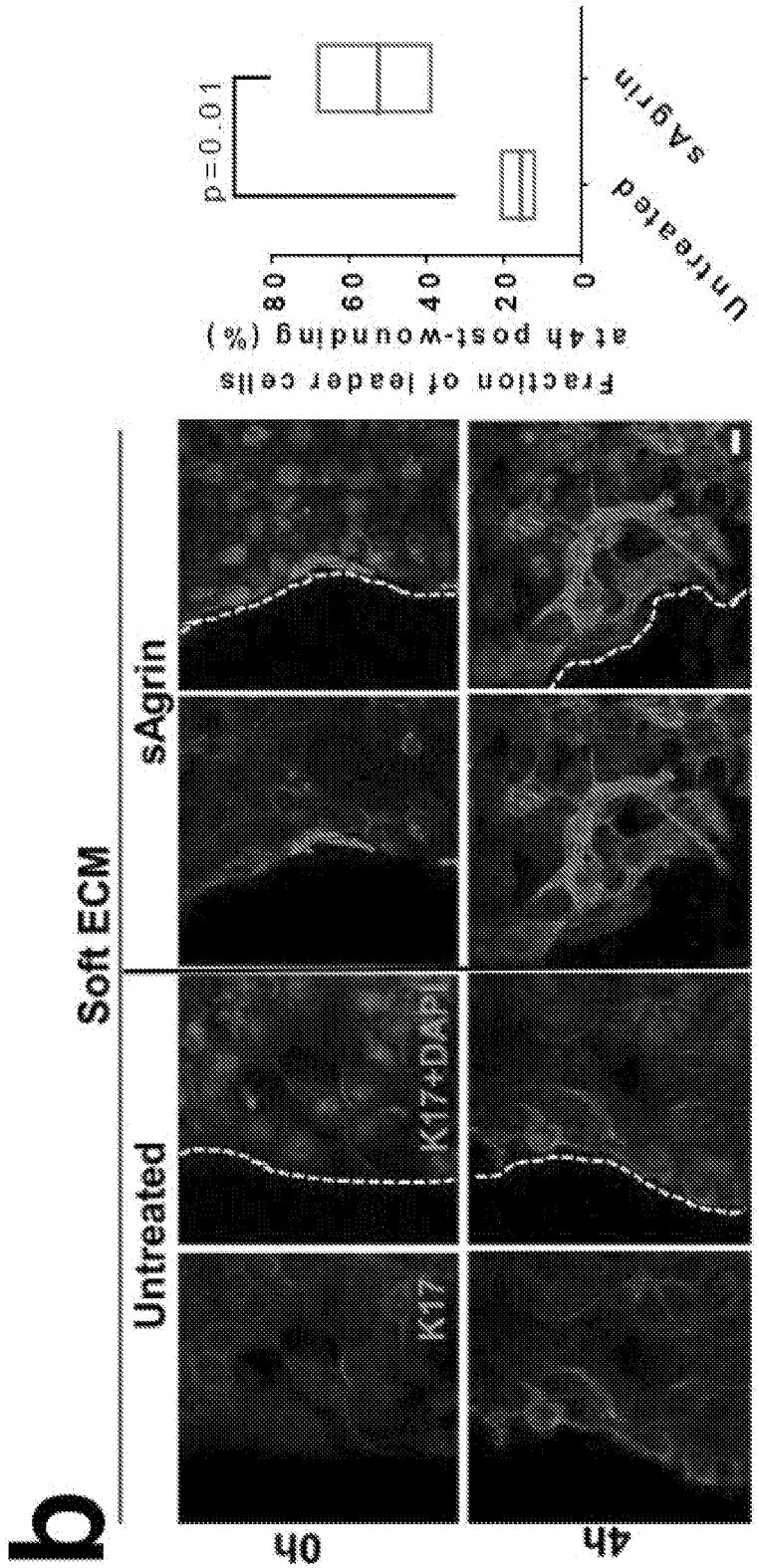


Fig. 7 (Continued)

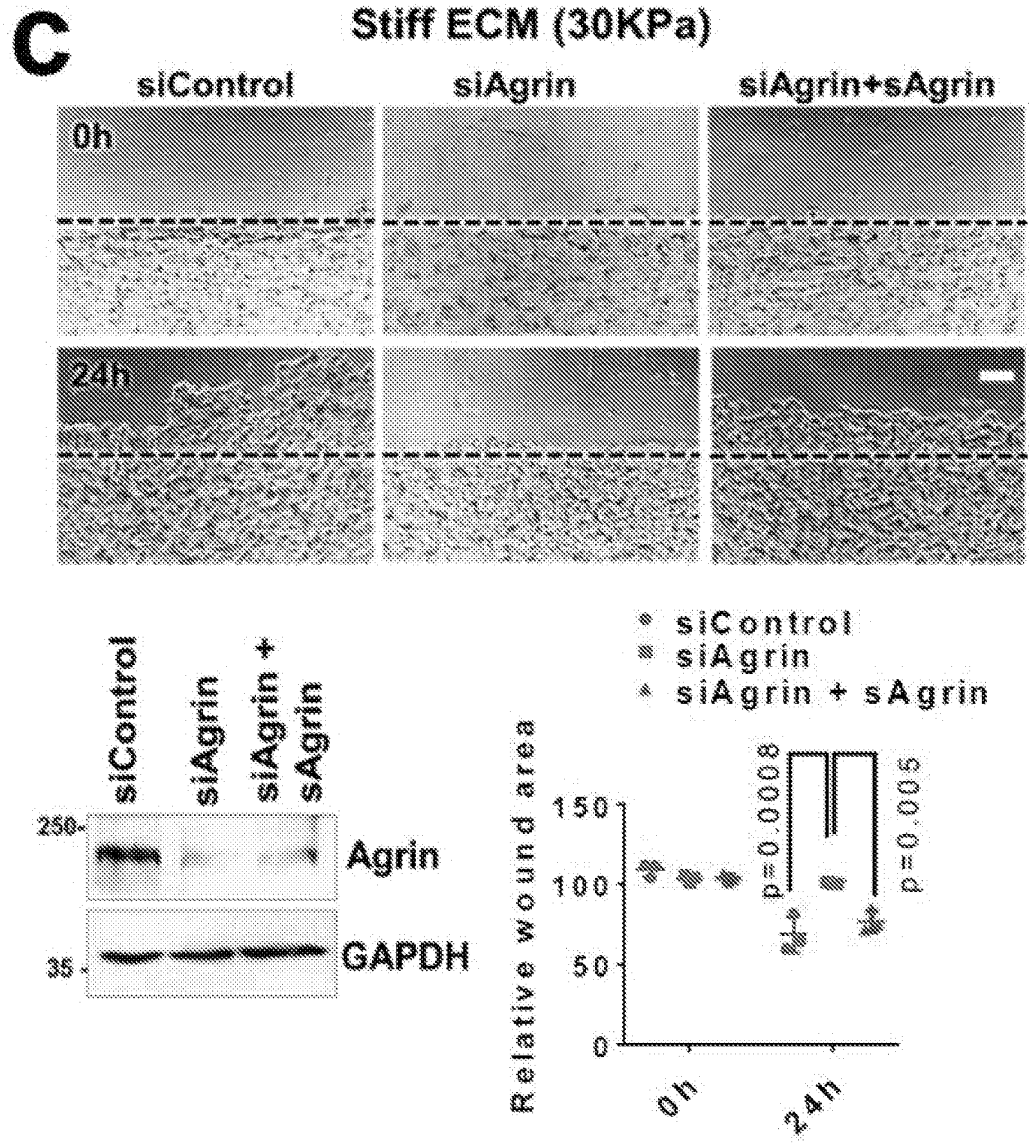


Fig. 7 (Continued)

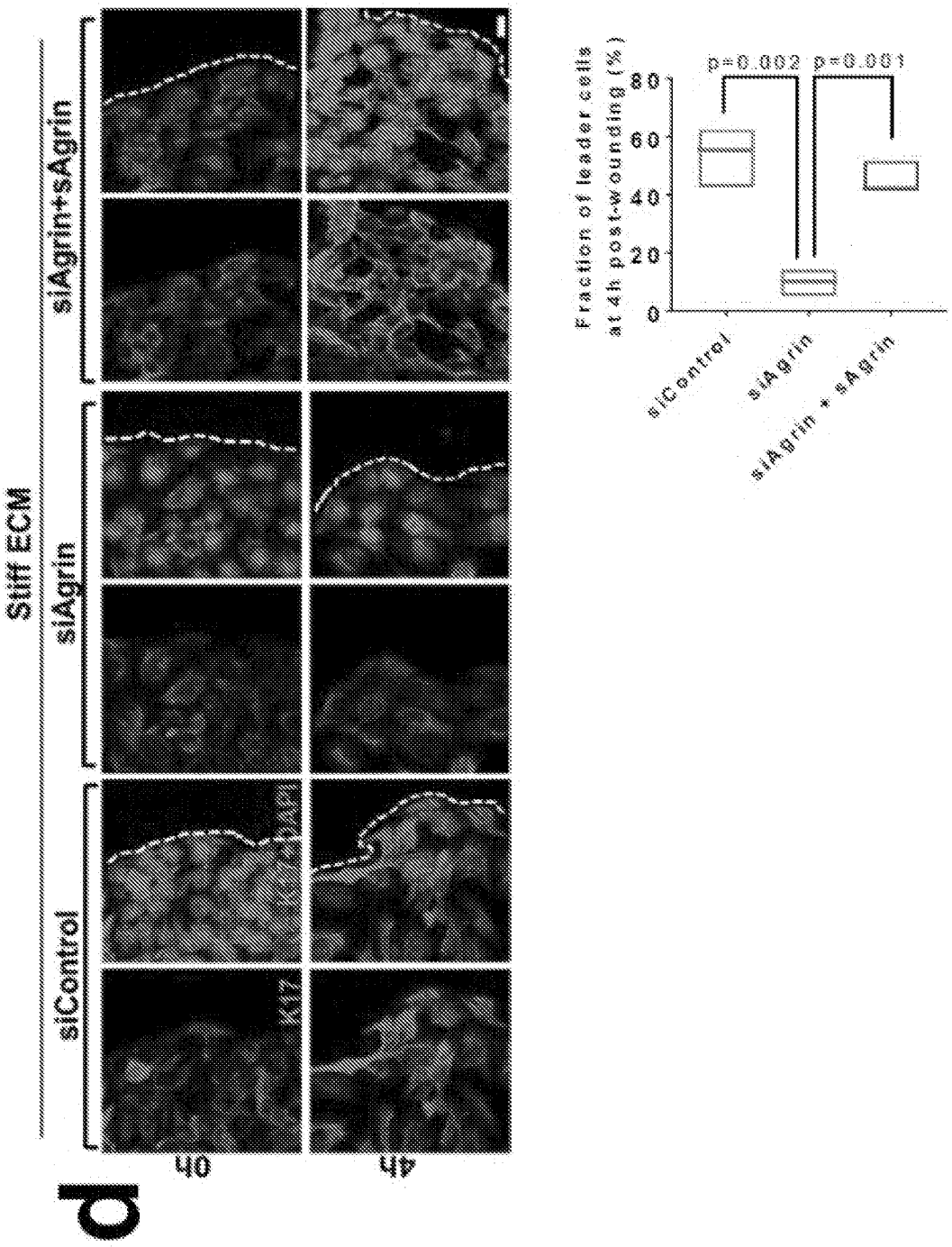


Fig. 7 (Continued)

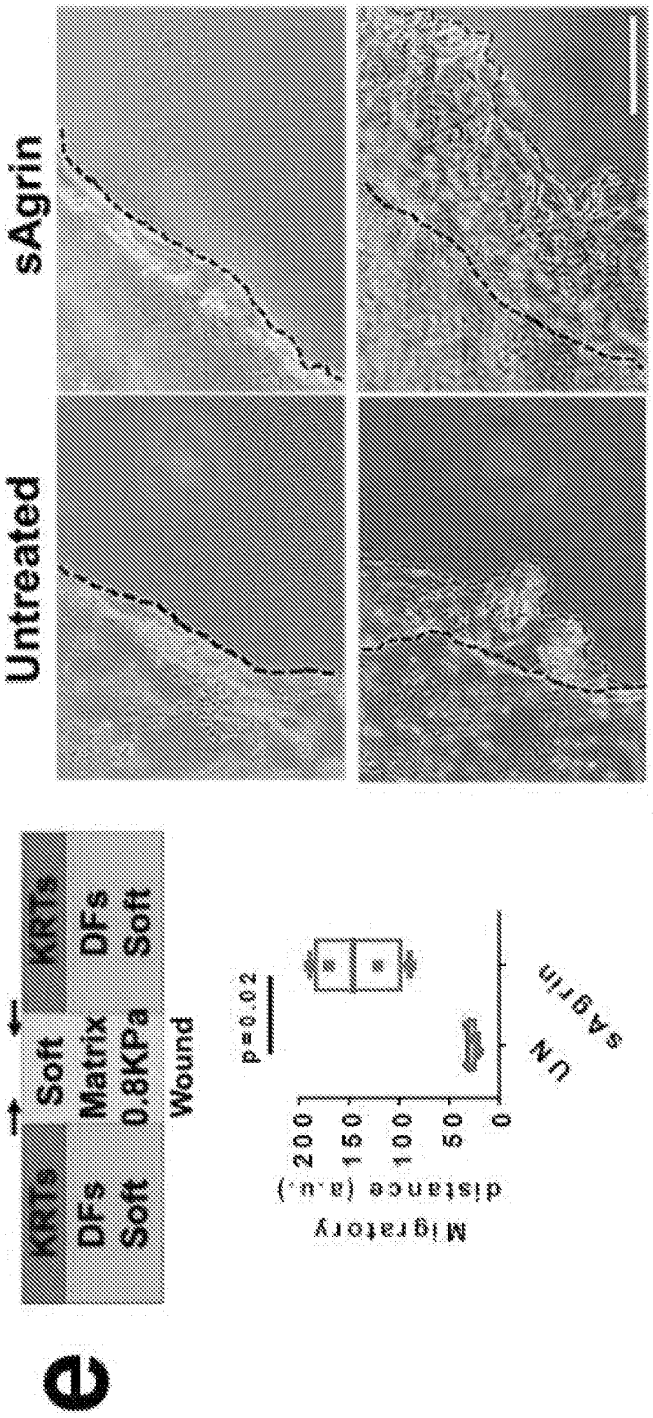


Fig. 7 (Continued)

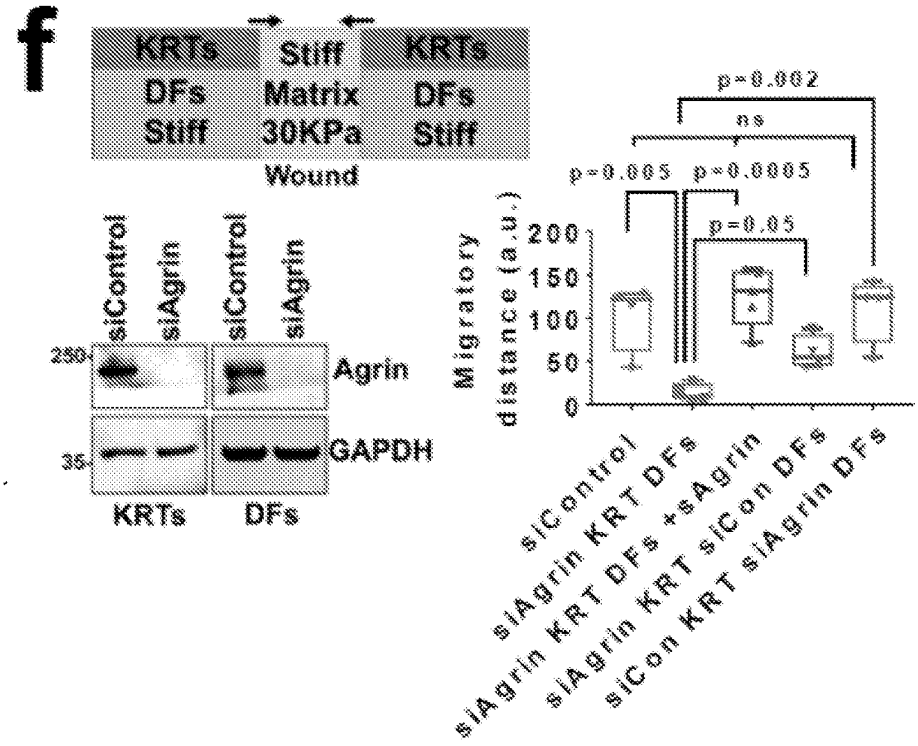


Fig. 7 (Continued)

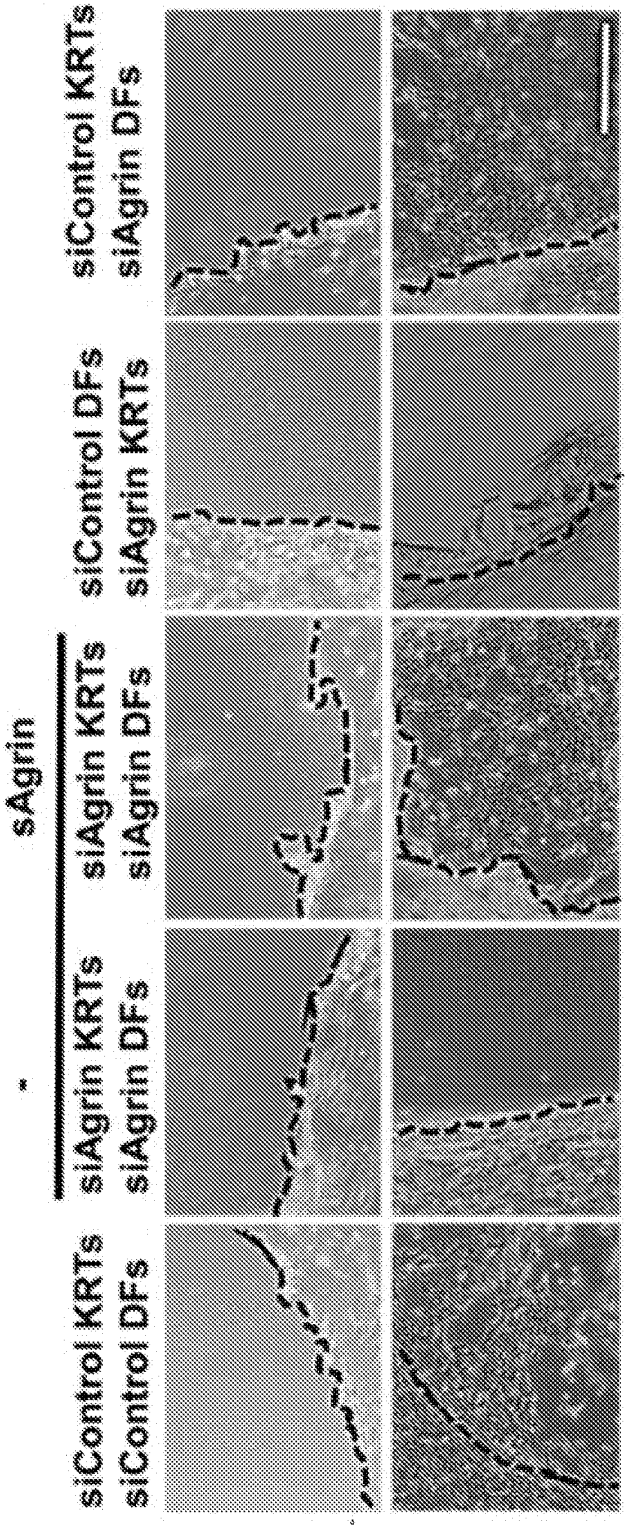
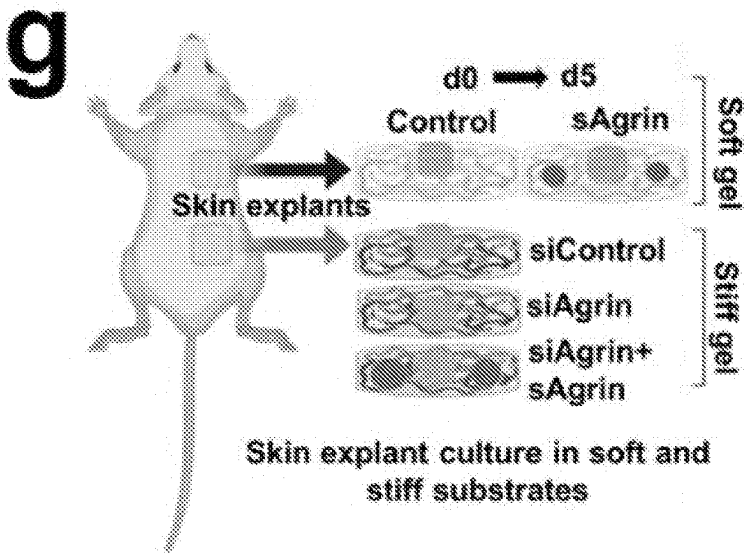


Fig. 7 (Continued)



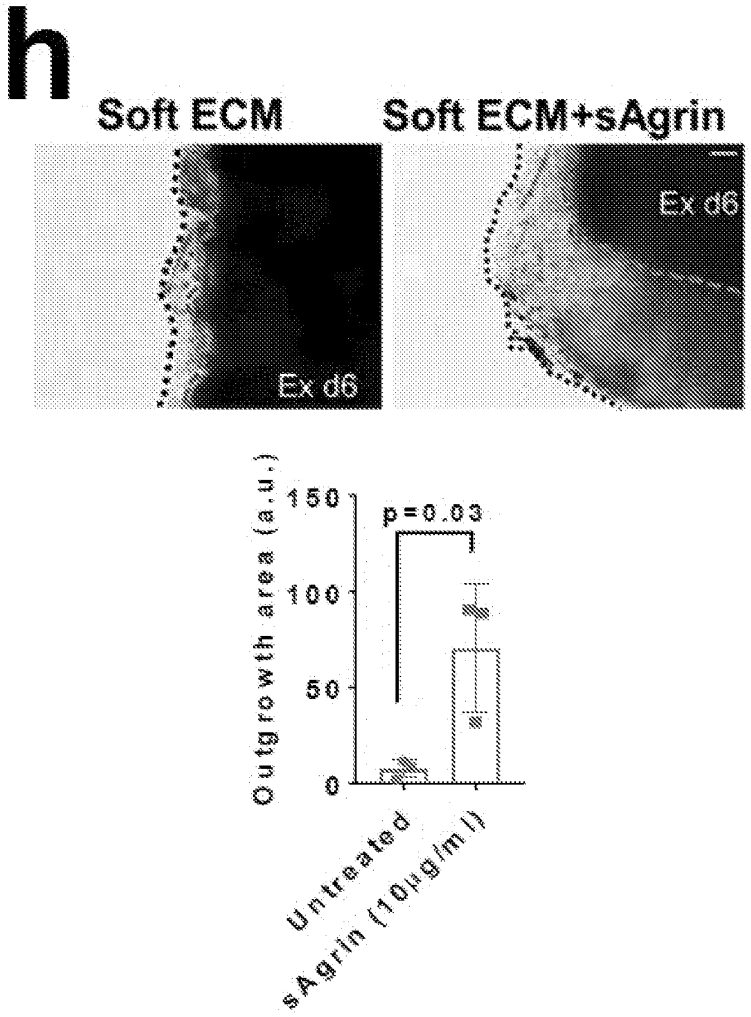


Fig. 7 (Continued)

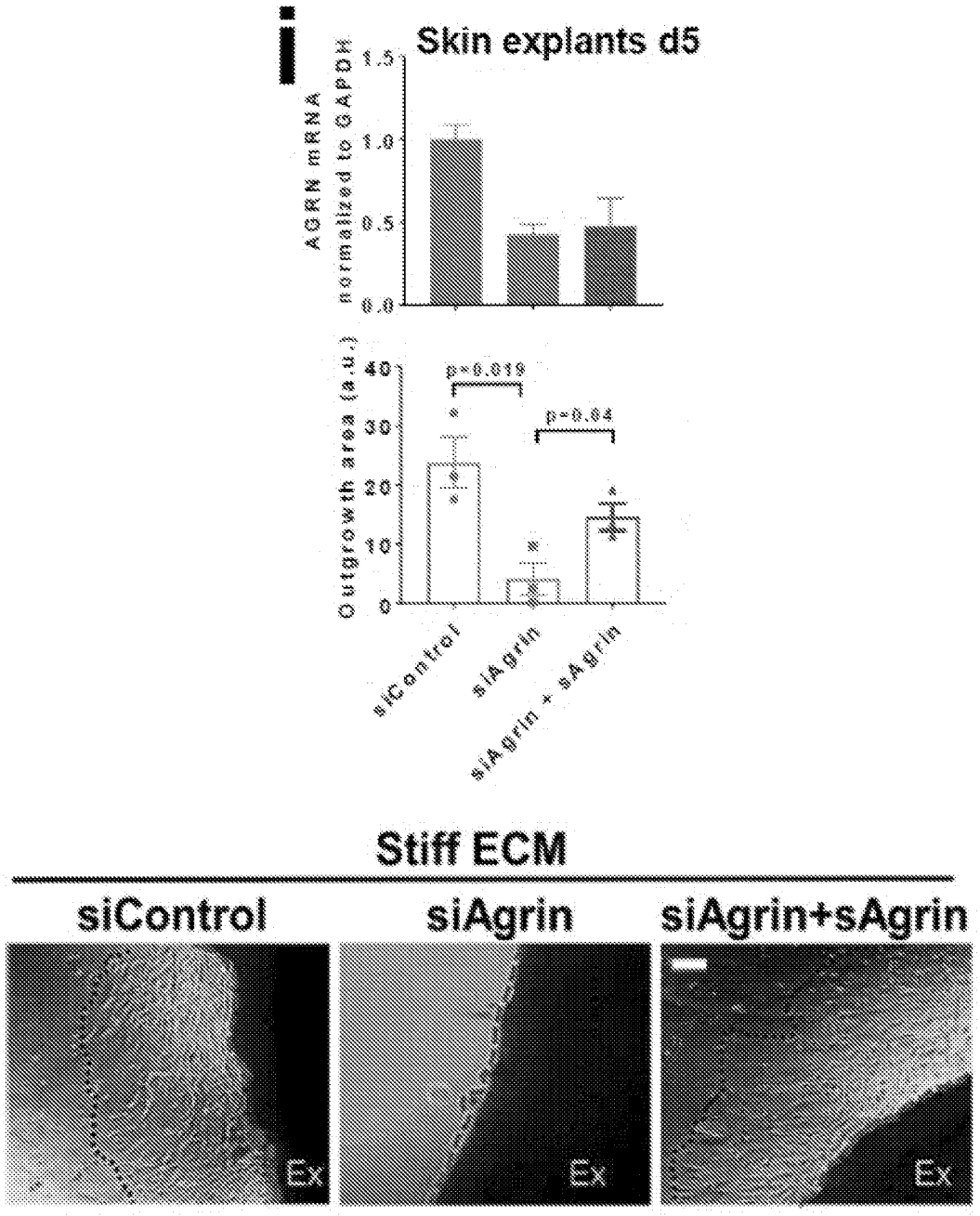


Fig. 7 (Continued)

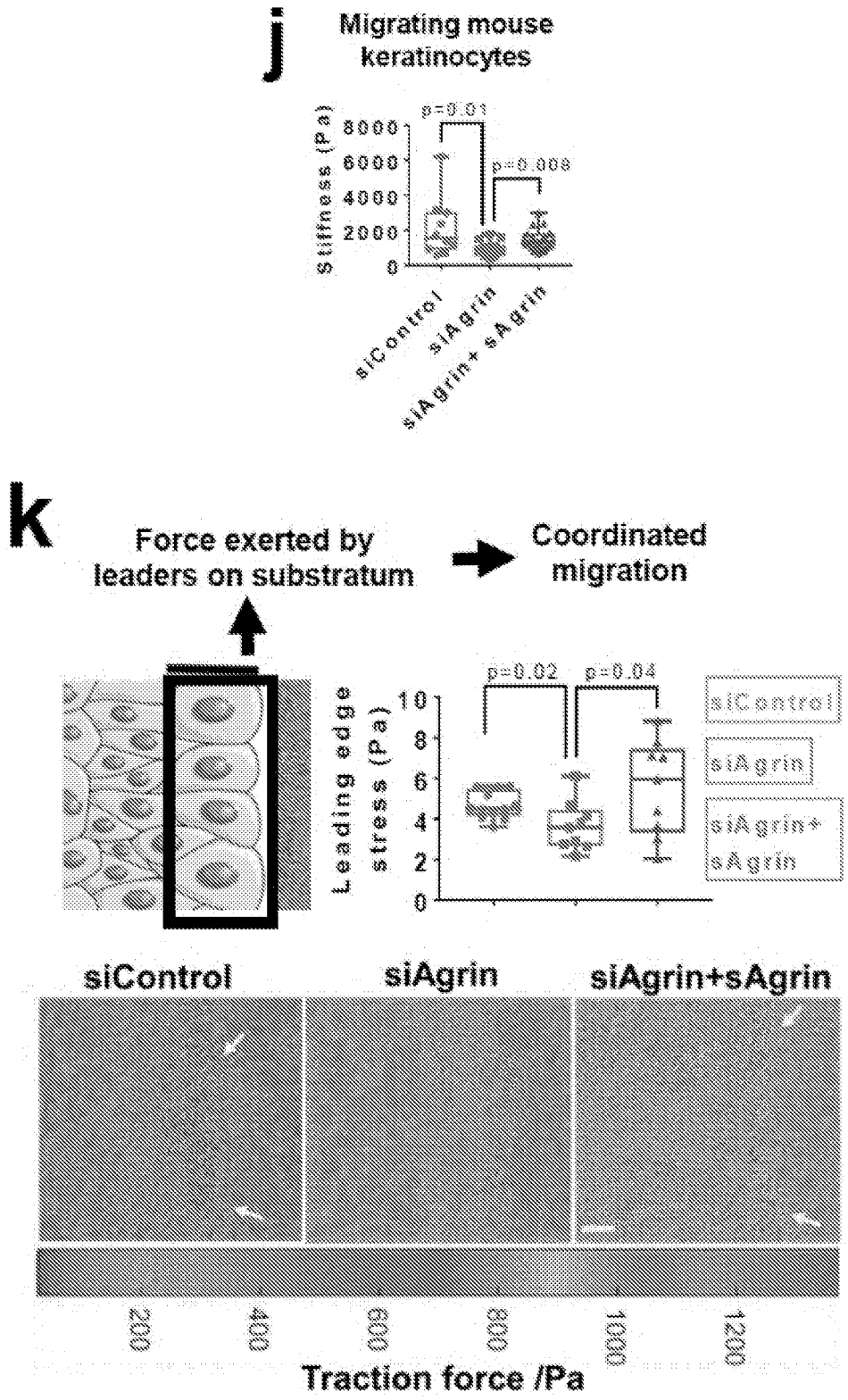


Fig. 7 (Continued)

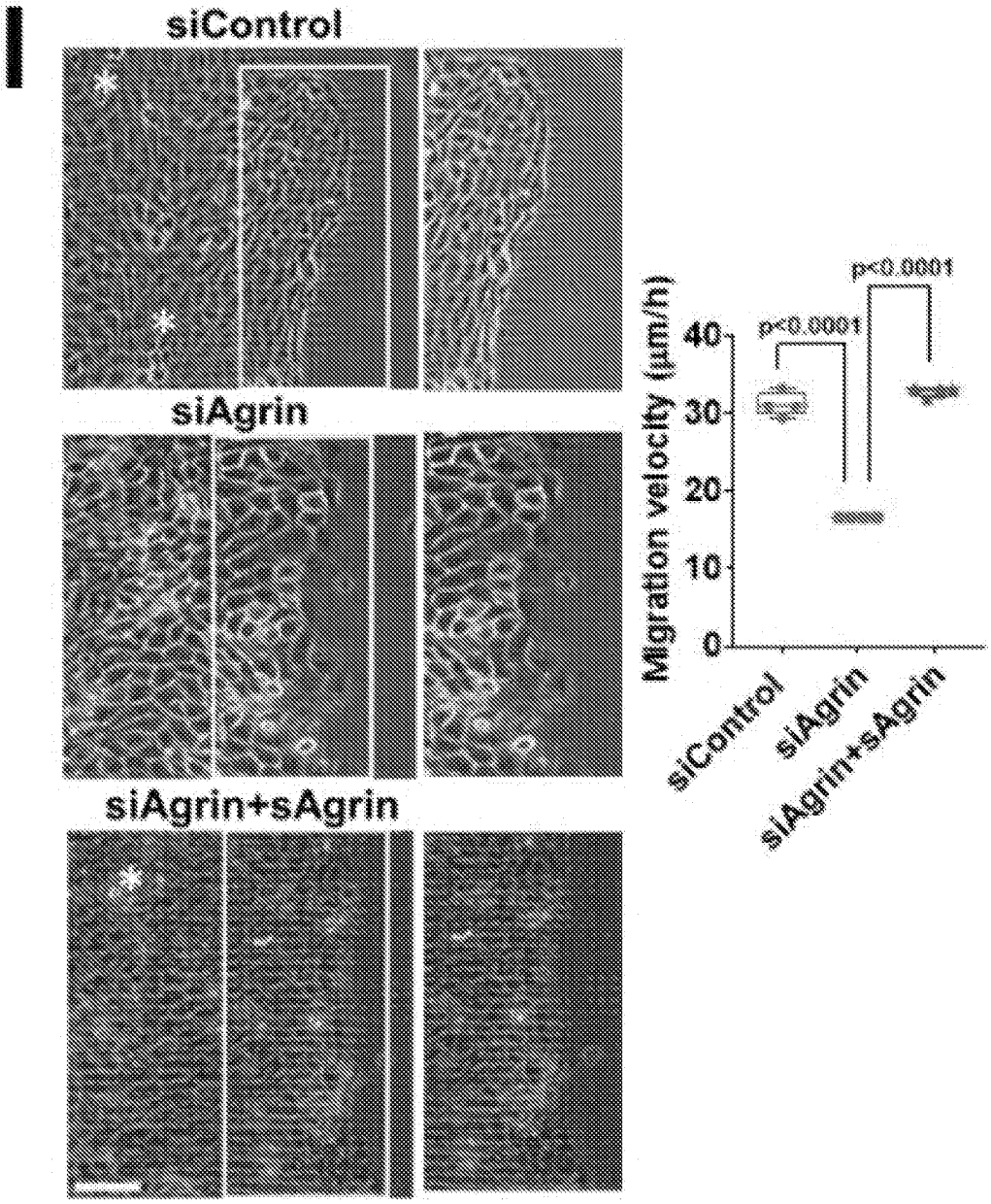


Fig. 7 (Continued)

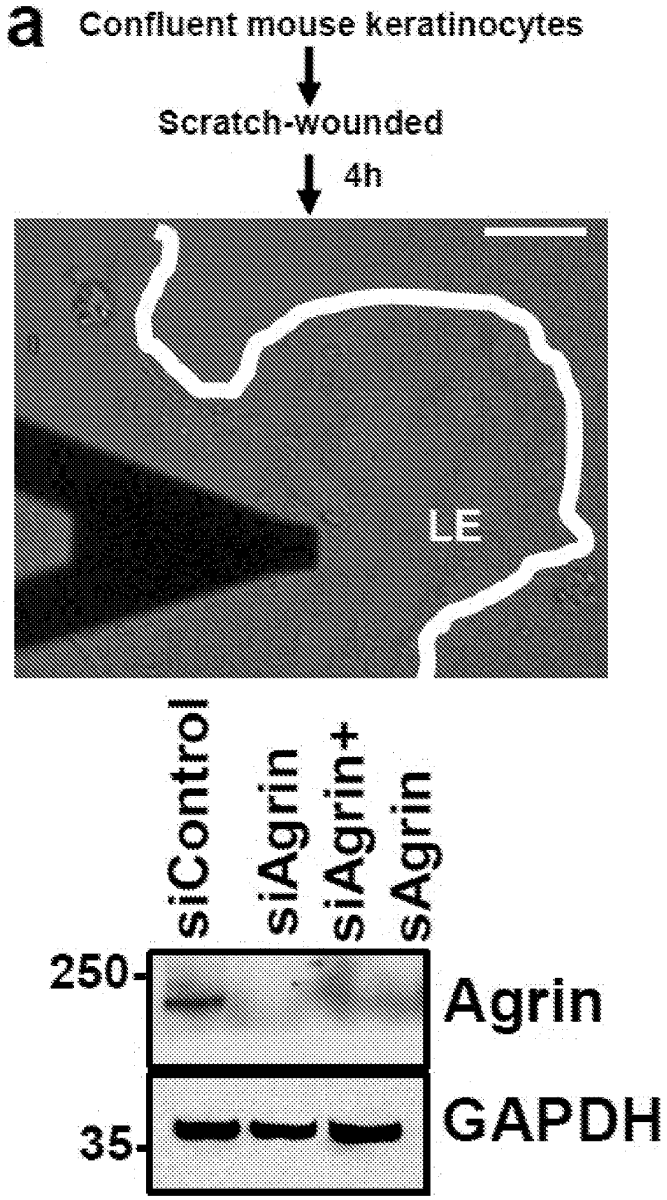

a
Confluent mouse keratinocytes
Scratch-wounded
4h
LE
siControl
siAgrin
siAgrin+
sAgrin
250
Agrin
35
GAPDH

Fig. 8

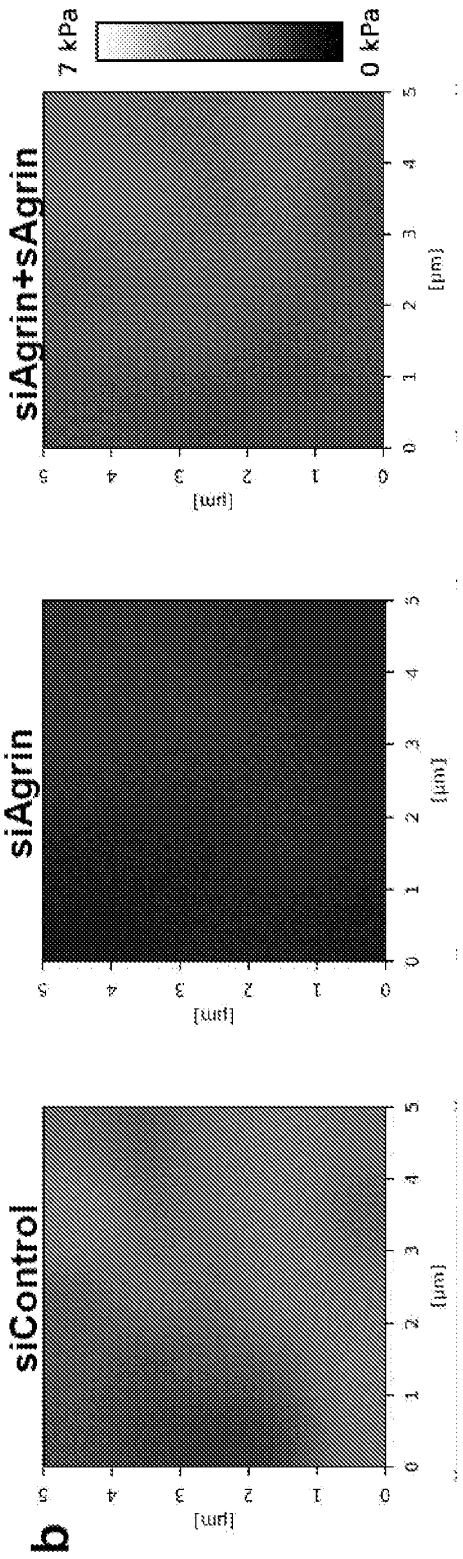


Fig. 8 (Continued)

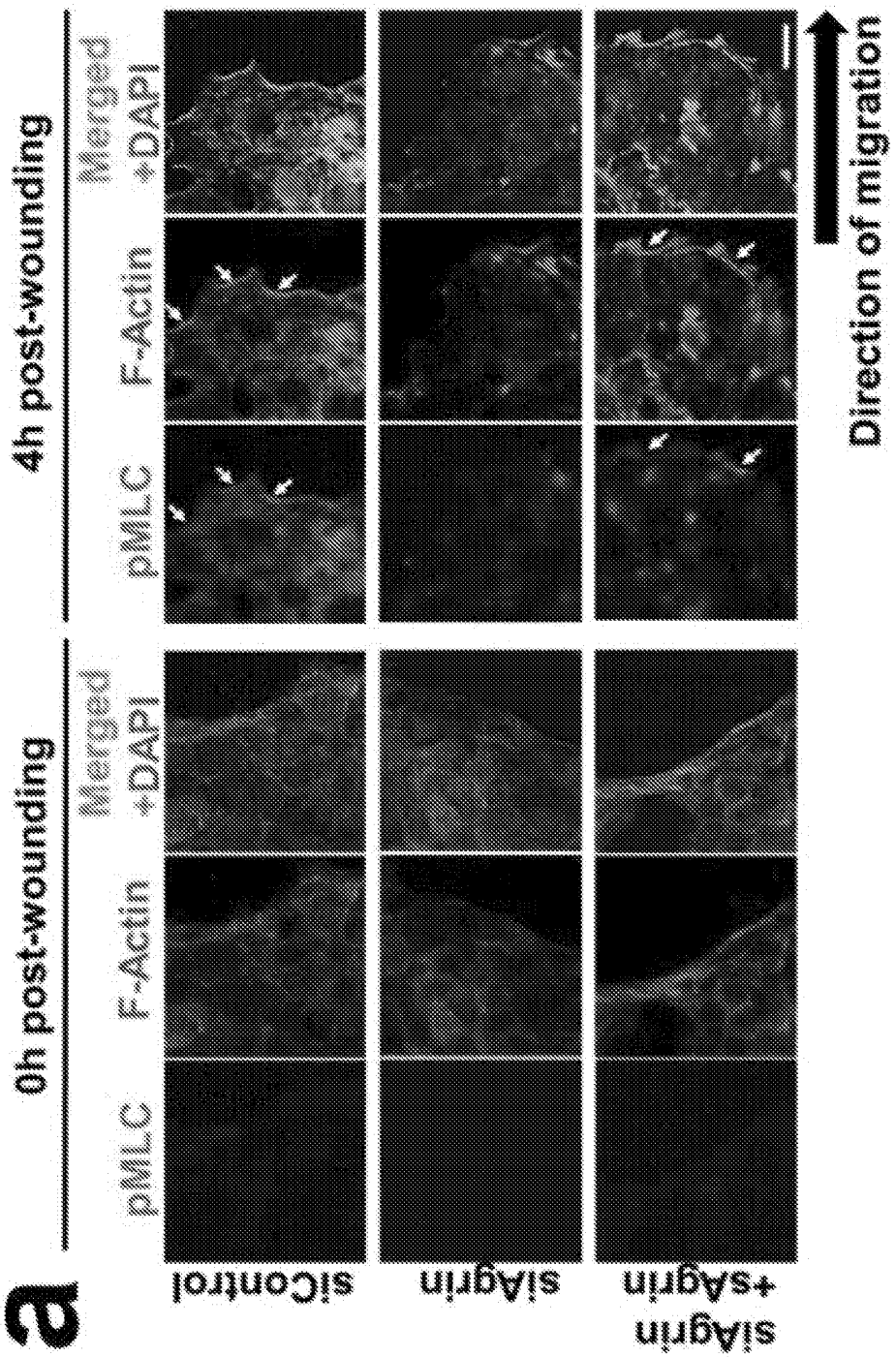

a
0h post-wounding
4h post-wounding
pMLC
F-Actin
Merged +DAPI
siControl
siAgrin
siAgrin +sAgrin
Direction of migration

Fig. 9

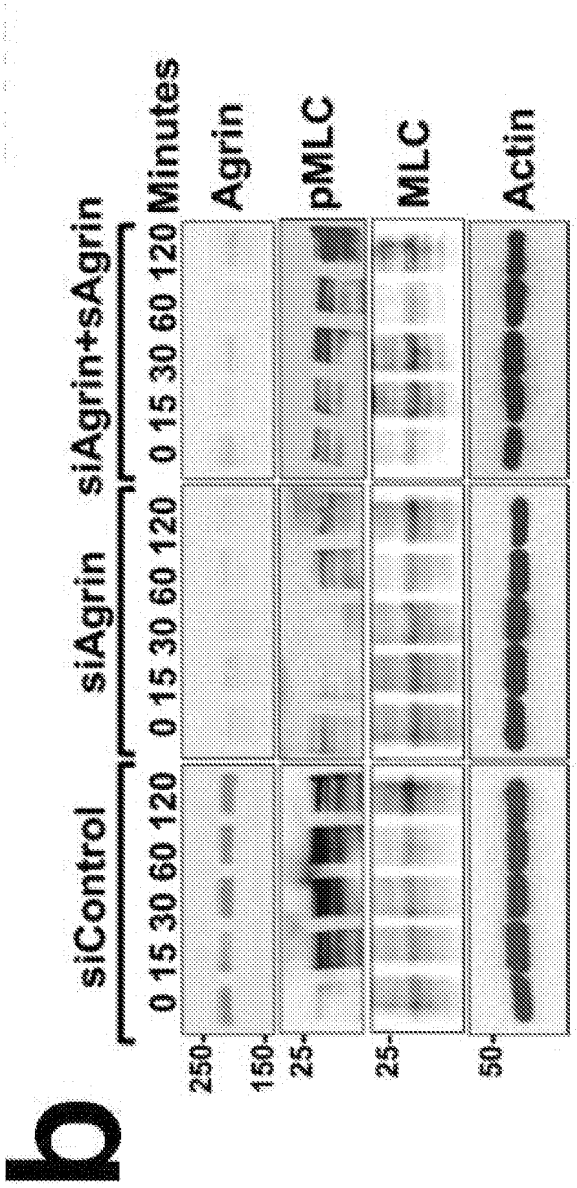


Fig. 9 (Continued)

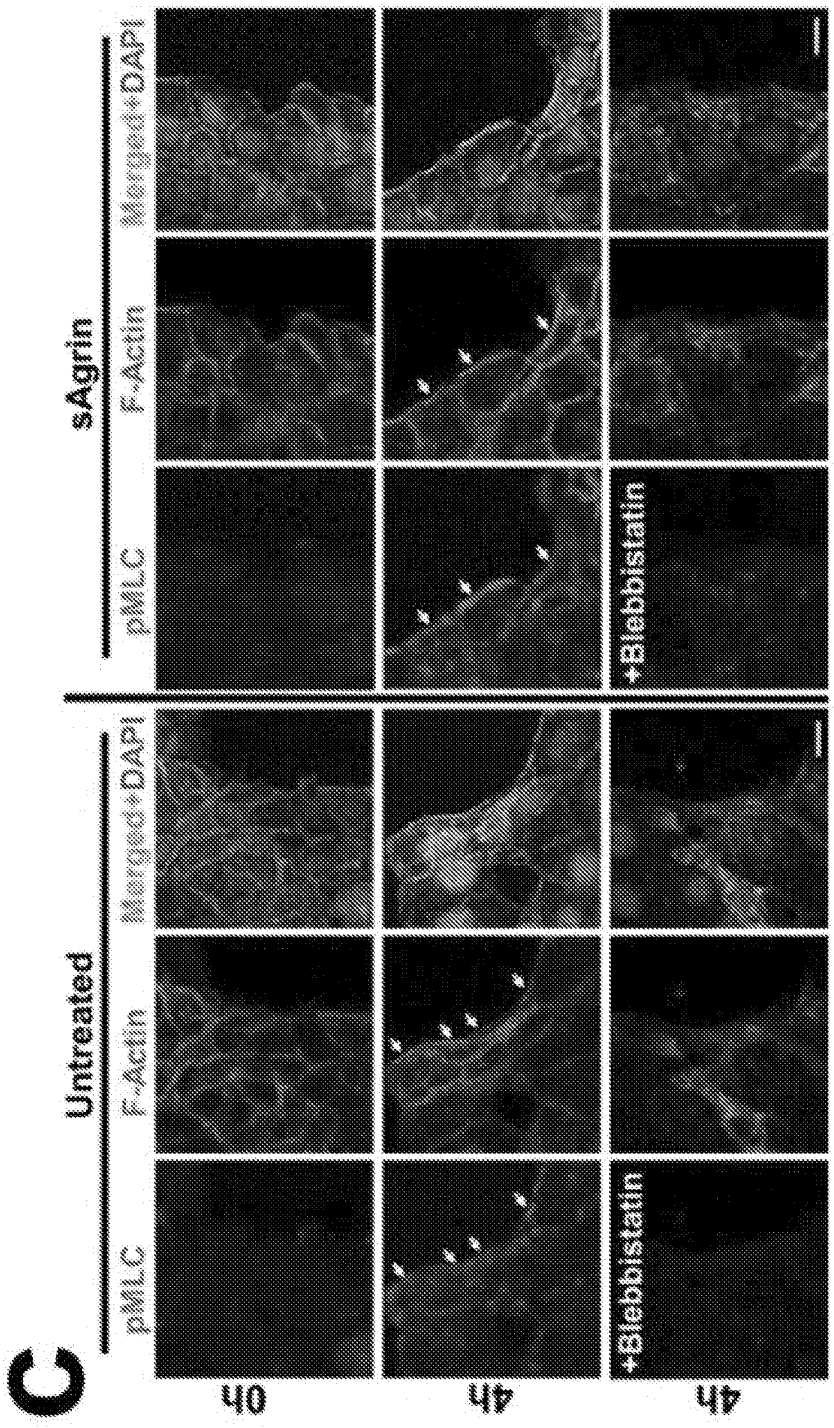


Fig. 9 (Continued)

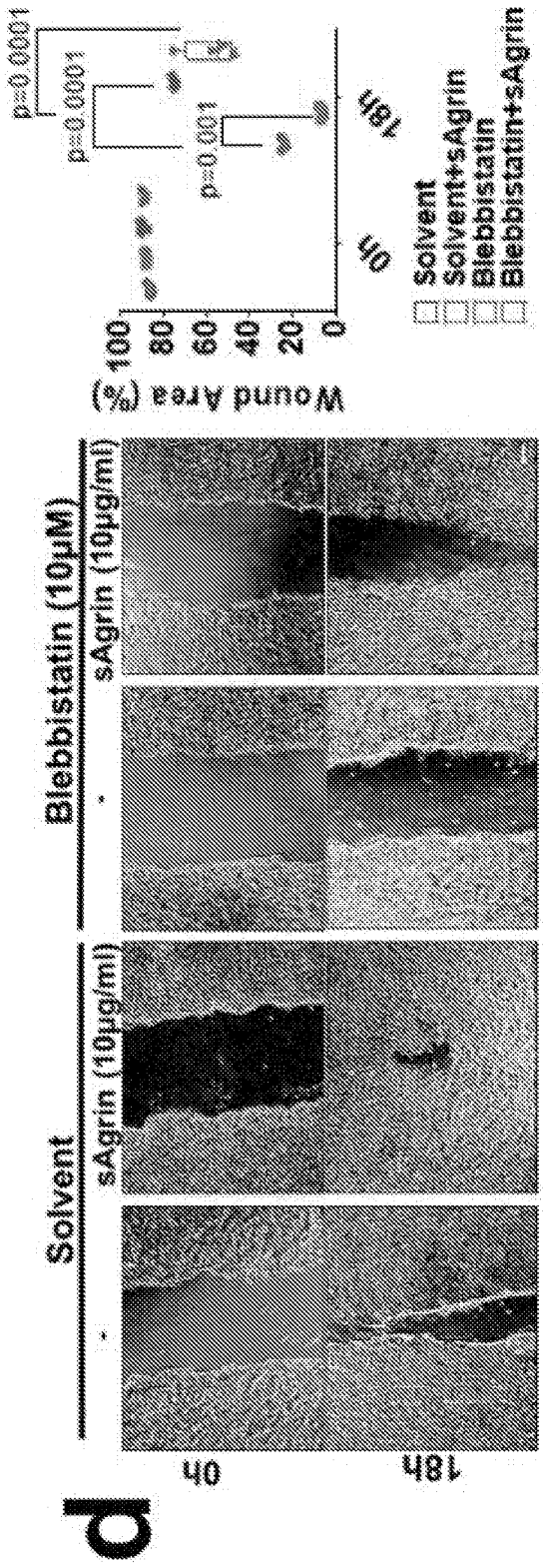


Fig. 9 (Continued)

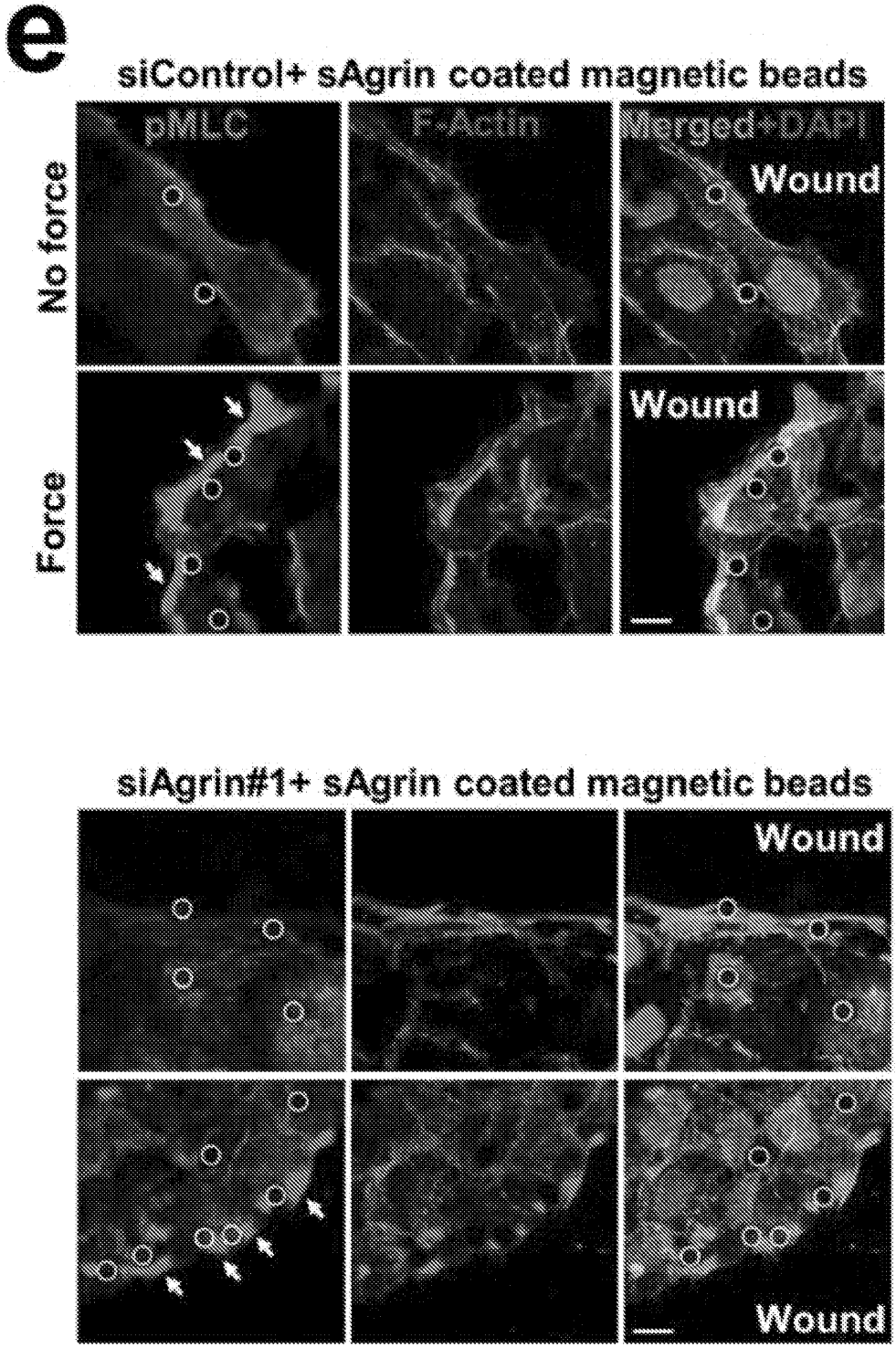


Fig. 9 (Continued)

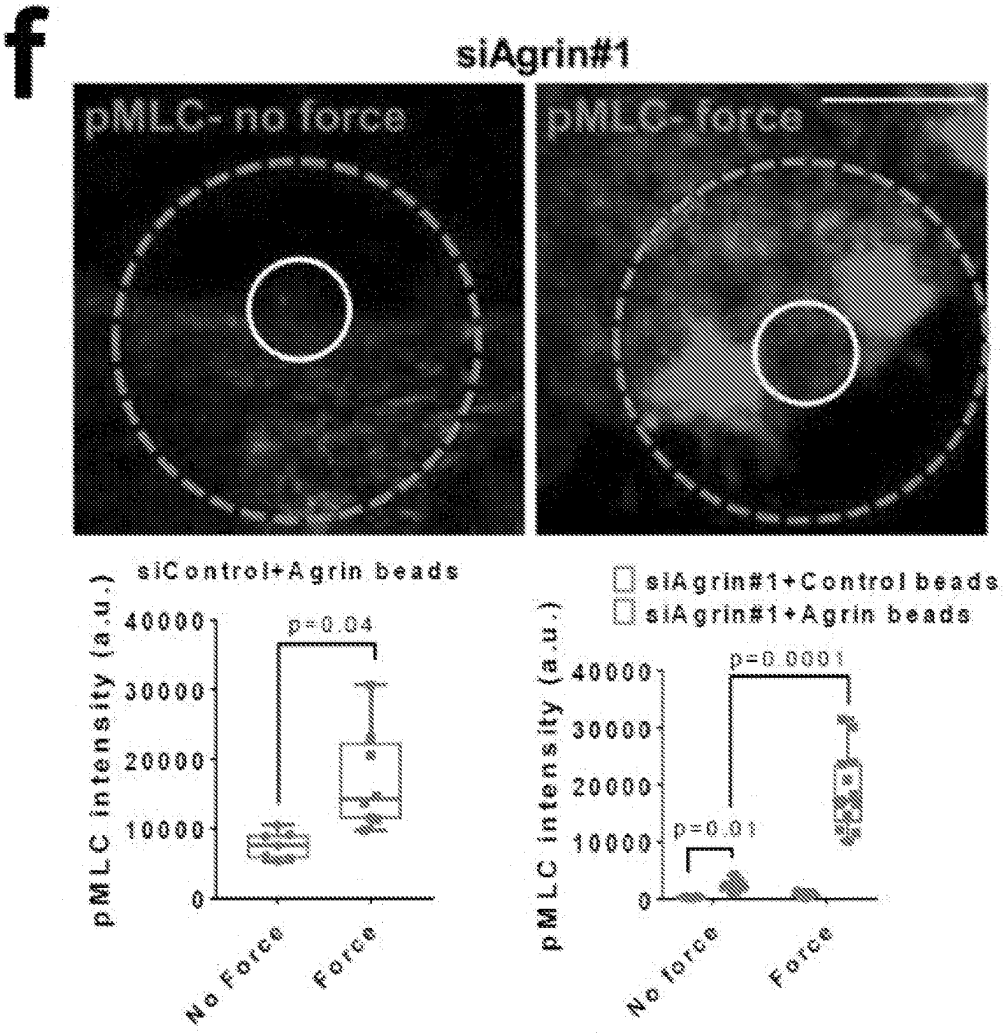


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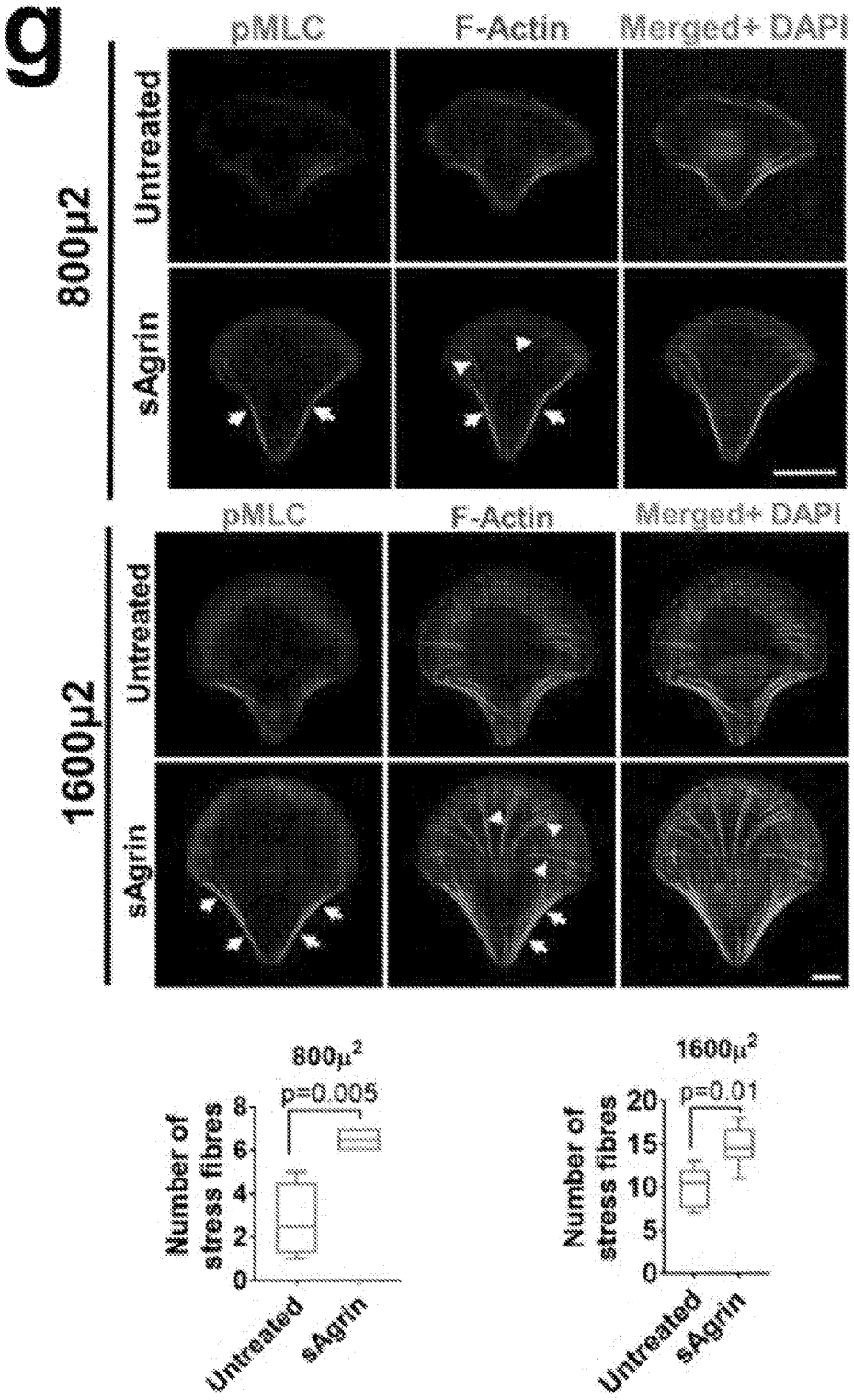


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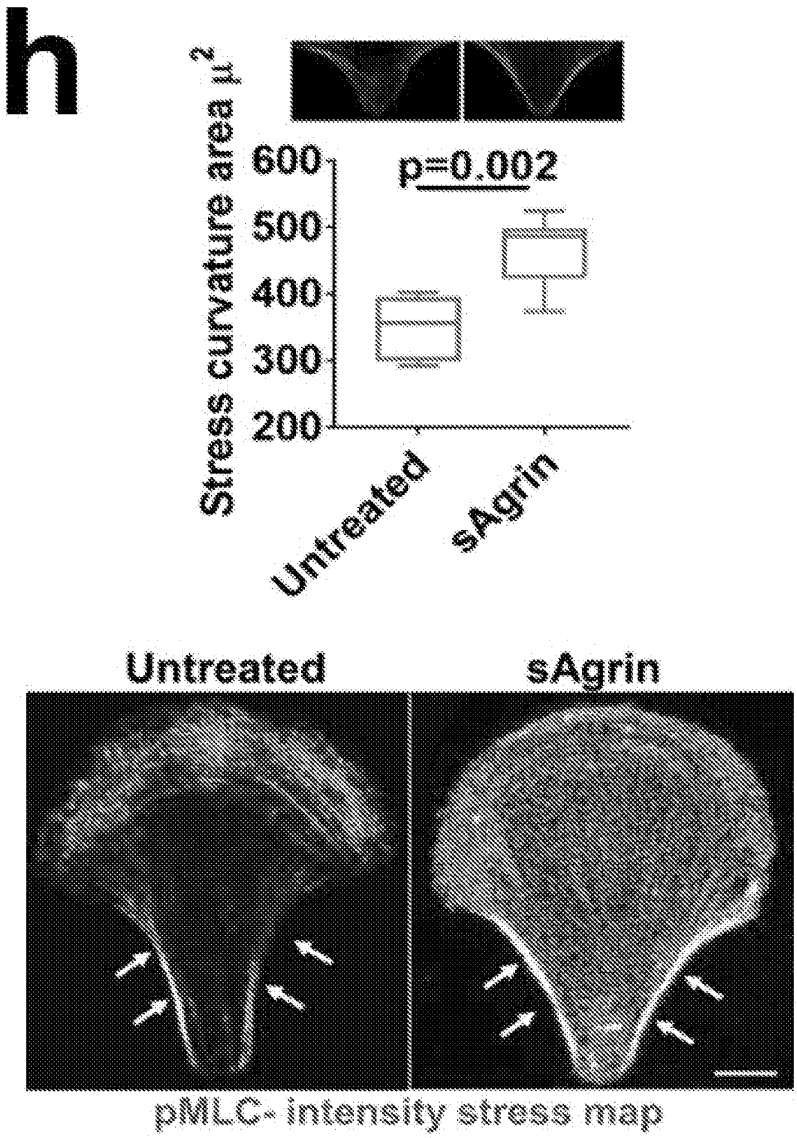


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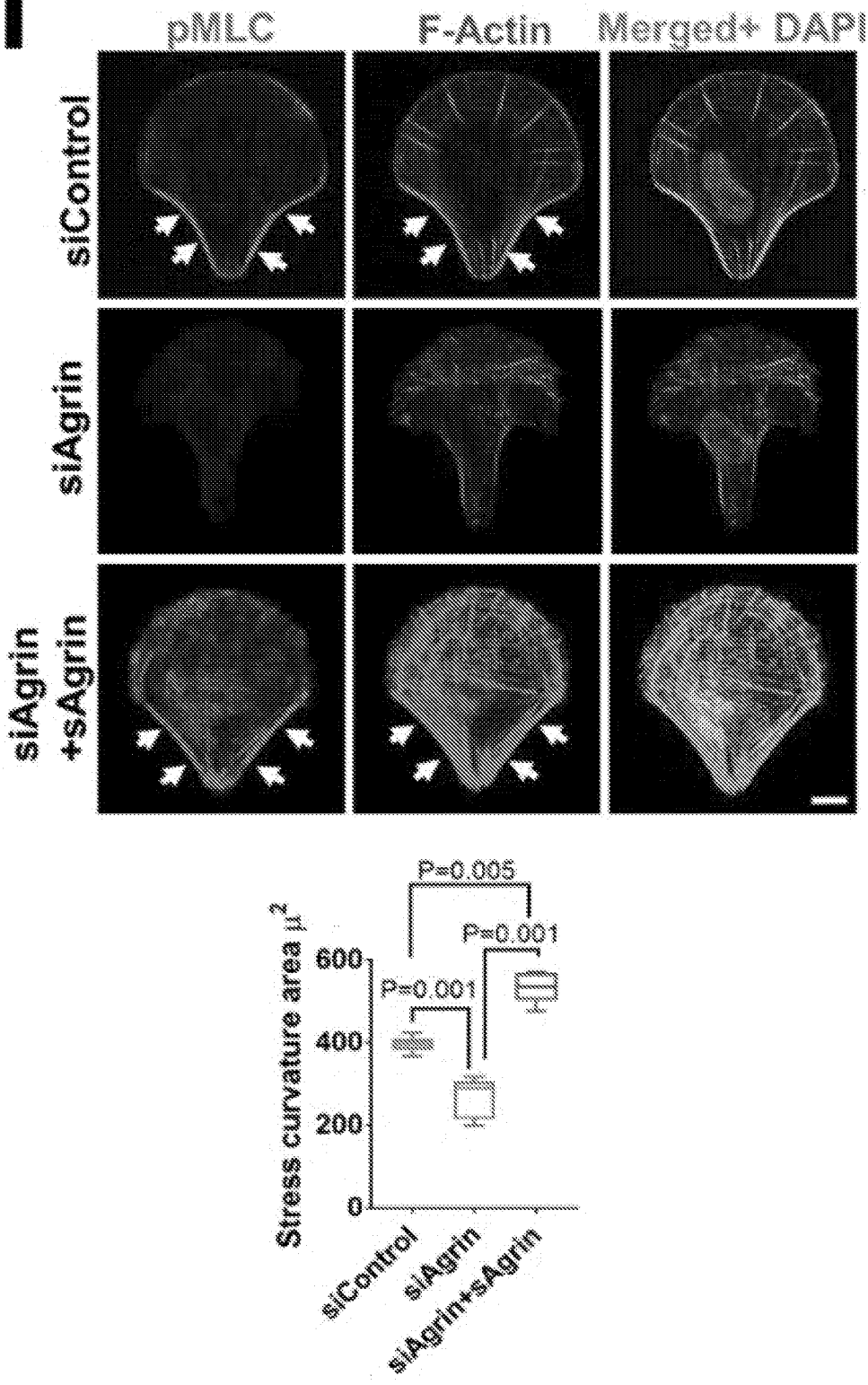


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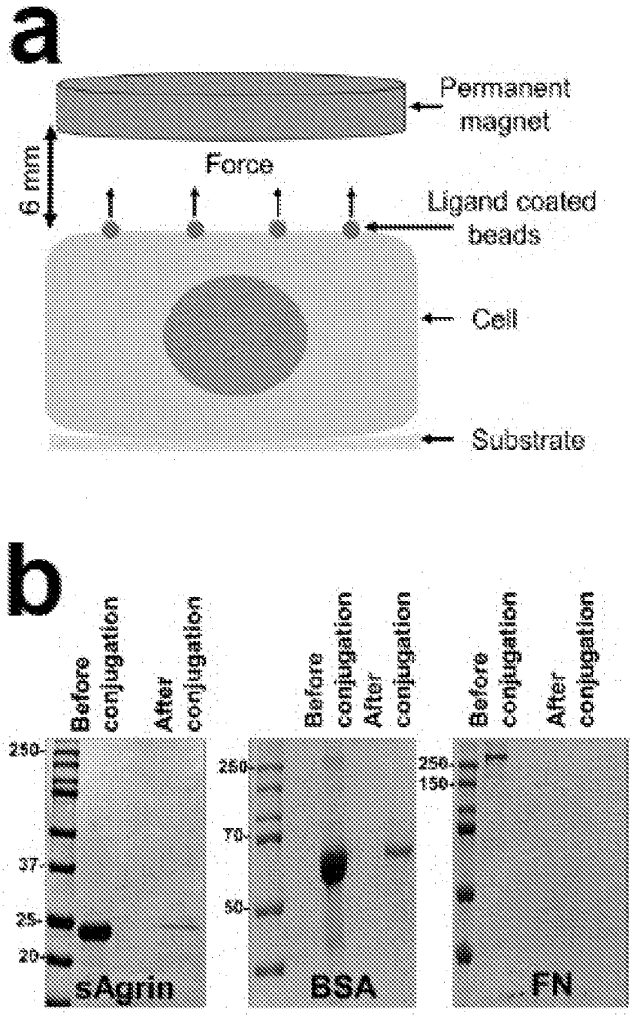

a
Permanent magnet
6 mm
Force
Ligand coated beads
Cell
Substrate
b
Before conjugation
After conjugation
250
37
25
20
sAgrin
Before conjugation
After conjugation
250
70
50
BSA
Before conjugation
After conjugation
250
150
FN

Fig. 10

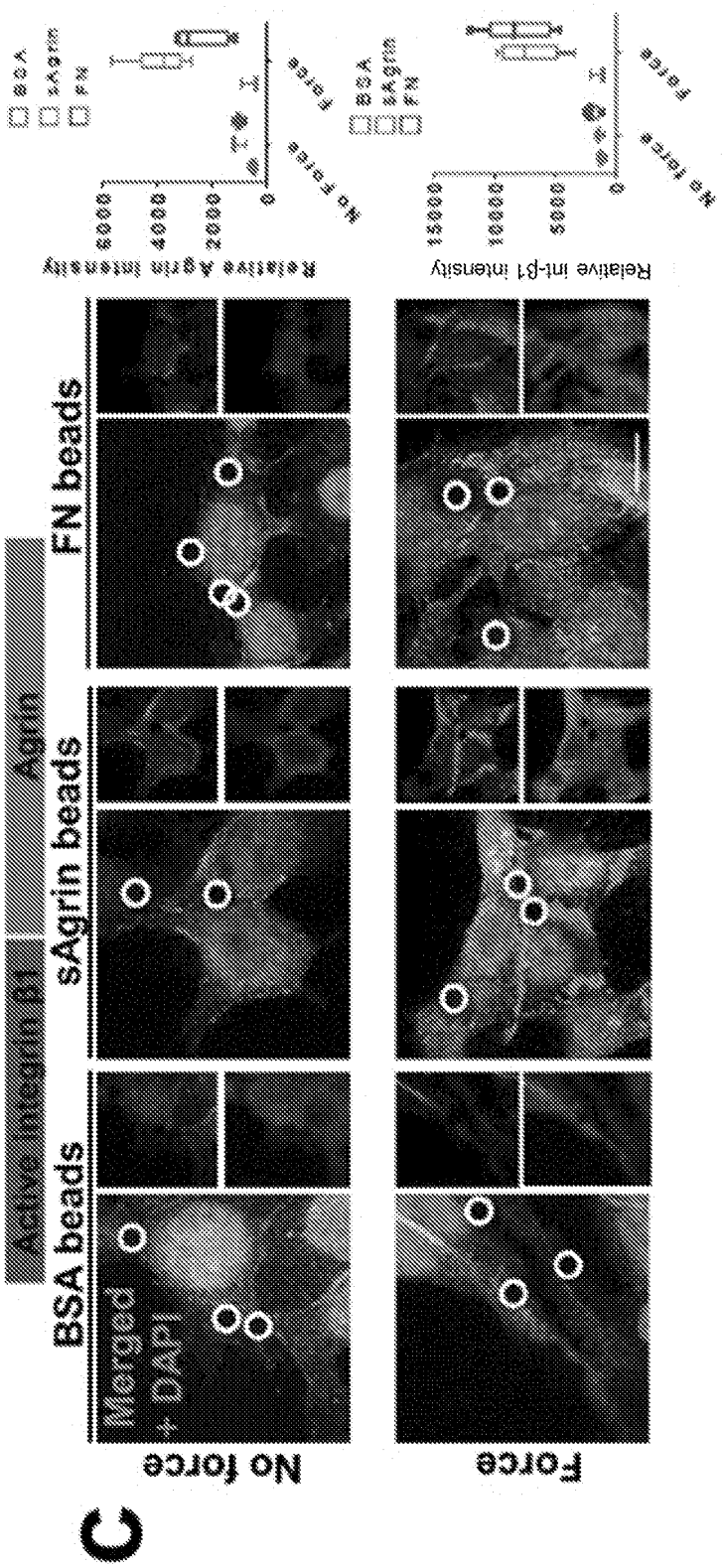


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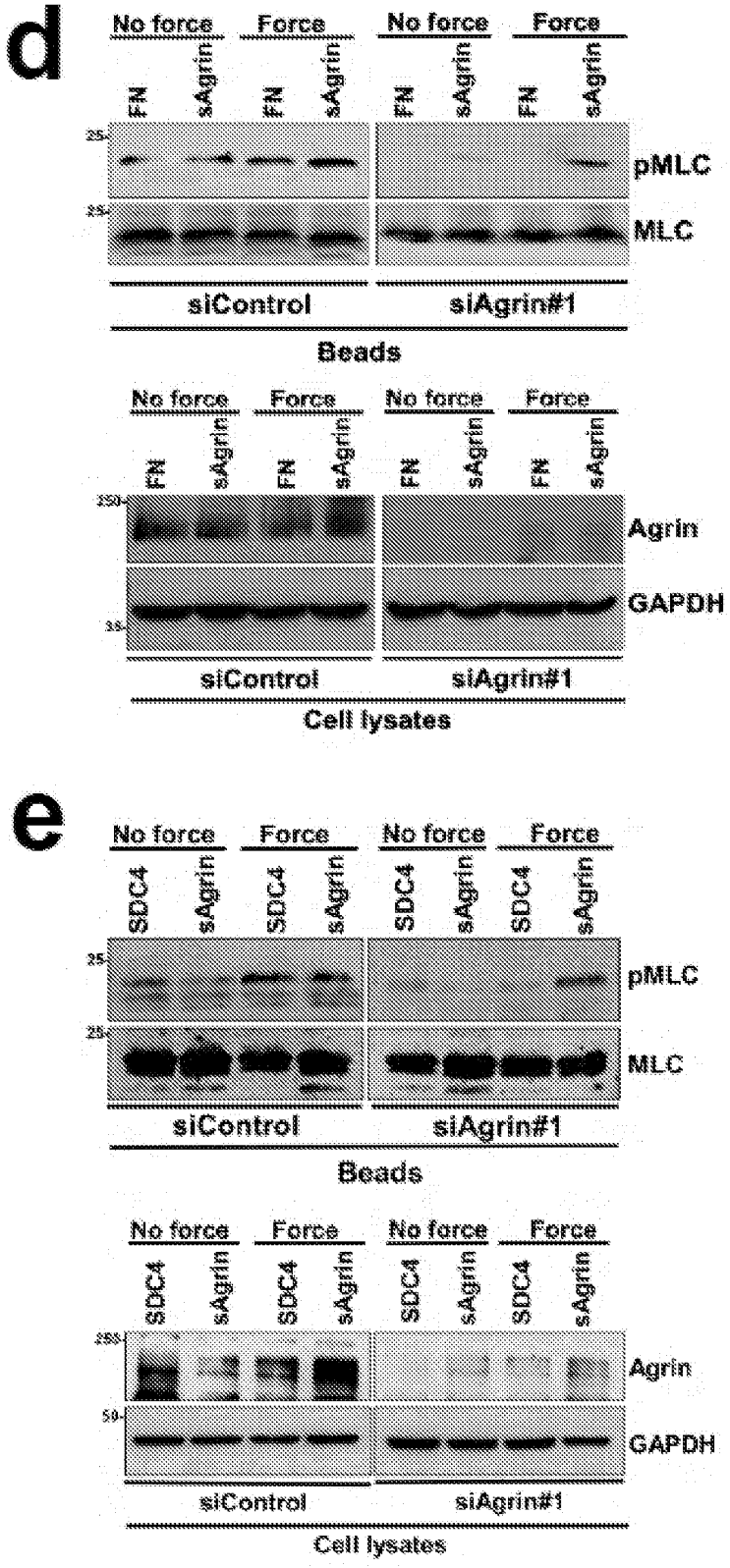


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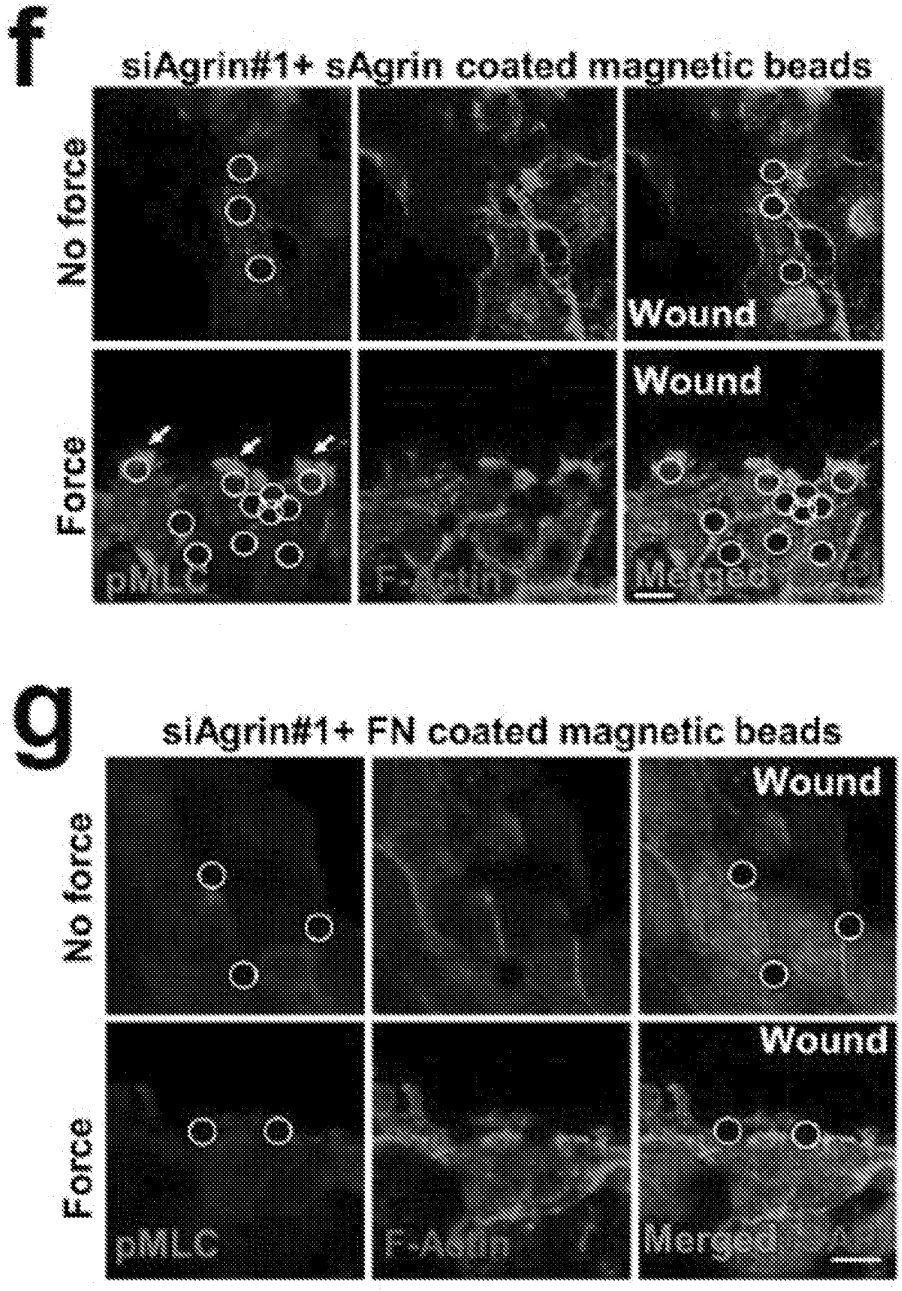


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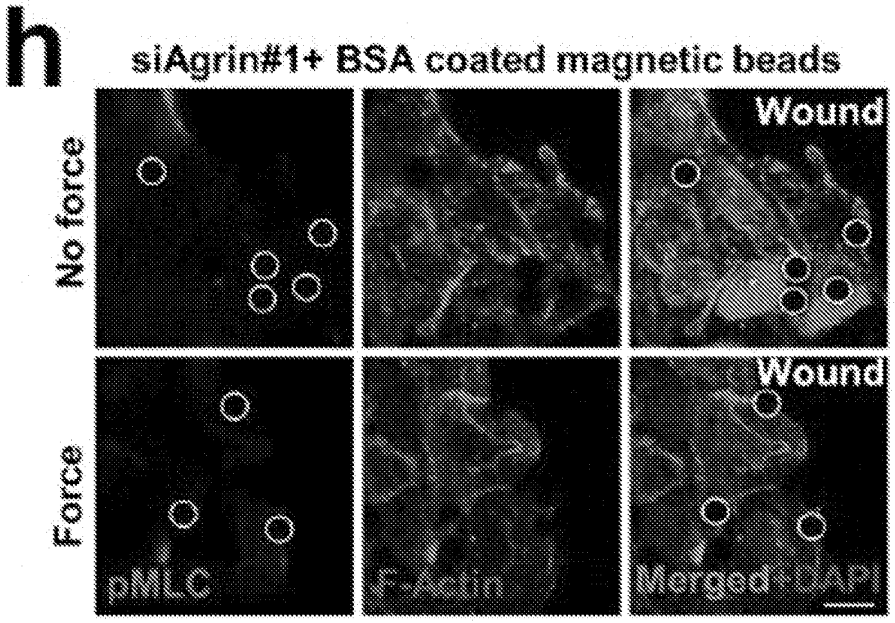
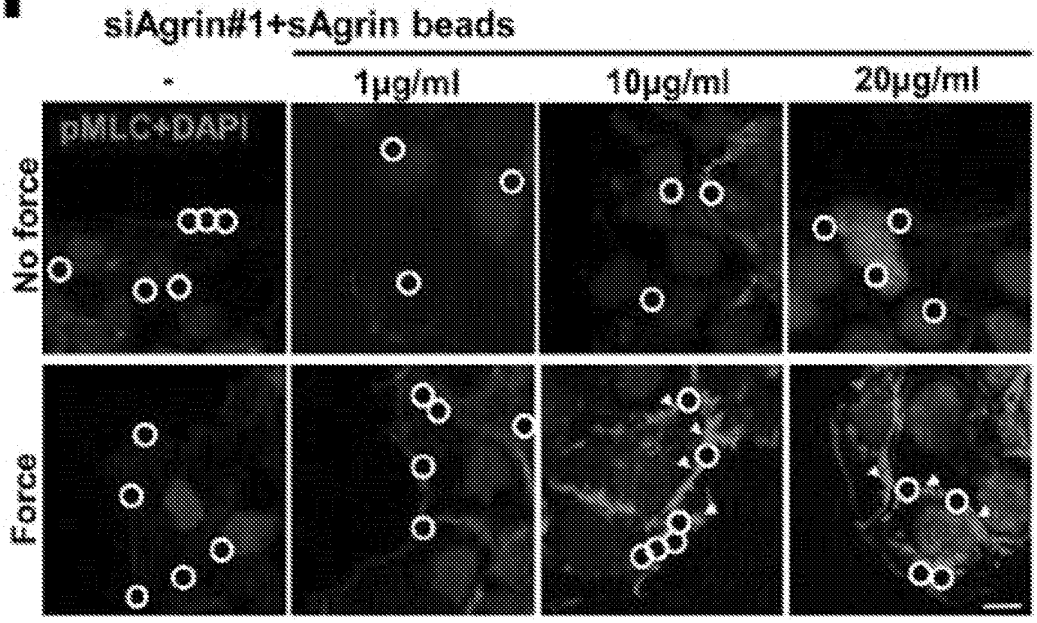


Fig. 10 (Continued)

i



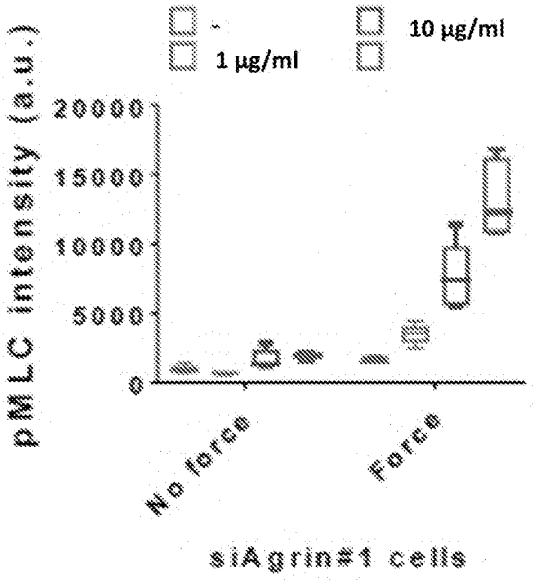


Fig. 10 (Continued)

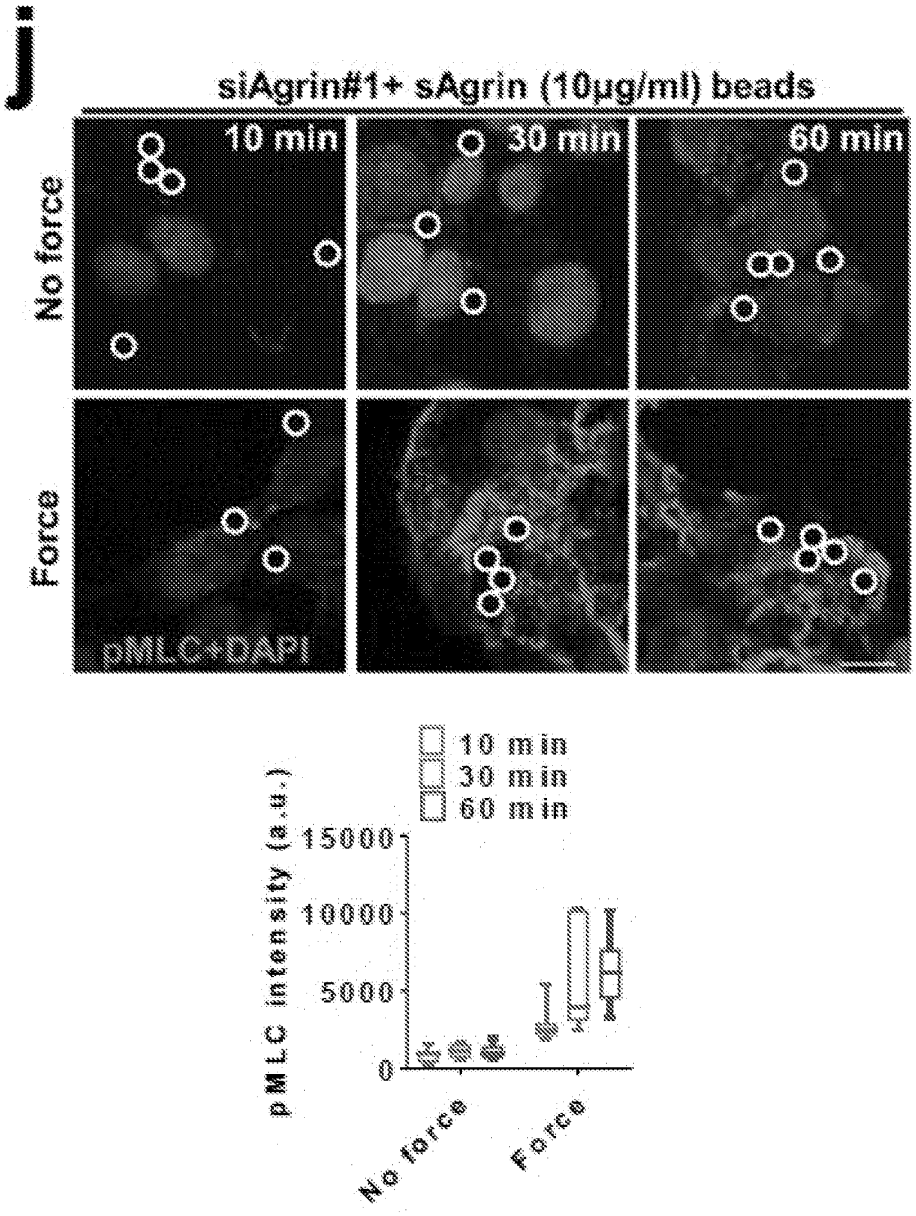


Fig. 10 (Continued)

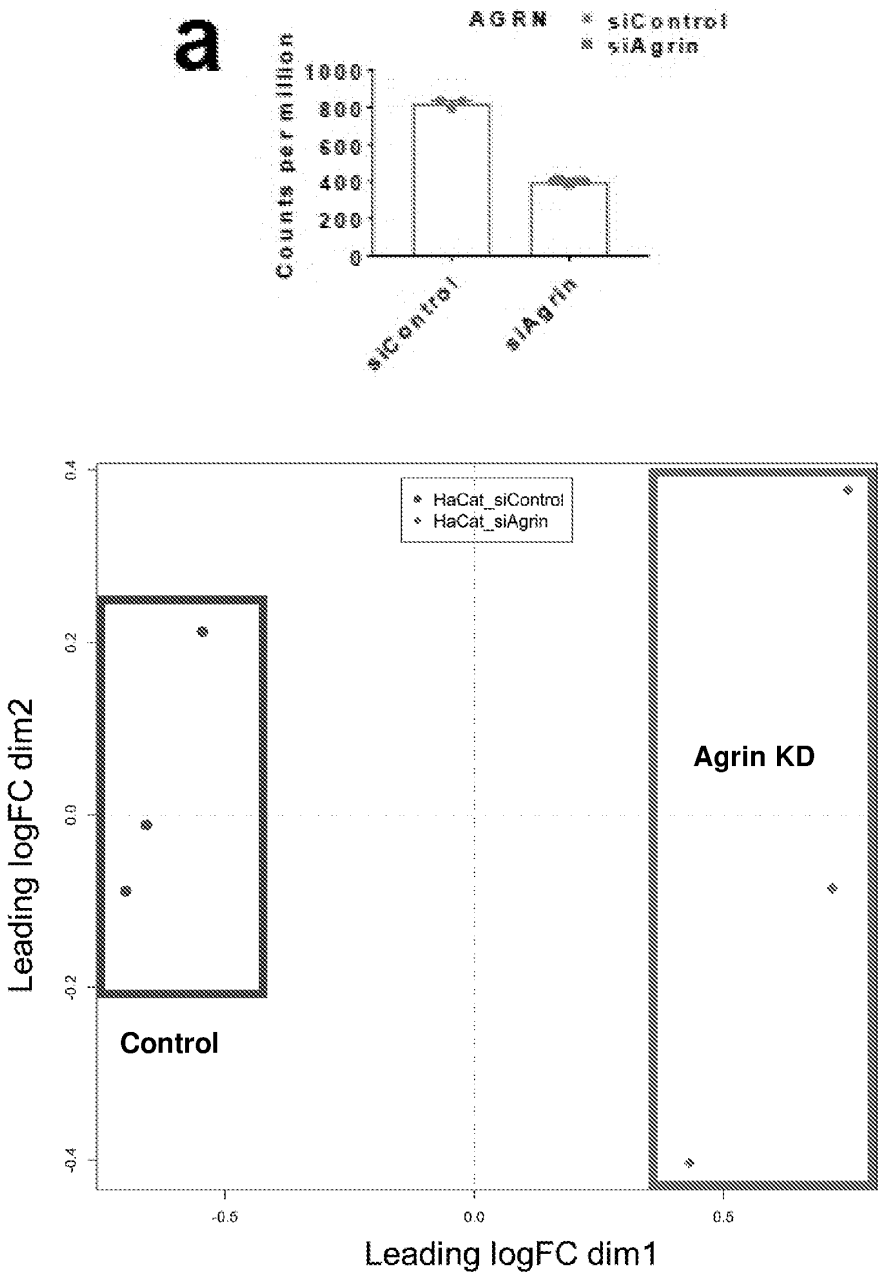

a
AGRN
siControl
siAgrin
Counts per million
1000
800
600
400
200
0
siControl
siAgrin
HaCat_siControl
HaCat_siAgrin
Agrin KD
Control
Leading logFC dim2
Leading logFC dim1
0.4
0.2
0.0
-0.2
-0.4
-0.5
0.0
0.5

Fig. 11

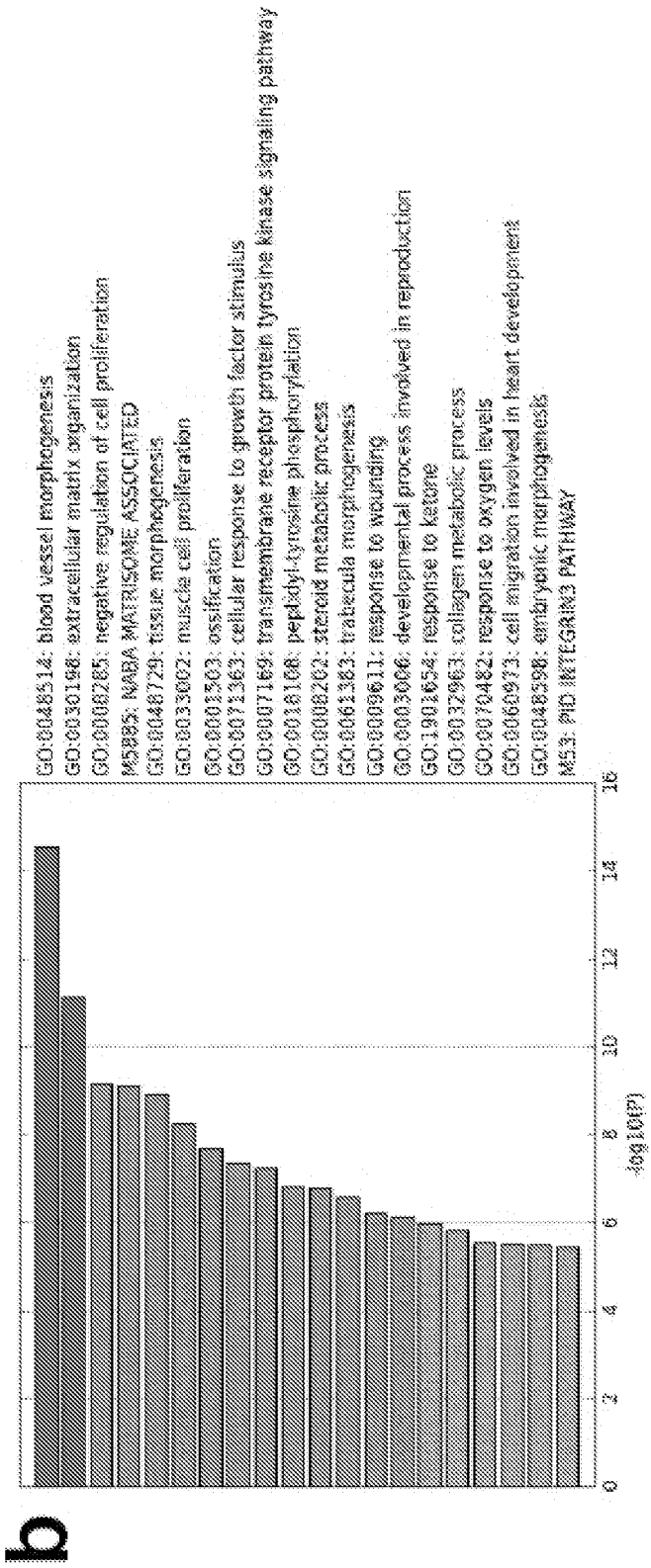


Fig. 11 (Continued)

c

GO_Extracellular matrix_constituents_enrichment plot

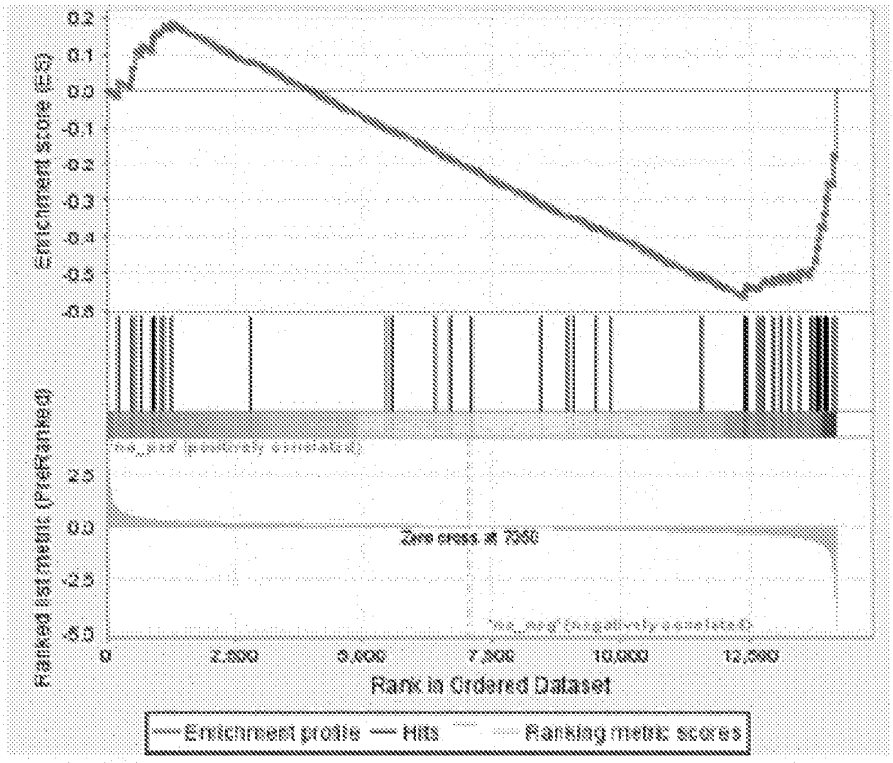


Fig. 11 (Continued)

d

Top 10 genes regulated

Gene	Log FC	P value
DKK3	1.217490735	1.5908E-12
IFI6	1.949568027	4.31383E-12
SERPINE2	1.559933701	4.70245E-12
SQLE	1.176672725	1.1468E-11
IFI27	2.390810676	1.38876E-11
DSP2	1.712664617	1.0363E-10
ELFN2	1.748537173	2.6594E-10
PTHLH	1.163873909	4.98709E-10
MFAP5	2.554695588	7.94297E-10
MMP12	-3.23873205	1.50405E-15
MMP10	-3.77153967	1.40921E-12
MMP1	-2.05967165	3.58854E-12
DUOX2	-1.52167939	1.70601E-11
AGRN	-1.03510194	2.04701E-11
GSDMB	-2.18196608	3.11526E-11
NNL	-2.7177322	8.59365E-11
RNF207	-1.43188112	1.042E-10
CTSS	-1.37321829	1.22908E-10

High

Low

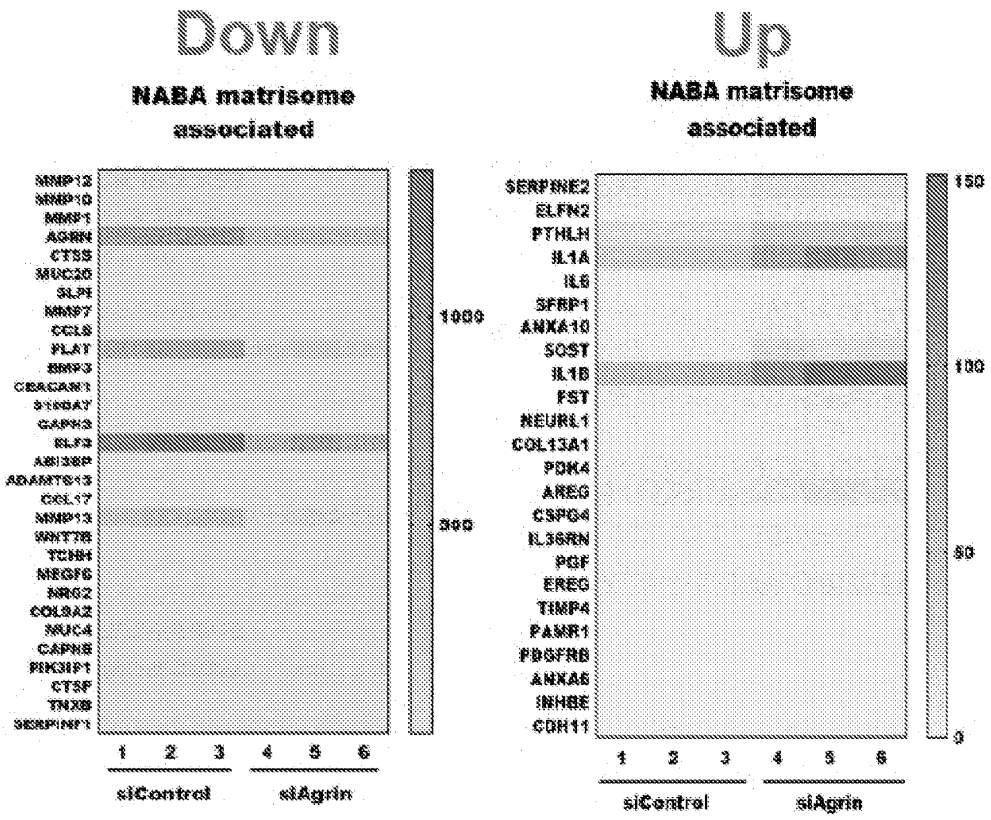


Fig. 11 (Continued)

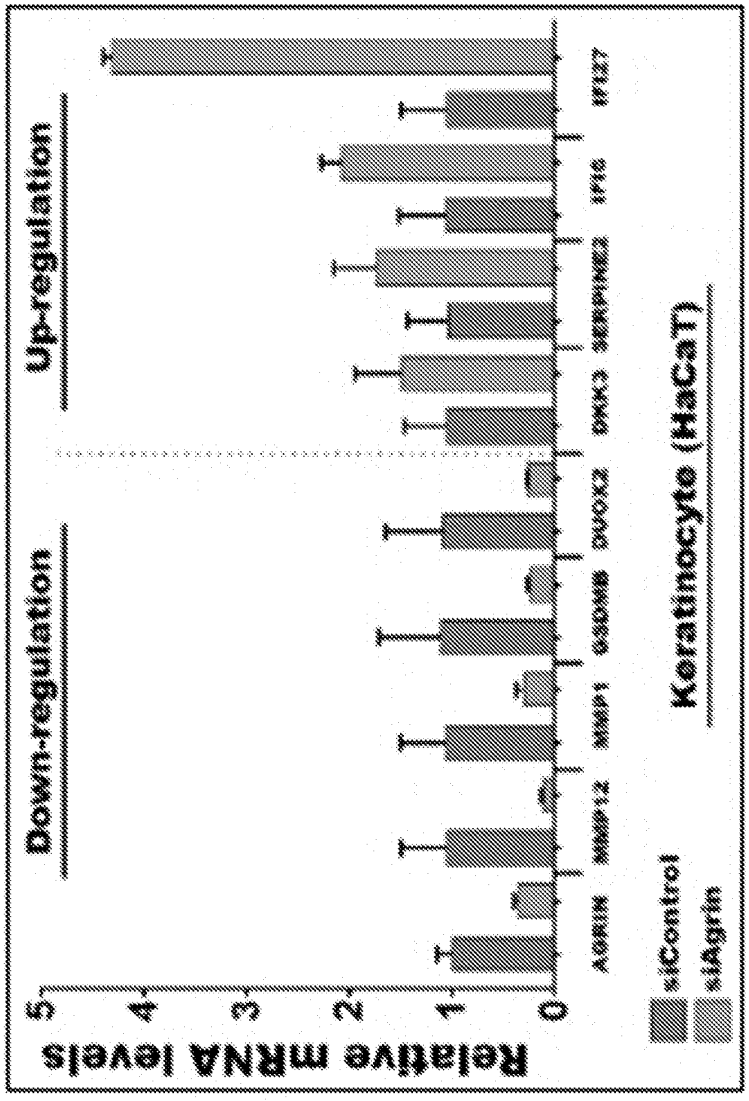


Fig. 11 (Continued)

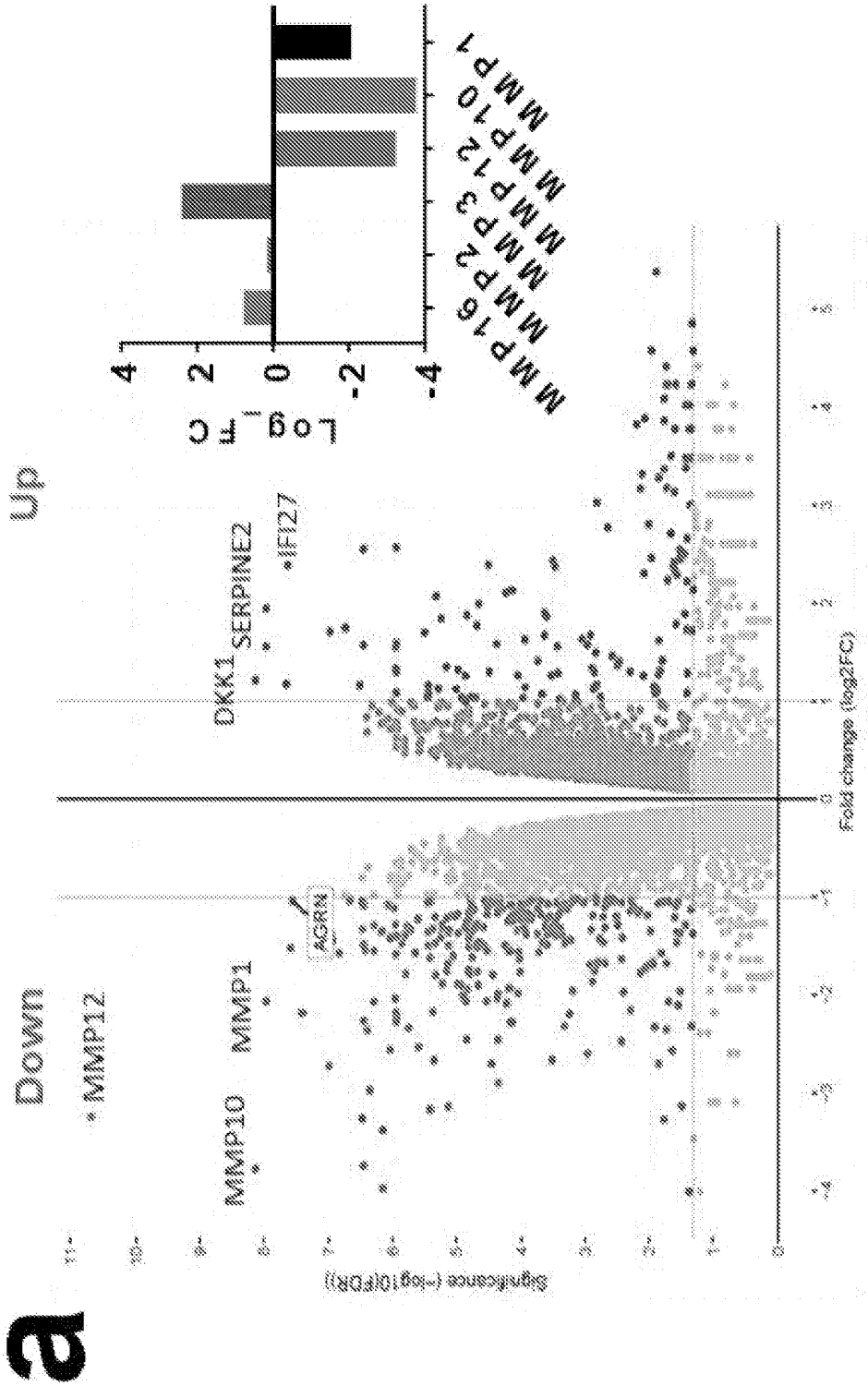

a
Up
Down
DKK1
SERPINE2
IFI27
MMP12
MMP10
MMP1
AGRN
Significance (−log10FDR)
Fold change (log2FC)
log_FC
MMP1
MMP2
MMP3
MMP12
MMP10
MMP16

Fig. 12

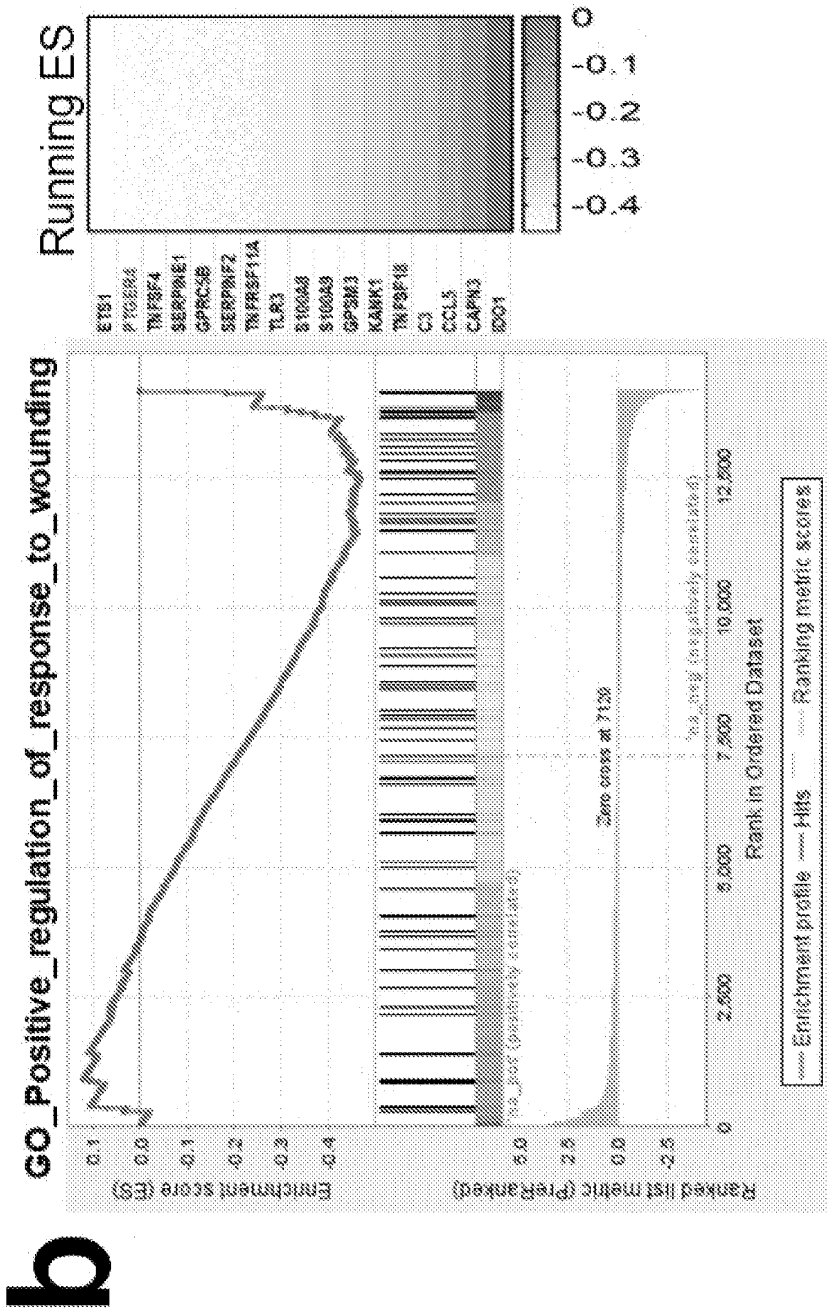


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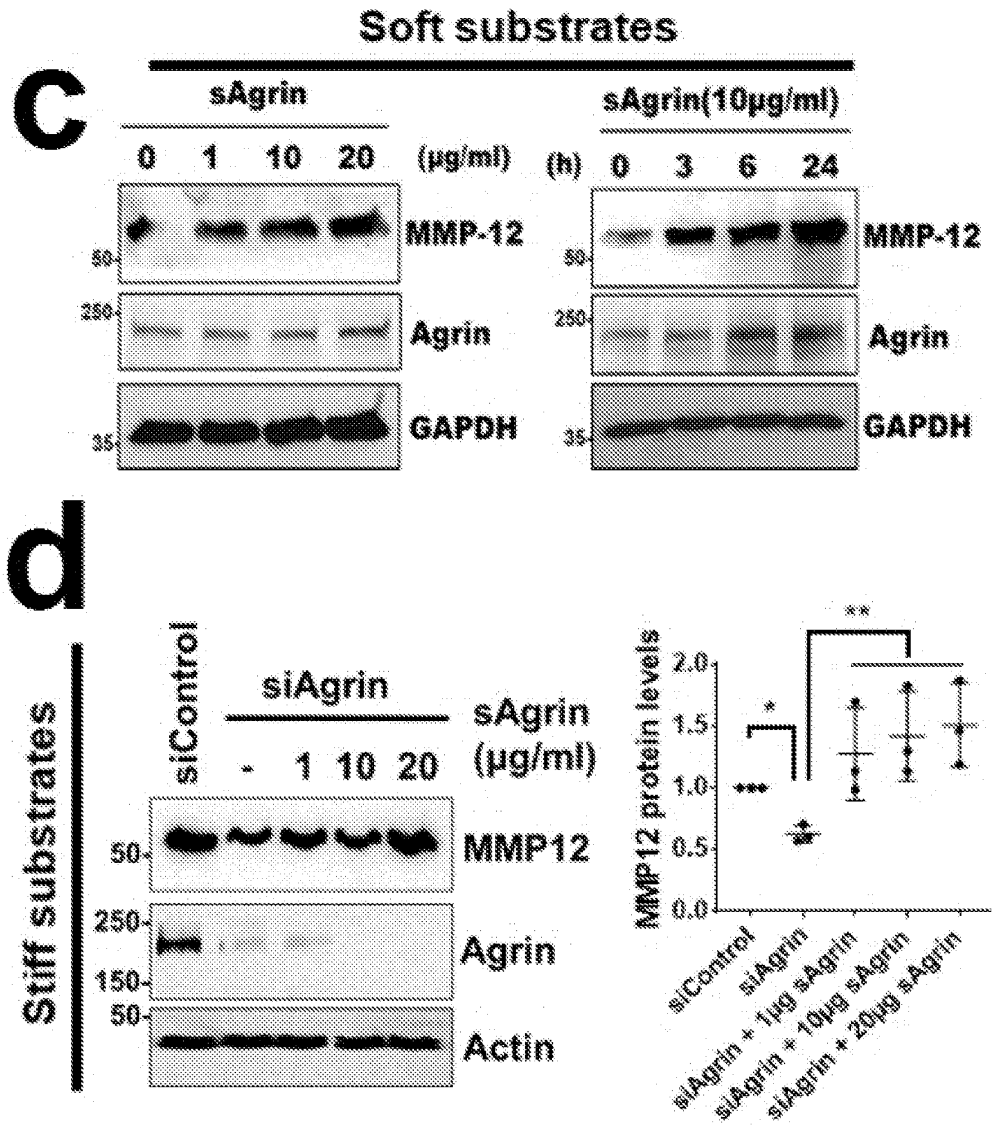


Fig. 12 (Continued)

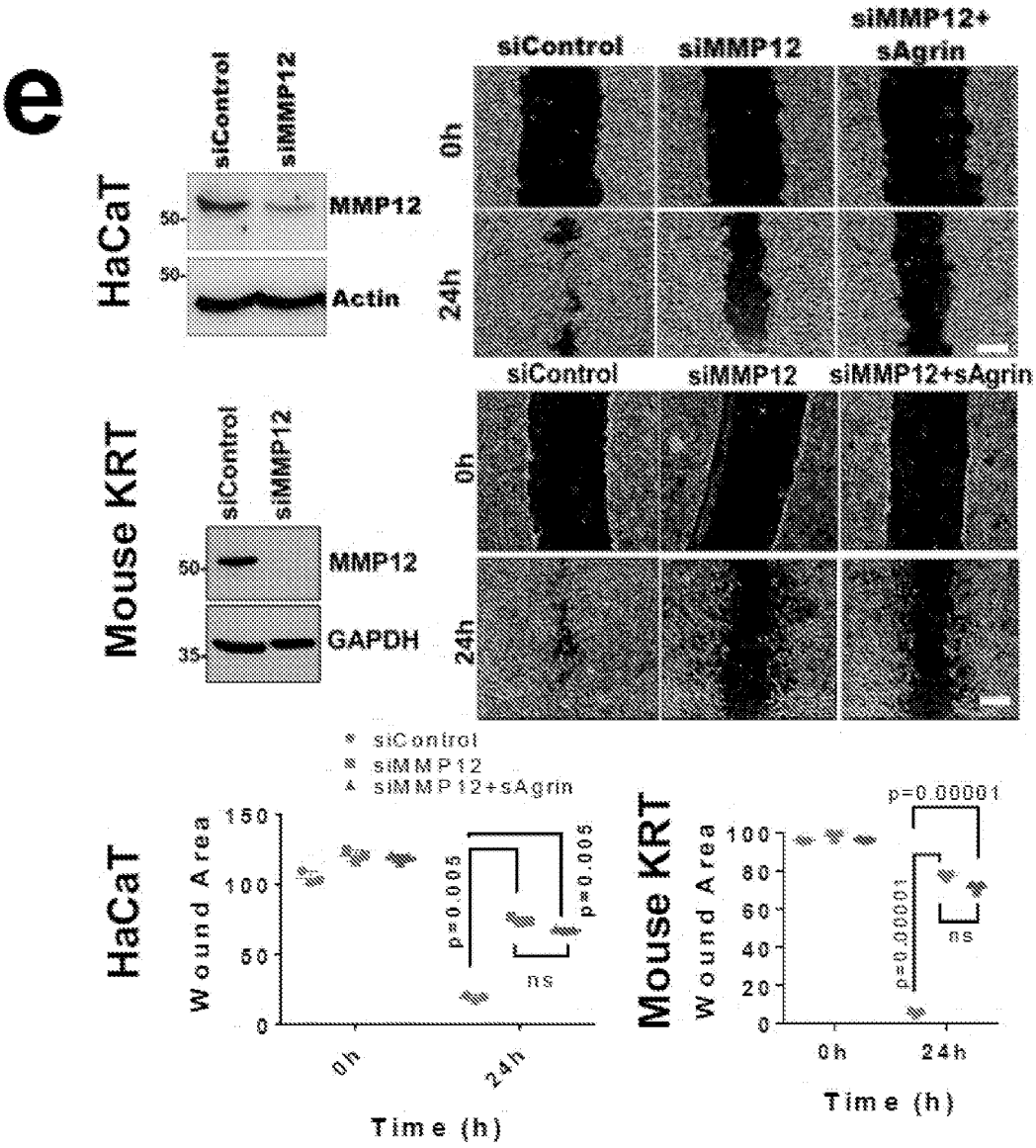


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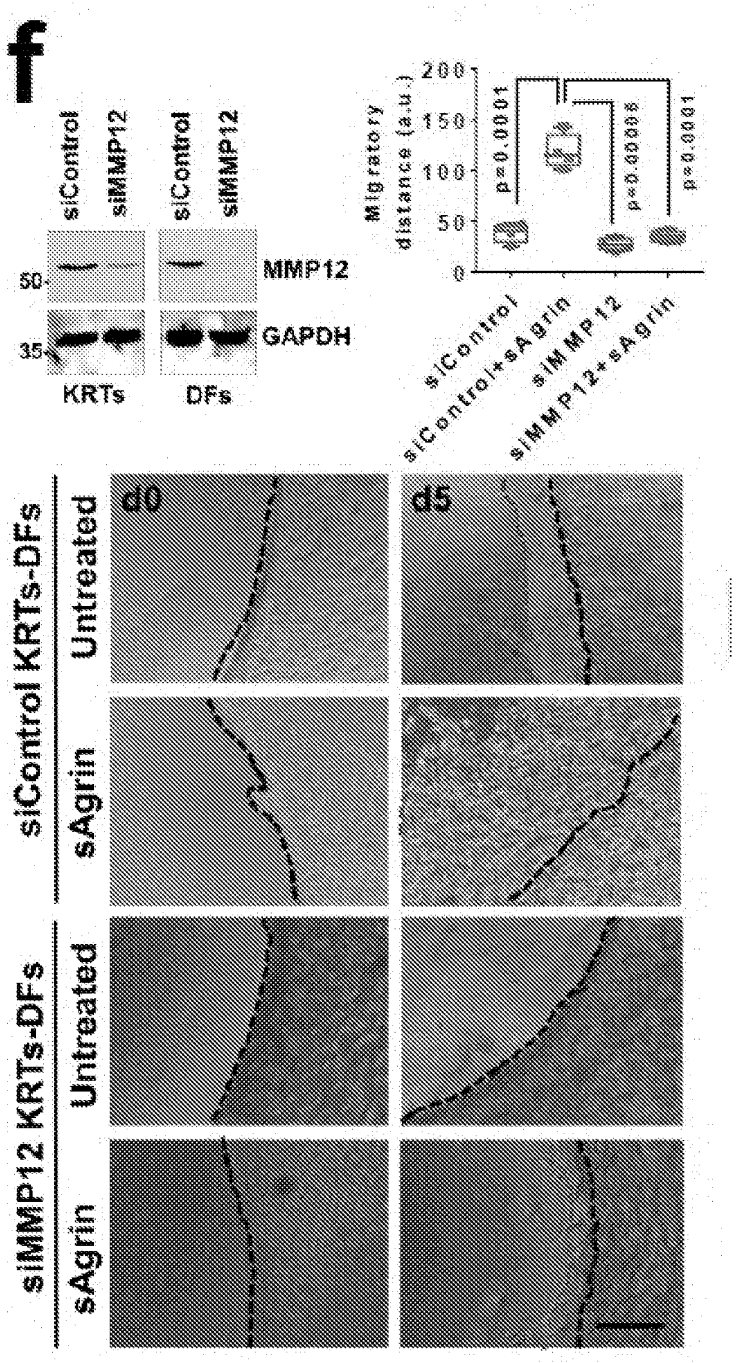


Fig. 12 (Continued)

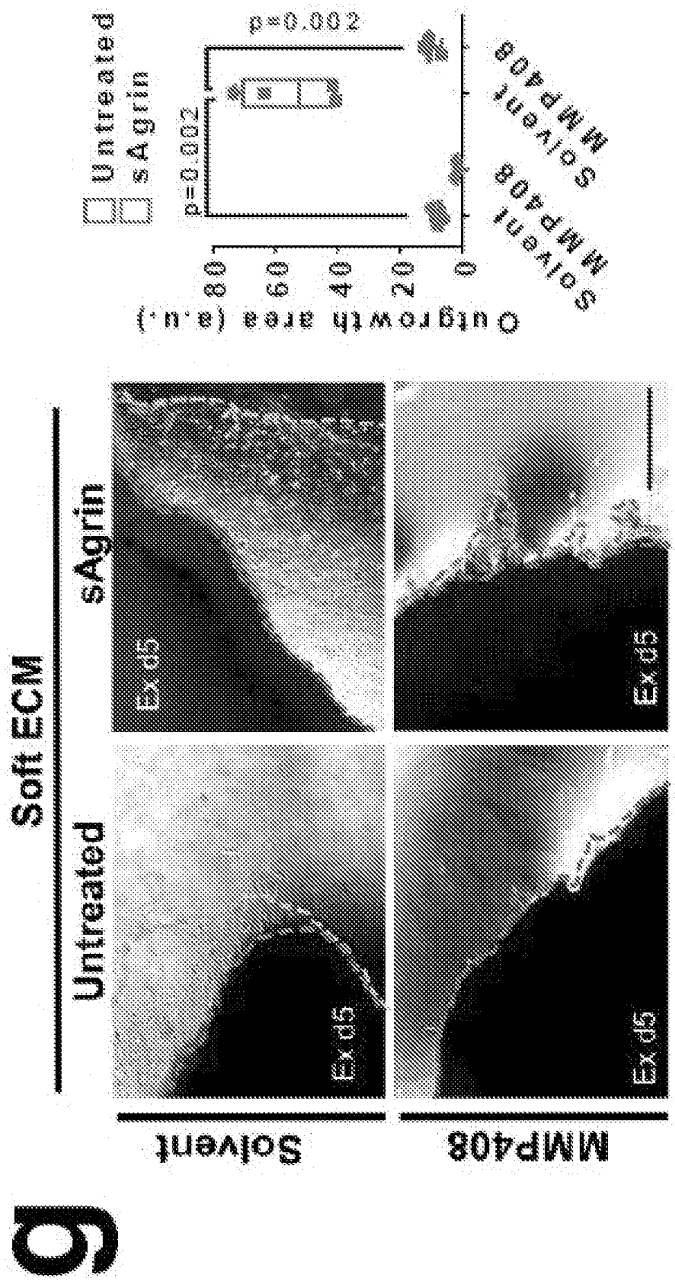


Fig. 12 (Continued)

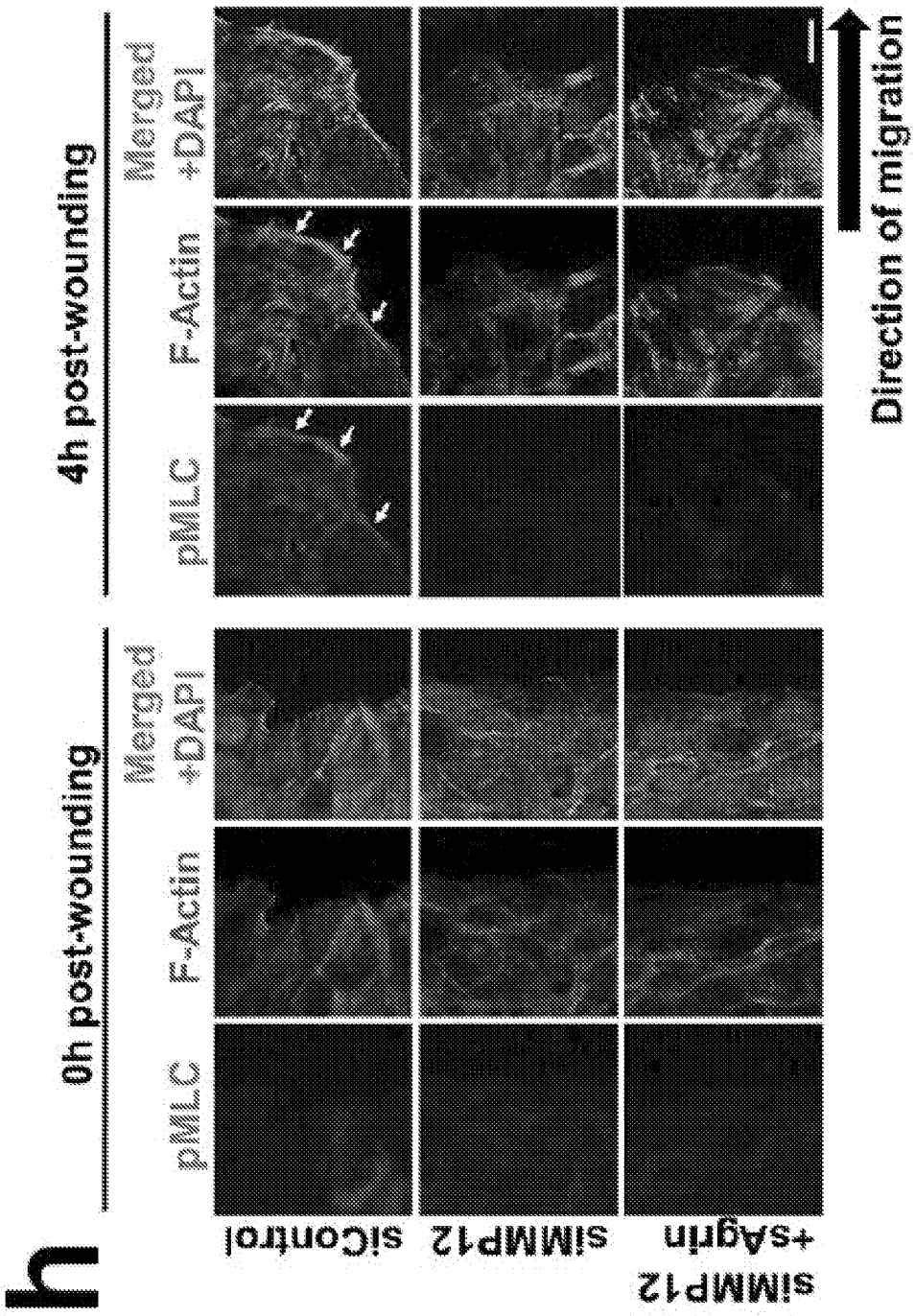


Fig. 12 (Continued)

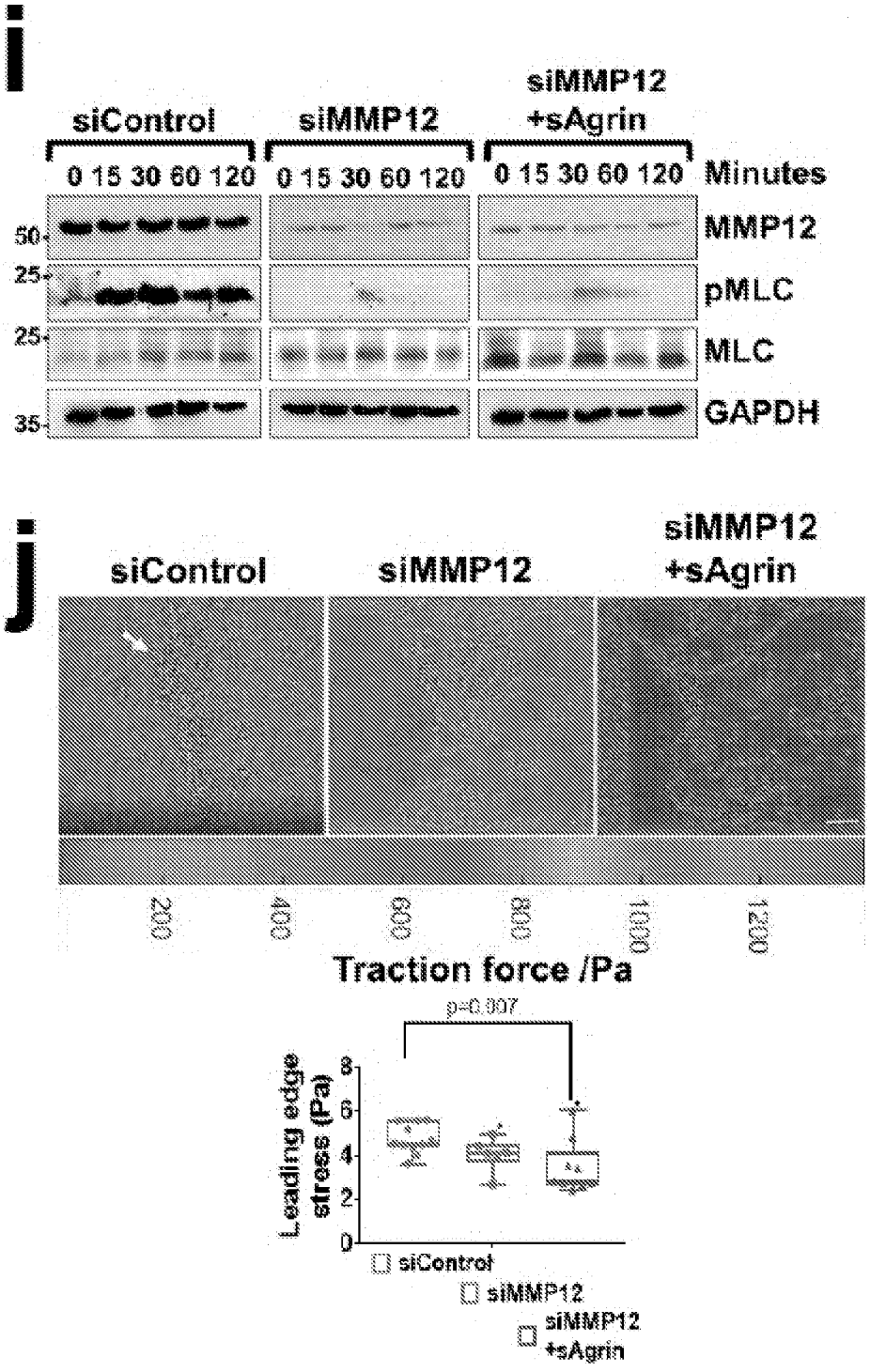


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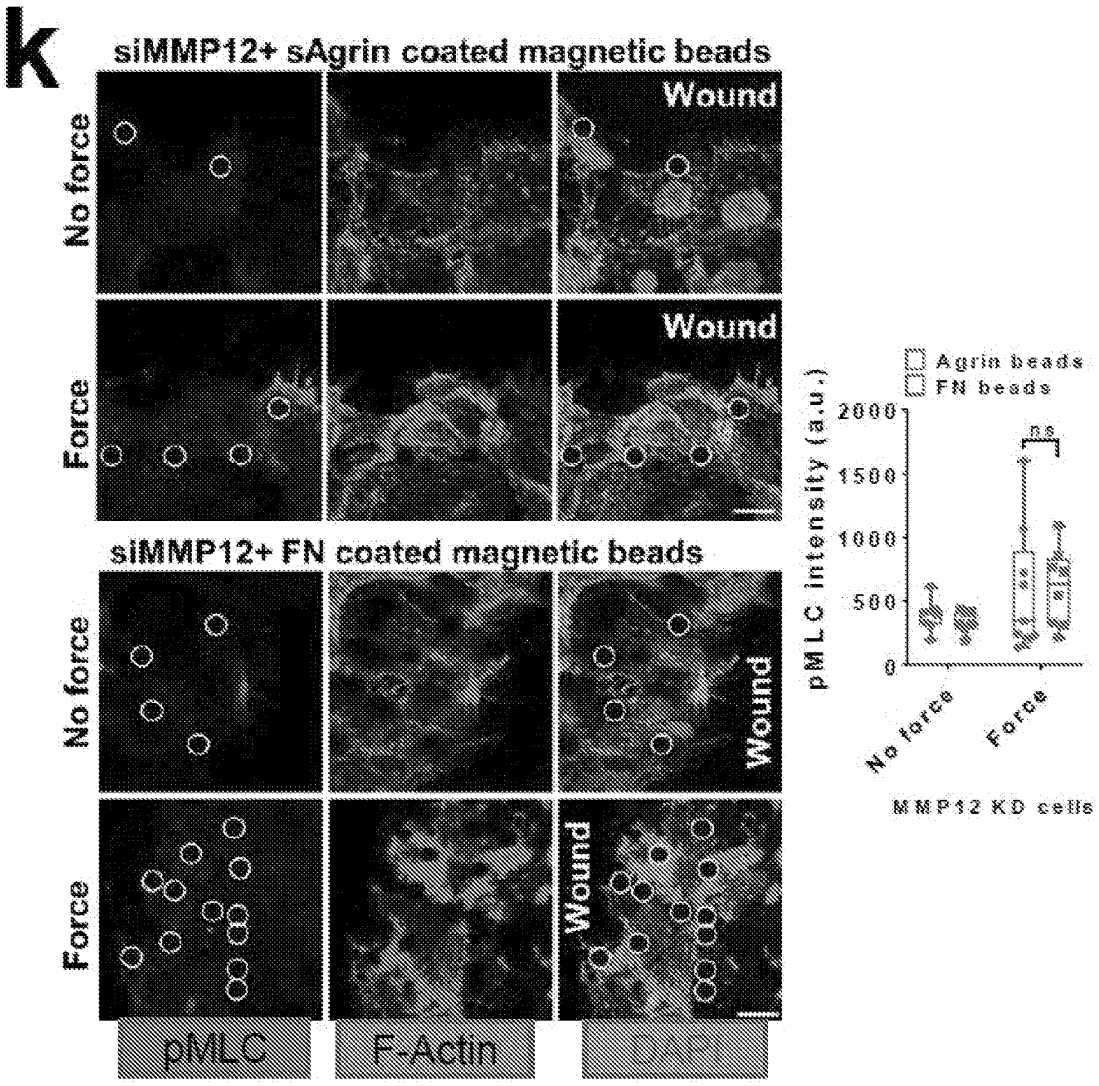


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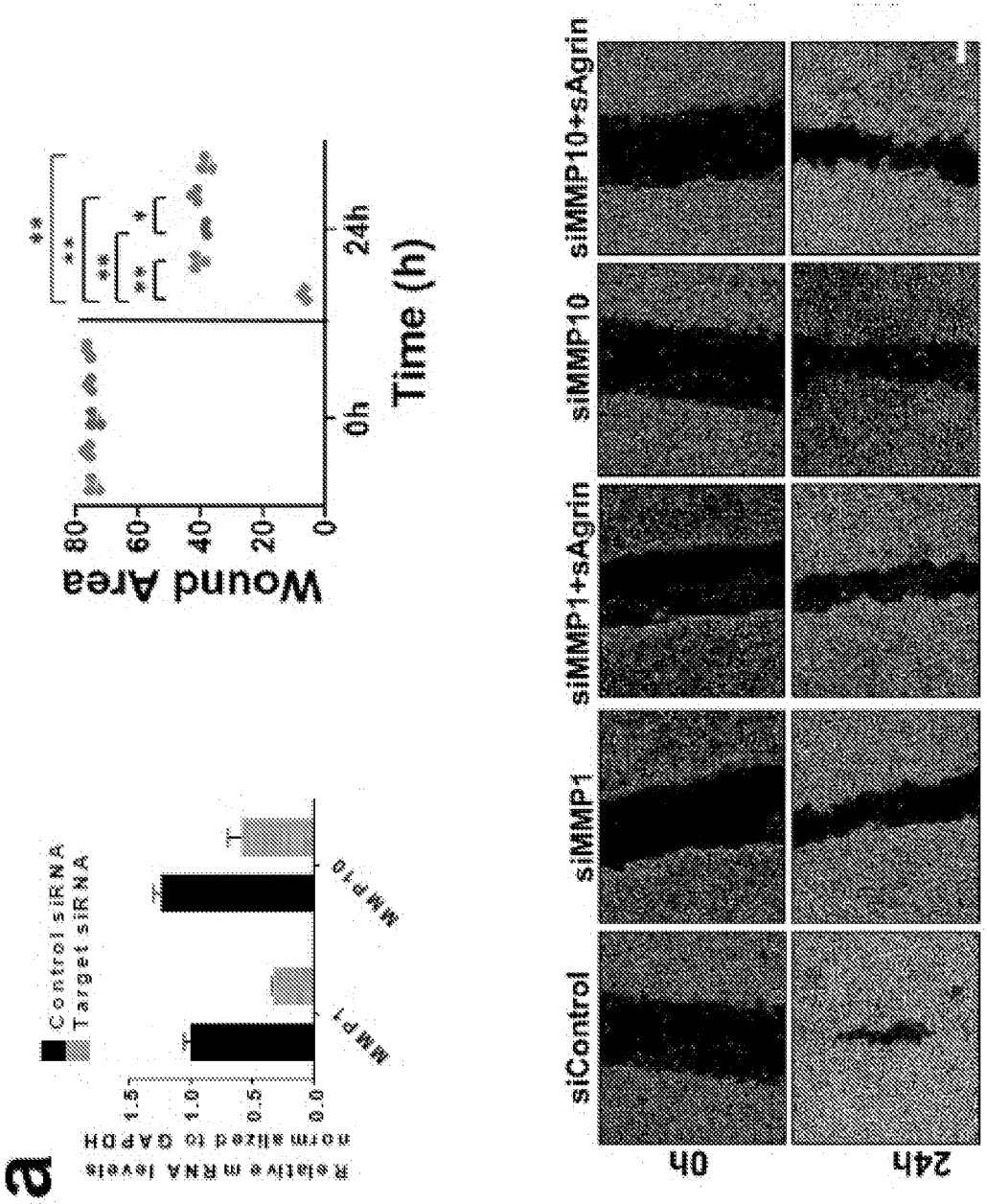

a
Relative mRNA levels norm alized to GAPDH
1.5
1.0
0.5
0.0
Control siRNA
Target siRNA
MMP1
MMP10
Wound Area
80
60
40
20
0
0h
24h
Time (h)
siControl
siMMP1
siMMP1+sAgrin
siMMP10
siMMP10+sAgrin
0h
24h

Fig. 13

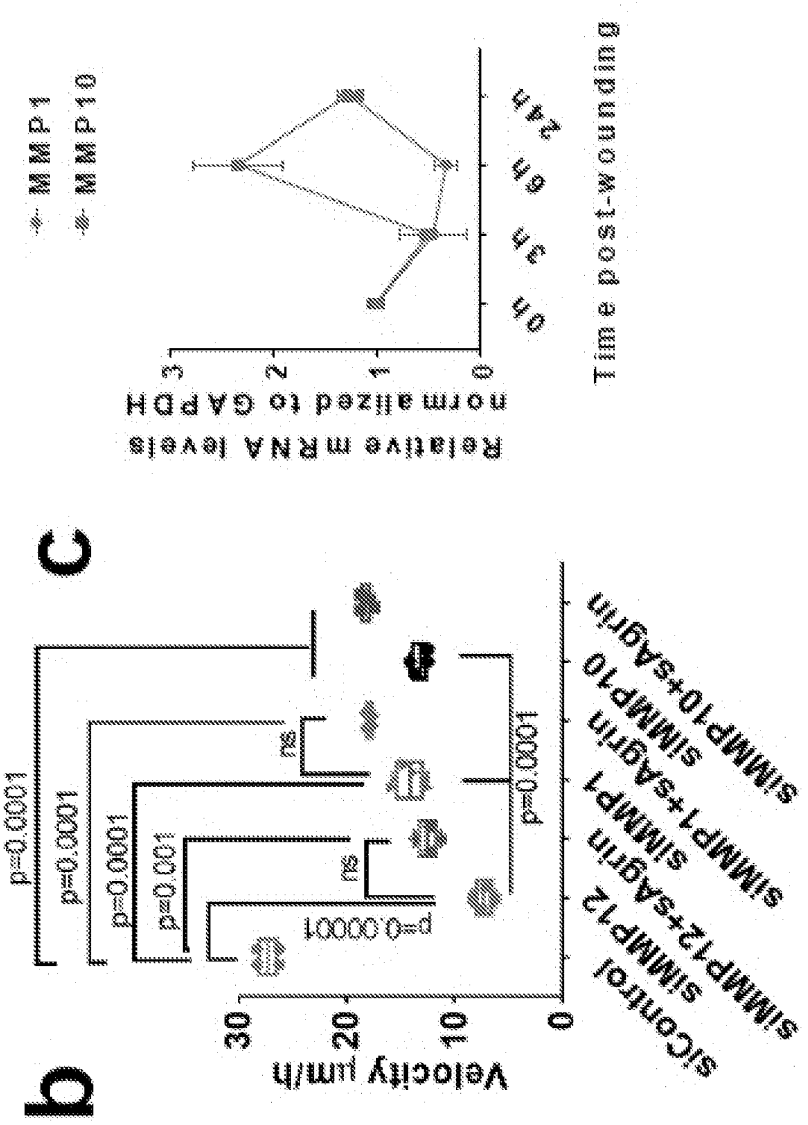


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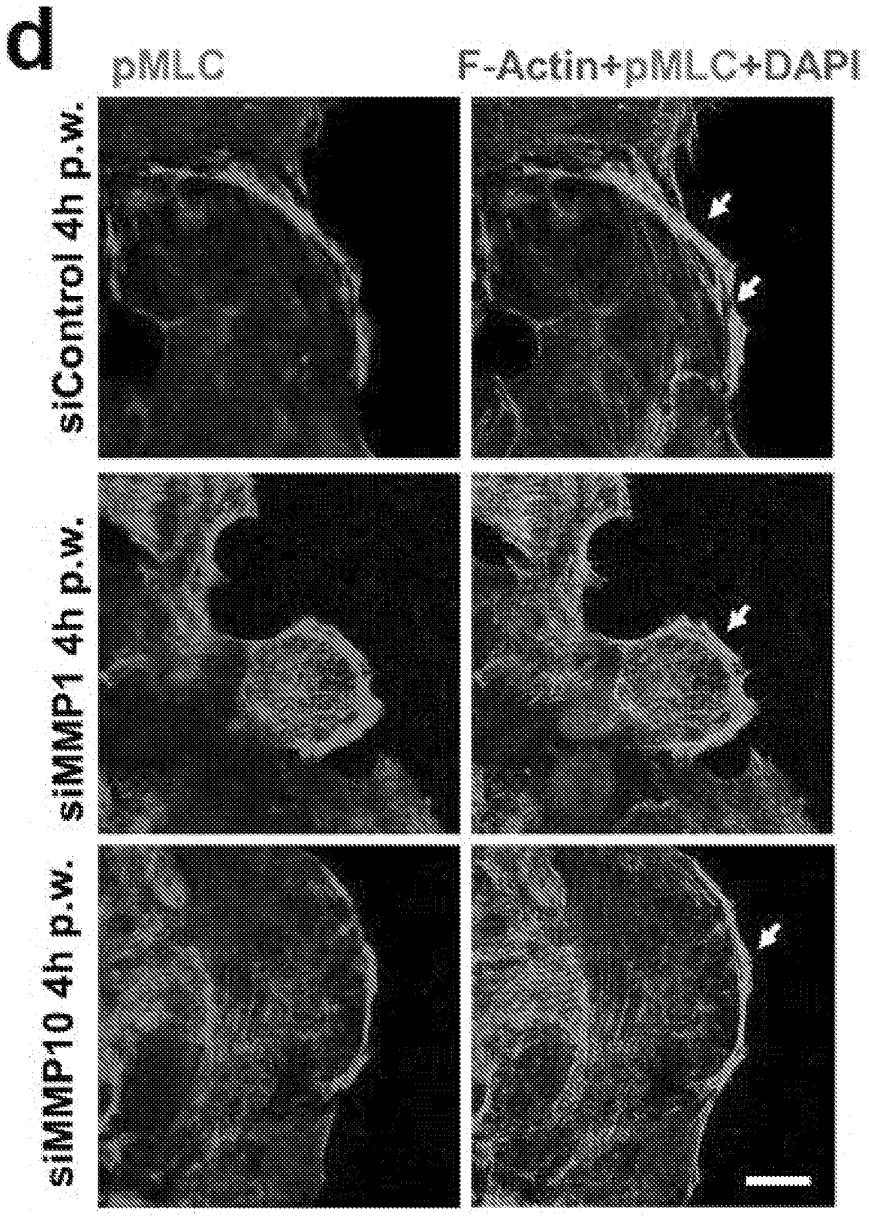


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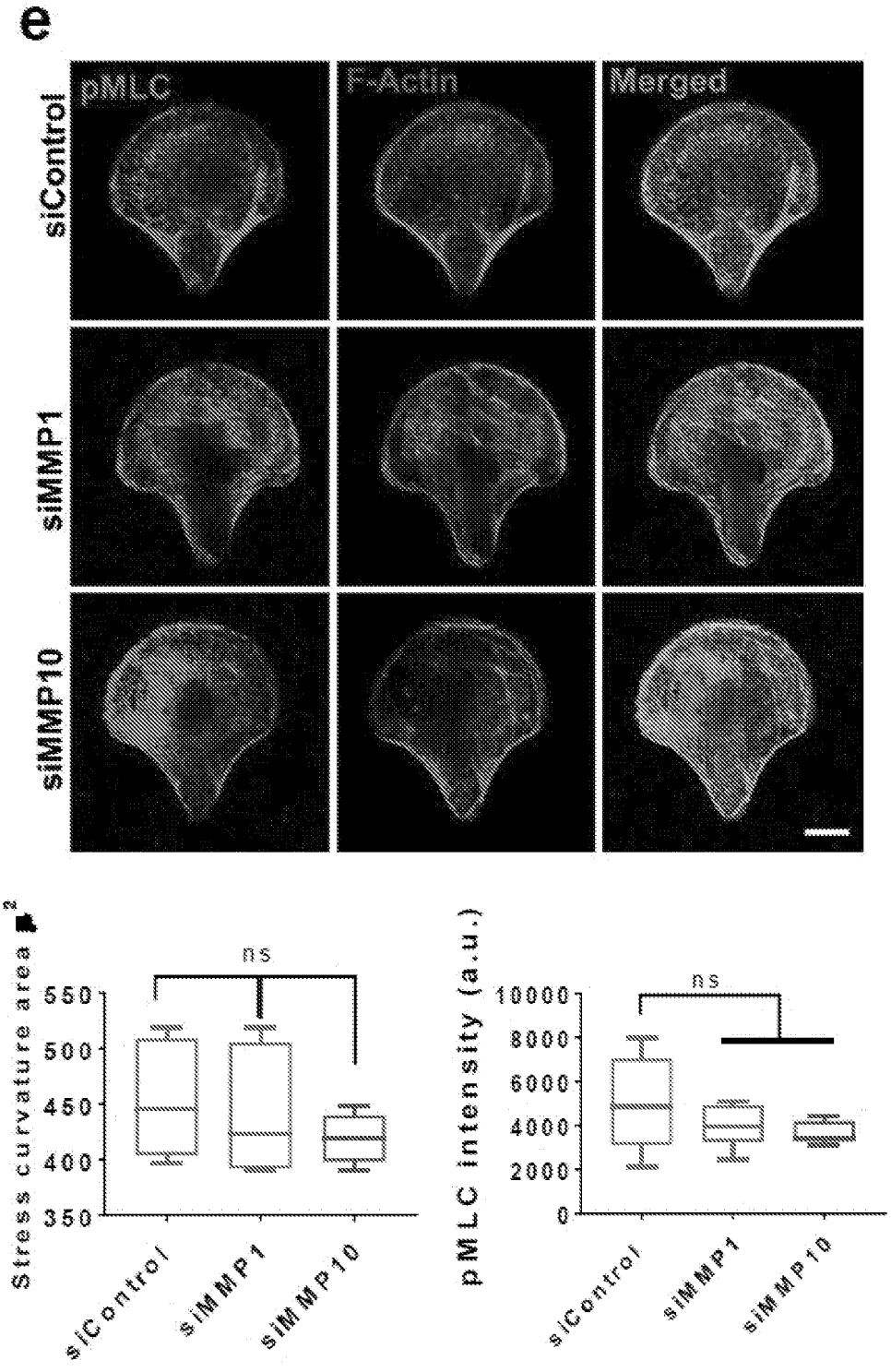


Fig. 13 (Continued)

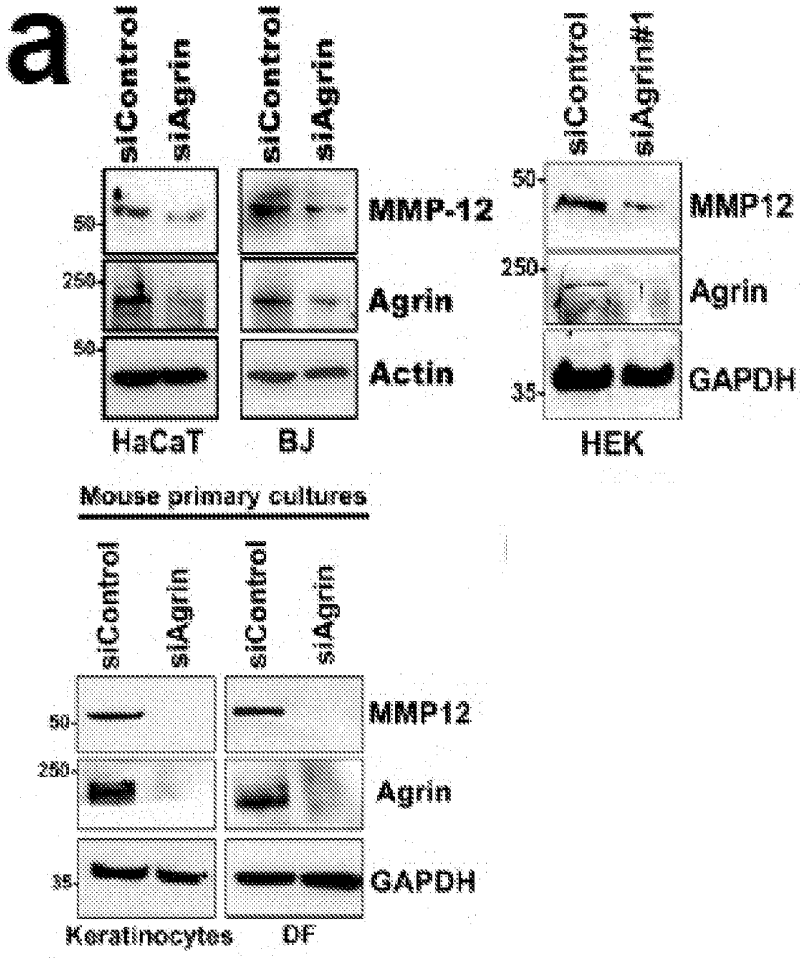
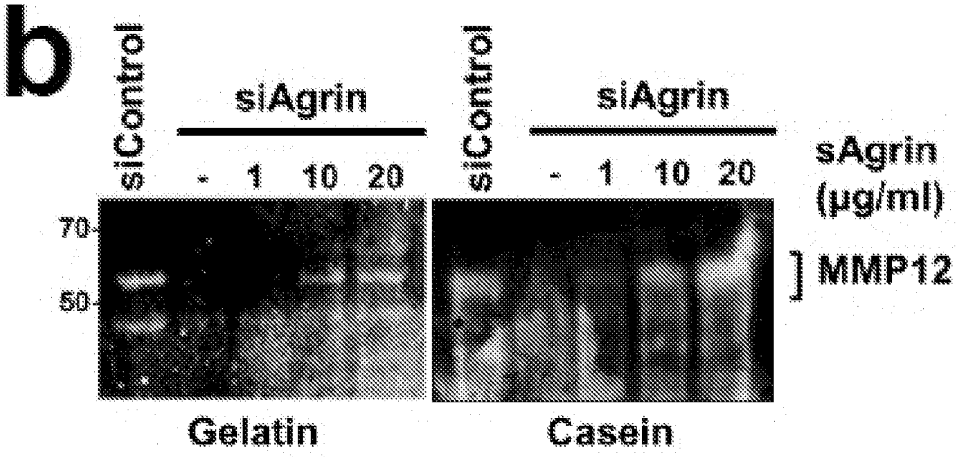

a
siControl
siAgrin
siControl
siAgrin
siControl
siAgrin#1
50
250
50
MMP-12
Agrin
Actin
HaCaT
BJ
50
250
35
MMP12
Agrin
GAPDH
HEK
Mouse primary cultures
siControl
siAgrin
siControl
siAgrin
50
250
35
MMP12
Agrin
GAPDH
Keratinocytes
DF

Fig. 14



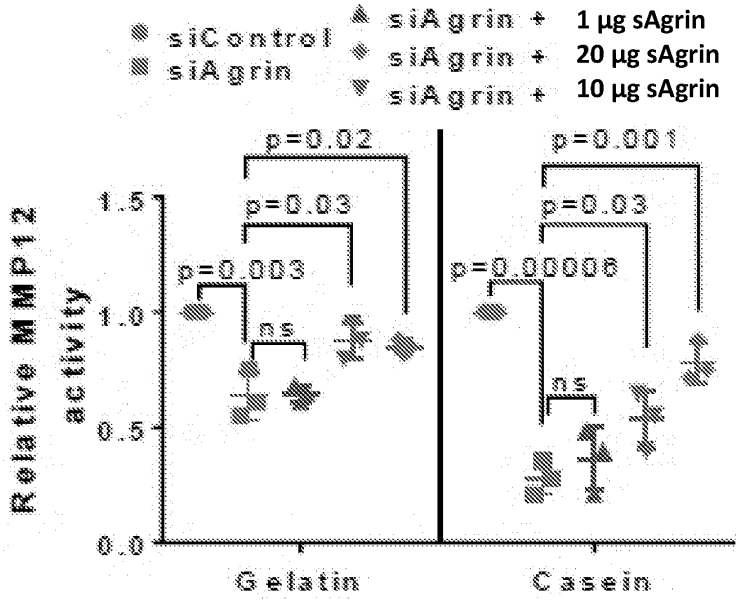


Fig. 14 (Continued)

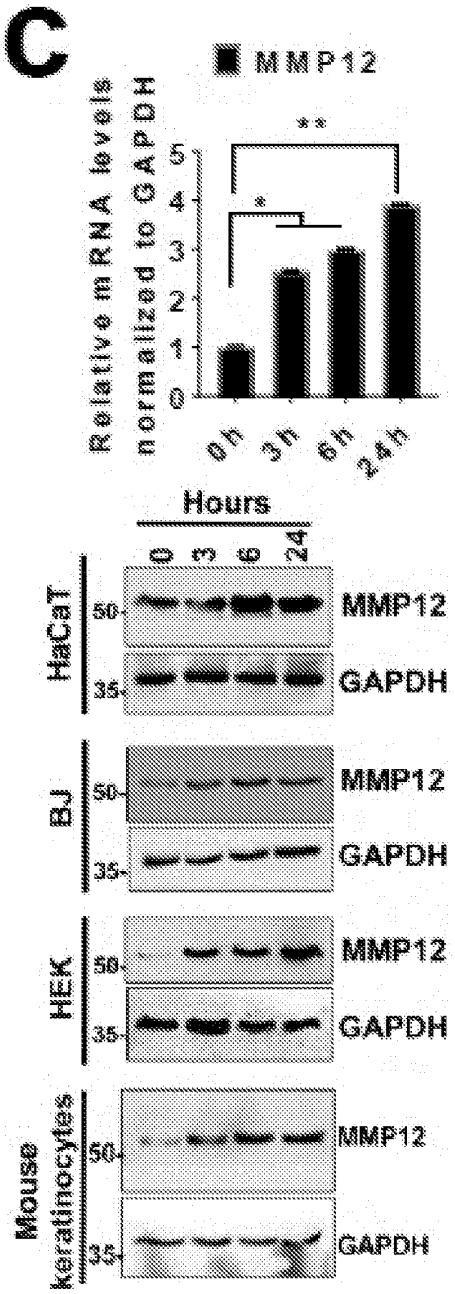


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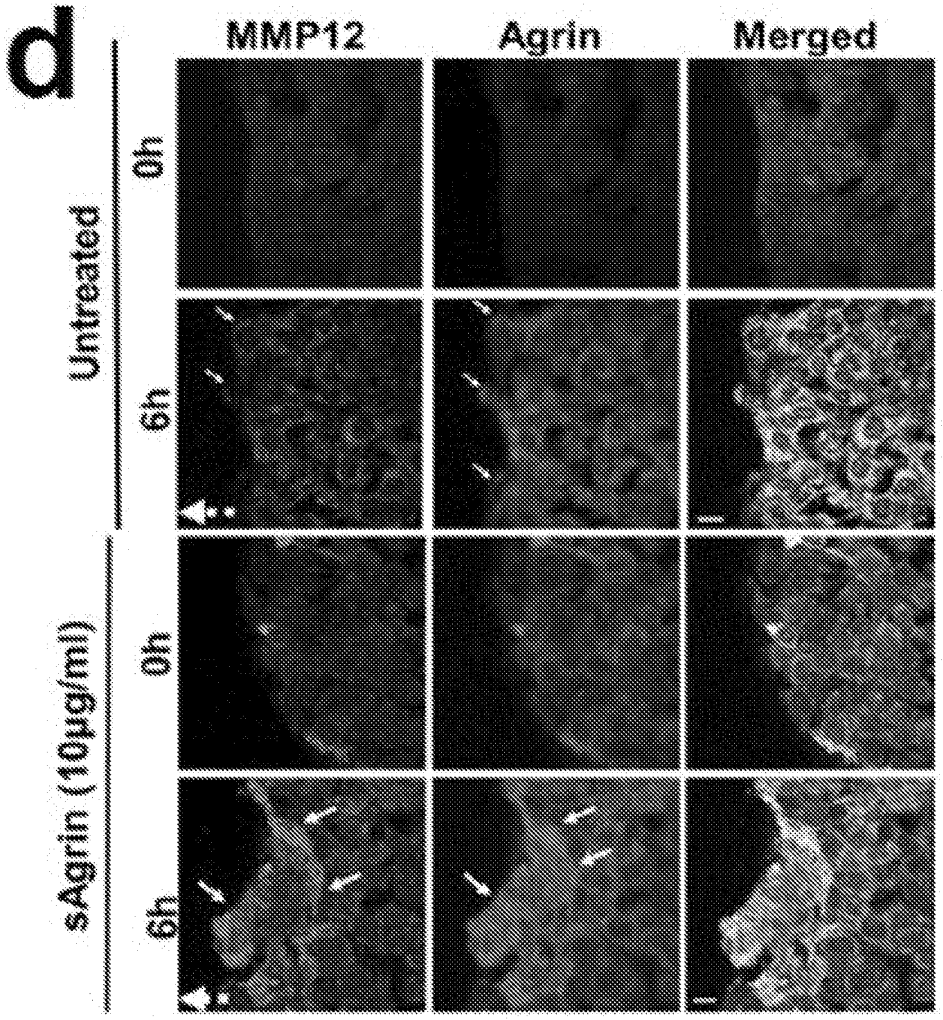


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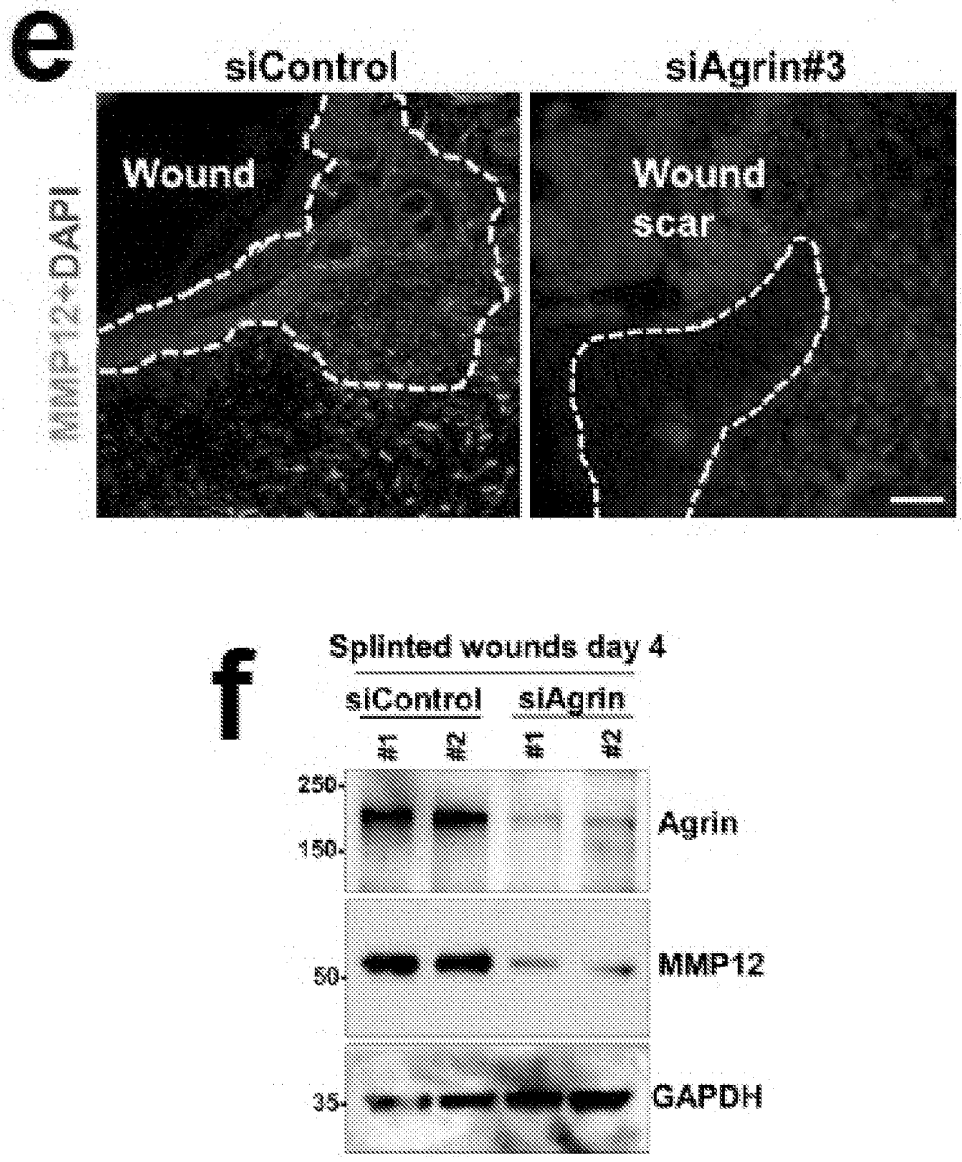
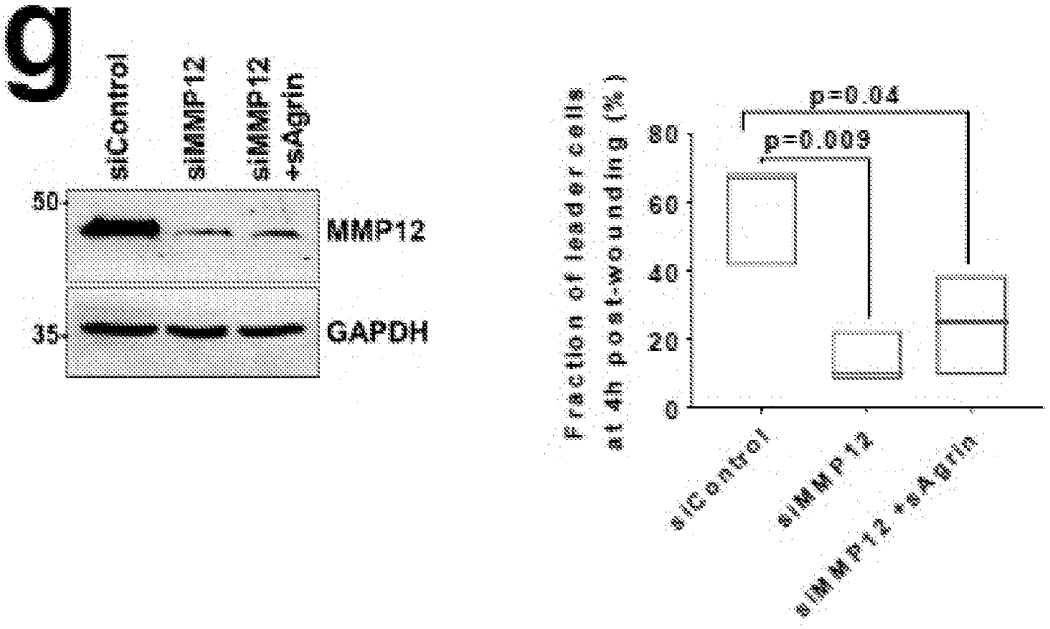


Fig. 14 (Continued)



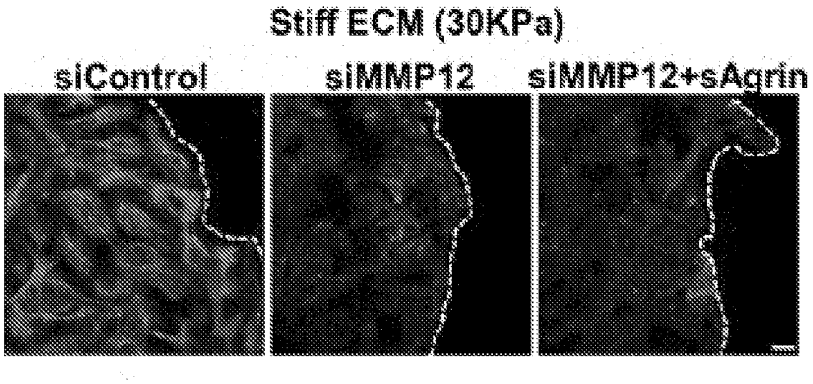
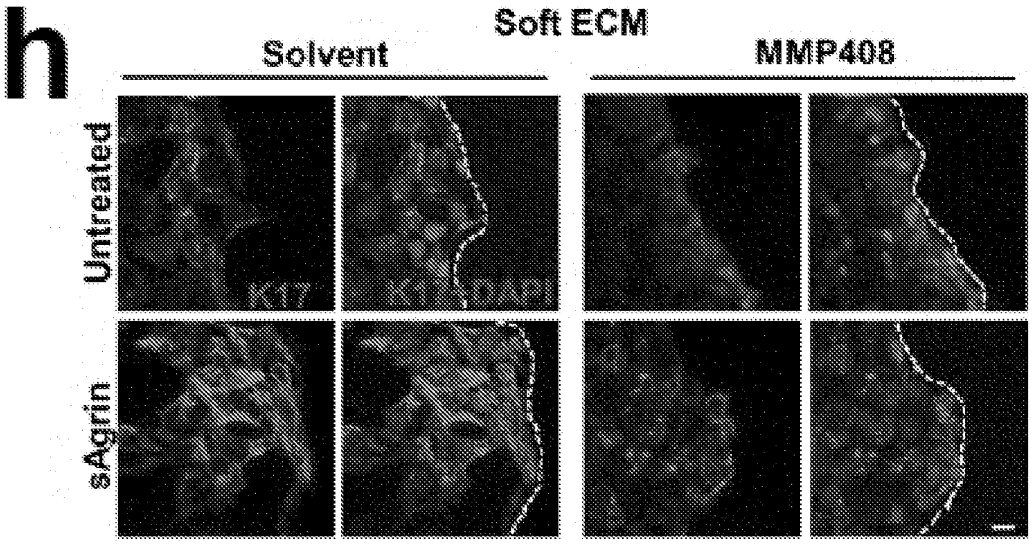
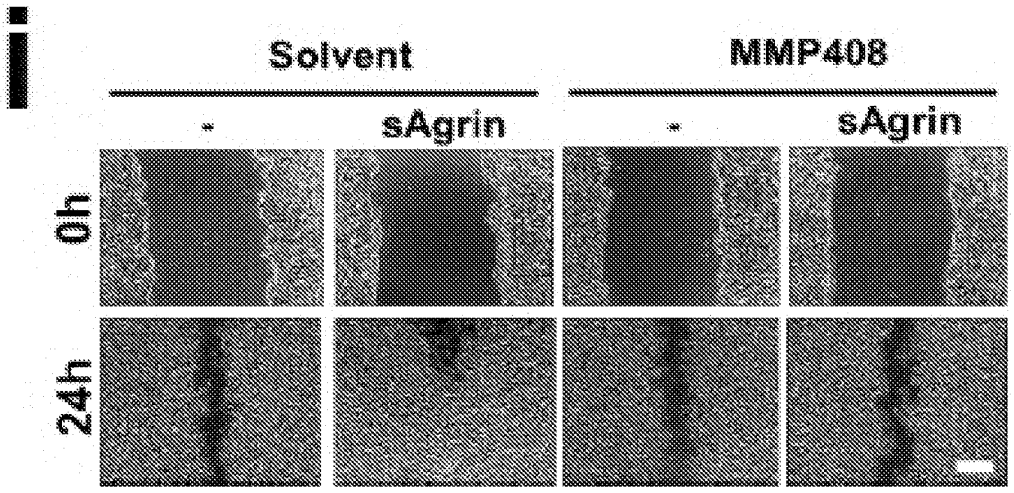


Fig. 14 (Continued)





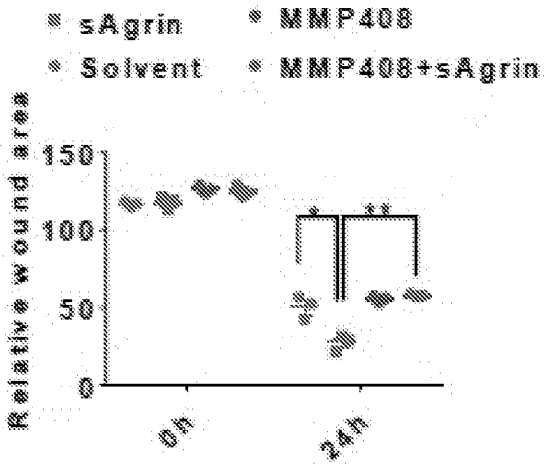


Fig. 14 (Continued)

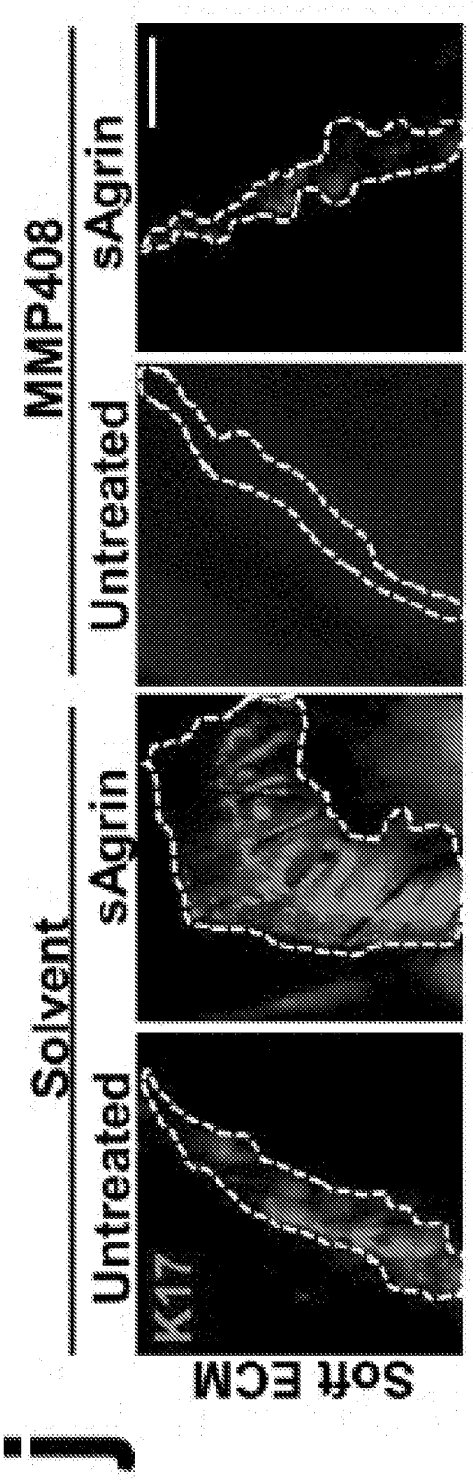


Fig. 14 (Continued)

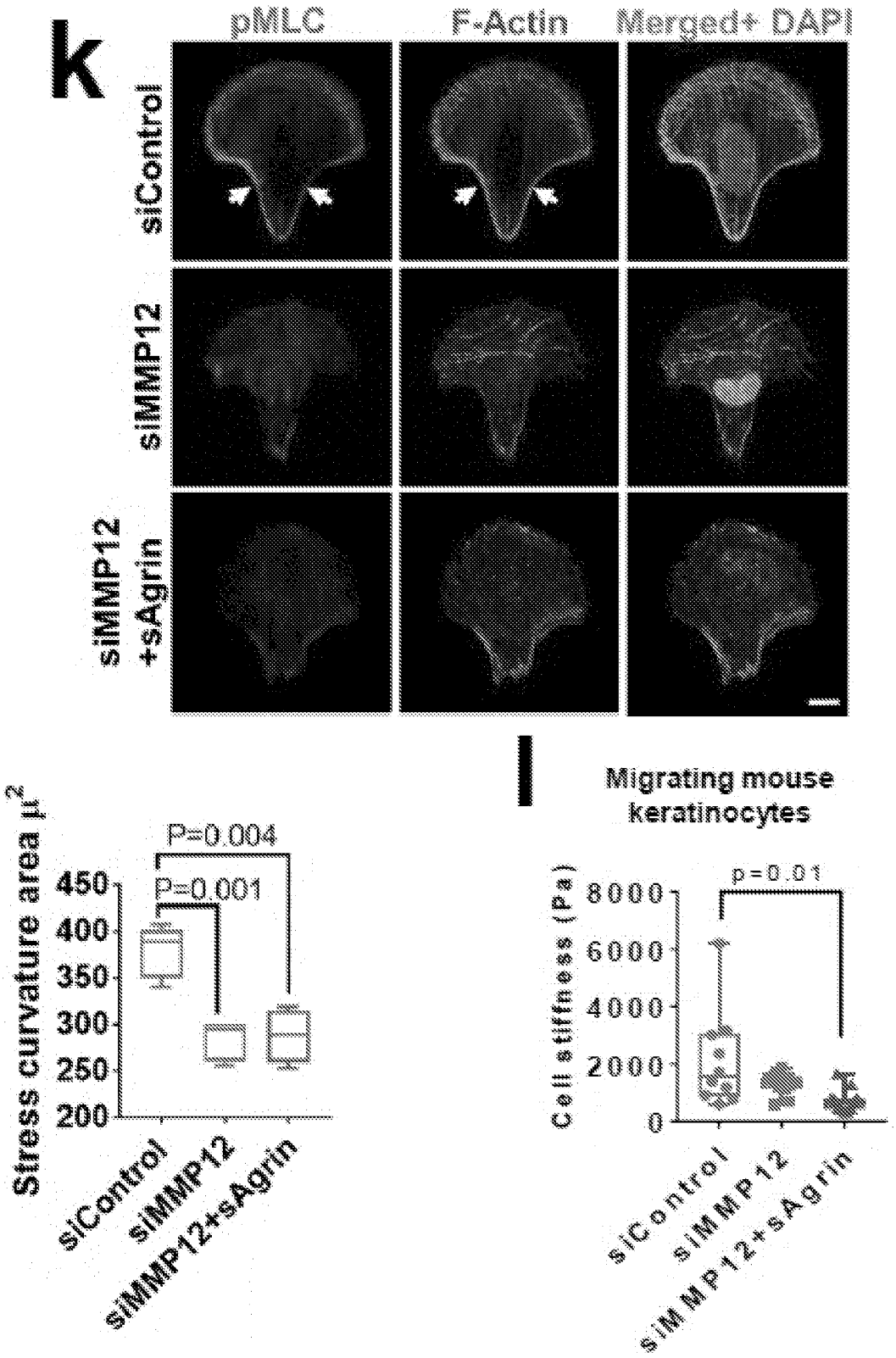


Fig. 14 (Continued)

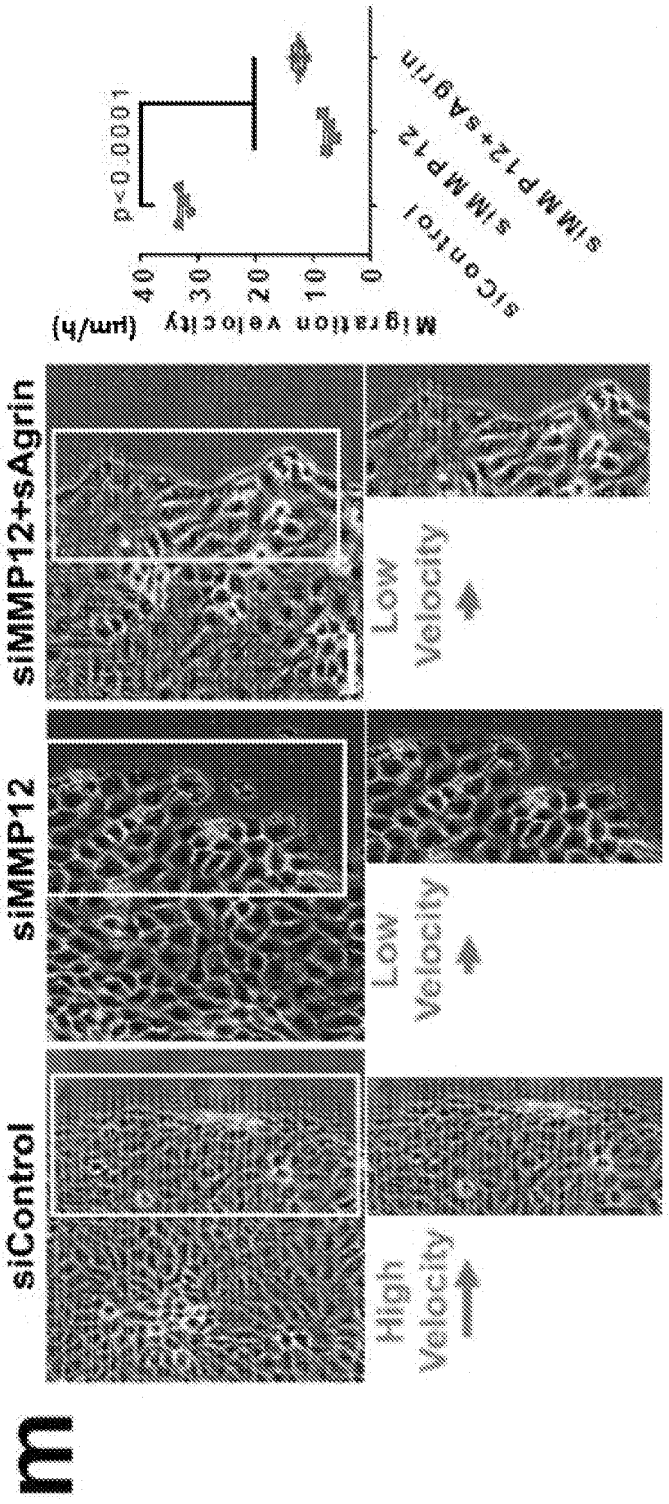
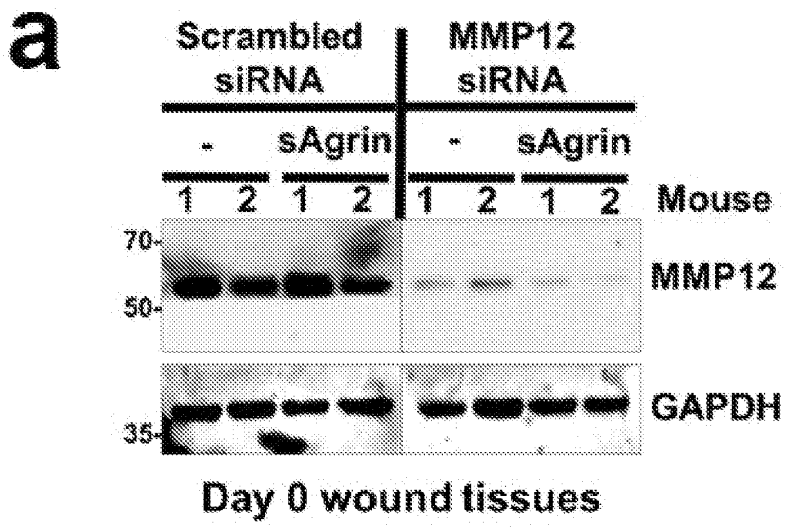


Fig. 14 (Continued)


a
Scrambled siRNA
MMP12 siRNA
-
sAgrin
-
sAgrin
1 2 1 2 1 2 1 2
Mouse
70-
50-
MMP12
GAPDH
35-
Day 0 wound tissues

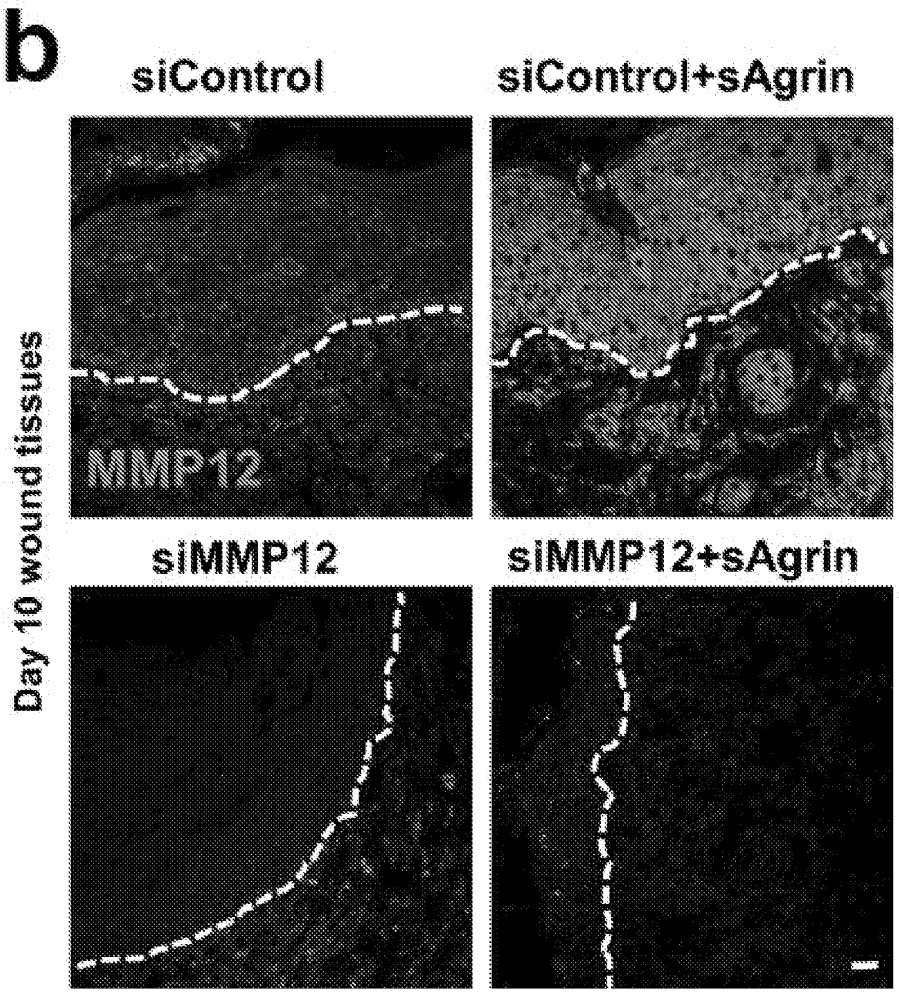

b
siControl
siControl+sAgrin
Day 10 wound tissues
MMP12
siMMP12
siMMP12+sAgrin

Fig. 15

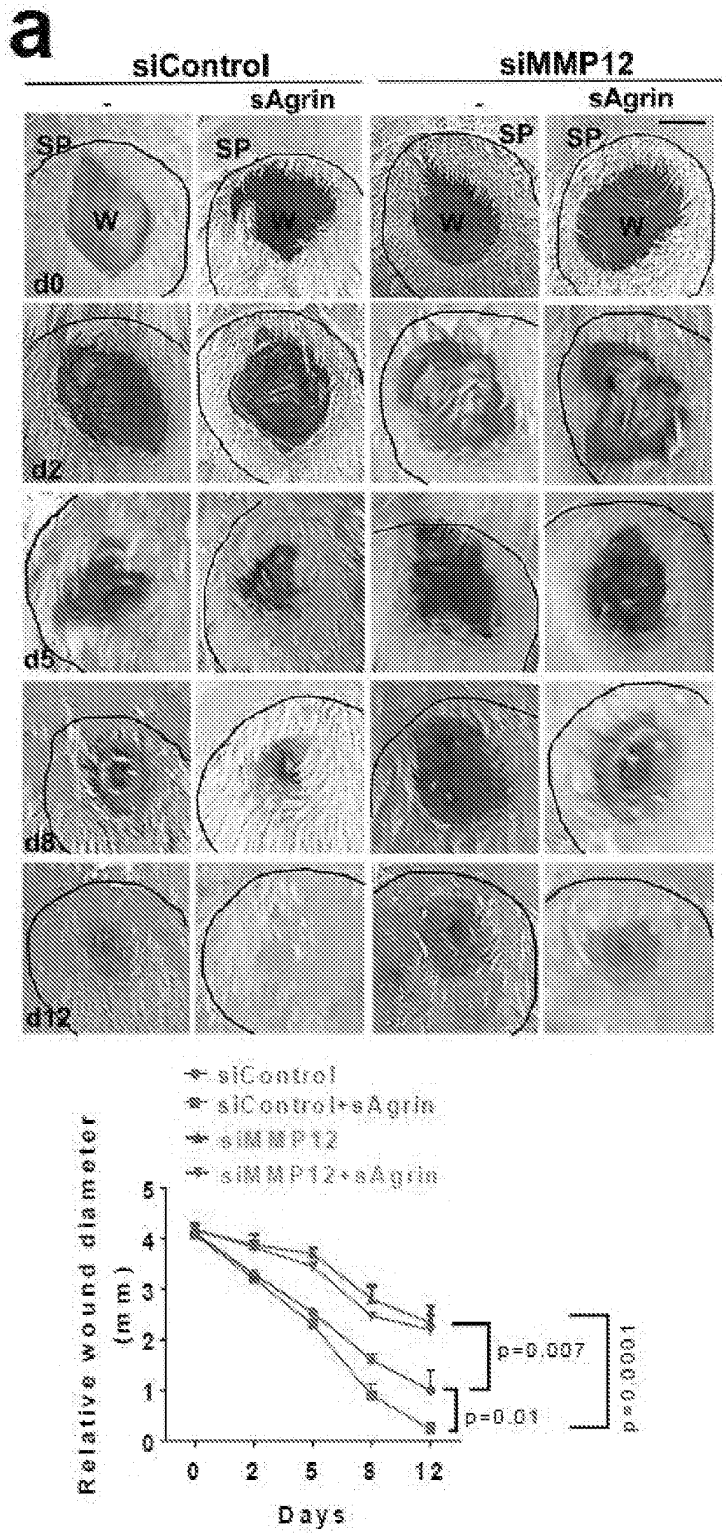
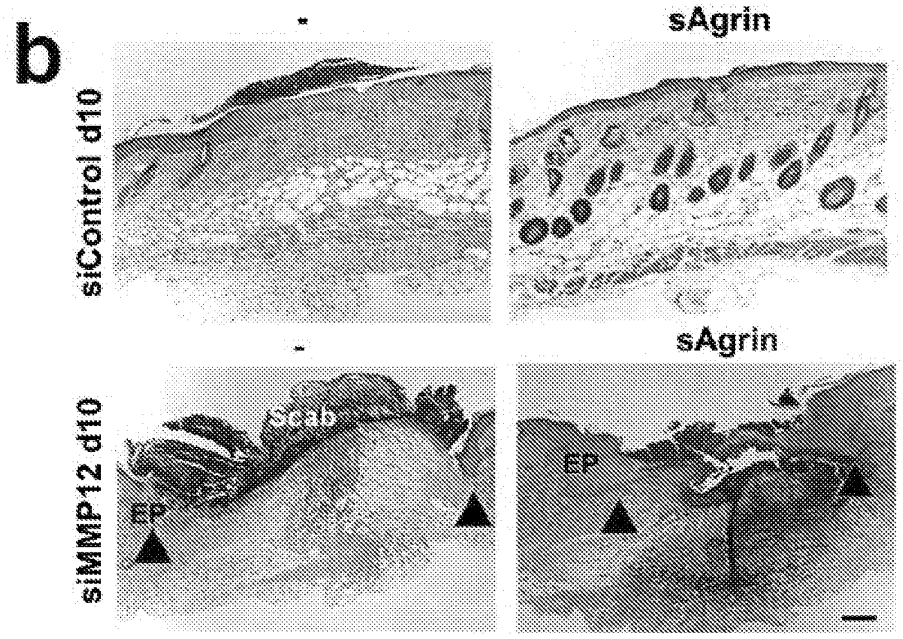

a
siControl
siMMP12
-
sAgrin
-
sAgrin
SP
W
d0
d2
d5
d8
d12
siControl
siControl+sAgrin
siMMP12
siMMP12+sAgrin
Relative wound diameter (mm)
0
1
2
3
4
5
0
2
5
8
12
Days
p=0.007
p=0.01
p=0.0001

Fig. 16



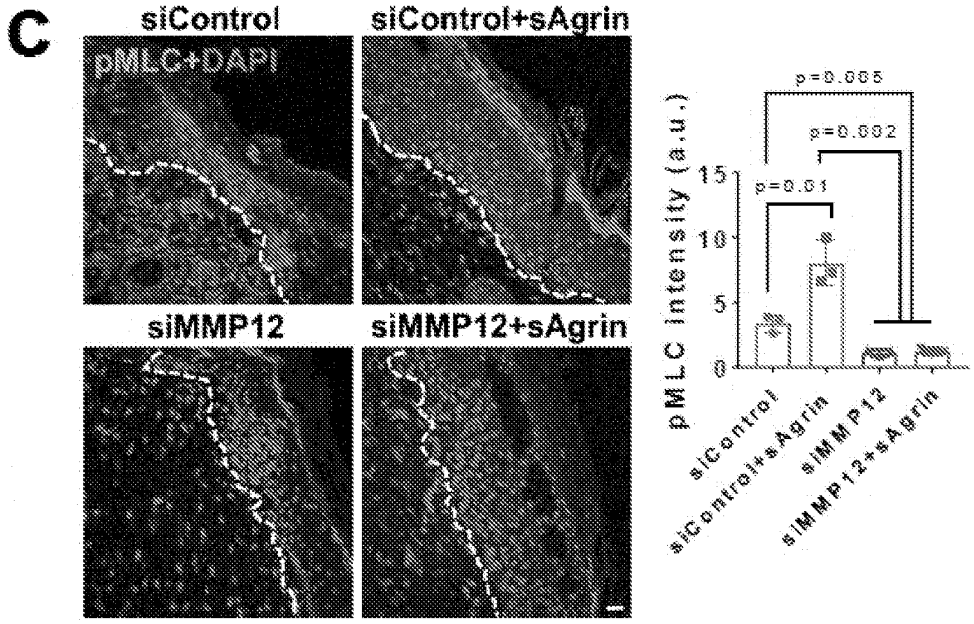


Fig. 16 (Continued)

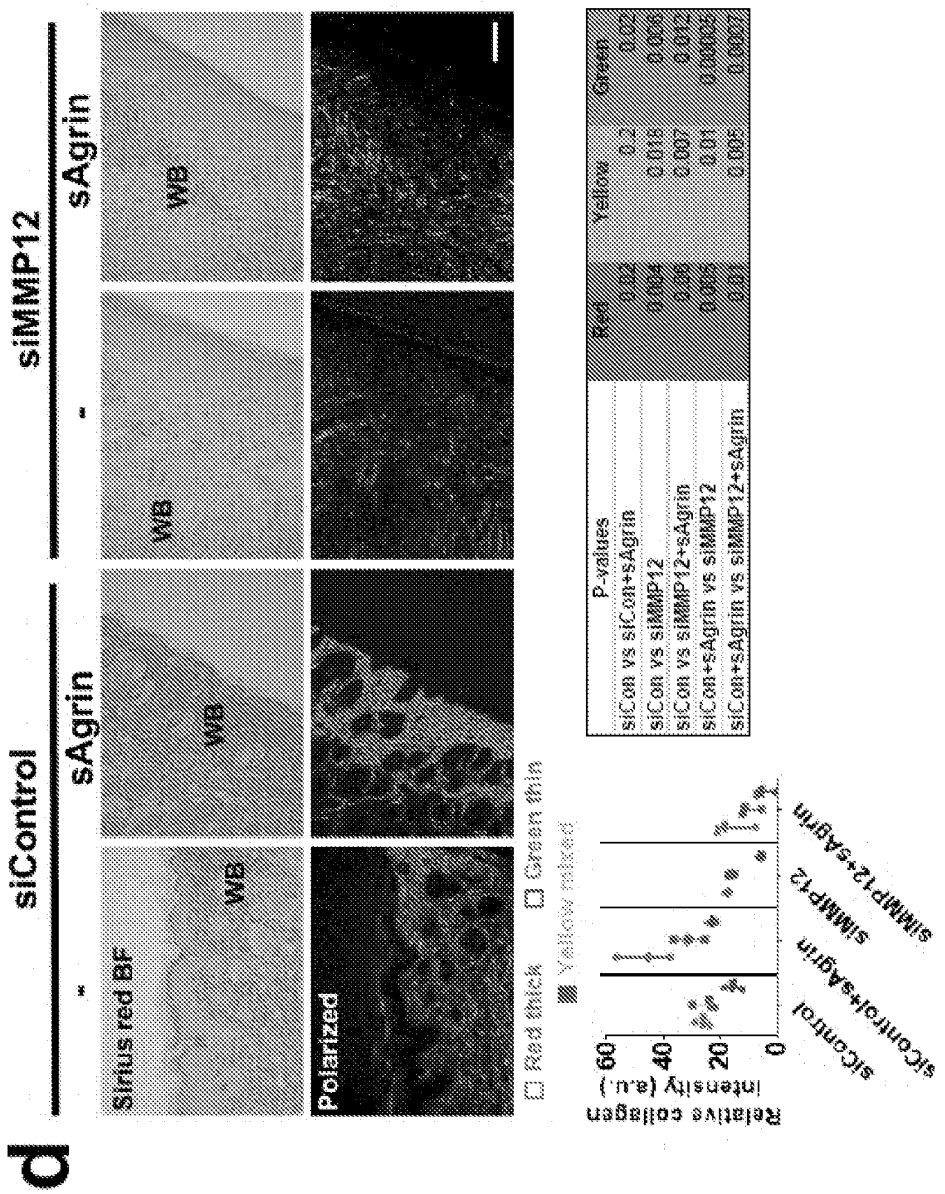


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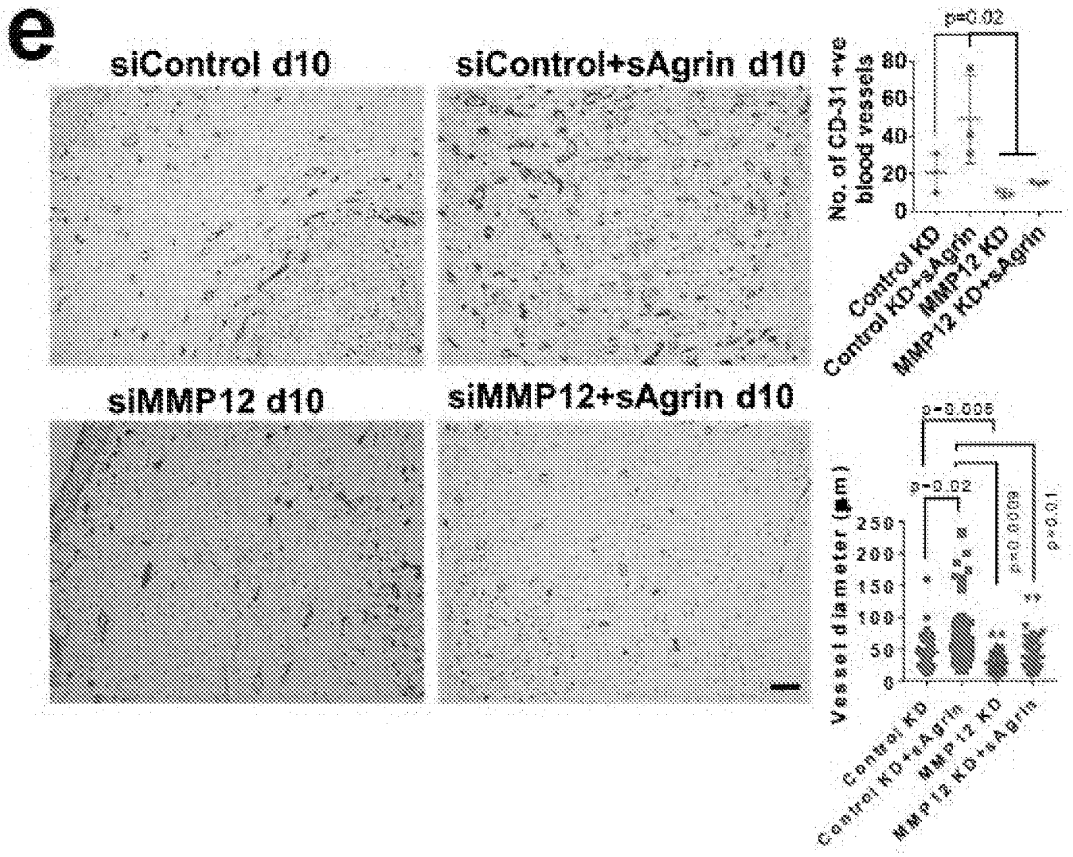


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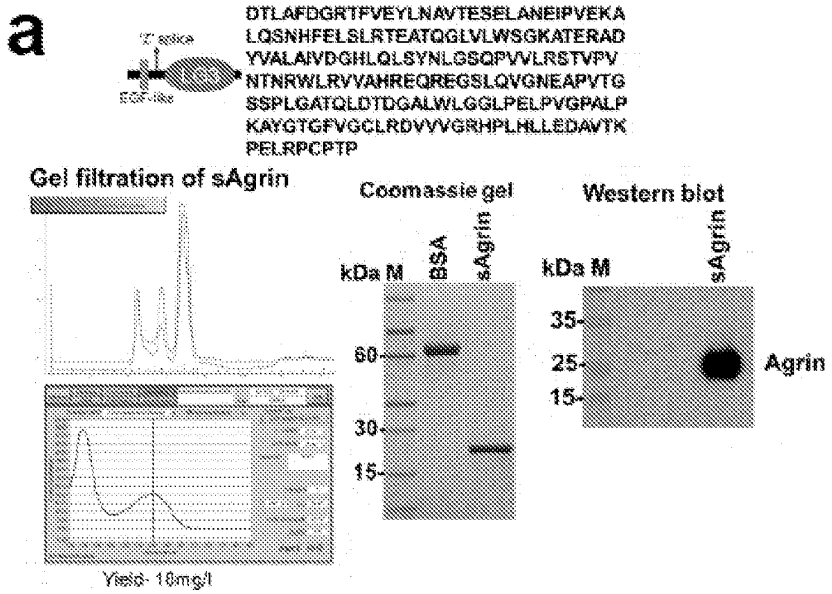


Fig. 17

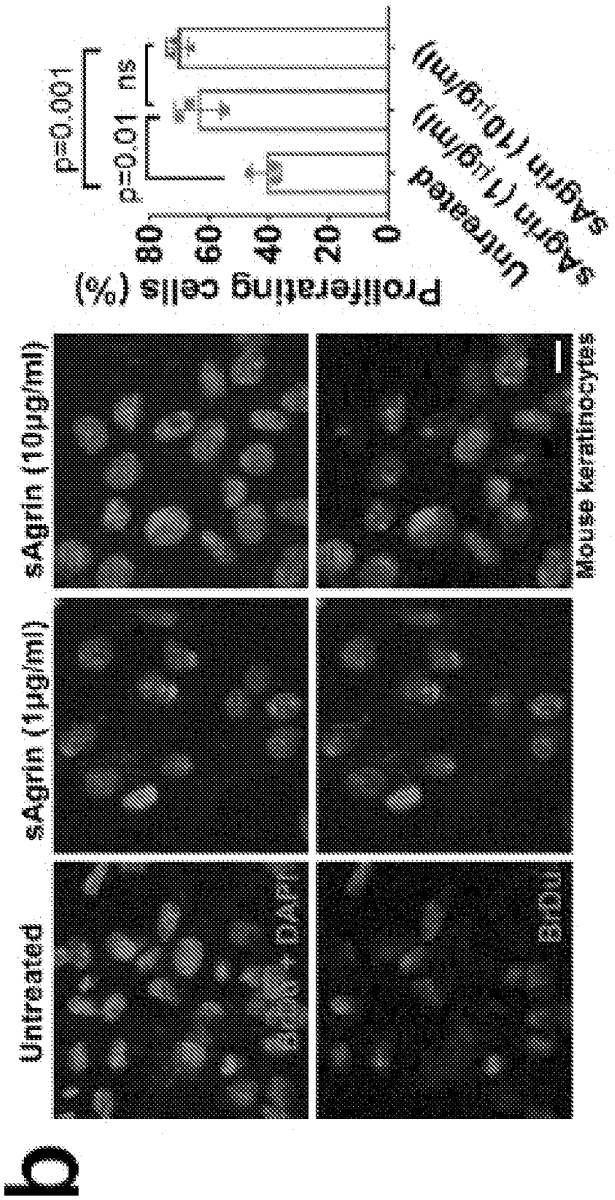


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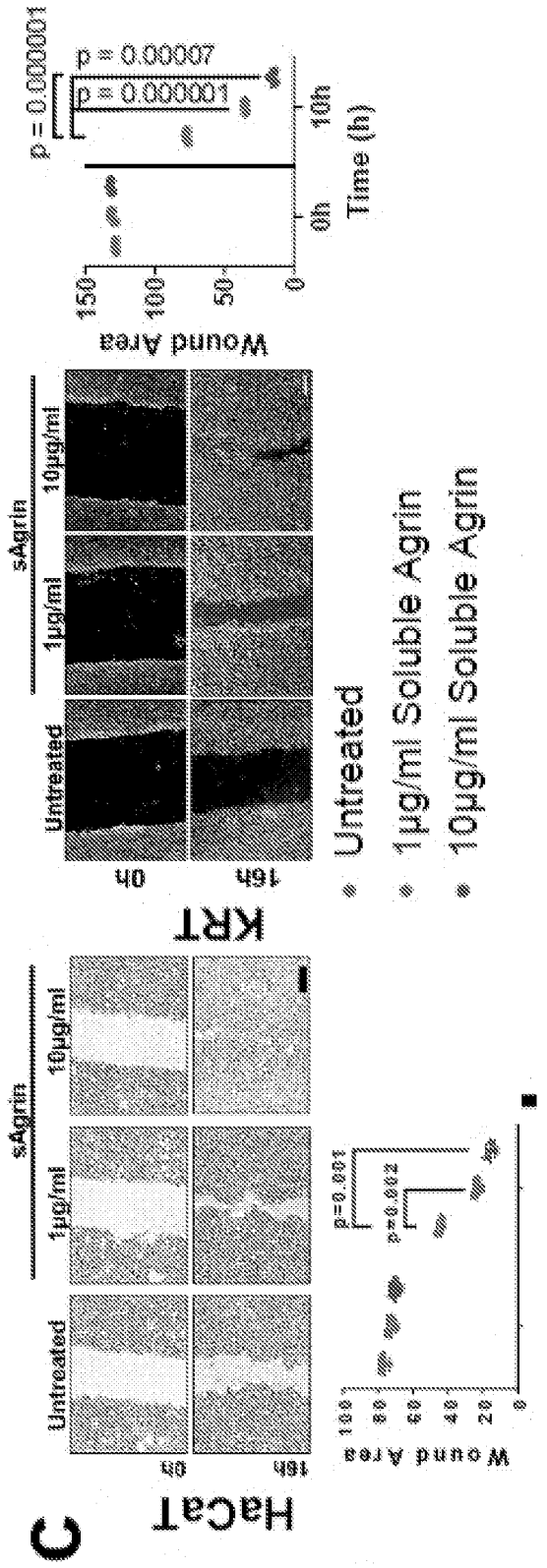
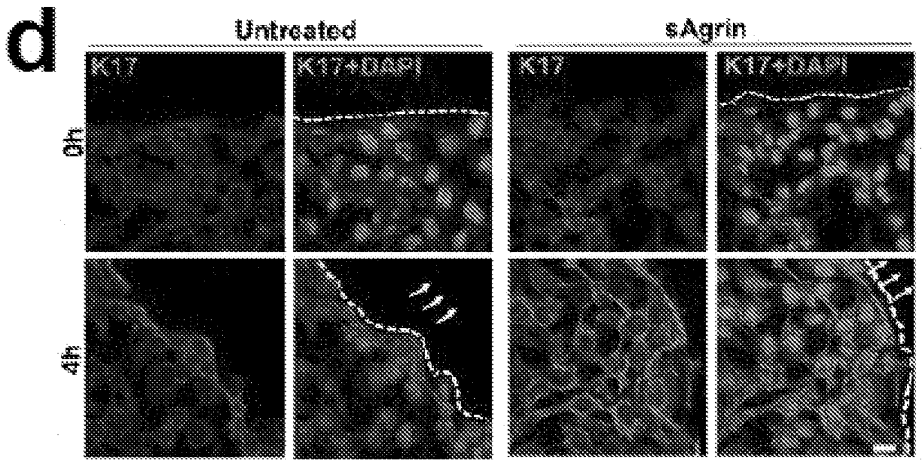


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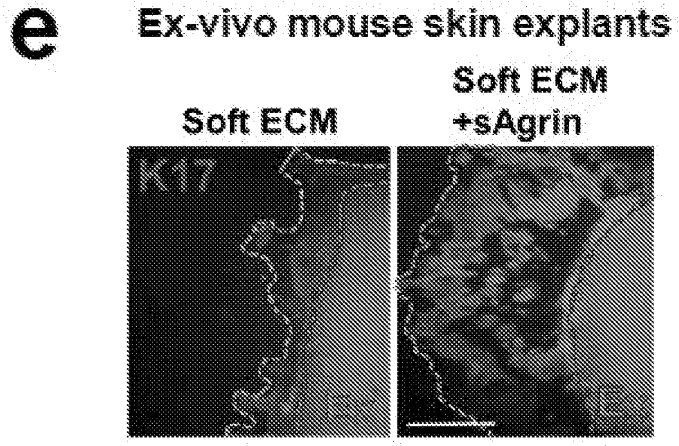


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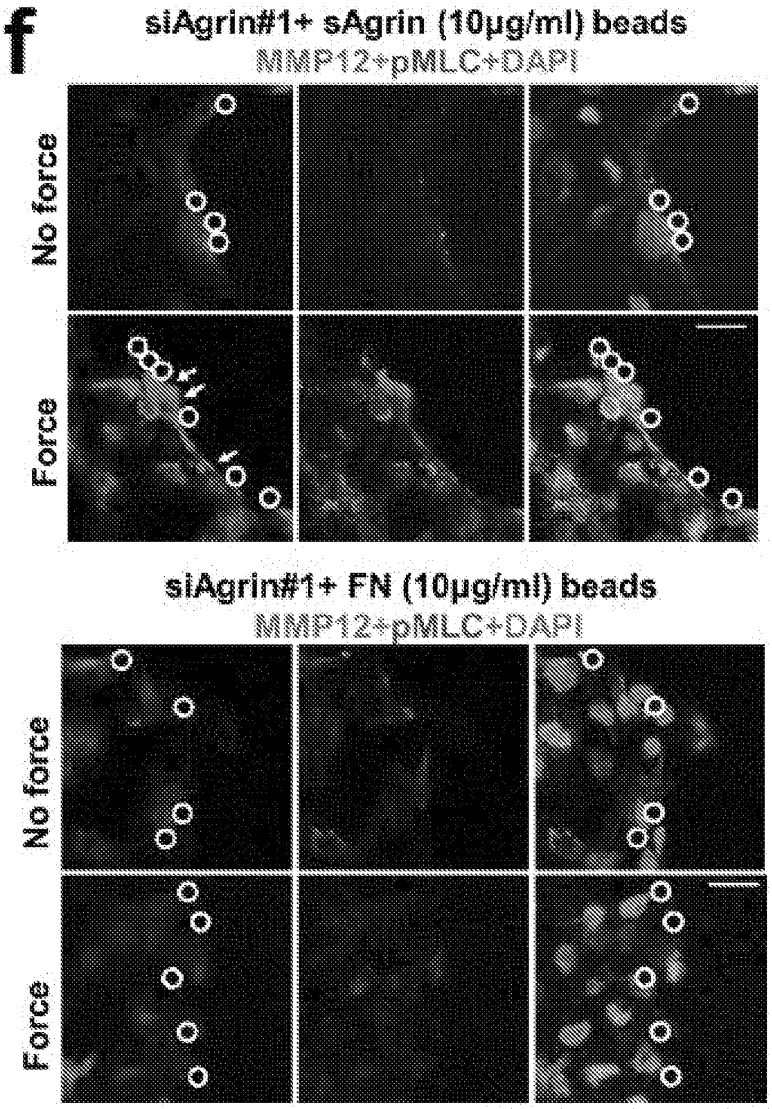


Fig. 17 (Continued)

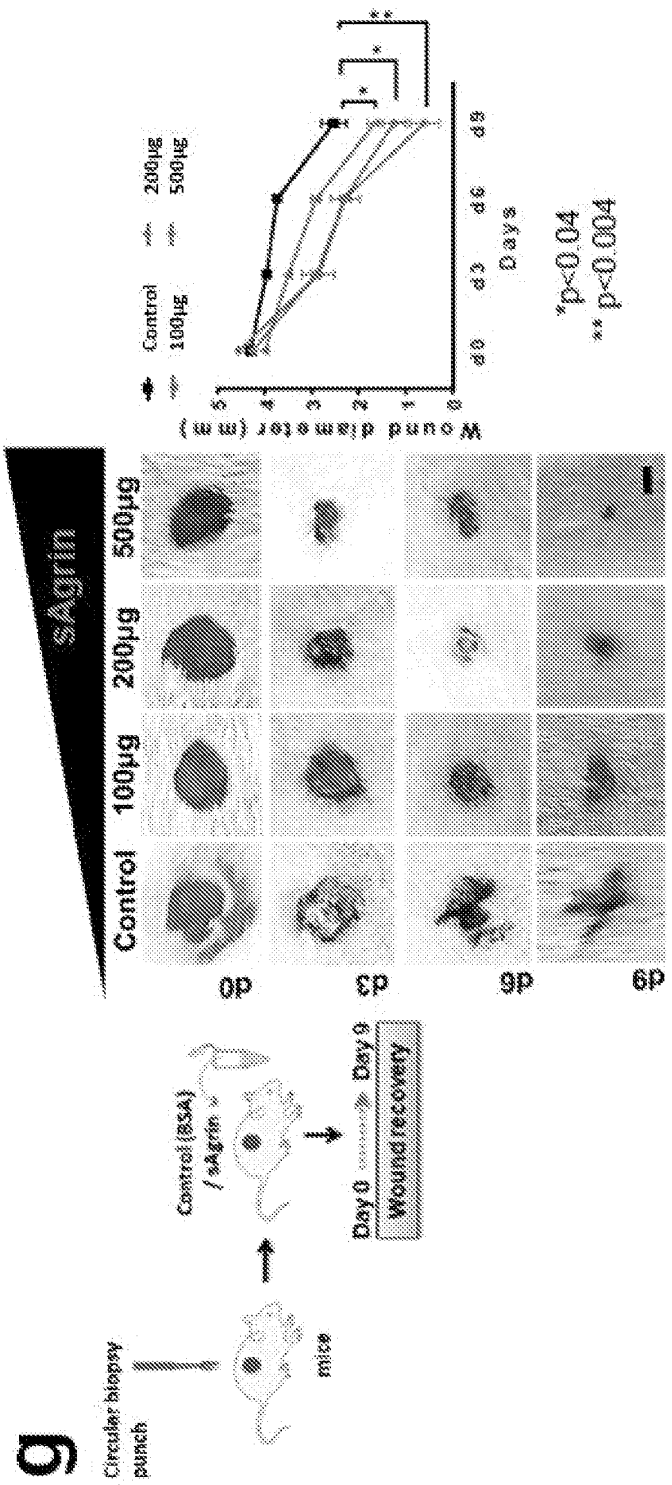


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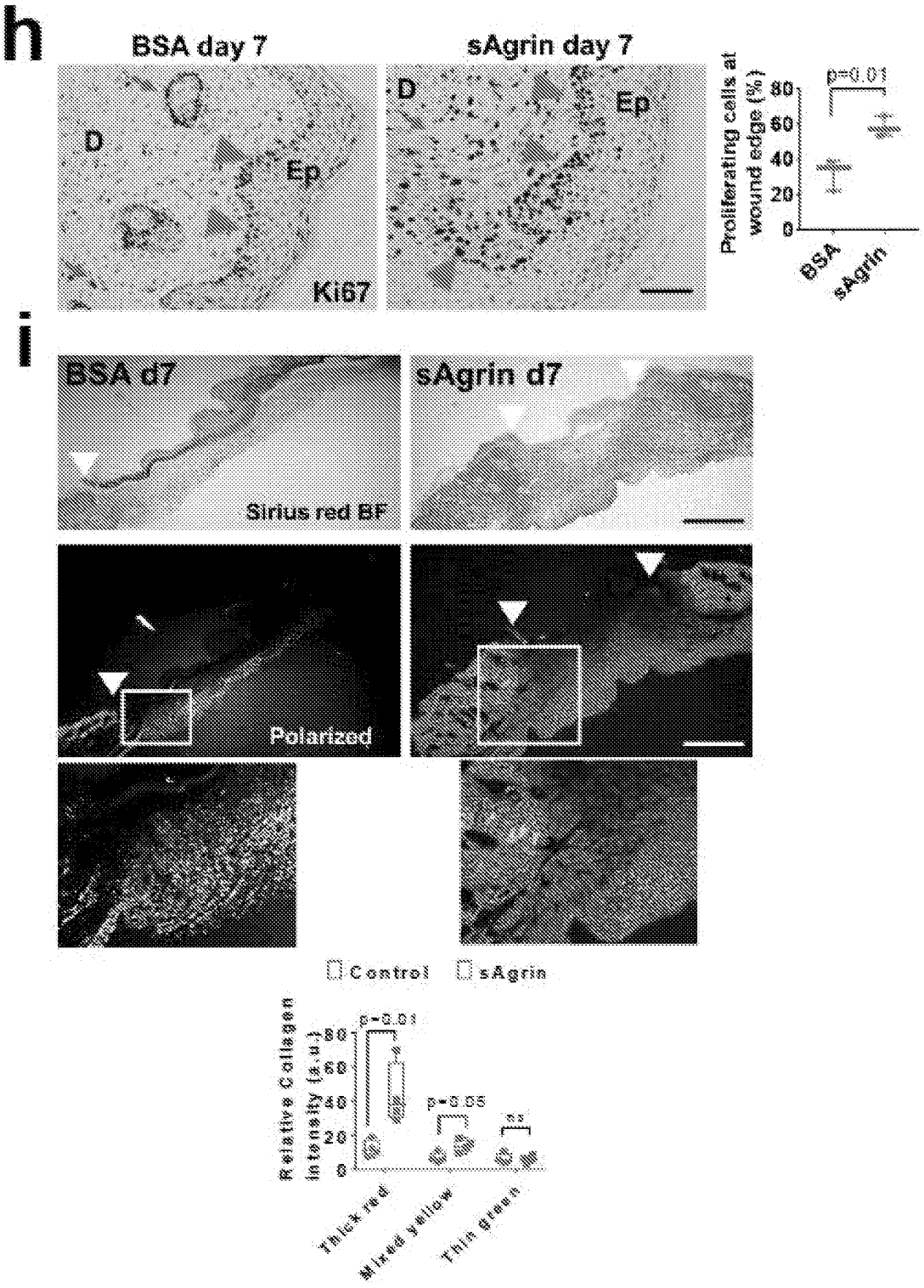


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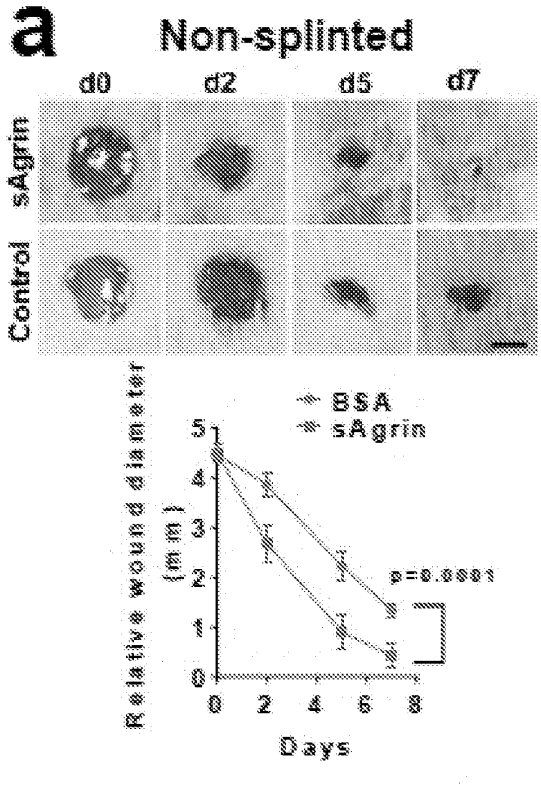

a
Non-splinted
d0
d2
d5
d7
sAgrin
Control
BSA
sAgrin
Relative wound diameter (mm)
0
1
2
3
4
5
0
2
4
6
8
Days
p=0.0001

Fig. 18

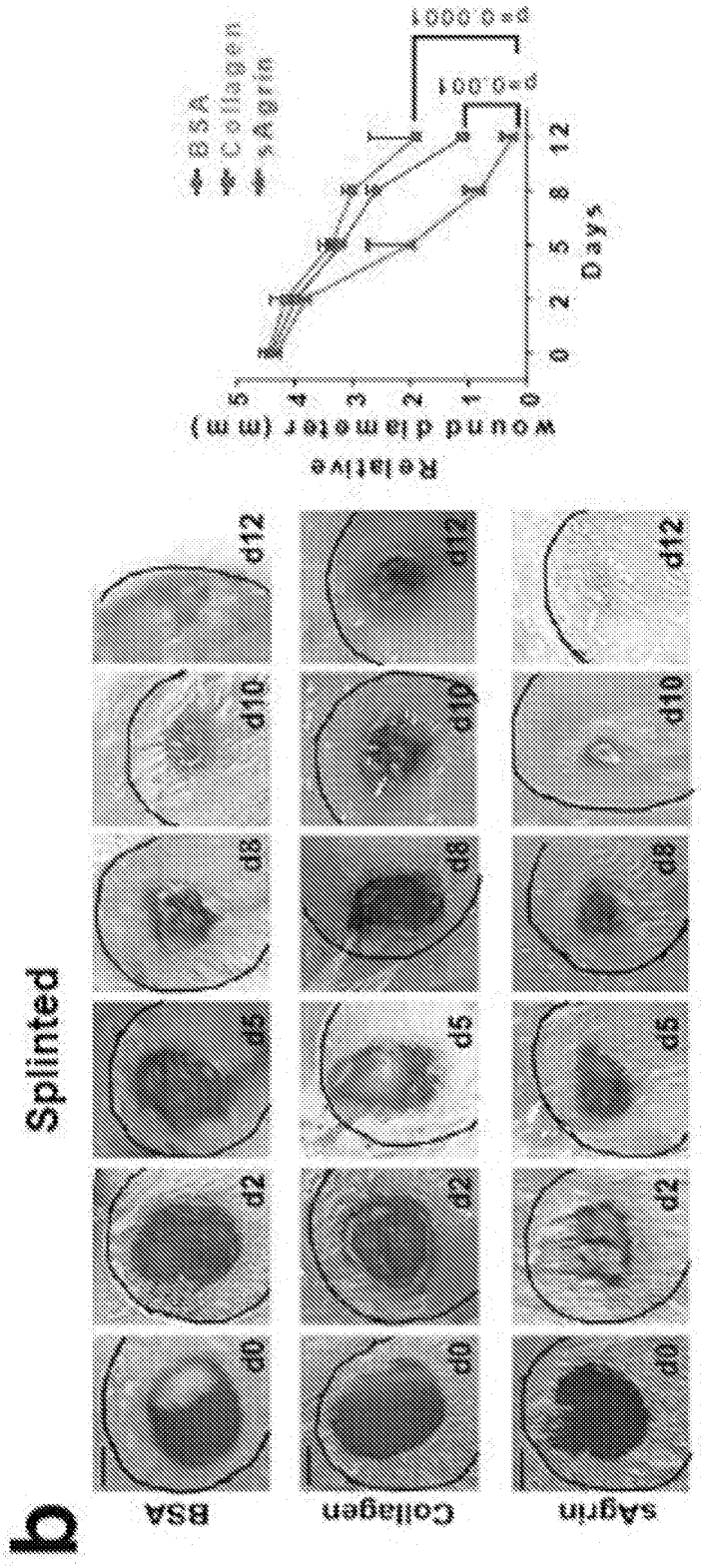


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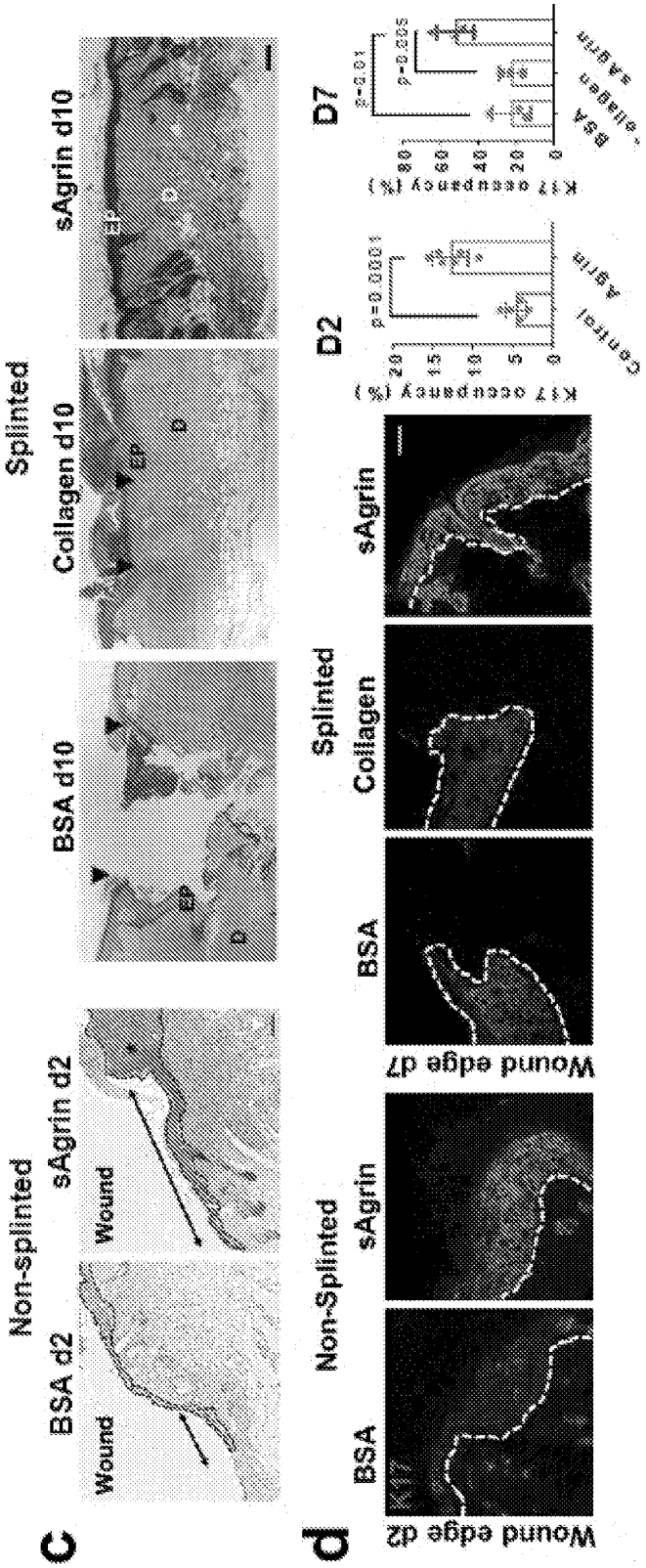


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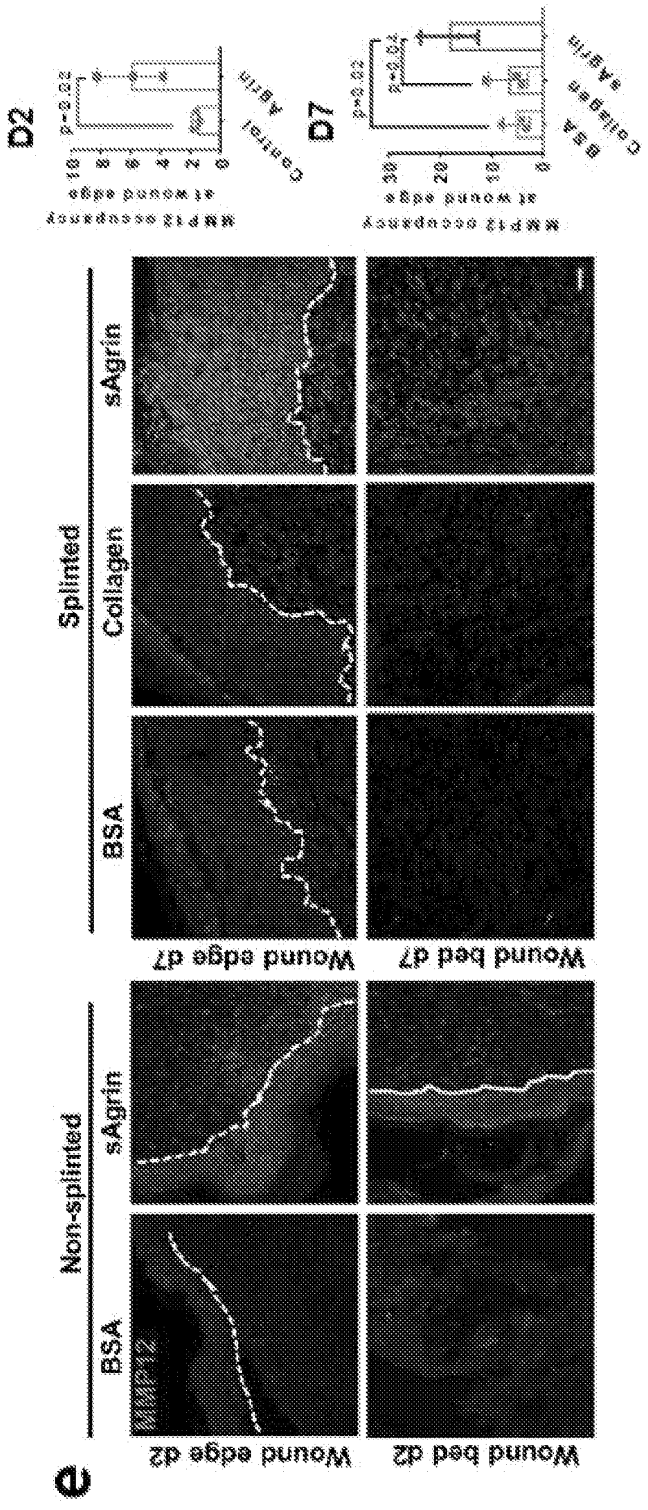


Fig. 18 (Continued)

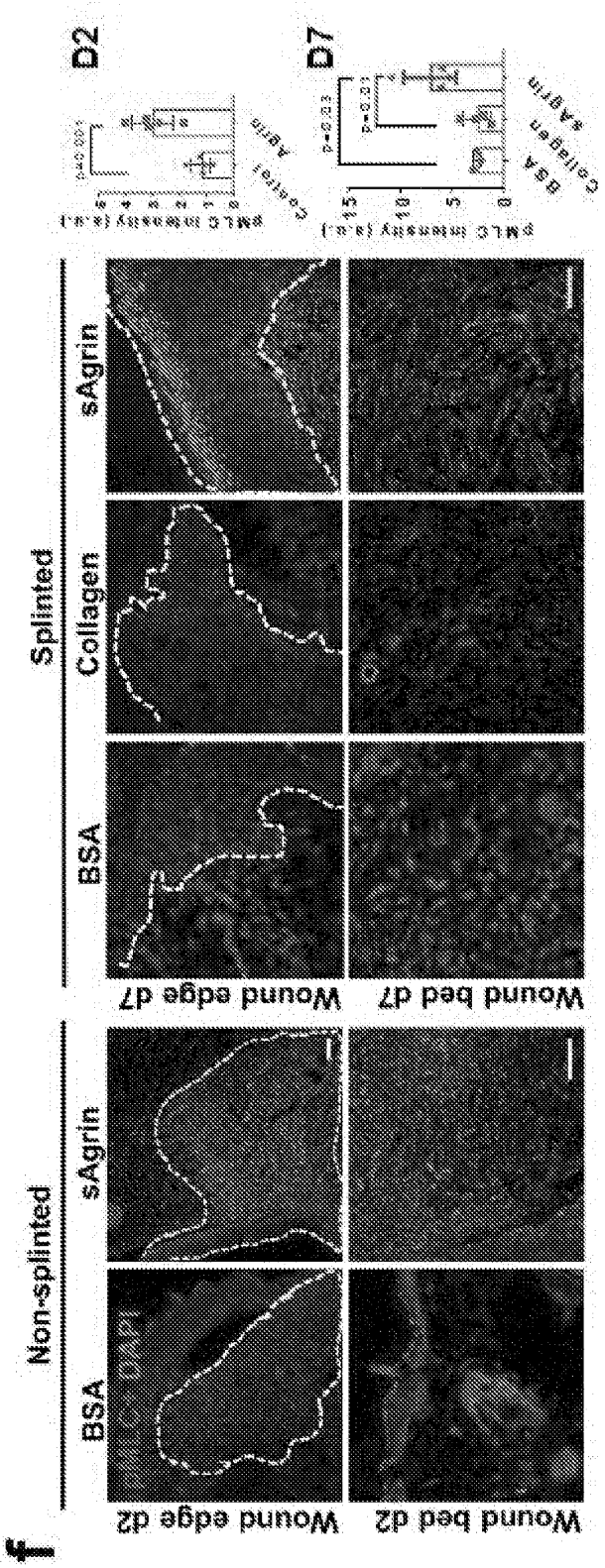


Fig. 18 (Continued)

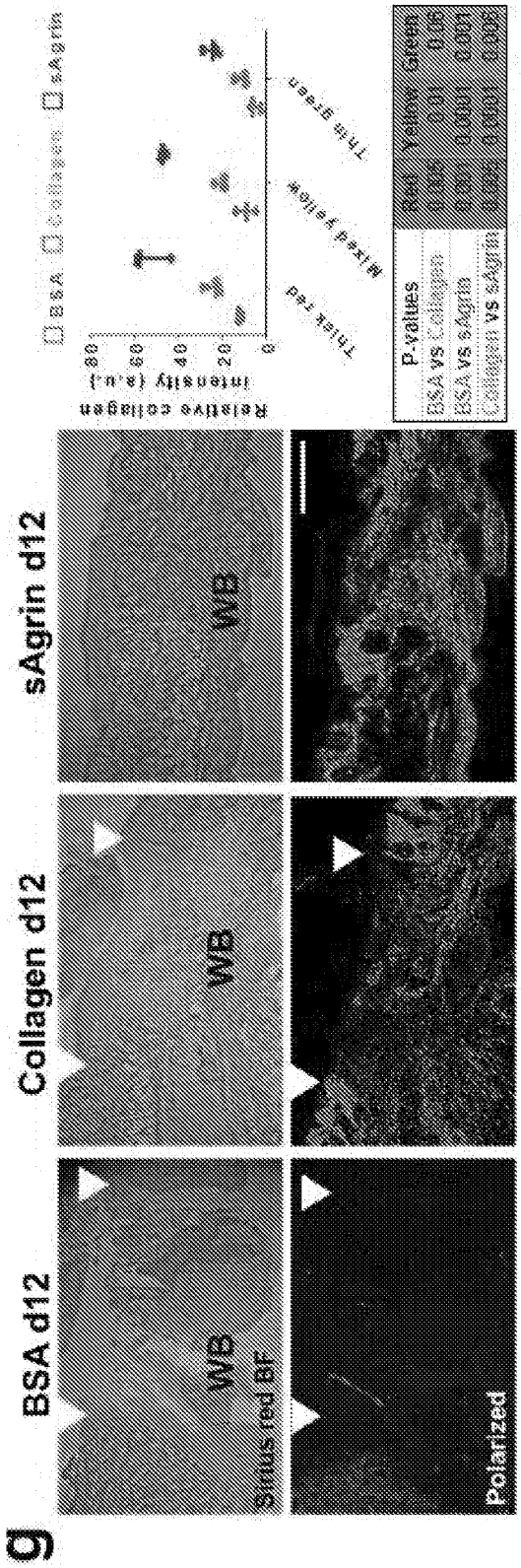


Fig. 18 (Continued)

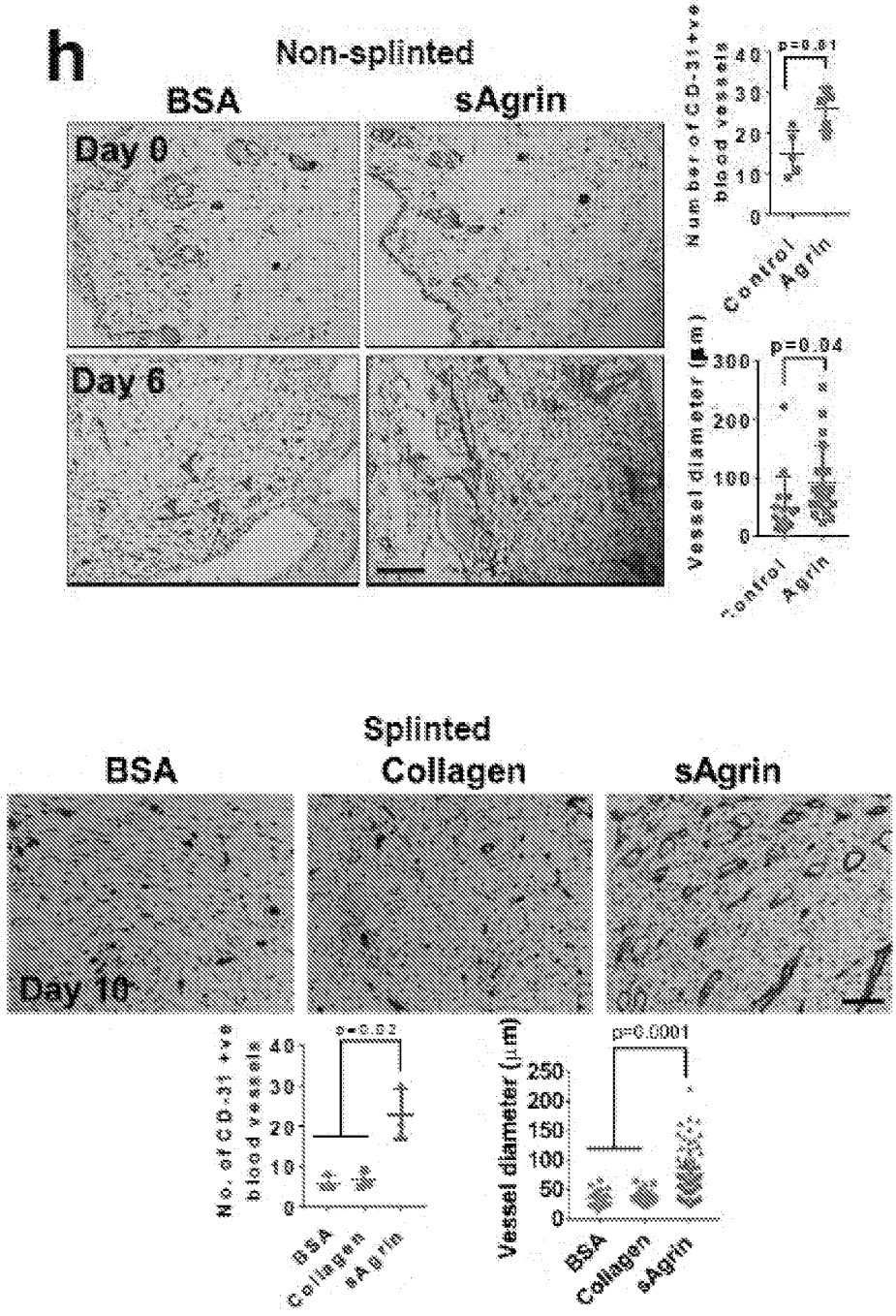
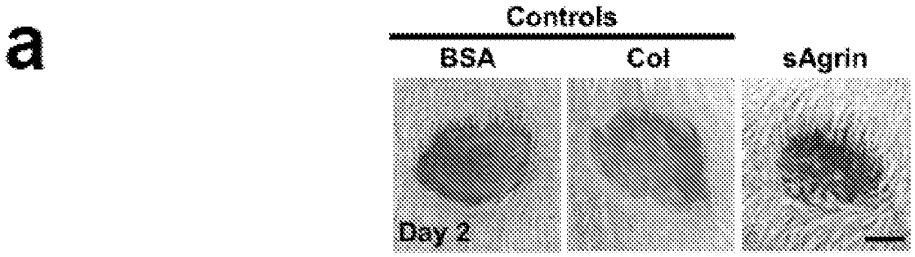
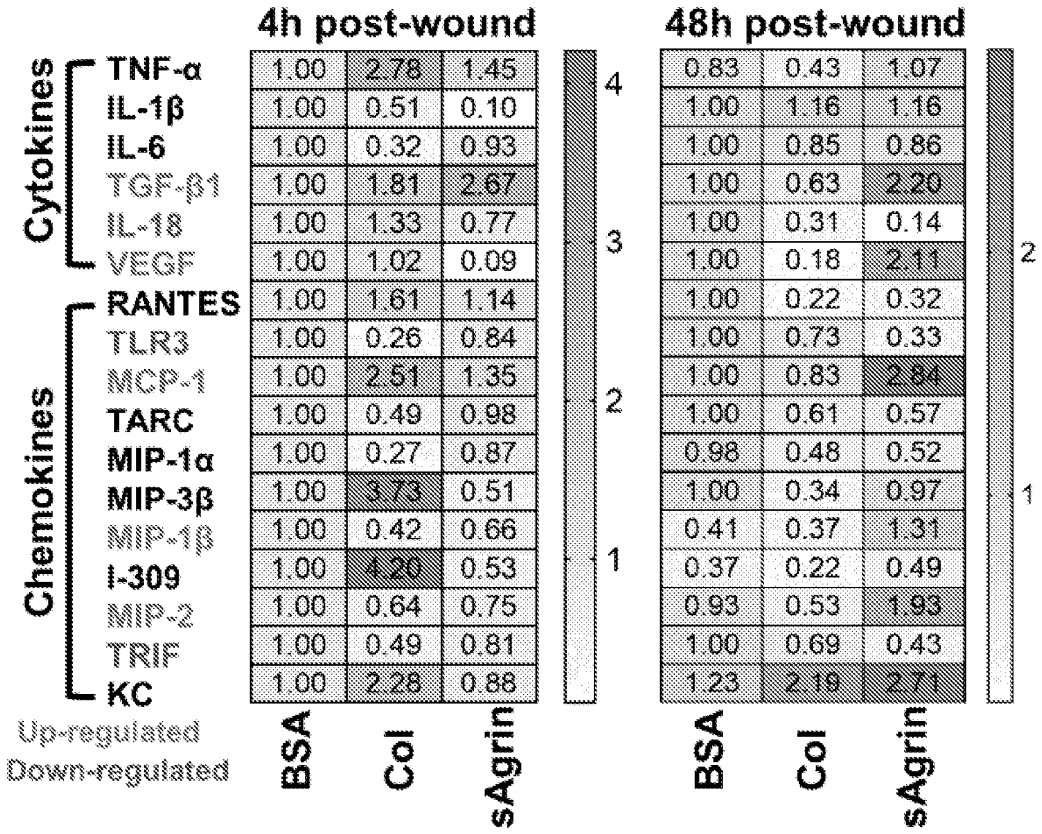


Fig. 18 (Continued)





Up-regulated pro-inflammatory genes	BSA vs Col	BSA vs sAgrin	Col vs sAgrin
TGF-β1	0.94	0.01	0.01
VEGF	0.01	0.005	0.0001
MCP-1	0.81	0.0006	0.03
MIP-1ß	0.32	0.01	0.01
MIP-2	0.22	0.01	0.008

Fig. 19

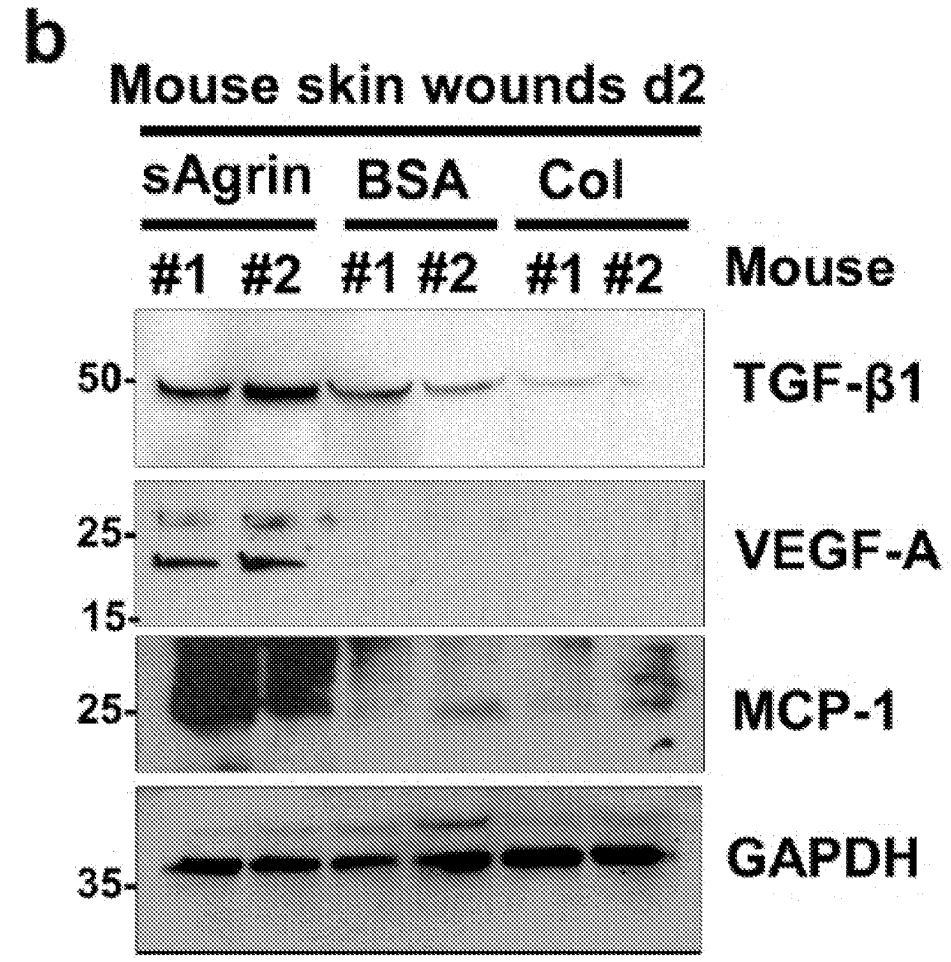


Fig. 19 (Continued)

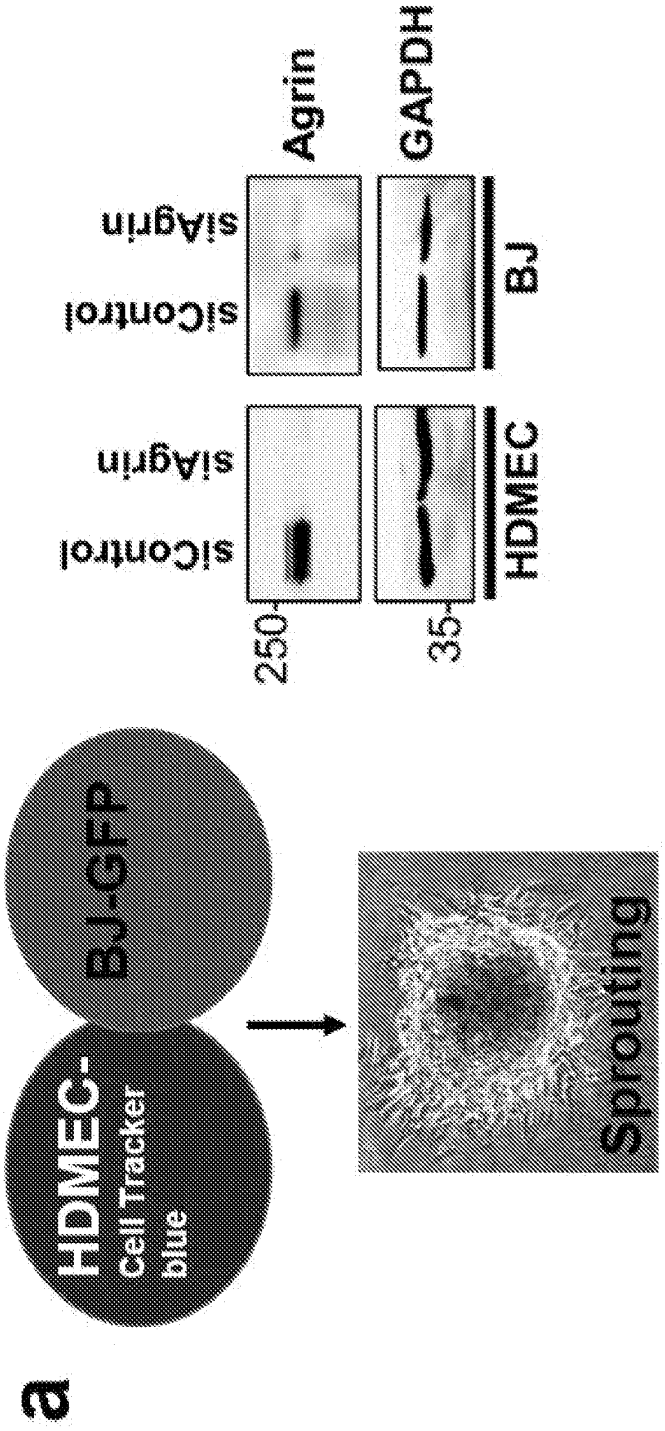

Agrin
GAPDH
siControl
siAgrin
siControl
siAgrin
BJ
HDMEC
250
35
a
BJ-GFP
HDMEC-
Cell Tracker
blue
Sprouting

Fig. 20

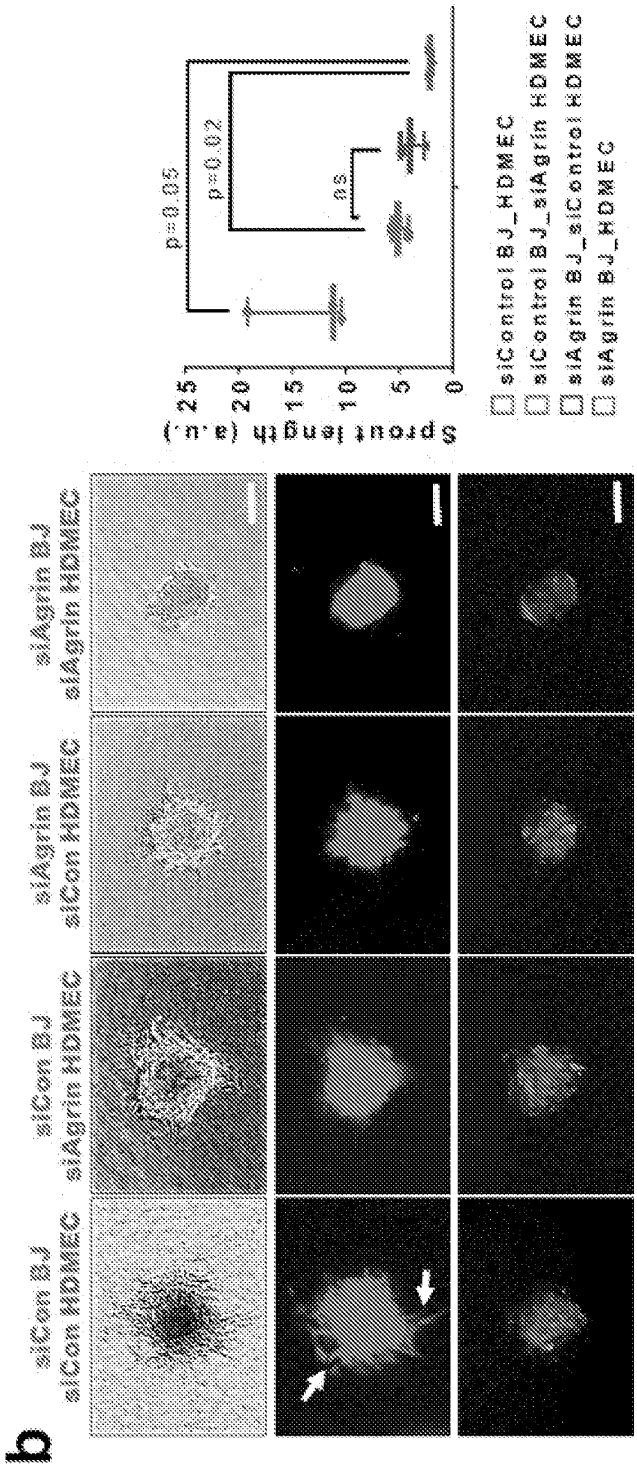


Fig. 20 (Continued)

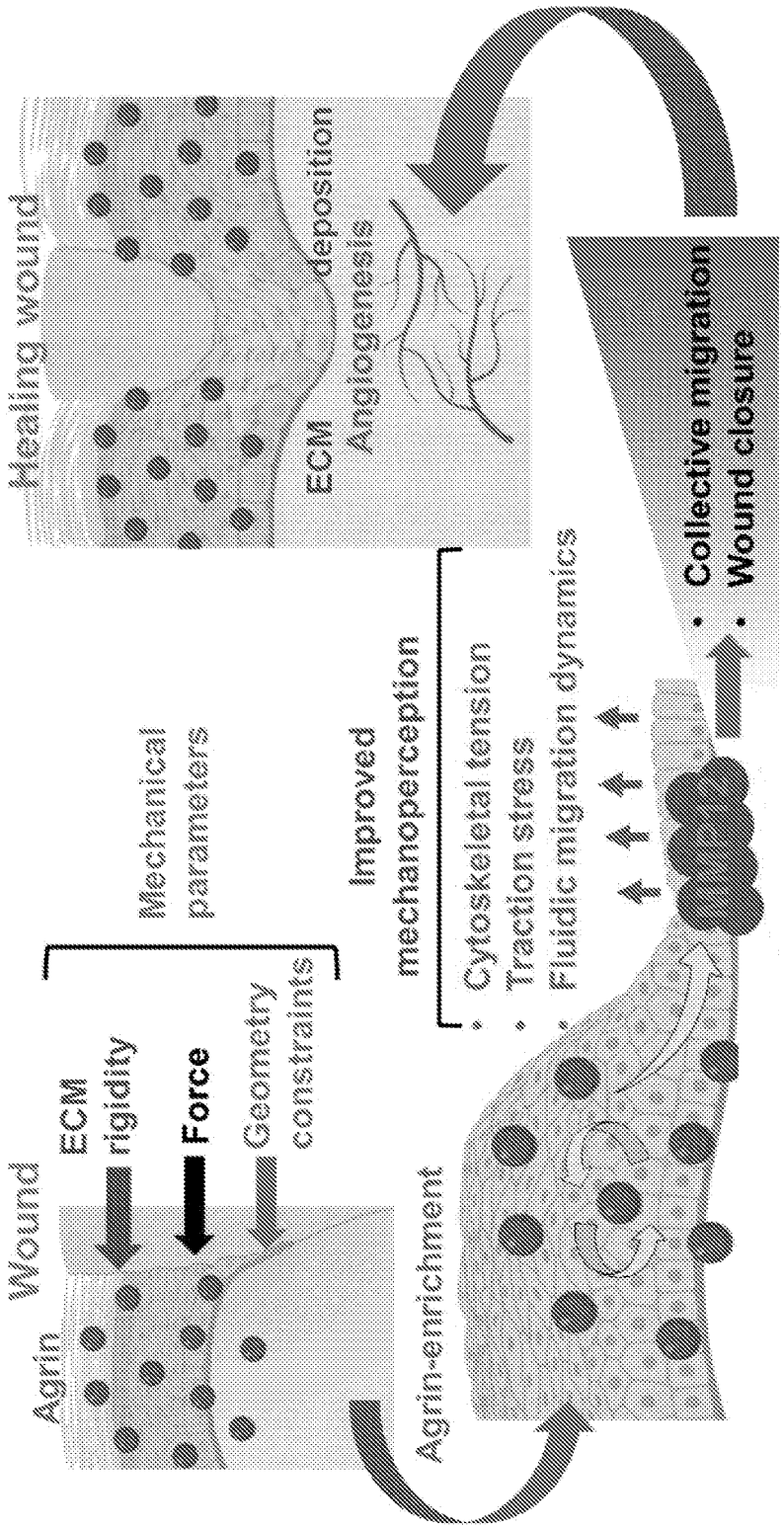
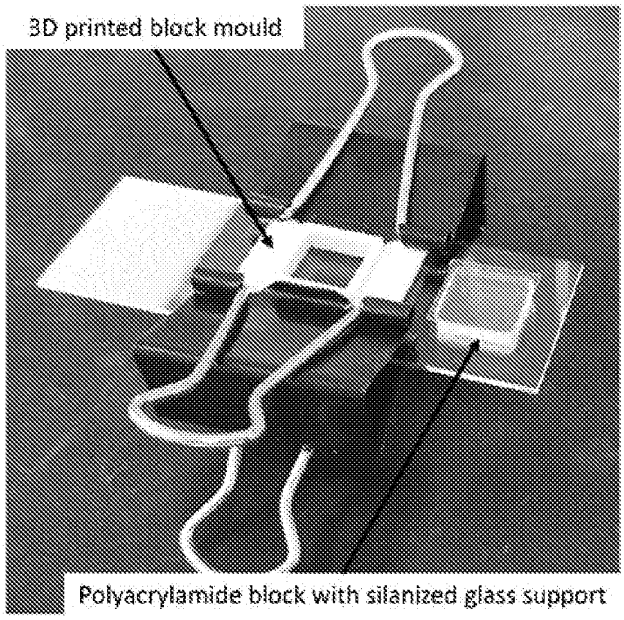

Healing wound
ECM deposition
Angiogenesis
Collective migration
Wound closure
Improved mechanoperception
Cytoskeletal tension
Traction stress
Fluidic migration dynamics
Mechanical parameters
ECM rigidity
Force
Geometry constraints
Wound
Agrin
Agrin-enrichment

Fig. 21

(a)


3D printed block mould
Polyacrylamide block with silanized glass support

(b)

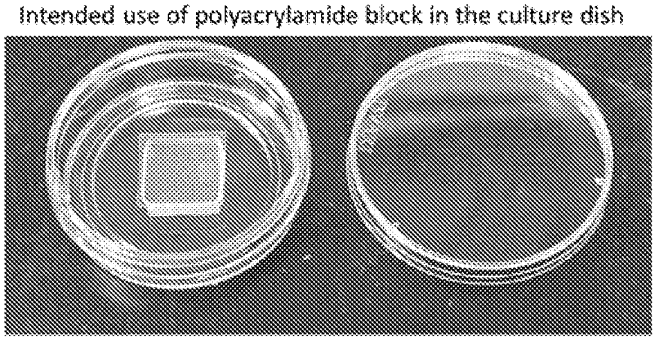

Intended use of polyacrylamide block in the culture dish

Fig. 22