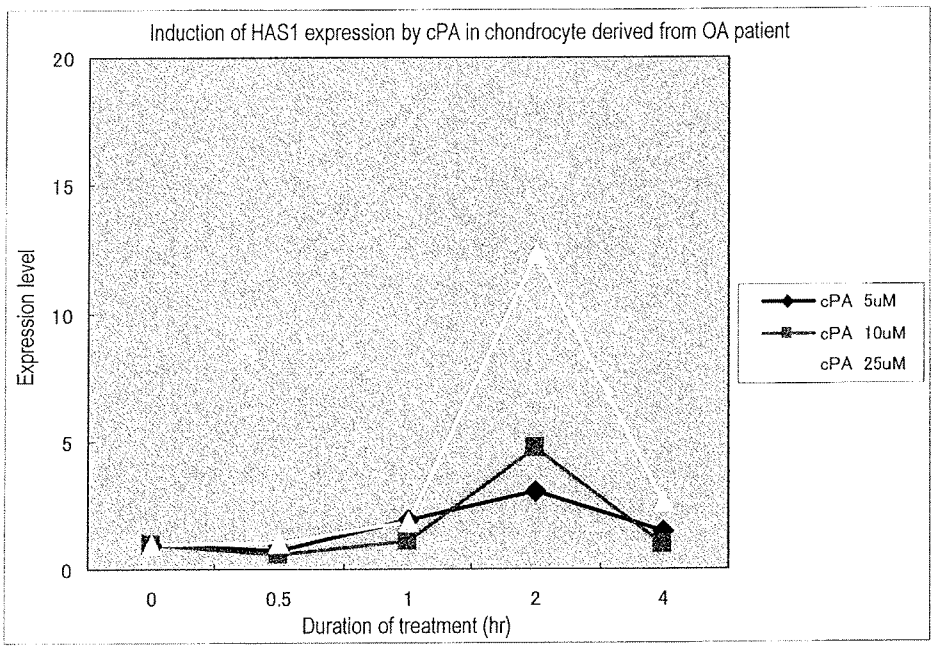
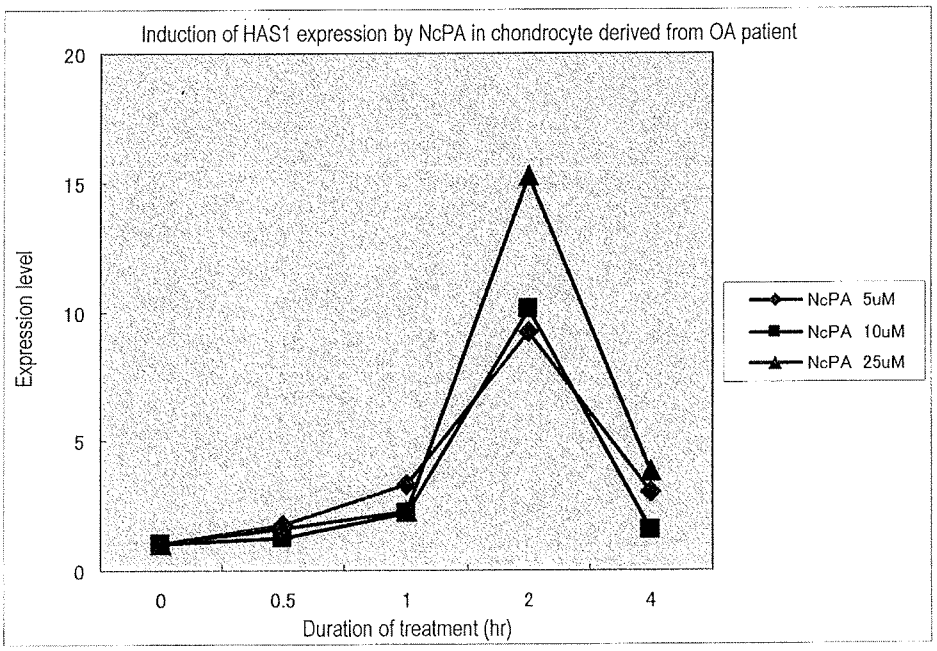
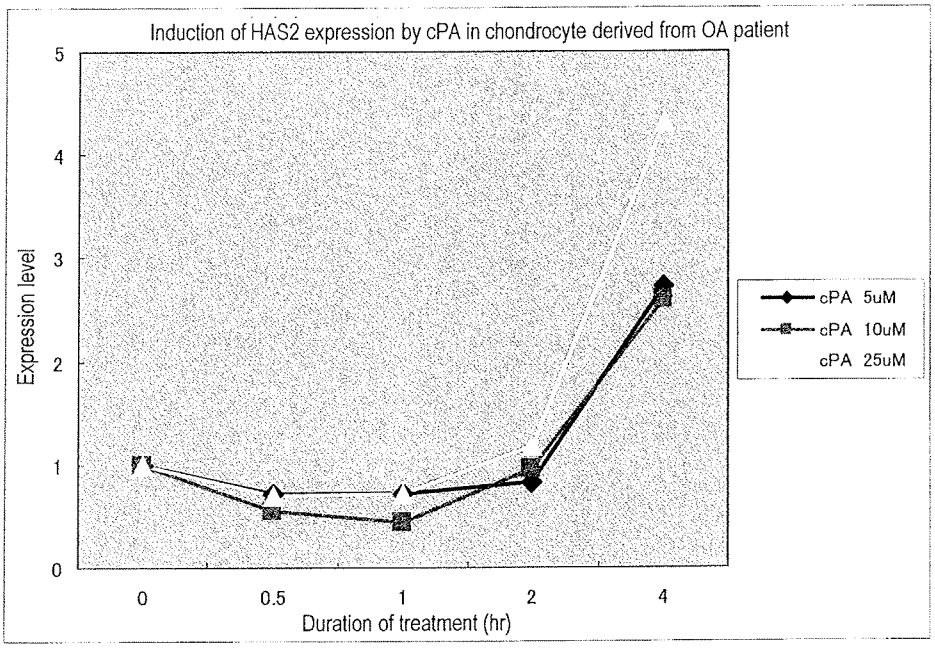
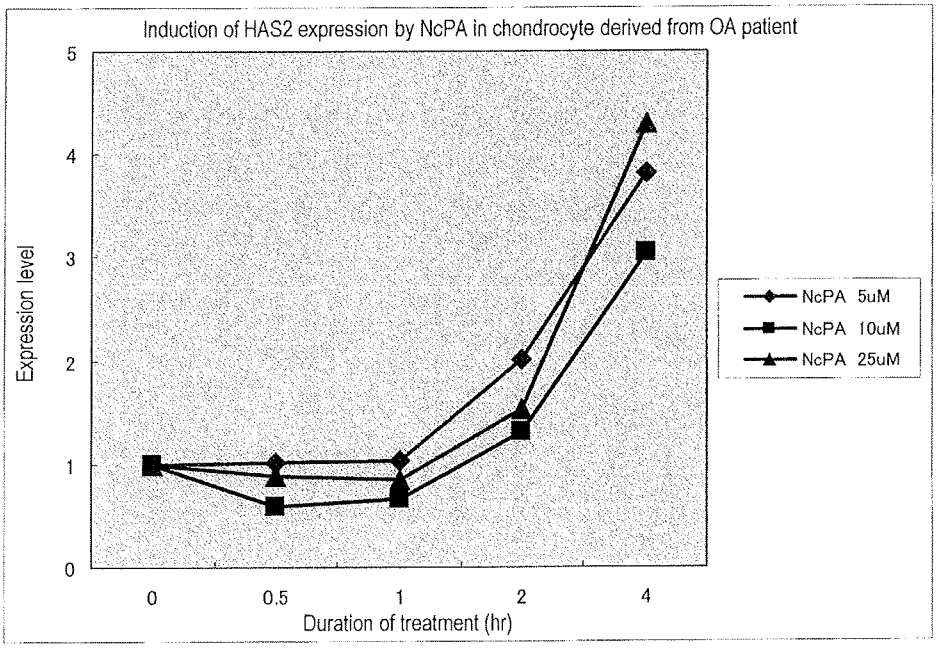
[Fig. 1]


Induction of HAS1 expression by cPA in chondrocyte derived from OA patient
Expression level
20
15
10
5
0
0
0.5
1
2
4
Duration of treatment (hr)
cPA 5uM
cPA 10uM
cPA 25uM

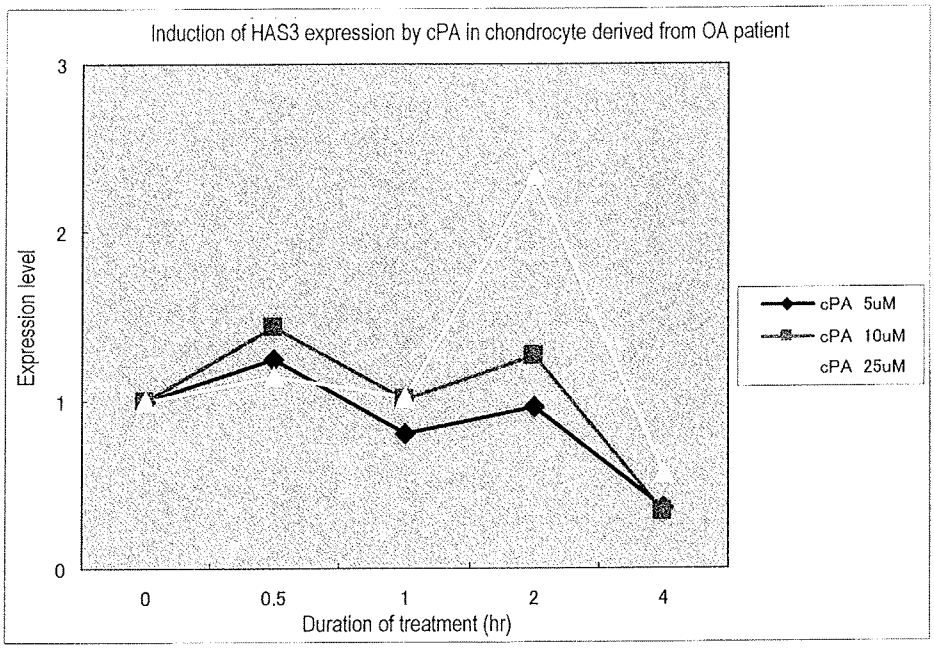

Induction of HAS1 expression by NcPA in chondrocyte derived from OA patient
Expression level
20
15
10
5
0
0
0.5
1
2
4
Duration of treatment (hr)
NcPA 5uM
NcPA 10uM
NcPA 25uM

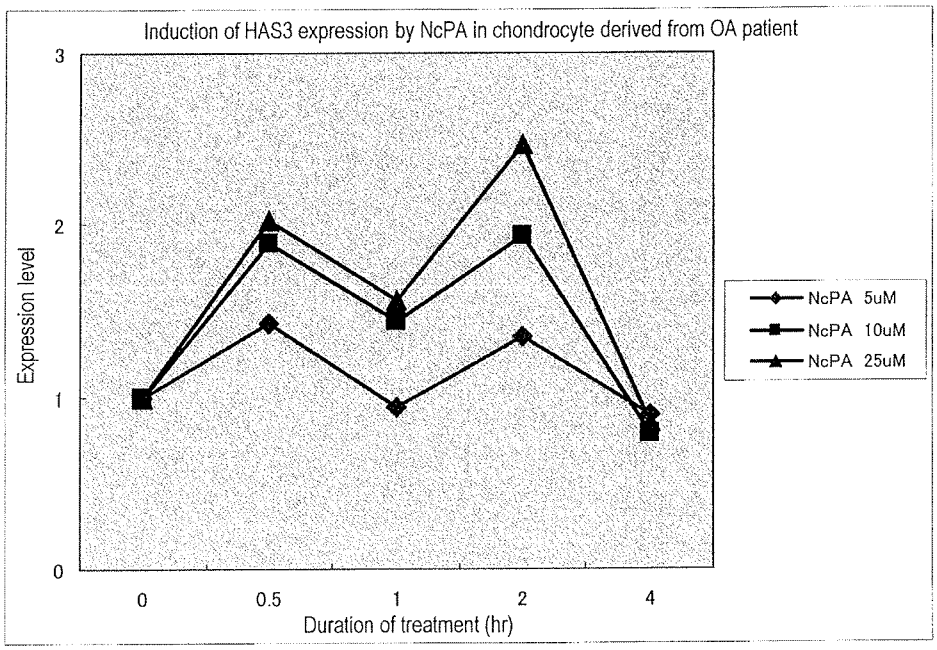
[Fig. 2]


Induction of HAS2 expression by cPA in chondrocyte derived from OA patient
Expression level
0
1
2
3
4
5
0
0.5
1
2
4
Duration of treatment (hr)
cPA 5uM
cPA 10uM
cPA 25uM

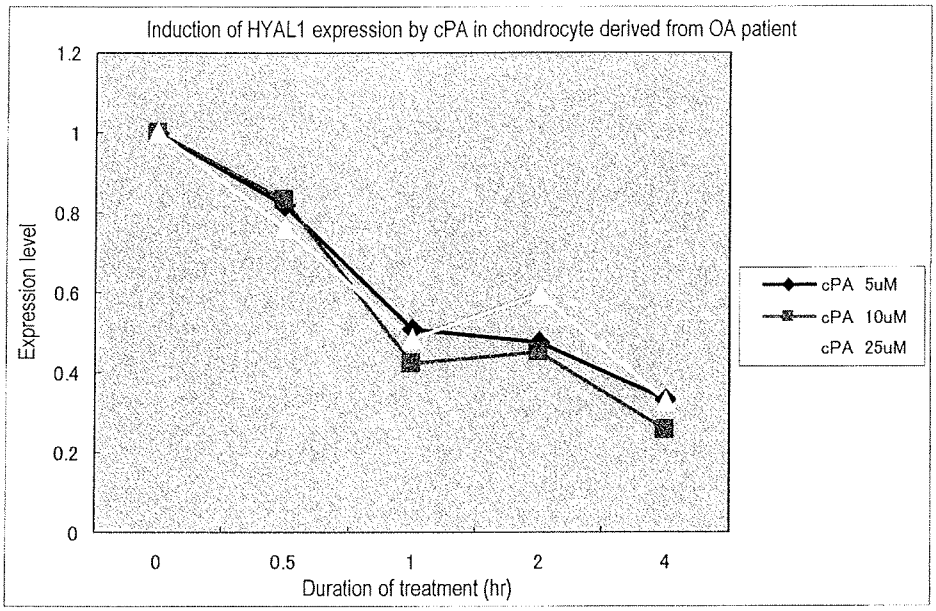

Induction of HAS2 expression by NcPA in chondrocyte derived from OA patient
Expression level
0
1
2
3
4
5
0
0.5
1
2
4
Duration of treatment (hr)
NcPA 5uM
NcPA 10uM
NcPA 25uM

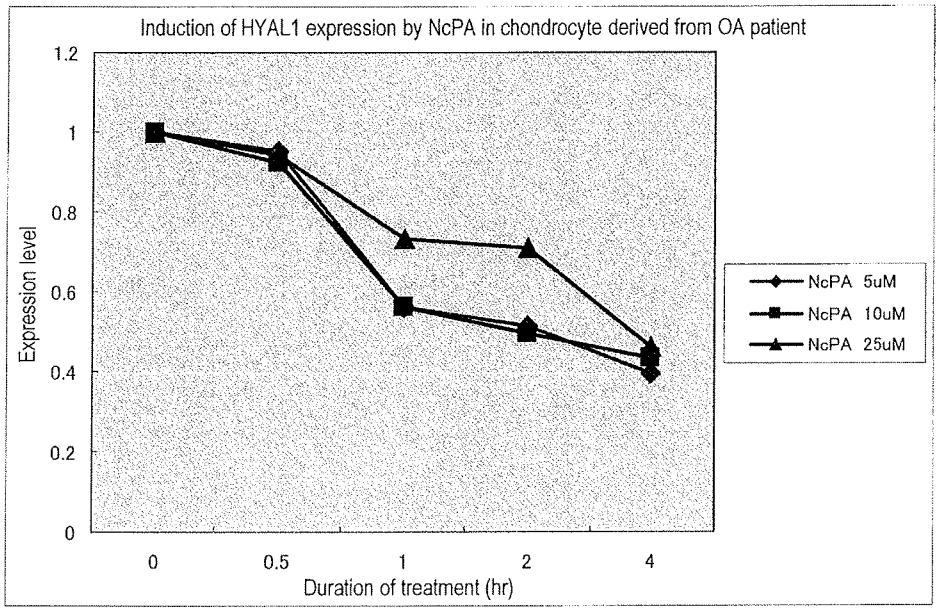
[Fig. 3]


Induction of HAS3 expression by cPA in chondrocyte derived from OA patient
Expression level
3
2
1
0
0
0.5
1
2
4
Duration of treatment (hr)
cPA 5uM
cPA 10uM
cPA 25uM

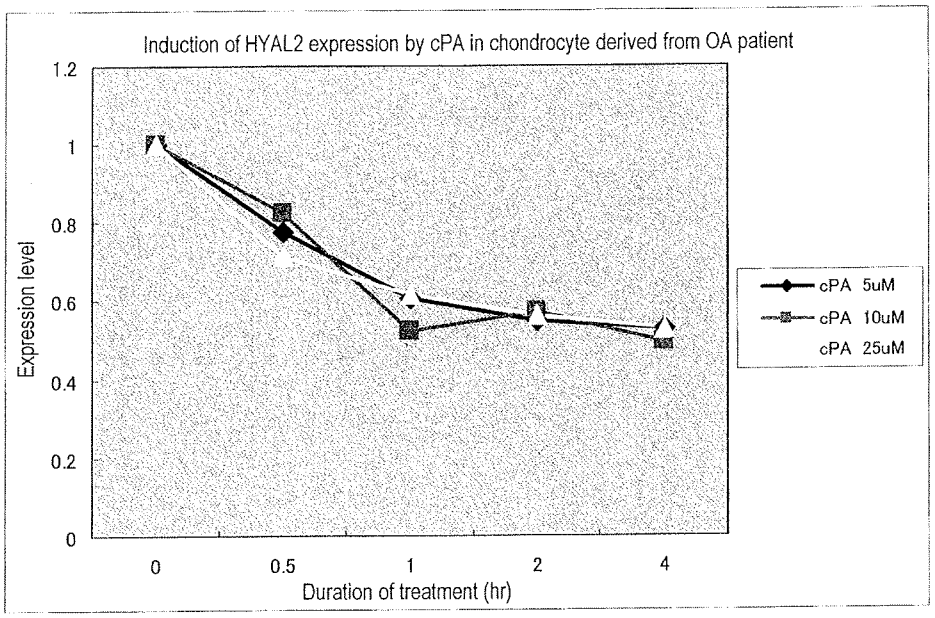

Induction of HAS3 expression by NcPA in chondrocyte derived from OA patient
Expression level
3
2
1
0
0
0.5
1
2
4
Duration of treatment (hr)
NcPA 5uM
NcPA 10uM
NcPA 25uM

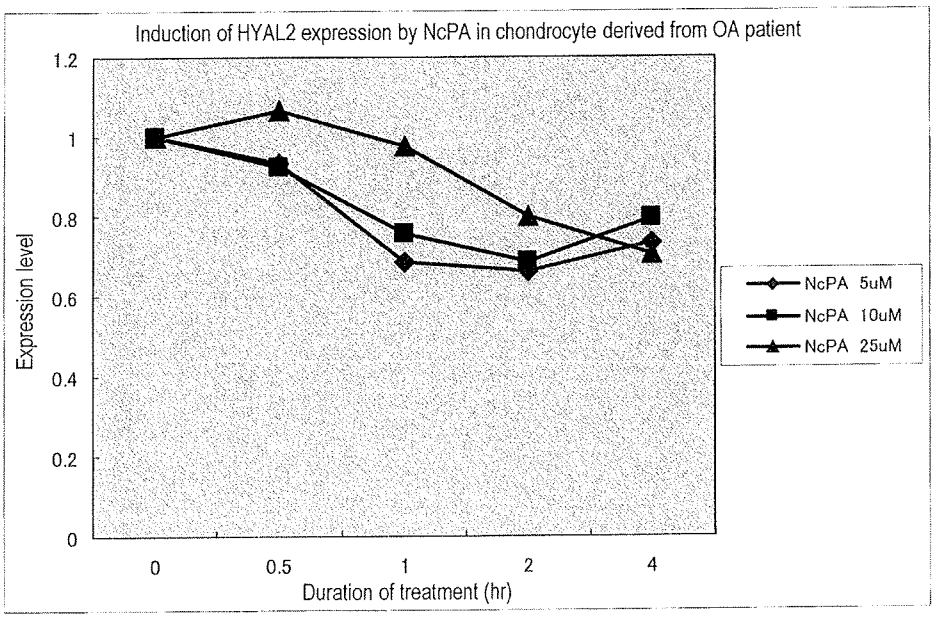
[Fig. 4]


Induction of HYAL1 expression by cPA in chondrocyte derived from OA patient
Expression level
1.2
1
0.8
0.6
0.4
0.2
0
0
0.5
1
2
4
Duration of treatment (hr)
cPA 5uM
cPA 10uM
cPA 25uM

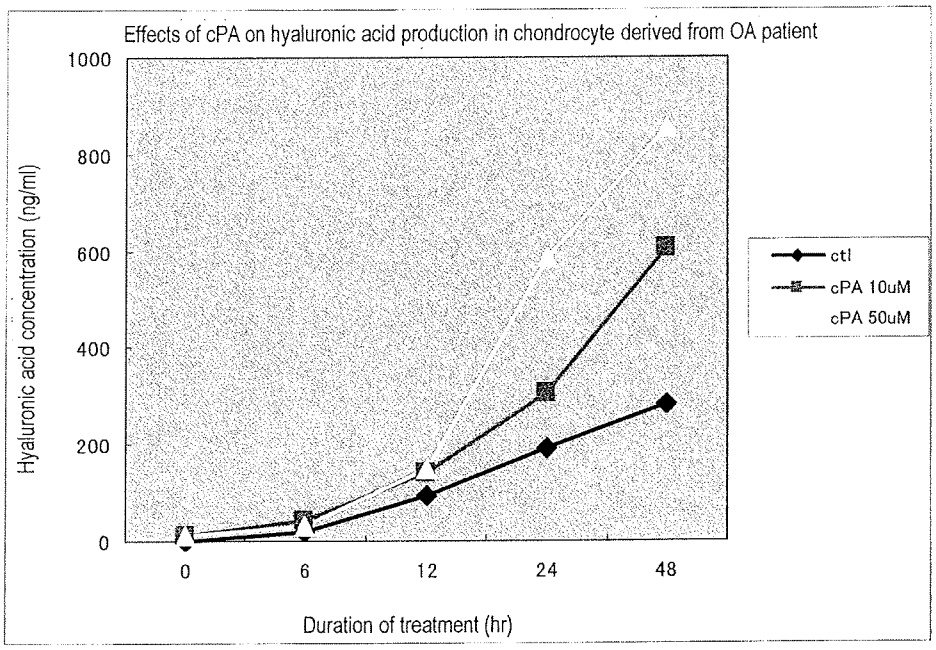

Induction of HYAL1 expression by NcPA in chondrocyte derived from OA patient
Expression level
1.2
1
0.8
0.6
0.4
0.2
0
0
0.5
1
2
4
Duration of treatment (hr)
NcPA 5uM
NcPA 10uM
NcPA 25uM

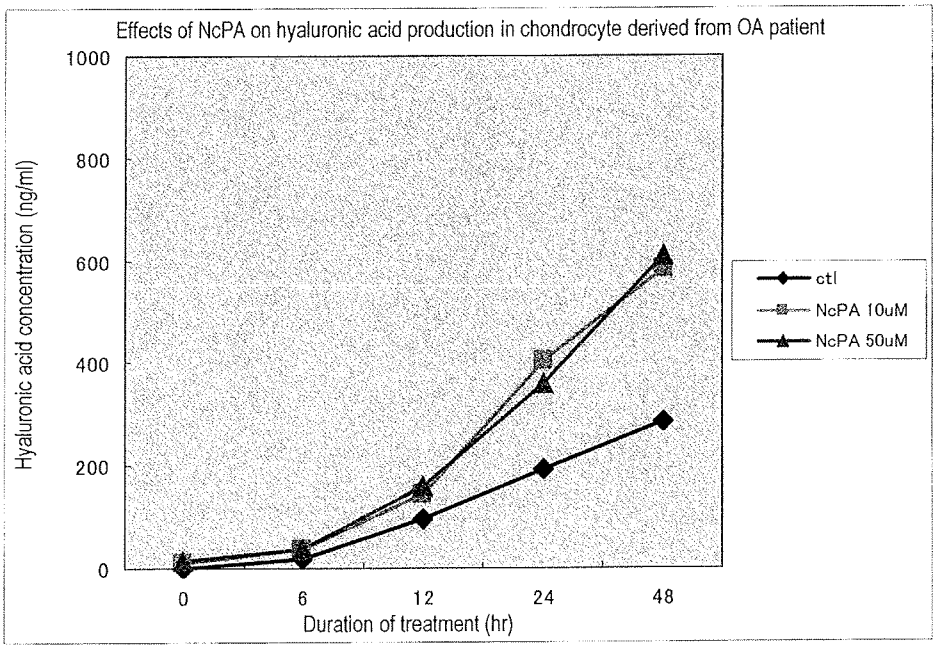
[Fig. 5]


Induction of HYAL2 expression by cPA in chondrocyte derived from OA patient
Expression level
1.2
1
0.8
0.6
0.4
0.2
0
0
0.5
1
2
4
Duration of treatment (hr)
cPA 5uM
cPA 10uM
cPA 25uM

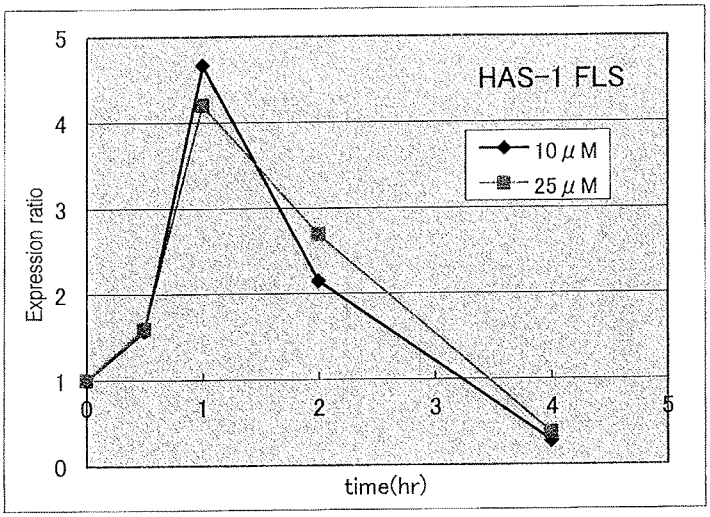

Induction of HYAL2 expression by NcPA in chondrocyte derived from OA patient
Expression level
1.2
1
0.8
0.6
0.4
0.2
0
0
0.5
1
2
4
Duration of treatment (hr)
NcPA 5uM
NcPA 10uM
NcPA 25uM

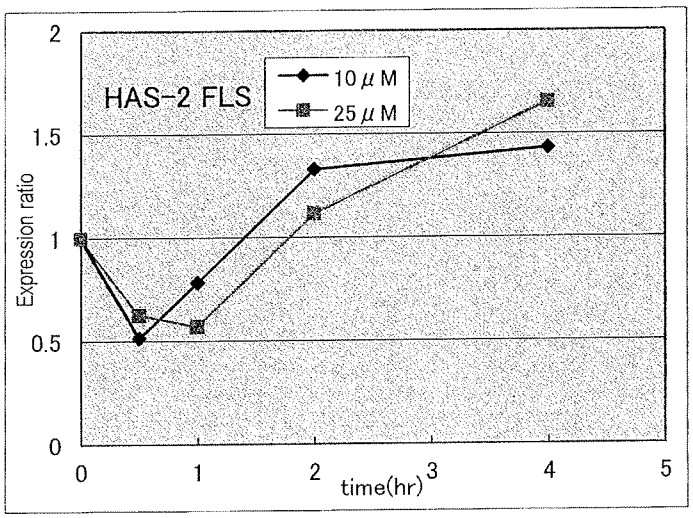
[Fig. 6]

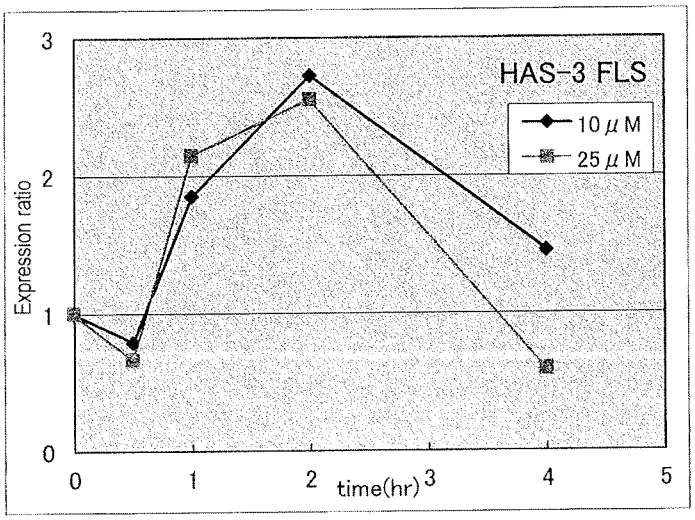

Effects of cPA on hyaluronic acid production in chondrocyte derived from OA patient
Hyaluronic acid concentration (ng/ml)
1000
800
600
400
200
0
0
6
12
24
48
Duration of treatment (hr)
ctl
cPA 10uM
cPA 50uM


Effects of NcPA on hyaluronic acid production in chondrocyte derived from OA patient
Hyaluronic acid concentration (ng/ml)
1000
800
600
400
200
0
0
6
12
24
48
Duration of treatment (hr)
ctl
NcPA 10uM
NcPA 50uM

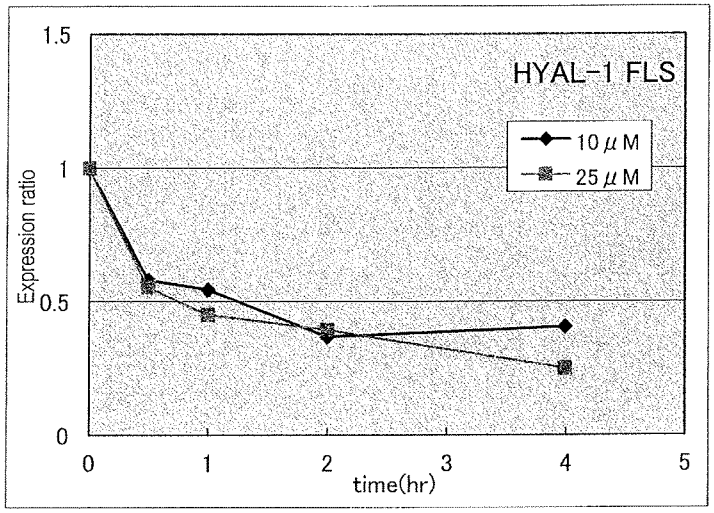
[Fig. 7]

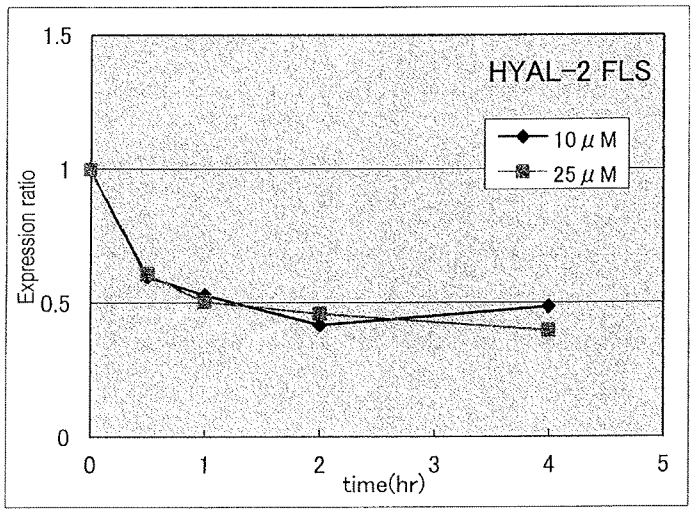

HAS-1 FLS
10 μ M
25 μ M
Expression ratio
time(hr)
0
1
2
3
4
5


HAS-2 FLS
10 μ M
25 μ M
Expression ratio
time(hr)
0
0.5
1
1.5
2
3
4
5

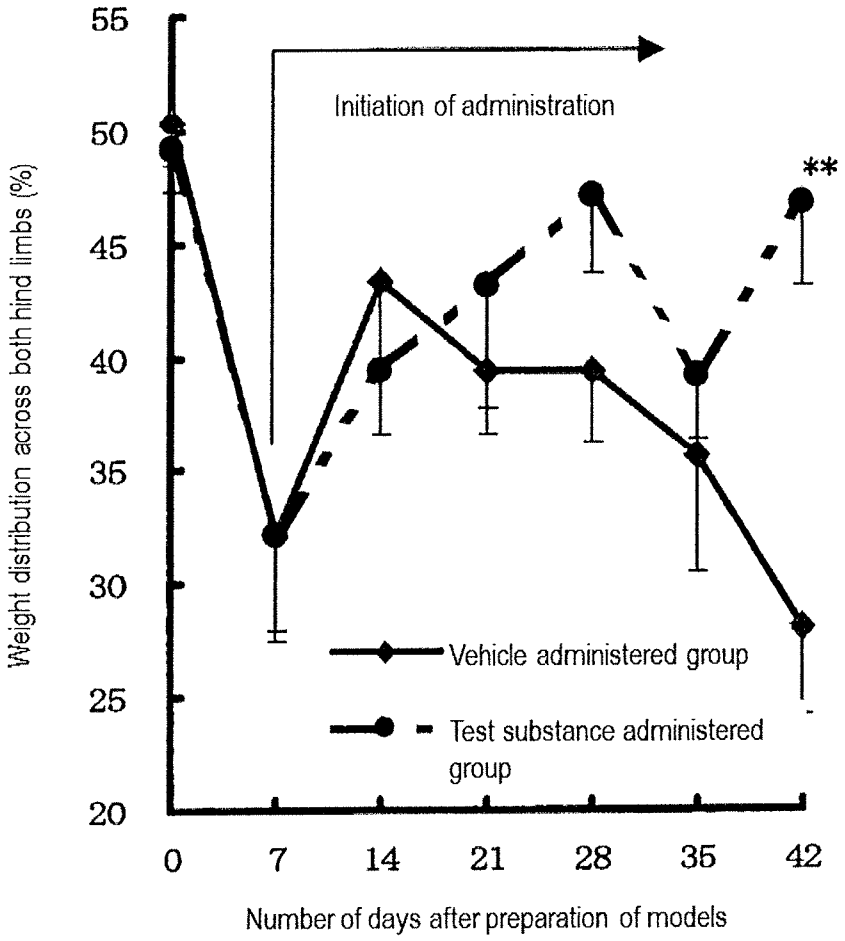

HAS-3 FLS
10 μ M
25 μ M
Expression ratio
time(hr)
0
1
2
3
4
5

[Fig. 8]

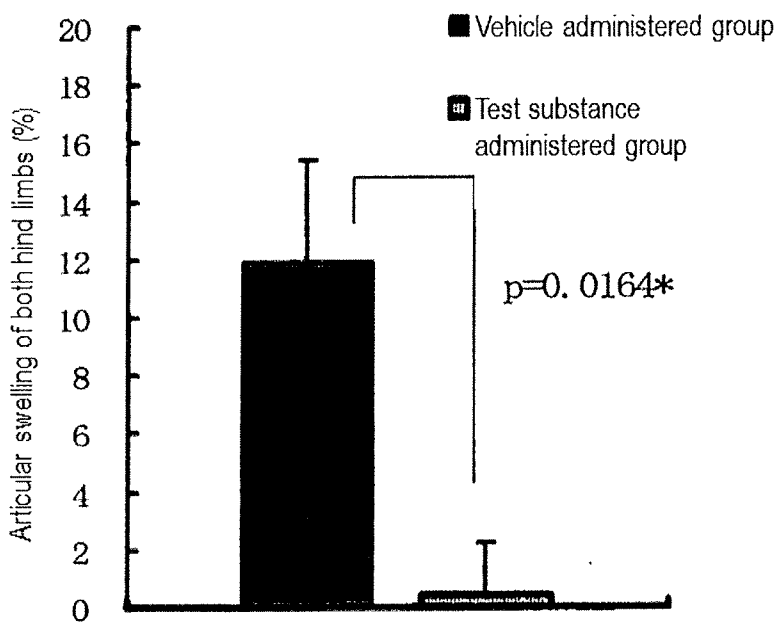

HYAL-1 FLS
10 μ M
25 μ M
Expression ratio
1.5
1
0.5
0
0
1
2
3
4
5
time(hr)


HYAL-2 FLS
10 μ M
25 μ M
Expression ratio
1.5
1
0.5
0
0
1
2
3
4
5
time(hr)

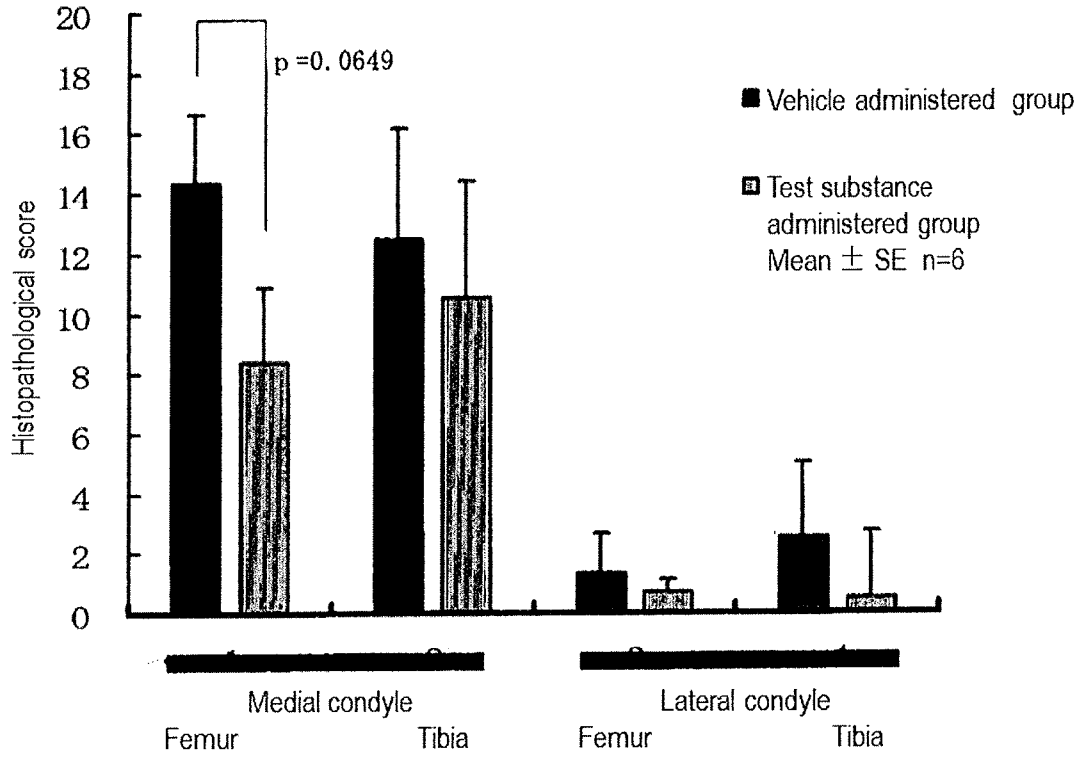
[Fig. 9]


55
50
45
40
35
30
25
20
Weight distribution across both hind limbs (%)
Initiation of administration
**
Vehicle administered group
Test substance administered group
0
7
14
21
28
35
42
Number of days after preparation of models

[Fig. 10]


Vehicle administered group
Test substance administered group
p=0. 0164*
Articular swelling of both hind limbs (%)
20
18
16
14
12
10
8
6
4
2
0

[Fig. 11]

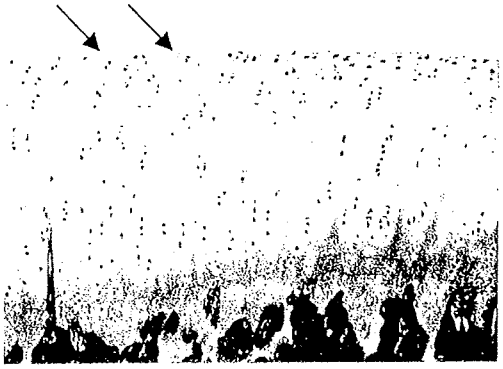

20
18
16
14
12
10
8
6
4
2
0
Histopathological score
p =0. 0649
Vehicle administered group
Test substance administered group
Mean ± SE n=6
Medial condyle
Femur
Tibia
Lateral condyle
Femur
Tibia

[Fig. 12]

A



B



C



D

