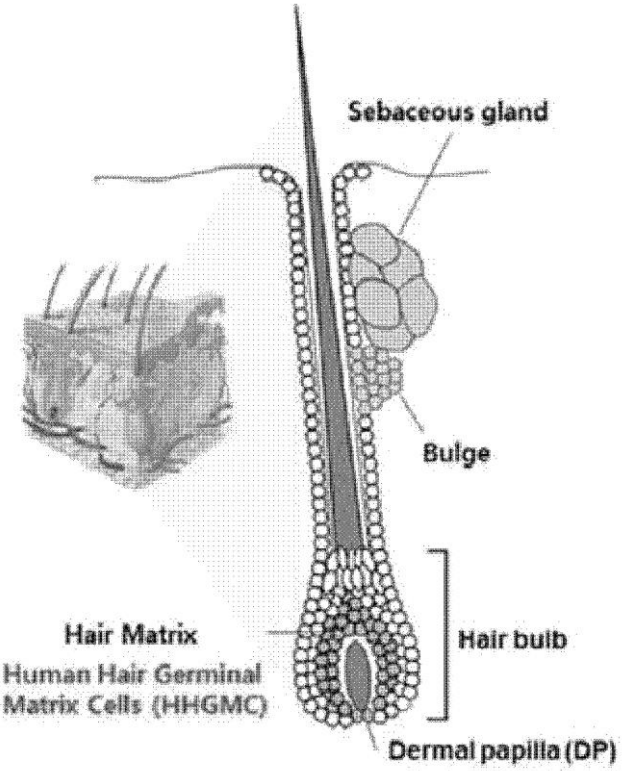
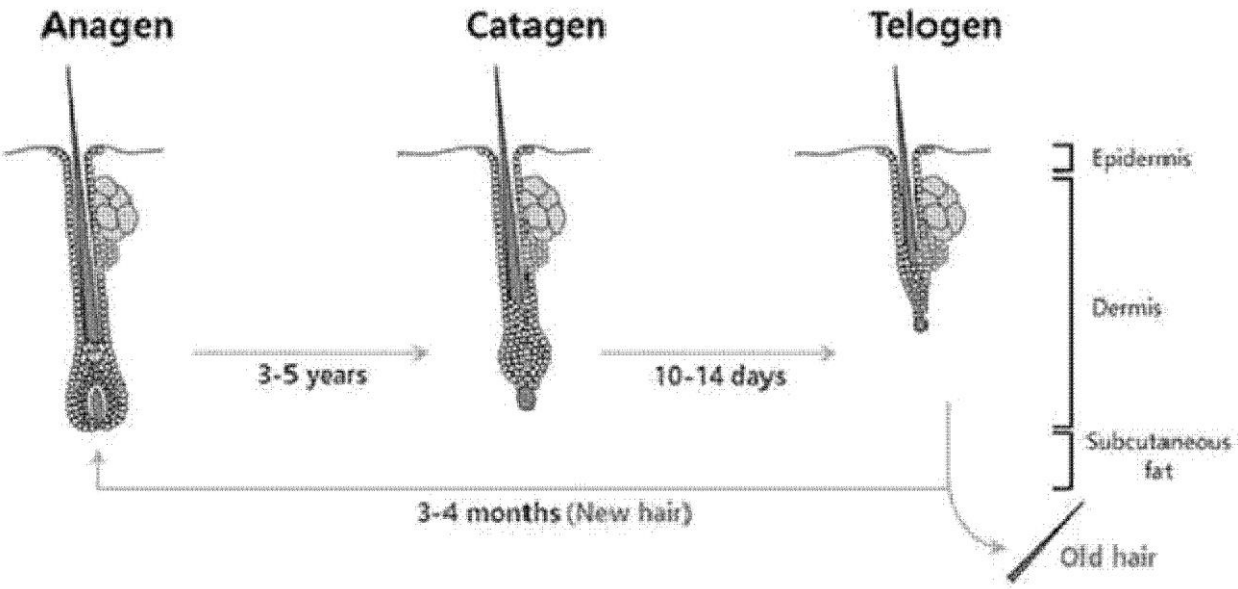
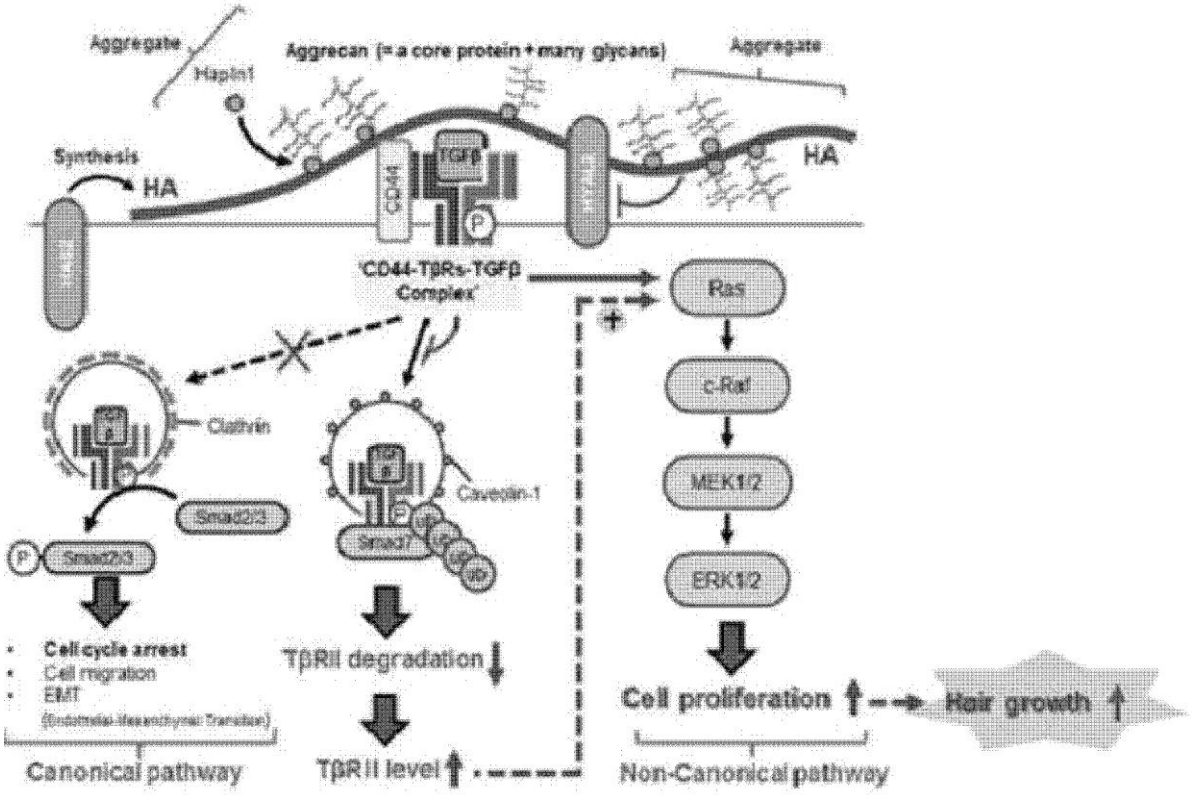
【FIG 1】


Sebaceous gland
Bulge
Hair bulb
Hair Matrix
Human Hair Germinal
Matrix Cells (HHGMC)
Dermal papilla (DP)

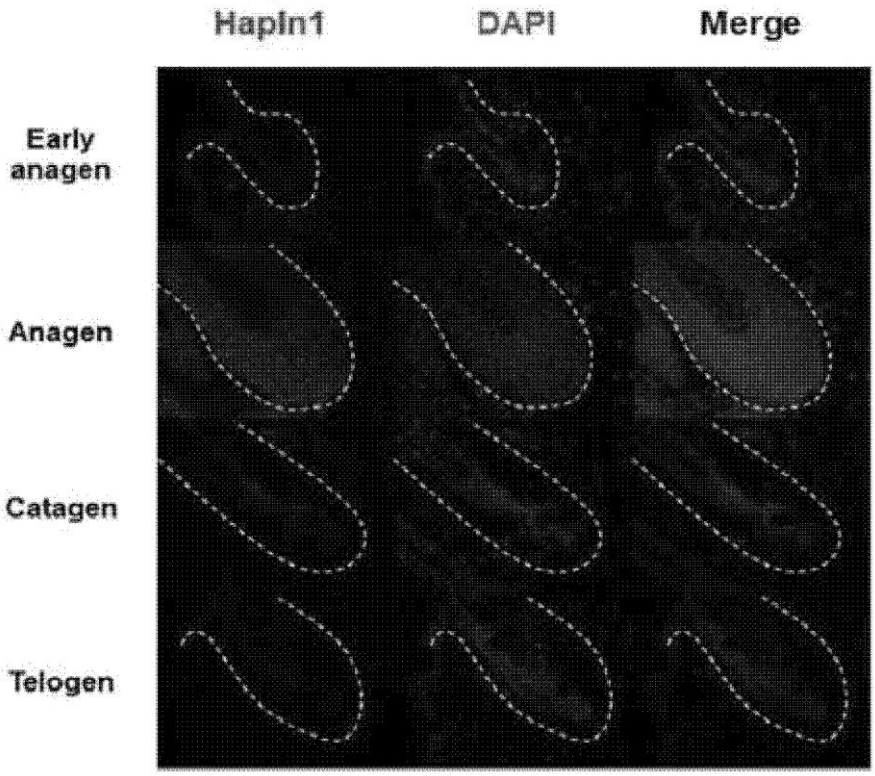
【FIG 2】


Anagen
Catagen
Telogen
3-5 years
10-14 days
Epidermis
Dermis
Subcutaneous fat
3-4 months (New hair)
Old hair

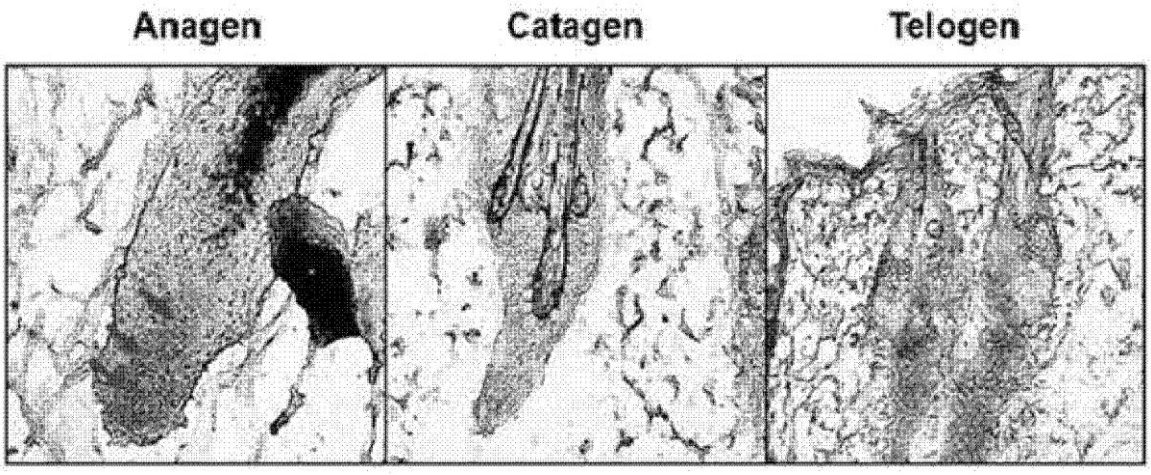
【FIG 3】


Aggregate
Hapln1
Aggrecan (= a core protein + many glycans)
Aggregate
Synthesis
HA
HA
CD44
TGFβ
P
'CD44-TβRs-TGFβ Complex'
Ras
c-Raf
MEK1/2
ERK1/2
Clathrin
Caveolin-1
Smad2/3
P
Smad2/3
Smad7
Ub
Cell cycle arrest
Cell migration
EMT
(Endothelial-Mesenchymal Transition)
Canonical pathway
TβRII degradation
TβRII level
Cell proliferation
Hair growth
Non-Canonical pathway

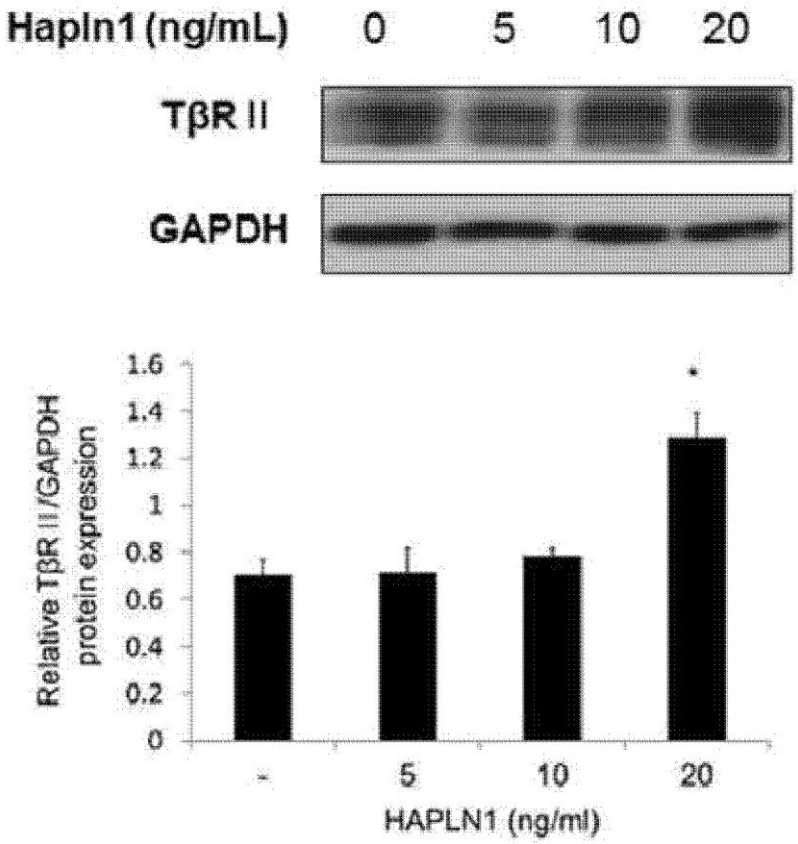
【FIG 4】


Hapln1
DAPI
Merge
Early anagen
Anagen
Catagen
Telogen

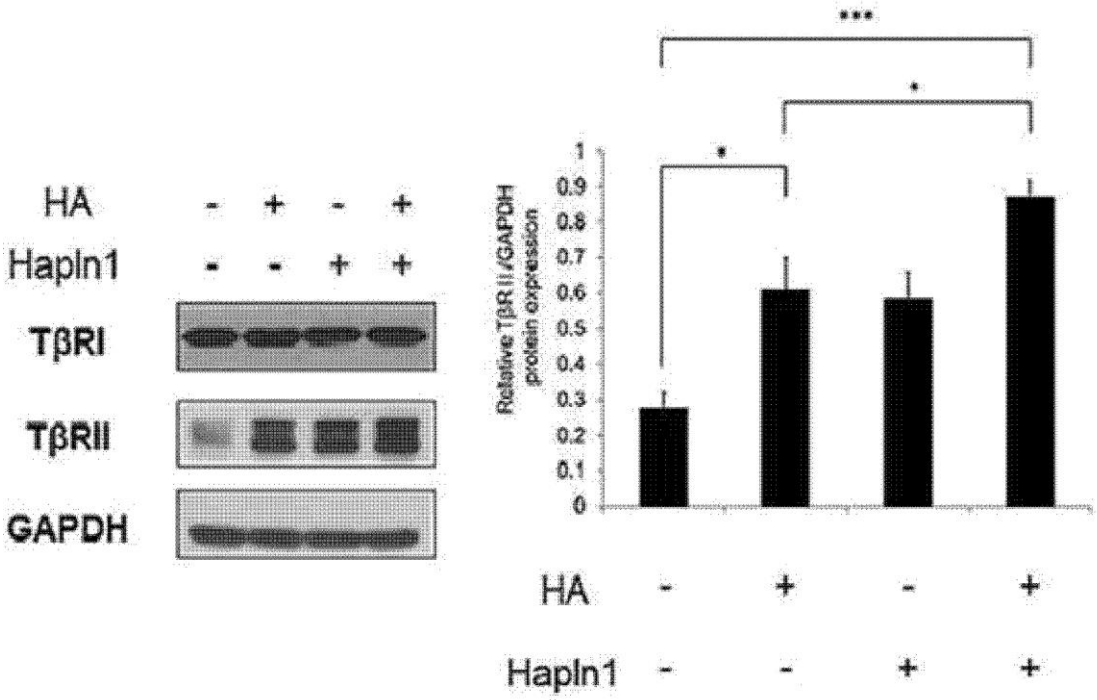
【FIG 5】


Anagen
Catagen
Telogen

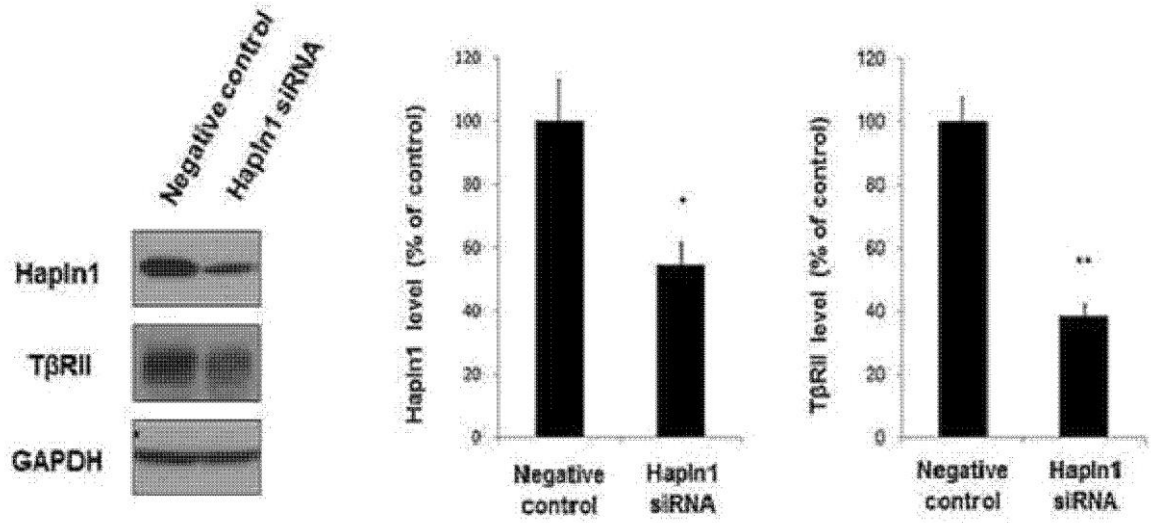
【FIG 6】


Hapln1 (ng/mL) 0 5 10 20
TβR II
GAPDH
Relative TβR II/GAPDH protein expression
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
*
-
5
10
20
HAPLN1 (ng/ml)

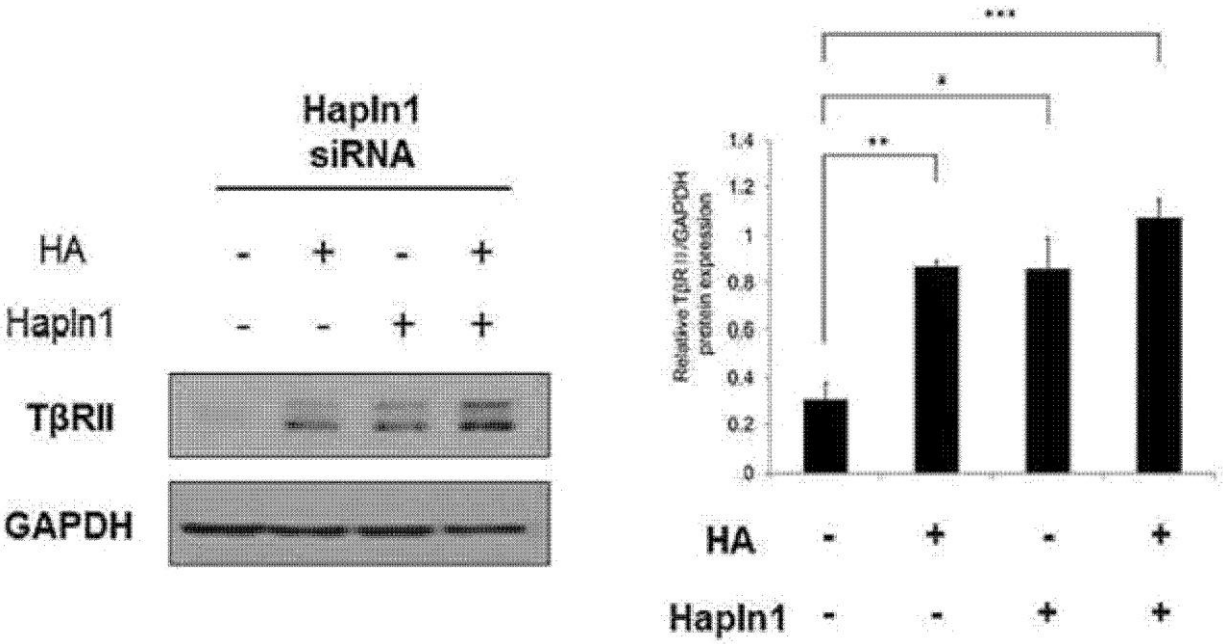
【FIG 7】


HA - + - +
Hapln1 - - + +
TβRI
TβRII
GAPDH
***
*
*
Relative TβR II/GAPDH protein expression
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
HA - + - +
Hapln1 - - + +

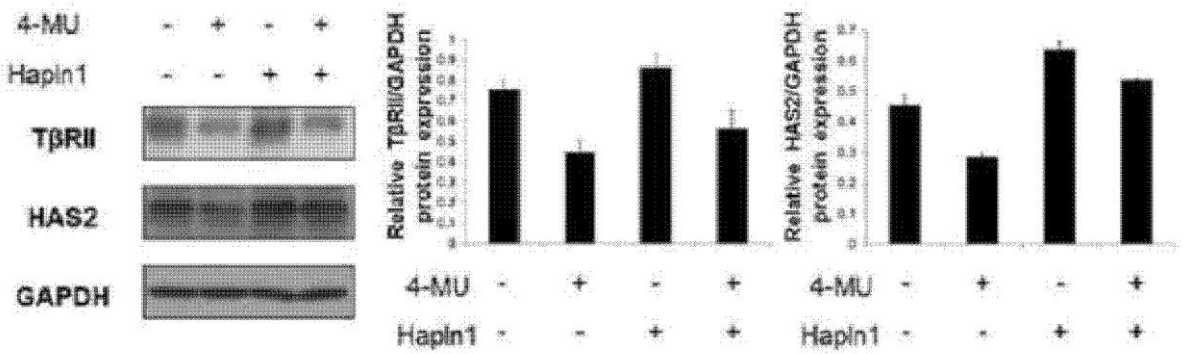
【FIG 8】


Negative control
Hapln1 siRNA
Hapln1
TβRII
GAPDH
Hapln1 level (% of control)
120
100
80
60
40
20
0
*
Negative control
Hapln1 siRNA
TβRII level (% of control)
120
100
80
60
40
20
0
**
Negative control
Hapln1 siRNA

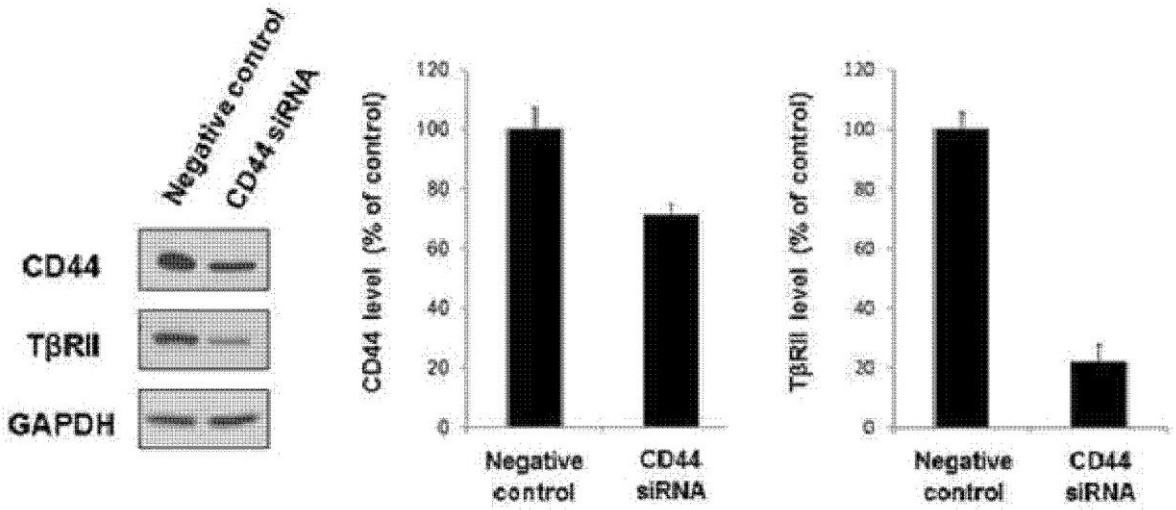
【FIG 9】


Hapln1 siRNA
HA - + - +
Hapln1 - - + +
TβRII
GAPDH
***
*
**
Relative TβRII/GAPDH protein expression
1.4
1.2
1
0.8
0.6
0.4
0.2
0
HA - + - +
Hapln1 - - + +

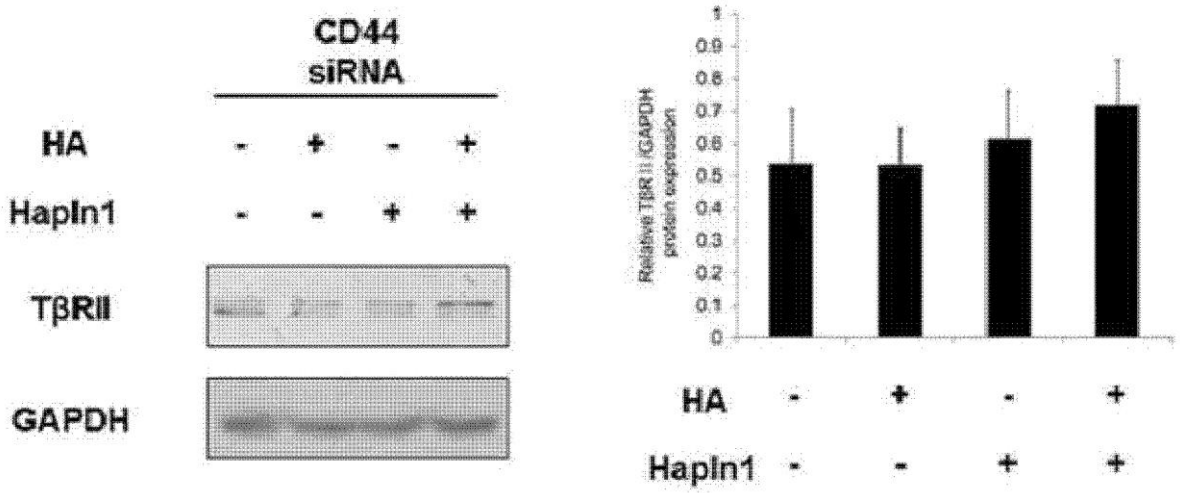
【FIG 10】


4-MU
Hapln1
TβRII
HAS2
GAPDH
Relative TβRII/GAPDH protein expression
Relative HAS2/GAPDH protein expression
4-MU
Hapln1

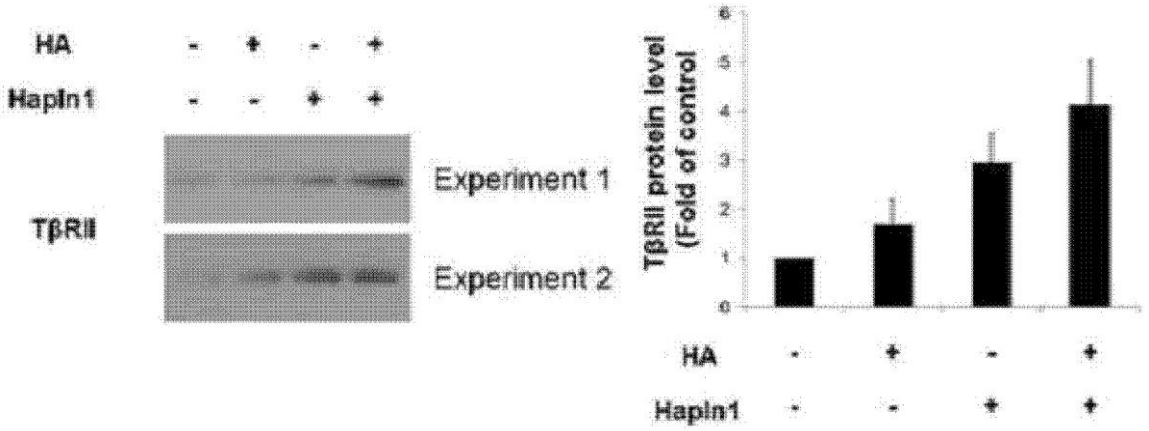
【FIG 11】


Negative control
CD44 siRNA
CD44
TβRII
GAPDH
CD44 level (% of control)
TβRII level (% of control)
Negative control
CD44 siRNA

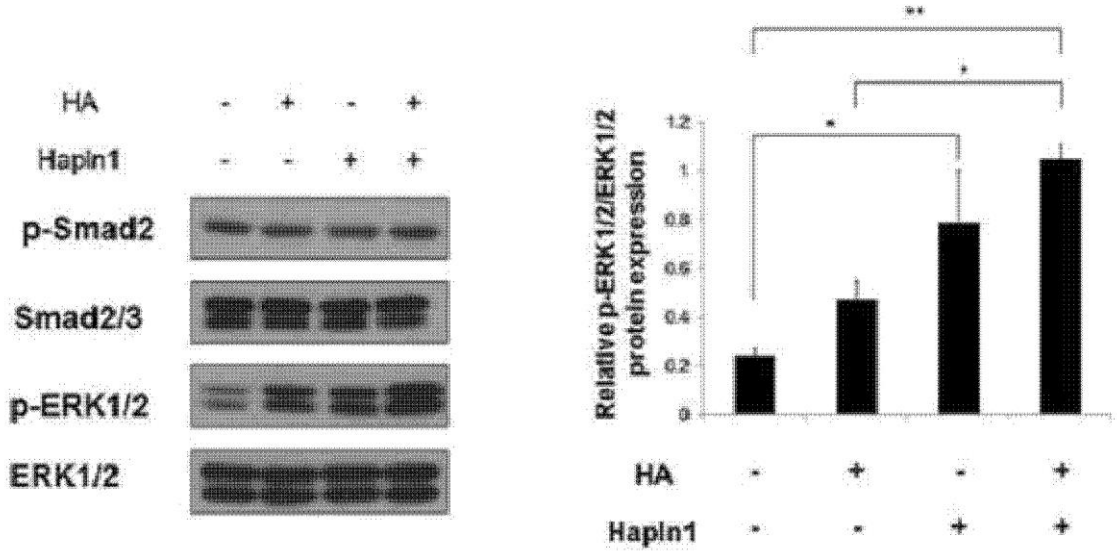
【FIG 12】


CD44
siRNA
HA
Hapln1
TβRII
GAPDH
Relative TβRII /GAPDH protein expression
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
HA - + - +
Hapln1 - - + +

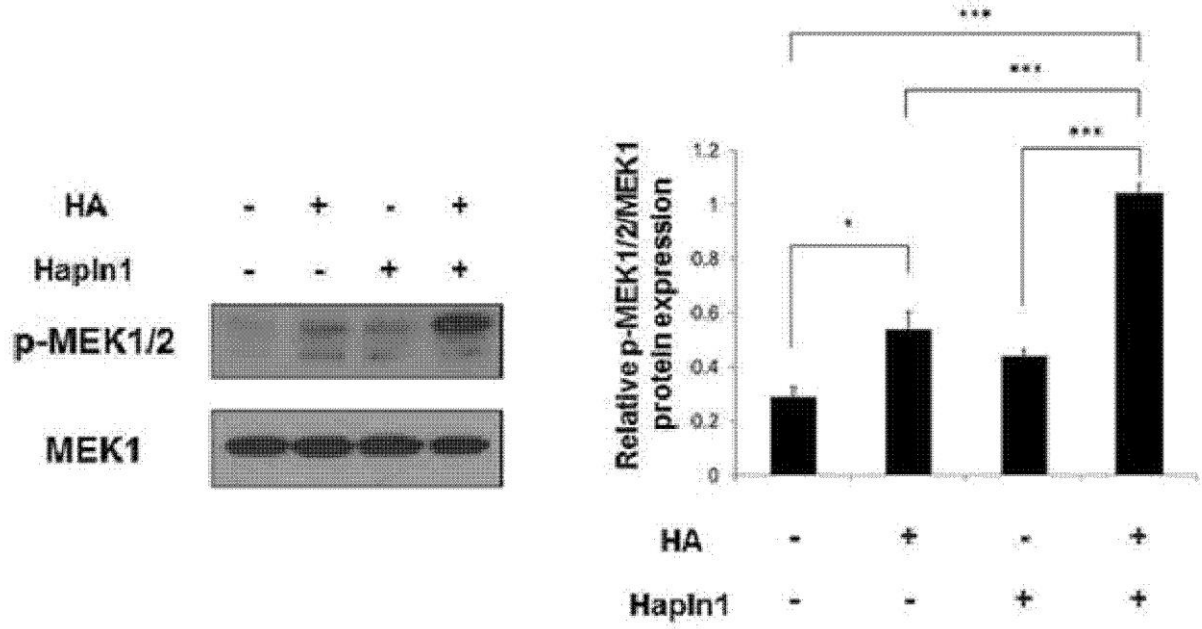
【FIG 13】


HA - + - +
Hapln1 - - + +
TβRII
Experiment 1
Experiment 2
TβRII protein level
(Fold of control)
6
5
4
3
2
1
0
HA - + - +
Hapln1 - - + +

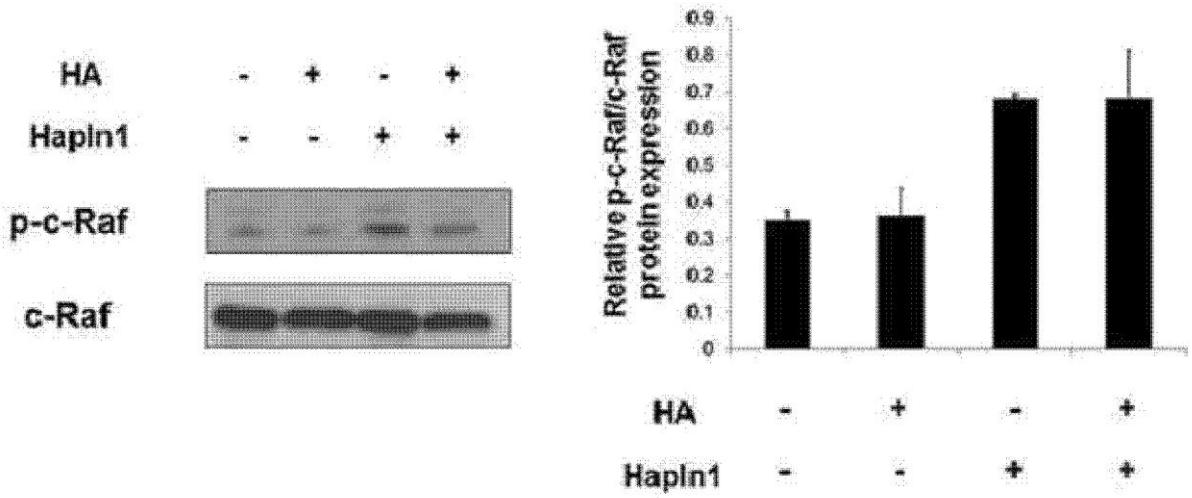
【FIG 14】


HA
Hapln1
p-Smad2
Smad2/3
p-ERK1/2
ERK1/2
Relative p-ERK1/2/ERK1/2 protein expression
0
0.2
0.4
0.6
0.8
1
1.2
*
*
**
HA
Hapln1

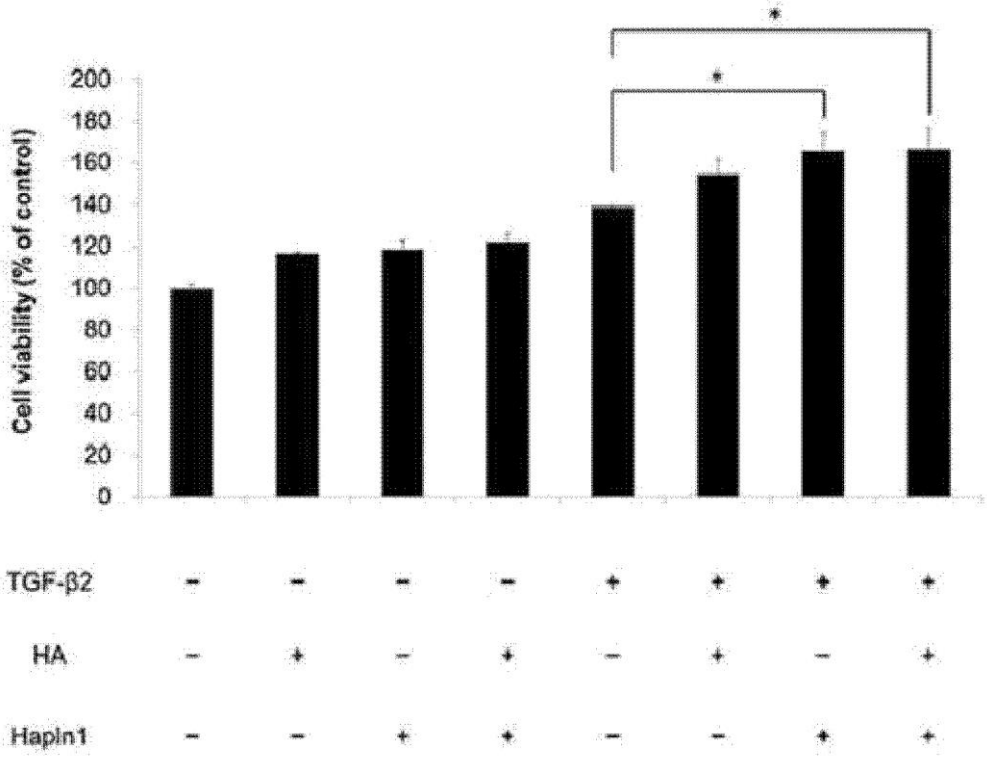
【FIG 15】


HA
Hapln1
p-MEK1/2
MEK1
Relative p-MEK1/2/MEK1 protein expression
0
0.2
0.4
0.6
0.8
1
1.2
*
***
***
***
HA
Hapln1

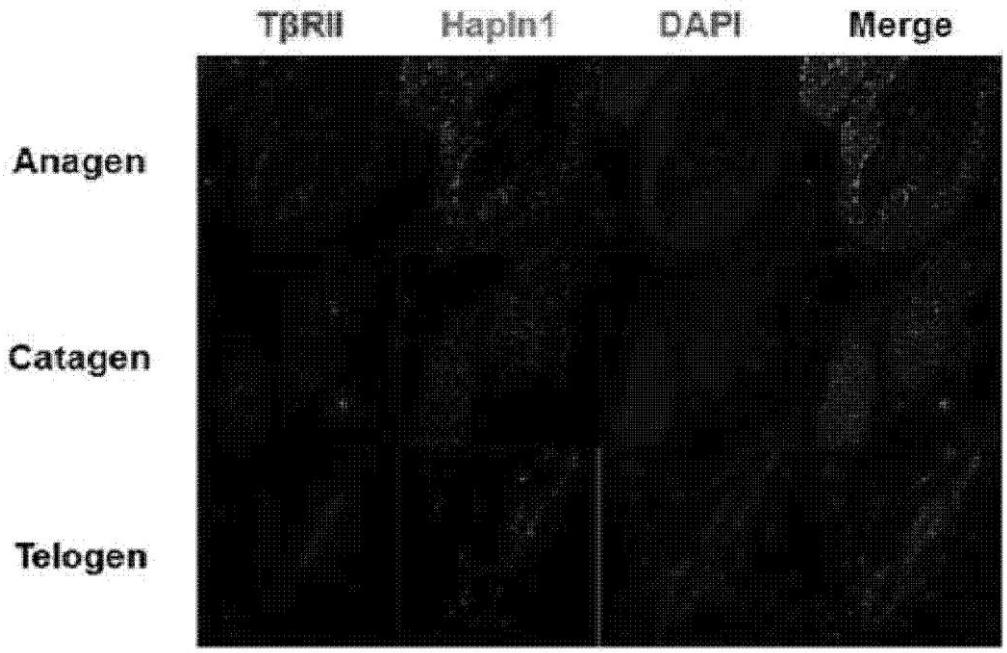
【FIG 16】


HA
Hapln1
p-c-Raf
c-Raf
Relative p-c-Raf/c-Raf protein expression
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
HA - + - +
Hapln1 - - + +

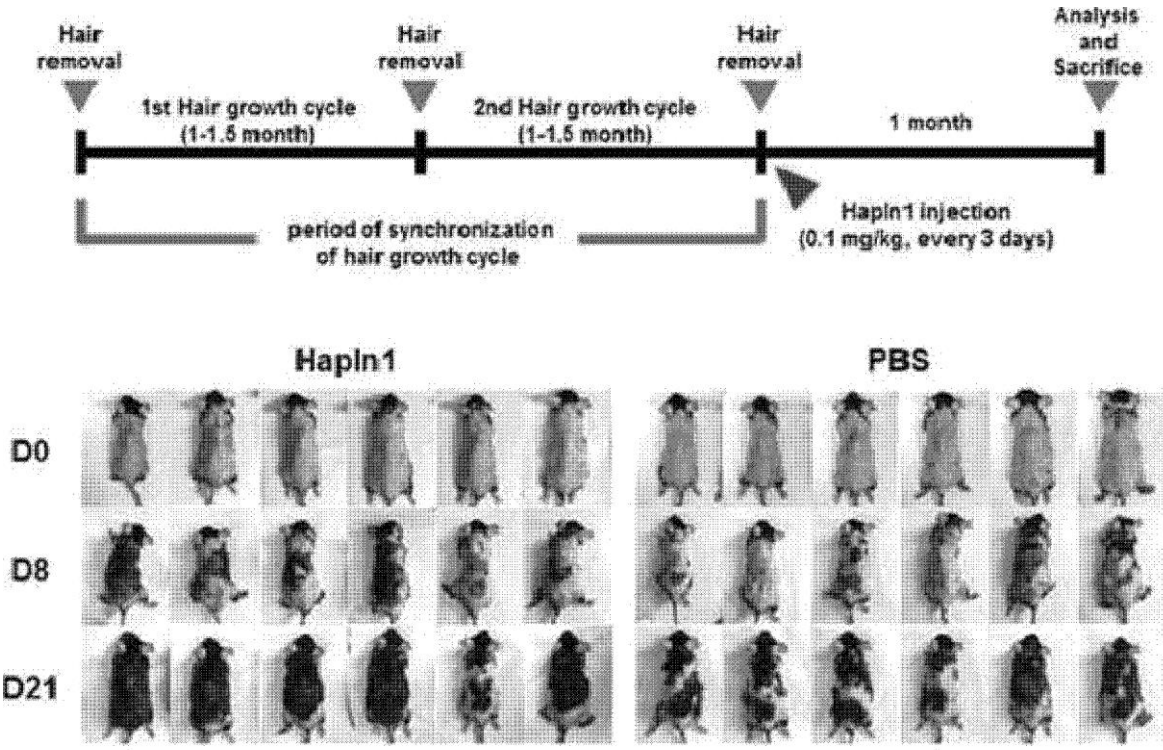
【FIG 17】


Cell viability (% of control)
200
180
160
140
120
100
80
60
40
20
0
*
*
TGF-β2 - - - - + + + +
HA - + - + - + - +
Hapln1 - - + + - - + +

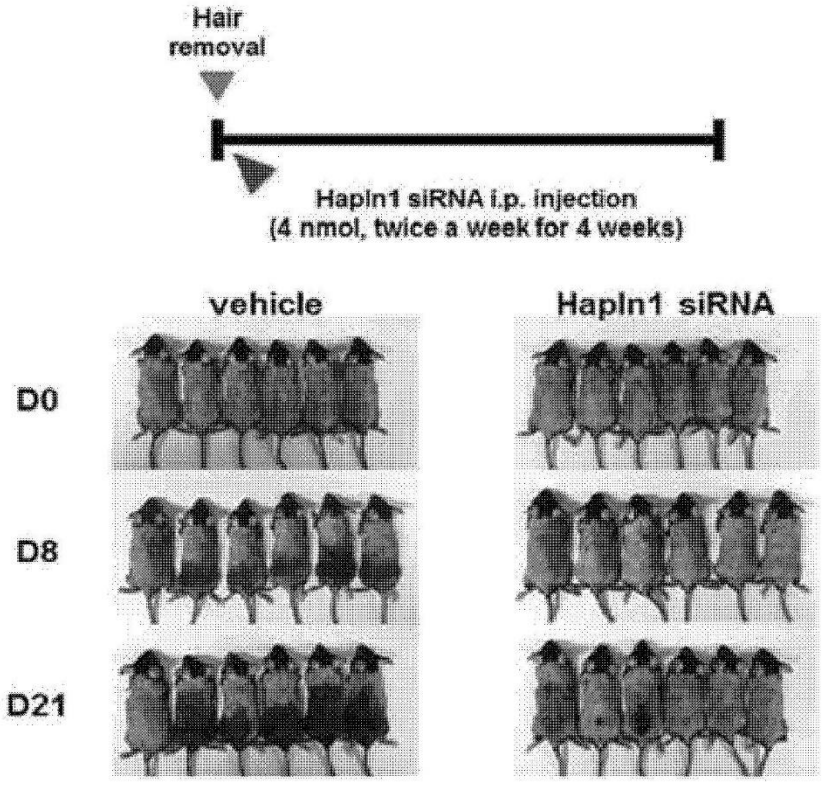
【FIG 18】


TβRII
Hapln1
DAPI
Merge
Anagen
Catagen
Telogen

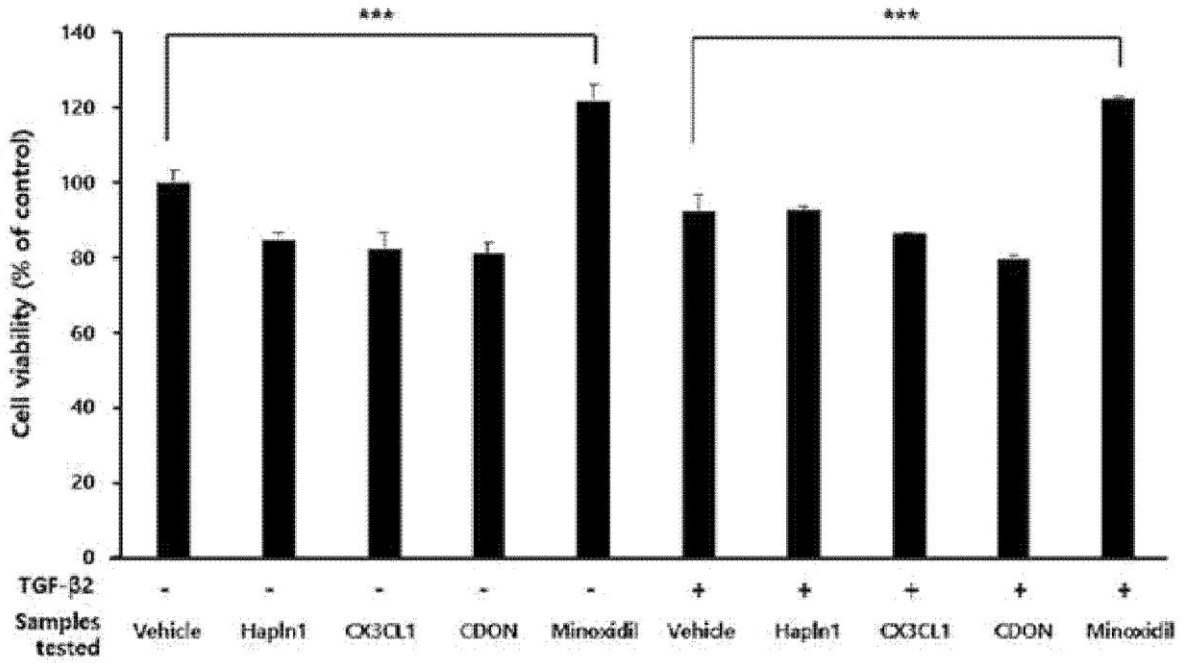
【FIG 19】


Hair removal
Hair removal
Hair removal
Analysis and Sacrifice
1st Hair growth cycle (1-1.5 month)
2nd Hair growth cycle (1-1.5 month)
1 month
period of synchronization of hair growth cycle
Hapln1 injection (0.1 mg/kg, every 3 days)
Hapln1
PBS
D0
D8
D21

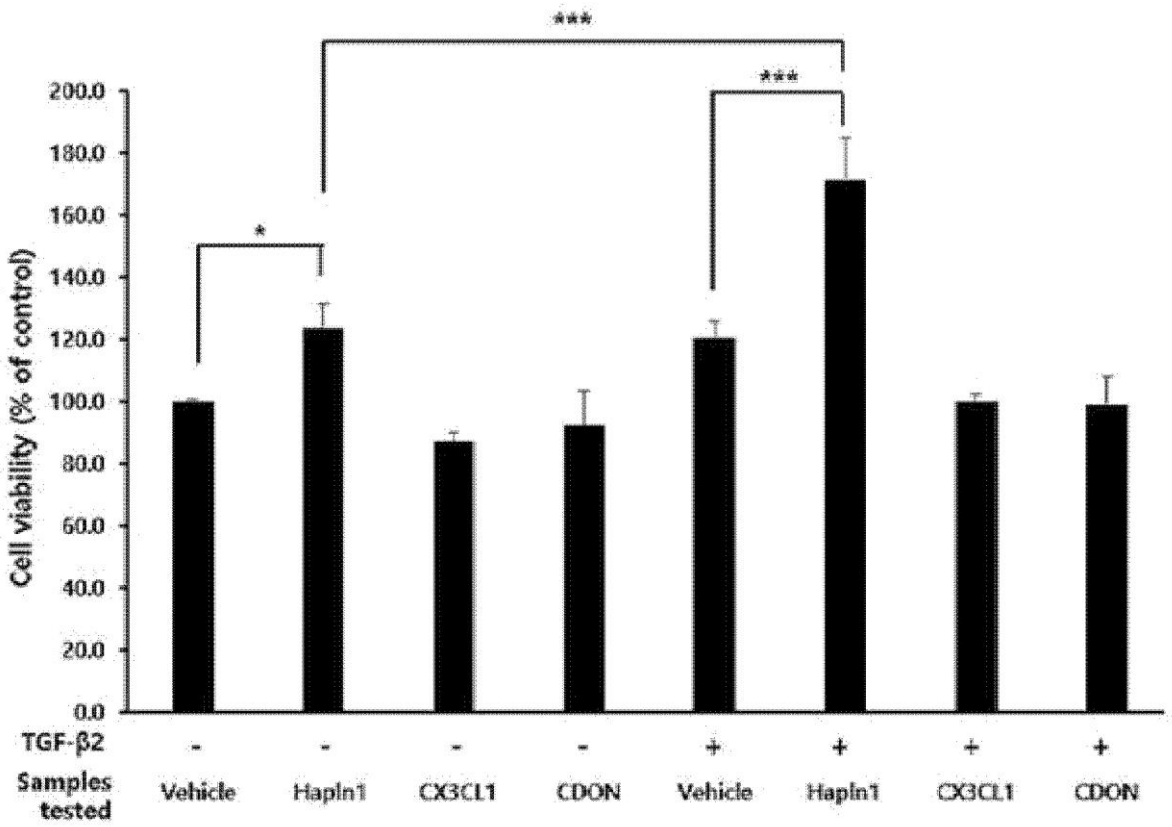
【FIG 20】


Hair
removal
Hapln1 siRNA i.p. injection
(4 nmol, twice a week for 4 weeks)
vehicle
Hapln1 siRNA
D0
D8
D21

【FIG 21】


***
***
140
120
100
80
60
40
20
0
Cell viability (% of control)
TGF-β2
- - - - - + + + + +
Samples tested
Vehicle
Hapln1
CX3CL1
CDON
Minoxidil
Vehicle
Hapln1
CX3CL1
CDON
Minoxidil

【FIG 22】


***
***
*
200.0
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
Cell viability (% of control)
TGF-β2
Samples tested
-
-
-
-
+
+
+
+
Vehicle
Hapln1
CX3CL1
CDON
Vehicle
Hapln1
CX3CL1
CDON