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(74)
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(54)

- 1 - 2 (extracellular signal regulated protein kinase - 1 and - 2; " ERK - 1/- 2")
MEK - 1 - 2 (MAP kinase kinase - 1/- 2)
, ERK - 1/- 2 MEK - 1/- 2
ERK - 1/- 2 MEK - 1/- 2
, ERK - 1/- 2 MEK - 1/- 2

1 ,

2 A ,

2 B ,

2 C ,

M : (monolayer culture),

A : (alginate gel bead)

3 A ERK - 1/ - 2 ,

3 B MEK - 1/ - 2 ERK - 1/ - 2 ,

3 C ERK - 1/ - 2 ,

4 A ERK - 1/ - 2 가 ,

NB : (Northern blot) ,

WB : (Western blot)

4 B ERK - 1/ - 2 ERK - 1/ - 2 가 ,

NB : , WB :

4 C ERK - 1/ - 2 가 가 ,

NB : , WB :

4 D ERK - 1/ - 2 가 가 ,

5 ERK - 1/ - 2 가 가 ERK - 1/ - 2 ,

A: P0 P2 ERK - 1/ - 2 ,

B: P0 P4 ERK - 1/ - 2

6 NO SNP(S - nitroso - N - acetyl penicillamine) NO ,

A: SNP NO ,

B: SNP NO

7 SNP ,

A: SNP II ,

B: SNP

8 ERK - 1/ - 2 가 SNP ,

A: SNP ERK - 1/ - 2 ,

B: SNP ERK - 1/ - 2 ,

C: ERK - 1/ - 2 II ,

D: ERK - 1/ - 2

9 1 - 가 MMP - 9 ,

10 A 1 - ERK - 1/ - 2 , B ERK - 1/ - 2
가 1 - MMP - 9 ,

11 1 - NO ERK - 1/ - 2 ,

12 1 - cox - 2(cyclooxygenase - 2) ERK - 1/ - 2 ,

13 ERK - 1/ - 2 .

- 1 - 2(extracellular signal regulated protein kinase - 1/ - 2; " ERK - 1/ - 2")
MEK - 1 - 2(MAP kinase - 1/ - 2)
, ERK - 1/ - 2 MEK

(chondrocytes)
(type - collagen) (proteoglycan)
- 1 (interleukin - 1 ; " IL - 1 ") - (tumor necrosis factor - ; " TNF

- ") (matrix metalloproteinase; (cytokine) " MMP") 가 (NO) 가 " PGE2") 가 MMP 가 E2(prostaglandin E2;) (, ,) (, ,) MMP 가 , (cell therapy) (tissue engineering) (de - differentiation)

- 1 TNF - MMP IL

가, , MMP ERK - 1/ - 2 MMP 가 , (cyclooxygenase - 2; " cox - 2" ERK - 1/ - 2 가 PGE2 가)

, ERK - 1/ - 2 MEK - 1/ - 2

SNP NO NO II NO NO ERK - 1/ - 2
 (7). NO SNP ERK - 1/ - 2
 ERK - 1/ - 2 NO NO
 (8). ERK - 1/ - 2 NO NO

ERK - 1/ - 2 MMP IL 1 -
 ERK - 1/ - 2 MMP - 9 가 (9). IL 1 -
 ERK - 1/ - 2 가 , ERK - 1/ - 2 ERK - 1/ - 2
 - 2 MMP - 9 (10 A 10 B). ERK - 1/
 MEK
 MMP

IL1 - NO ERK - 1/ - 2 NO
 - 2 , IL1 - NO ERK - 1/ - 2 ERK - 1/
 NO 가 (11). NO ERK -
 1/ - 2 MMP ERK -
 MEK NO

ERK - 1/ - 2 cox - 2 IL1 - IL1 -
 ERK - 1/ - 2 cox - 2 가 IL1 - cox - 2 가 ERK - 1/ - 2
 1/ - 2 PGE2 (12). ERK -
 cox - 2 PGE2 cox - 2 ERK - 1/ - 2
 MEK cox - 2

ERK - 1/ - 2 MEK
 가 가

가 가

(Propylene glycol), (witepsol), (tween) 61,
 가 (carrier)
 (ascorbic acid) 가 (antioxidants), (chelatin
 g agents), (stabilizers)

0.001 - 100 mg/kg, 0.01 - 150 mg/kg

1 - 3

(single dose) (fractionated treatment protocol) , (bolus) , (multiple dose) (infusion)

가

ERK - 1/ - 2

MEK

NO , ERK - 1/ - 2 MEK
 MMP , ERK - 1/ - 2 MEK
 MMP PGE2 cox - 2
 , ERK - 1/ - 2 MEK

< 1 >

< 1 - 1 >

가 (Hamburger - Hamilton stage 24 -
 25 chicken embryo) (limb bud) (microass culture)
 (1). , 10%
 (Ham 's F - 12 medium, GibcoBRL, Gaithersburg, MD, USA) 2×10^7 /Ml
 (spot) 15 μ l 37 2 10%
 (50 μ g/Ml), (50 units/Ml)
 가 가 , 5
 3
 (glycosaminoglycan) 가
 (alcian blue) 3 5
 (2A).

< 1 - 2 >

2 - 4
 (1). , 0.2% (colag
 enase type , Sigma) 6 (sin
 gle cells) 10% , 50 µg/Ml 50 units/Ml
 DMEM(Dulbecco 's modified Eagle 's medium GibcoBRL, Gaithersburg, MD, USA)
 5 x 10⁴ /cm² 37 2
 5 P0
 5 x 10⁴ /cm² (subculture) ,
 P1, P2 P6
 P0 P6 P1
 P3
 (glycosaminoglycan) ,
 alcian blue) (2B).

< 2> ERK - 1/ - 2

ERK - 1/ - 2 가
 (2A 1 - 1) ERK - 1/ - 2 ERK - 1/ - 2
 가 가 3
 가
 (3A). ERK - 1/ - 2 가 ERK - 1/ - 2
 (3A). ERK - 1/ - 2 MEK -
 1 MEK - 2 2 - (2 - - 3 -) - 4H - 1 - - 4 - (PD98059) E
 RK - 1/ - 2 (3B), (ERK - 1/ - 2
 alcian blue) 가 (3C)
 가 (3A). ERK - 1/ - 2 가
 , ERK - 1/ - 2

< 3> ERK - 1/ - 2

< 3 - 1> ERK - 1/ - 2

ERK - 1/ - 2 5 x 10⁴ /
 cm² 2 5 P6
 P0 가 (2B).
 P0 가 , P1 , P3
 (4A). ERK - 1/ - 2 P0 ,
 ERK - 1/ - 2 ERK - 1/ - 2 (5A). ERK - 1/ - 2
 ERK - 1/ - 2 가 ERK - 1/ - 2

< 3 - 2> ERK - 1/ - 2

ERK - 1/ - 2
 - 3 -) - 4H - 1 - - 4 - (PD98059)
) - 4H - 1 - - 4 - (PD98059) 가 20 μM ERK - 1/ - 2 2 - (2 - - 3 -
 , ERK - 1/ - 2 ERK - 1/ - 2
 (5B) (5C). ERK - 1/ - 2
 P0 가 P2 가
 ERK - 1/ - 2
 P0 2.6 , P2 6.4 가 (5D).
 ERK - 1/ - 2

< 3 - 3 > ERK - 1/ - 2 II

ERK - 1/ - 2
 , 0 2 20 μM ERK - 1/ - 2 2 - (2 - - 3 -) - 4H -
 1 - - 4 - (PD98059) 가 2 , 3% (paraformaldehyde)
 10 , 0.2% X - 100 (Triton X - 100)
 (10 μg/ml) 가 1 TRITC가 2 가 1
 II
 , P0 (6). ERK - 1/ - 2
 ERK - 1/ - 2 가 가
 / - 2 P2 , ERK - 1
 가 가 (5).
 ERK - 1/ - 2

< 4 > ERK - 1/ - 2 NO

< 4 - 1 > NO

NO NO SNP(S - nitroso - N - ac
 etyl penicillamine) NO 가 (6). SNP SNP

< 4 - 2 > NO

SNP NO NO ()
 7A) (7B)
 SNP 24 0.1 mM 1 mM
 1 mM SNP 12 24
 (7A). SNP (7B), SN
 P NO

< 4 - 3 > ERK - 1/ - 2 NO

ERK - 1/- 2 NO SNP
 ERK - 1/- 2 , 1 mM SNP 3 ERK - 1/-
 2 가 12 36 (8A). SNP
 ERK - 1/- 2 가 0.5 mM SNP SNP 가 가 ERK - 1/- 2 가
 (8B). SNP ERK - 1/- 2 가 20 μM ERK - 1/- 2 2 - (2 -
 - 3 -) - 4H - 1 - - 4 - (PD98059) 가
 ERK - 1/- 2 SNP II (8C),
 SNP (8D). E
 ERK - 1/- 2 NO ERK - 1
 / - 2 NO

< 5> ERK - 1/- 2 MMP

ERK - 1/- 2 MMP MMP
 MMP - 9 (gelatin zamography)
 (IL) 1 - (10 ng/Mℓ) IL 1 - 24
 2% MMP
 37 12 MMP - 9
 MMP - 9
 , 9 (IL) 1 - (10 ng/Mℓ) 24
 2 MMP - 9 가 IL1 - ERK - 1/-
 가 (10 A), ERK - 1/- 2 10 uM 2 - (2 - - 3 -
) - 4H - 1 - - 4 - (PD98059) MMP - 9 (10
 B). ERK - 1/- 2
 , MMP

< 6> ERK - 1/- 2 NO

IL1 - NO ERK - 1/- 2 NO
 NO (Nitrite) IL1 - 24
 , IL1 - NO 5 uM 2 - (2 - - 3 -) - 4H - 1 - - 4 - (PD98059)
 ERK - 1/- 2 NO (11). NO
 NO 가 MMP
 ERK - 1/- 2 NO

< 7> ERK - 1/- 2 cox - 2

ERK - 1/- 2 cox - 2
 IL1 - 24 cox - 2 cox - 2

가 IL1 - (cyclooxygenase - 2; cox - 2)
 ERK - 1/- 2 가 2 - (2 - - 3 -) - 4H - 1 - - 4 - (PD980
 59) (12).
 PGE2 . PGE2 cox - 2 ERK - 1/- 2 ERK - 1
 / - 2 cox - 2 ERK - 1/- 2 cox
 - 2

< 8 >

6 (SPF) SD 2
 2 - (2 - - 3 -) - 4H - 1 - - 4 - (PD98059) 0.5%
 50, 30, 10 mg/kg/15 Ml

2 - (2 - - 3 -) - 4H - 1 - - 4 - (PD98059) 50 mg/kg
 (LD₅₀) 50 mg/kg

< 9 >

ERK - 1/- 2 MEK ERK - 1/- 2
 ERK - 1/- 2
 3B, 4B, 8C

ERK - 1/- 2 MEK MMP
 , MMP NO ERK - 1/- 2 M
 PGE2 cox - 2 ERK - 1/- 2 MEK
 EK

NO , ERK - 1/- 2 MEK - 1/- 2
 MMP , MMP
 , ERK - 1/- 2 MEK
 PGE2 cox - 2

(57)

1.

) ERK - 1/- 2 - 1/- 2(extracellular signal regulated protein kinase; " ERK - 1/- 2"
 MEK(MAP kinase kinase)

2.

1 , ERK ERK - 1, ERK - 2 95% ERK

3.

1 , MEK MEK - 1, MEK - 2 95% MEK

4.

1 , ERK ERK MEK 2 - (2 - - 3 -
) - 4H - 1 - - 4 - (2 - (2 - amino - 3 - met hoxo phenol) - 4H - 1 - benzopyran - 4 - one) (PD98059)
 1,4 - - 2,3 - - 1,4 - (2 -) (1,4 - diamino - 2,3 - dicyano - 1,4 - bis(
 2 - aminophenylthio) butadiene)(U - 0126)

5.

4 , ERK ERK MEK 2 - (2 - - 3 -
) - 4H - 1 - - 4 -

6.

ERK ERK MEK

7.

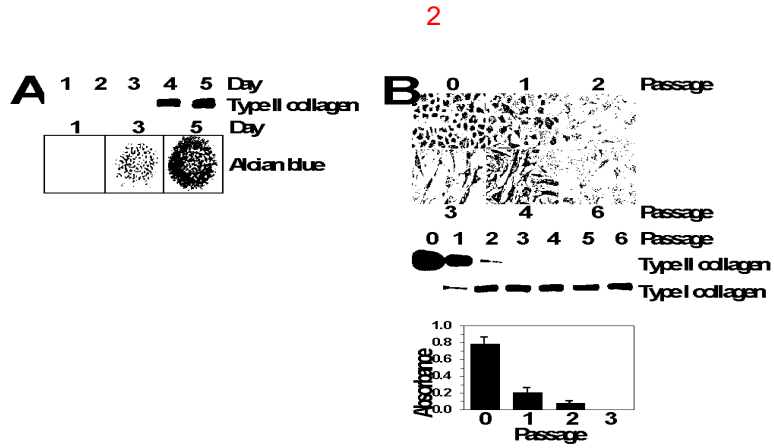
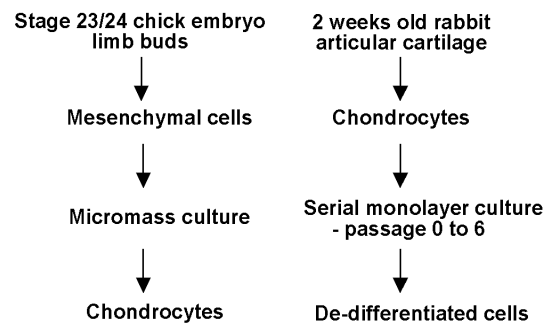
6 , ERK ERK - 1, ERK - 2 95% ERK

8.

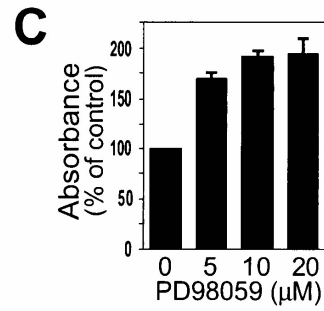
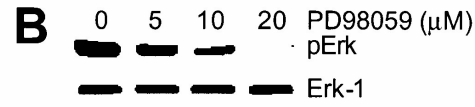
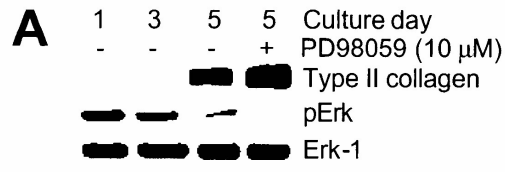
6 , MEK MEK - 1, MEK - 2 95% MEK

1

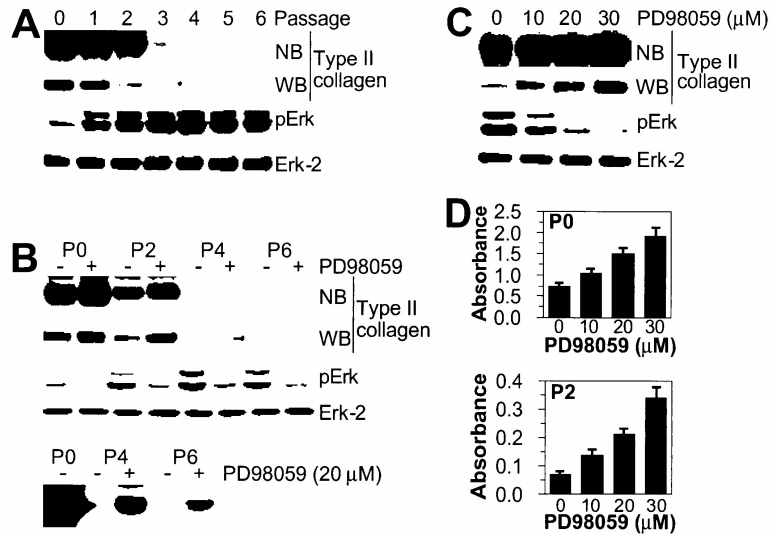
분화 탈분화
Differentiation Dedifferentiation



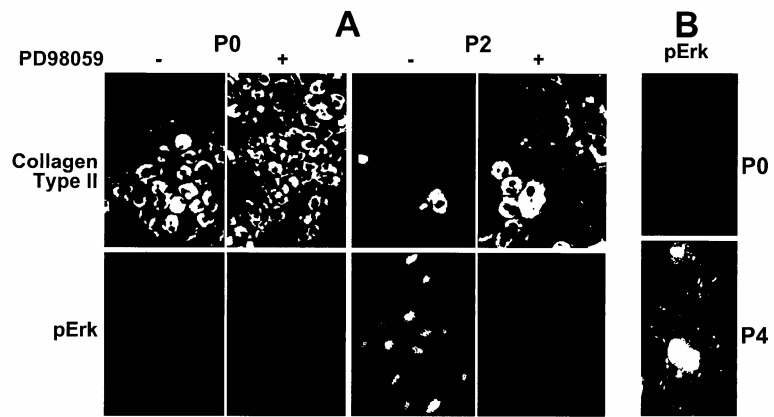
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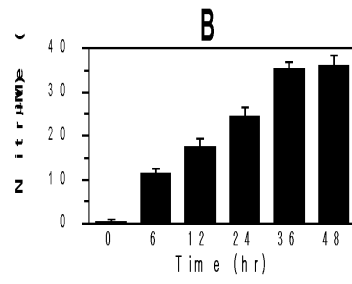
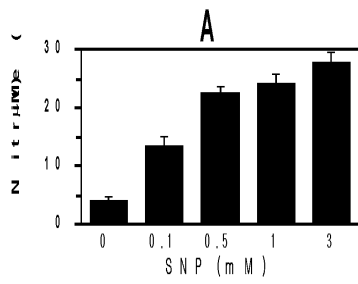
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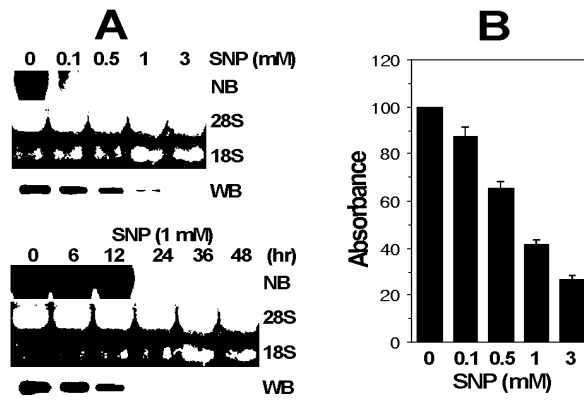
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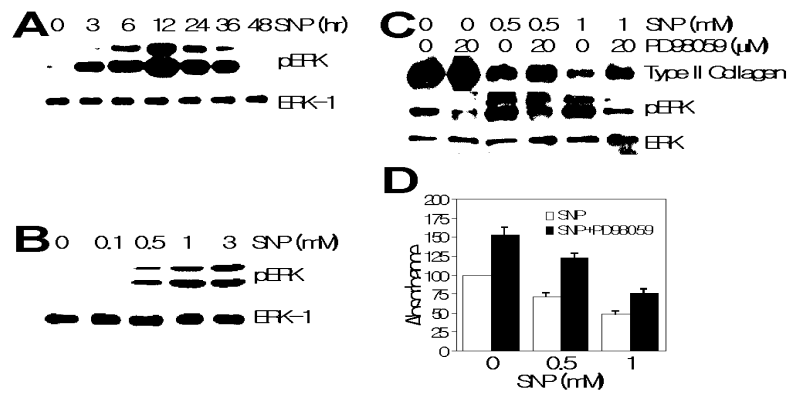
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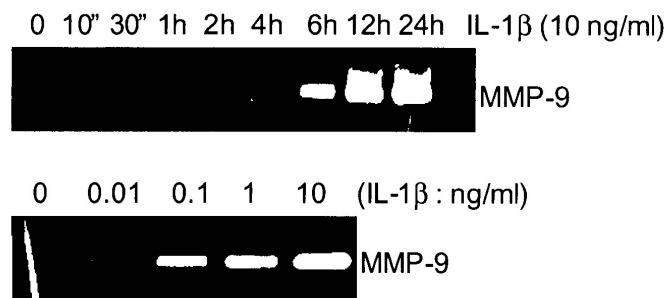
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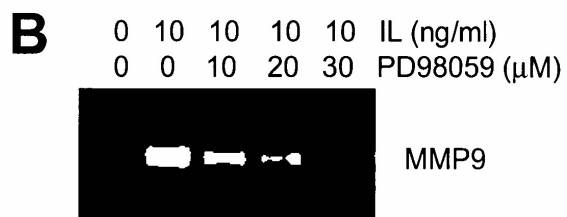
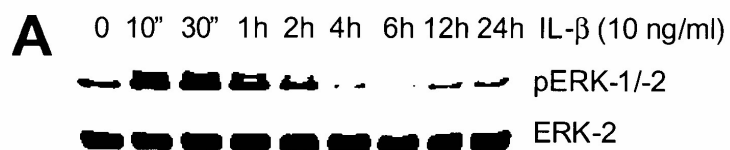
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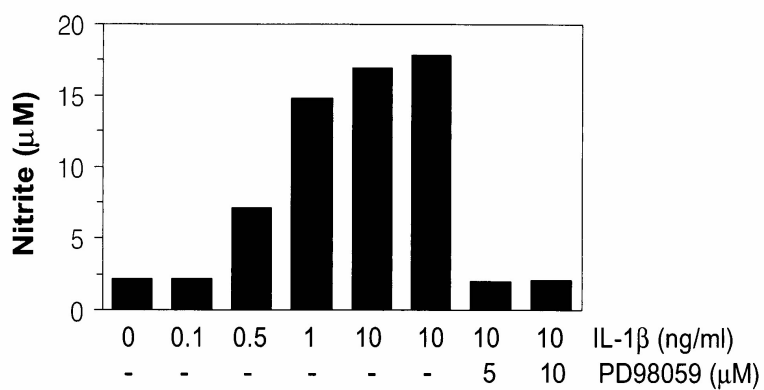
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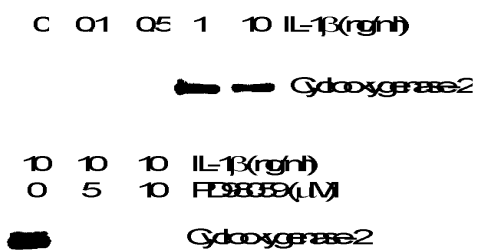
10



11



12



13

