

(19)
(12)

(KR)
(A)

(51) 。 Int. Cl.⁷
C07K 14/00
C07K 14/435
C07K 14/475
C07K 14/52

(11)
(43)

10-2004-0065249
2004 07 21

(21)
(22)
(62)

10-2004-7009015 ()
2004 06 11
10-1996-0703590
: 1996 07 03
2004 06 11

1999 12 28

(86)
(86)

PCT/US1994/014553
1994 12 28

(87)
(87)

WO 1995/18858
1995 07 13

(30)

08/176,553
08/185,607
08/196,689
08/223,263
08/249,376
08/348,657
08/348,658

1994 01 03
1994 01 21
1994 02 15
1994 04 04
1994 05 25
1994 12 02
1994 12 02

(US)
(US)
(US)
(US)
(US)
(US)
(US)

(71)

,
940080-4990

460

(72)

, , .
94901
94404

75
166

(74)

:

(54)

(TPO), TPO
TPO가

DNA, TPO

(TPO),

1 mpl (hML) cDNA (SEQ ID NO:1) (SEQ ID NO:2) 5' 3' (ML) Ser1 N- 3

2 mpl 3 H- 24 5% CO₂ 96 1 uCi 3 H- 24 RPMI 20ul (Star vation). IL-3 , mpl P Ba/F3 , 6 8 96 가 .

3 , DTT APP Ba/F3 mpl APP Affi-gel10(Biorad) . APP PP APP 80 18 4 가 37 100 uM DTT PBS . A

4 (phenyl toyopearl), (blue sepharose) (ultra link)-mpl 4 8 mpl .

5 -mpl SDS-PAGE 2 8 200 ul , 1mM HCl 1 ml -20 가 . 3 , -20 30 ul SDS 가 100 uM DTT 2 -20 90 5 가 . 4-20% SDS-

6 SDS-PAGE mpl . mpl 6 4-20% SDS- 12 1/20 PBS Mr Novex Mark 12 .

7 mpl APP (700 ug mpl-IgG/ml NHS-10 % APP 10% mpl , Pharmacia) 1 ml . mpl APP 1ml mpl 12 .

8 APP 12 . 0, 2 4 mpl-IgG mpl-IgG(0.5 ug) ANP-R-IgG(0.5 ug) 가 10 % AP . 12 2 .

9 mpl DNA 390 bp . ' 3' (SEQ ID NO:3), (SEQ ID NO:4), (SEQ ID NO:5) .

10 mpl (hML)(SEQ ID NO:6) (hEPO)(SEQ ID NO:7) mpl .

N- 2 hML hEPO .

11 mpl hML (SEQ ID NO:6), hML2(SEQ ID NO:8), hML3(SEQ ID NO:9) hML4(SEQ ID NO:10)

12a, 12b, 12c mpl Ba/F3-mpl (A), GPII_b III_a (B) IgG (C)

293 pRK5 pRK5-hML pRK5-ML₁₅₃ CaPO₄ (Gorman, C in DNA Cloning:A New Approach 2:143-190[1995])(pRK5-ML₁₅₃ PCR hML₁₅₃ 15 3 36 1(A) Ba/F3-mpl (A) (B) 125 I IgG (HP1-1D) [Grant et al., Blood 69:1334-1339] GPII_b III_a ML(rML) [T.P. Proc.Soc. Exp. Biol. Med. 144:1006-10012(1973)] (C) rML ML 200 ml PBS 2M PBS NaCl 2 ml Blue-Separeose PBS BSA 가 1 mg/ml 16000 rML 1 2 (t 6 ailed) T - . p

13 Ba/F3 mpl mpl hML, (mock), hML 2, hML3, hML(R153A, R154A) hML₁₅₃ 1

14a, 14b 14c mpl (hML) TPO(hTPO) (SEQ ID NO:1) DNA (SEQ ID NO:11)

15 293-rhML₃₃₂ 293-rhML₁₅₃ SDS-PAGE

16 (ML (SEQ ID NO:13)) (open reading frame) cDNA (SEQ ID NO:12) mpl 331 mML 4 mML2 N-

17 ML (mML) cDNA (SEQ ID NO:14) (SEQ ID NO:15) Ser1 mML mpl 335 가 (splicing)(mML2 mML3) 5' 3' 2 4 7 N-

18 ML hML3 (SEQ ID NO:9) ML mML3 (SEQ ID NO:16) mpl

19 ML(SEQ ID NO:17), -ML(SEQ ID NO:18) -ML(SEQ ID NO:6) N- 가

. 4

(ML2)

20	ML	(pML)	cDNA	(SEQ ID NO:19)	pML	(SEQ ID NO:18)
	mpl		332			mpl
						Ser1
21	ML	(pML2)	cDNA	(SEQ ID NO:20)	pML2	(SEQ ID NO:21)
	4	mpl	328			mpl
		가				
		Ser1				
22	ML	pML3		(SEQ ID NO:18)	ML	pML2
	(SEQ ID NO:21)		pML		pML2	
23	CHO-rhTPO	332	CHO-DP12			pSV15.ID.LL
	.MLORF(	TPO 332)				
24	CHO-rhTPO	153	CHO-DP12			pSV15.ID.LL
	.MLEPO-D(	TPO 153)				
25a, 25b,	25c	E.coli-rhTPO(Met ⁻¹ , 153)		(A),	(B)	
(C)	. 6	C57 B6		2	PBS	0.3
ug E. coli-rhTPO(Met ⁻¹ , 153)(100 ul,		)		. 0 3 7	, 40 ul	
		10 ml			Serrono Baker Hematology Analyzer 9018	
			±			
26a, 26b	26c	E.coli-rhTPO(Met ⁻¹ , 153)		(A),		
(B)	(C)	. 10	C57 B6	2	137 Cs	
	750 cGy	PBS		3.0 ug E. coli-rhTPO(Met ⁻¹ , 153)(100 ul,		
)	. 0	, 40 ul				
10 ml		Serrono Baker Hematology Analyzer 9018				
	±					
27a, 27b	27c	CHO-rhTPO	332	(A),	(B)	(C)
	. 6	C57 B6		2	PBS	0.3 ug CHO-
rhTPO 332 (100 ul,		)		. 0 3 7	, 40 ul	
	10 ml				Serrono Baker Hematology Analyzer 9018	
		±				
28	rhTPO	rhTPO	: CHO	hTPO 332 (		
); hTPO Met ⁻¹ 153 (N-	가	E.coli		); hTPO 332 (	293	
TPO); Met 155 E Coli(		E.coli		[rhTPO 155]). 6		C57B6
7	rhTPO		40 ul			(met 153 E.Coli)
					5	
	7		'met 153 E.Coli'			
	±					
29	CHO	rhTPO		E. coli		
	. 6	C57B6			rhTPO	0.3 ug
. 2	7	40 ul				E.coli
TPO	TPO 153 ;	80-90%		10-20%	TPO	TPO 3
(Mix	); TPO332(30K	)=	'Mix'		; TPO332(70K	)=
32	TPO	TPO		±		'Mix

30	TPO		KIRA ELISA			(	)
	MPL/Rse.gD					(	)
31			KIRA ELISA				
32a	32I	17	Rse.gD		pSVI17.ID.LL		(SEQ ID N
O:22)							
33			pMP1				
34			pMP21				
35			pMP151				
36			pMP202				
37			pMP172				
38			pMP210				
39	pMP210			가	5	TPO	
40			pMP41				
41			pMP57				
42			pMP251				

< >

, , , , , mpl ,

< >

1.

T- B- 가

가

()

[(Dexter et al., Ann. Rev. Cell Biol.,3:423-441 [1987])].

(Cronkite et al., Blood Cells, 2:263-284 [1976]).

, 가 가 .
가 , 가
CFC-Mix (가)
(T- B-
, CFC-Mix
(GM-CFC), (CFU-E), /
(Meg-CFC),
(Bas-CFC) 가
가 가
가 가 가
가 가 가
-3(IL-3) /
(GM-CSF) GM-CFC
(interalia) 가
, IL-3 GM-CSF
-6(IL-6) -11(IL-11)
, IL-3 (Yonemura et al., Exp. Hemato
I., 20: 1011-1016 [1992]).

,
,
,
(epo)
(SCF) IL-3 가
(BFU-MK), (CFU-MK) 3 (LD-CFU-
MK)가
MK. meg) 가
가 , 20

II. -

[: Exp. Hematol., 15:248 [1987]] [: Blood, 74:11
96-1212 [1989]]
(BFU-MK), (CFU-MK) 3 (LD-CFU-
MK)가
MK. meg) 가
가 , 20

30 um . , 32 () , 가 , 1
 0% 가 50% . (,)
 가 .(Williams et al., Hematology, 1972).

가 (Williams et al., Br. J. Hematol., 52: 173 [1982])
 82] Williams et al., J. Cell Physiol., 110:101[1982]). CFU-MK
 (Burststein et al., J. Cell Physiol., 109:333[1981] Kimura et al., Exp. Hematol., 13:1048[1985]).
 (Odell et al., Blood, 48:765[1976] Ebbe et al. Blood, 32:787 [1968]).

(MK-CSF) (Mazur, Exp. Hematol., 15:340-350 [1987]).
 30 / 가
 30 MK-CSF(TPO) .
 (Hill et al., Exp. Hematol., 14 : 752[1986]) [CM]
 (McDonald et al., J. Lab. Clin. Med. 85:59[1975]), (Kawakita et al., Blood, 6:556[1983]) (Hoffman et al., J. Clin. Invest., 75:1174[1985])
 purpura) MK-CSF가
 (poke weed) (PWM-SpCM) (murine) WEHI-3(W
 EHI-3CM) (potentiators) PWM-SpCM CFU-MK
 (Metcalf et al., Pro. Natl. Acad. Sci., USA, 72:1744-1748[1975]; Quesenberry et al., Blood, 65:214[1985]; Iscove, N. N., in Hematopoietic Cell Differentiation, ICN-UCLA Symposia on Molecular and Cellular Biology, Vol. 10, Golde et al., eds. [New York, Academy Press] pp 37-52[1978]),
 (multi-CSF)[Burstien, Blood Cells, 11:469[1989]) -3(IL-3)
 WEHI-3 IL-3 GM-CSF
 IL-3 (Ihle et al., J. Immunol., 13:282[1983]). IL-3
 (EPO) -1(IL-1)
 (Bartelmez et al., Cell Physiol., 122:362-369 [1985] Warren et al., J. Cell, 46:667-674[1988]).

(Mazur, Exp. Hematol., 15:340-350[1987])
 T- 가 (Geissler et al., Br. J. Hematol. 15:340-350 [1987])가 T- MK
 (Geissler et al., Exp. Hematol. 15:845-853 [1987]). (EPO)
 (Vainchenker et al., Blood, 54:940 [1979]); McLeod et al., Nature, 261:492-4 [1976] Williams et al., Exp. Hematol. 12:734 [1984])가 MK 가
 et al., Exp. Hematol. 12:734 [1984]). EPO 4 PWM-SpCM
 2 가
 MK 가 가 GM-CSF IL-3
 , B- IL-6 (Ikebuchi et al., Proc. Natl. Acae. Sci. USA, 84:9035 [1987]). IL-11 (LIF)가 IL-3
 가 (Yonemura et al., British Journal of Hematology, 84:16-23 [1993]; Burststein et al., J. Cell Physiol., 153:305-312 [1992]; Metcalf et al., Blood, 76:50-56 [1990]; Metcalf et al., Blood, 77:2150-2153 [1991]; Bruno et al., Exp. Hematol., 19:378-381 [1991] Yonemura et al., Exp. Hematol., 20:1011-1016 [1992]).

(Eppstein et al., 4.962,091; Chong et al., 4.879,111; Fernardes et al., 4.604,377; Wissler et al., 4.512,971; Gottlieb et al., 4.468,379; Bennet et al., 5.215,895; Kogan et al., 5.250,732; Kimura et al., Eur. J. Immunol., 20(9): 1927-1931[1990]; Secor et al., J of immunol., 144(4):1484-1489 [1990]; Warren et al., J of Immunol., 140(1):94-99 [1988]; Warren et al., Exp. Hematol., 17(11):1095-1099 [1989]; Bruno et al., Exp. Hematol., 17(10):1038-1043 [1989]; Tanikawa et al., Exp. Hematol., 17(8):883-888 [1989]; Koike et al., Blood, 75(2):2286-2291[1990]; Lotem et al., Blood, 75(5):1545-1551 [1989]; Rennick et al., Blood, 73(7):1828-1835 [1989]; Clutterbuck et al., Blood, 73(6):1504-1512 [1989]).

III

가 150×10^9 (1) ; (2) () (3) 가(: 가) . , (severity), , 가 20×10^9 100×10^9 , 가 20×10^9 . , 가가 , 가 [Schafner, A.I. 'Thrombocytopenia and Disorders of Platelet Function', Internal Medicine, 3rd Ed., John J. Hutton et al., Eds., Little Brown and Co., Boston/Toronto/London[1990]

(a) _____

() () , , , , ; 가 , (B_{12}) , 가 (DIC) , 가

(b) _____

가 , 50×10^9 ,

(c) _____

가 , , 가

(DIC)가
[Braunwald et al., (eds), Harrison's Principles of Internal Medicine, 11th Ed.,
p.1478, McGraw Hill[1987]
(mild) (moderate)

(d) _____

100

(e) (가) (ITP)

가 ITP 가 가 가 GPII_b III_a
IgG ITP 가 가
ITP ITP 가 (:
) (:)

(f) HIV- ITP

ITP HIV [Morris et al., Ann. Intern. Med., 96:714-717[1982],
, AIDS AIDS HIV
HIV
CD₄ T [Lane
et al., Ann. Rev. Immunol., 3:477[1985]]. CD₄ / T
AIDS (H. Lane supra).

HIV ITP , HIV ITP [Walsh
et al., N. Eng. J. Med., 311:635-639[1984]; Ratner Am. J. Med., 86:194-198[1989].

IV. _____

-HIV , 가 HIV
(:) 가
가 가 HIV ITP , 가 20×10^9
AIDS
-1-]6H- [3,2,f][1,2,4] [4,3,a][1,4] (WEB 2086) HIV- ITP
가 37000-58000/uI WEB 2086 1
2 가 140000 190000/uI 가 .(361.077 Lohman et al., Lancet, 1147
[1988]).

(AATP) ([Trimble et al., Am. J. Hem
ATG)(atol., 37:126-127[1991]). , ATG 가 ,
(ATG) (Panella et al., Cancer Research, 50:4429-4435[1990]).

가 가 가

ITP), 2 3 , (: HIV - AIDS
 HIV ITP , (: (AZT,))
 가 '(TPO)
 TPO
 (TSF), (MK-CSF), 가 TPO
 1959 (Rak et al., Med. Exp., 1:125) 가
 TPO 가 (, Tayrien et al., J. Biol. Chem.,
 262:3262[1987] Hoffman et al., J. Clin. Invest. 75:1174[1985]), TPO 가
 가 (IL-3) 가 [Sparrow et al., Prog. Clin. Biol. Res., 21
 5:123[1985]]. 가
 TPO , mpl()

V. mpl

가
 IL-2(β y)(Hatakeyama et al., Science, 244:551-556[1989]; Tak
 eshita et al., Science, 257:379-382[1991]), IL-3(Itoh et al., Science, 247:324-328[1990]; Gorman et al., Pr
 oc. Natl. Acad. Sci. USA, 87:5459-5463[1990]; Kimura et al., Cell, 66:1165-1174[1991a]; Kitamura et al., P
 roc. Natl. Acad. Sci. USA, 88:5082-5086[1991b]), IL-4(Mosely et al., Cell, 59:335-348[1989]), IL-5(Taka
 ki et al., EMBO J., 9:4367-4374[1990]; Tavernier et al., Cell, 66:1175-1184[1991]), IL-6(Yamasaki et al.,
 Science, 241:825-828[1988]; Hibi et al., Cell, 63:1149-1157[1990]), IL-7, (Goodwin et al., Cell, 60:941-95
 1[1990]), IL-9(Renault et al., Proc. Natl. Acad. Sci. USA, 89:5690-5694[1992]),
 (GM-CSF)(Gearing et al., EMBO J., 8:3667-3676[1991]; Hayashida et al., Proc. Natl. Acad. Sci. USA, 2
 44:9655-9659[1990]), (G-CSF)(Fukunaga et al., Cell, 61:341-350[1990a]; Fukunag
 a et al., Proc. Natl. Acad. Sci. USA, 87:8702-8706[1990b]; Larsen et al., J. Exp. Med., 172:1559-1570[1990
]), EPO(D'Andrea et al., Cell, 57:277-285[1989]; Jones et al., Blood, 76:31-35 [1990]), (LI
 F)(Gearing et al., EBMOL.10:2839-2849[1991]); M(OSM)(Rose et al., Proc. Natl. Acad. Sci. USA,
 88:8641-8645[1991] (Boutin et al., Proc. Natl. Acad. Sci. USA, 88:7744-774
 8[1988]; Edery et al., Proc. Natl. Acad. Sci. USA, 86:2112-2116[1989], (GH)(Leung et al., Natur
 e, 330:537-543[1987] (CNTF)(Davis et al., Science, 253:59-63[1991])가

([Nicola et al., Cell, 67:1-
 4[1991]]). (EPO-R) (G-CSF-R)
 (domain)
 . α - -6 (IL6-R)
 , - (GM-CSF-R), -3 (IL3-R α)
 . α -
 가 α - β - β c)
 (: IL3-R α GM-CSF-R 3 α - β - β c)

mpl (Gearing, EMBO J., 8:3667-3676[1988]; Bazan,
 Proc. Natl. Acad. Sci. USA, 87:6834-6938[1990]; Davis et al., Science, 253:59-63[1991] Vigon et al., Pr
 oc. Natl. Acad. Sci. USA, 89:5640-5644[1992]

c-mpl

465

1

가

2

N-

C-

4

LIF β - (Barrel fold) 가 2
IL-3, IL-5 GM-CSF
(Vigon et al., Oncogene, 8:2607-2615[1993]). , mpl

mpl , N- C- mpl P , 81%가
91% 75% 80%가 . 가 mpl
, mpl 가 (Vigon supra).

mpl 가
mpl , IL-4R G-CSFR 1
가 . Vigon G-CSFR c-mpl
(chimera)
G-CSFR IL-3 G-CSFR
IL-3 G-CSF
[: EMBO J., 12(7):2645-2653[1993],
Skoda mpl IL-4 IL-3
3 Ba/F3 (hIL-4-R) hIL-4 R Ba/F3 hIL-4(IL-3
Ba/F3 hIL-4R/mpl Ba/F3 mpl)

mpl 가 , mpl
3 (1) , IL-3 α - 2가 가 , mpl EPO-R G-CSFR
(3) (Skoda et al. supra). 가 β - (

VI. Mpl (TPO)

(TPO) , . mpl
 , mpl 가
(Methia et al., Blood, 82(5):
1395-1401[1993]).

IL-1 α , IL-3, IL-4, IL-6, IL-11, SCF, EPO, G-CSF GM-CSF 가 mp
I c-mpl
mpl
(RT)-PCR , Methia mpl mRNA CD34 BM
(BM) CD34 +
+ , 1% (: ,)
가 .

mpl ([MK-CSF]) 가
CD34 + .

mpl 가 mpl
 , mpl , mpl
(Vigon at al, supra[1993]).

VII.

가 mpl () 가

가 ()

mpl

가

mpl

mpl EPO 가 가

mpl (immunogen), mpl

가

ML) ' (TPO), 'mpl '(

(1) mpl 가 (source),

mpl, mpl, (2) mpl 가

, (3)

mpl

mpl-IgG

mpl

'mpl 70% 가

mpl (hML) 가

'EPO- ML 가

'TPO' mpl 1(SEQ ID NO:1)

(porcine) mpl 80% 가

'EPO- mpl (hML) 80%

가

X-hML(7-151)-Y

hML(7-151) Cys⁷ Cys¹⁵¹ (Cys¹⁵¹) TPO(hML) ; X Cy
 s⁷ (: Xa hML) ,
 s¹⁵¹ hML ; Y Cy
 .

mpl ().
 1, EPO, GM-CSF, LIF , (KL), IL-1, IL-3, IL-6, IL-1
 , IgG
 , IgG1, IgG2, IgG3, IgG4, IgA, IgE, IgD, IgM .

IL-3 Ba/F3 DNA (: ³H-) mpl
 . mpl
³⁵S . mpl
 R154A), hML2, hML3, hML4, mML, mML2, mML3, pML pML2 hML₁₅₃, hML(R153A,
 .

mpl . mpl
 mpl
 mpl
 mpl
 mpl

가 , mpl
 , mpl
 가 (stringent)
 mpl
 mpl RNA DNA, cDNA
 DNA , 가 DNA가
 가 3'-5' DNA 가 cDNA
 CHO mpl DNA , mpl
 A mpl
 .

가 mpl
 . mpl
 ,
 (KL), LIF, G-CSF, GM
 -CSF, M-CSF, EPO, IL-1, IL-3, IL-6 IL-11 .

(1) TPO ,

(2) 가 TPO ,

(3) 가 TPO

(4) TPO 가 ,

(5) TPO ,

(6) TPO TPO , TPO TPO

가 , 가 TPO가 TPO ,

'mpl ' 'TPO ' 가
 mpl () N- C- . mpl
 mpl EPO 10, 15, 20, 25, 30, 40
 가 N- hML₁₅₃ TPO(Met⁻¹ 1-153) .
 1) 'mpl ' 'mpl 1(SEQ ID NO:
 가 가 mpl
 100% 가 mpl
 mpl (1(SEQ ID NO:1)) 70% 가
 가 . 75% , 80% , 85
 % , 90% 가 95% .
 ' mpl ' 2 m
 pl 2 , , mpl
 ' mpl ' , ' mpl ' , m
 pl (1) (spinning Cup sequenator) 가 ,
 15 , 20 N- (2)
 mpl SDS-PAGE 가 5% .
 'mpl ' ' mpl ' 가
 mpl (가) 가
 , mpl , DNA , () ,
 ' mpl
 . mpl mpl 10⁻⁶ I/
 가 mpl . 가 mpl 10⁻⁷ I/
 mpl 가
 'mpl ' ' mpl ' 가
 pl mpl (³H-) mpl P IL-3
 Ba/F3 DNA 35 S
 ((GPII_b III_a) . mpl
 mpl ' ,
 1 (SEQ ID NO:1) 가 mpl ,
 C- mpl , N- ,
 가 mpl

-mpl , -mpl mpl 가 .

'mpl (microsequencing)' .

, SDS (PTH) 가 HPLC 120A .

() (:CNBr, , 2- -5- (Clostripain), (staphylococcal) . PTH

(:HPLC) mpl .

(chromperfect) (Justice Innovationa, Palo Alto, CA) .

VAX 11/785 Digital Equipment Co. (Henzel et al., Chromatography, 40 4:41-52[1978]). , HPLC 5 20% SDS-PAGE , PVDF (Matsurdi ara, J.Biol. Chem., 262:10035-10038[1987]). (blot)

N- . H

PLC (SpeedVac), , Lys- Lys-C(Wako Chemicals, Richmond, VA) Asp-N(Boeringer Mannheim, Indianapolis, IN) 0.1% TFA

C4 HPLC .

가 150×10^{-9} .

가 , ()

(CMK) (anti-GPII_b III_a) (DAMI) .

(TPO)' 가 가 가 10% , 가 50 % 가 가 150×10^{-9} .

mpl ' mpl 16 , 20 RNA DNA RNA DNA RNA DNA , DNA , RNA DNA , 90% , 80% , 95% , 85% , 75% , mpl , 가 (promoter), DNA (operator) , 가 (enhancer) . , 가 DNA가 , 가 가 DNA (linking) , (ligation) 가 ,

가 .

DNA
 가
 가
 'p' ()
 가
 DNA
 DNA
 DNA
 DNA
 DNA
 20 ul 1 2 (unit) 1 37 1 ug DNA
 5' 5' DNA가
 [Sambrook et al., Molecular Cloning: A Laboratory Manual[
 New York: Cold Spring Harbor Laboratory Press, 1989] 1.56-1.61
 DNA 가
 가 DNA
 DNA
 [Lawn et al., Nucleic Acids Res., 9:6103-6114[1981] Goe
 ddel et al., Nucleic Acids Res., 8:4057[1980]
 (southern analysis)' (southern blotting)' DNA DNA-
 DNA 가 DNA , DNA
 DNA [Sambrook et al., supra 9.37-9.52
].
 (northern) , DNA , cDNA RNA
 RNA ³²P RNA Sambrook et al., supra 7.39-7.52
 가
 (ligation)'
 (staggered) (blunt)
 가 , DNA 4 (klebnow) 10 15 15 D
 NA I T4 DNA , DNA
 DNA 가 DNA 0.5 ug ATP, 가 (ligase)
 , T4 DNA 가 10 DNA가
 가

DNA ' , ' DNA DNA . DNA
 Sambrook et al., supra 1.25-1.33
 . DNA가 , Sambrook et al., supra 1.40
 .
 ' (: 1988 5 4 266,032 (solid pha
 se) , [Froehler et al., Nucl. Acids Res., 14:5399-5407[1986]
 H- ,)
 , 가
 [Engels et al., Agnew. Chem. Int. Ed. Engls. 28:716-734[1989]]
 .
 , 가
 .
 ' 'PCR' 1987 7 28 4,683,195
 , RNA () DNA ,
 , 가
 5'
 . PCR DNA, RNA
 cDNA, RNA DNA RNA
 [Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263[1987]; Erlich, ed., PCR
 Technology, (Stockton Press, NY, 1989) . PCR
 , 가
 .
 ' (stringent) ' (1) , 0.015 M NaCl/0.0015 M
 /0.1 % NaDodSO₄ (SDS) 50 (2)
 , 750 mM NaCl, 75 mM 0.1%
 /50 mM (pH 6.5) 50% /0.1% Ficoll/0.1%
 Cl, 0.075 M), 50 mM (pH 6.8), 0.1% , 5× , 5×SSC(0.75 M Na
 's solution), DNA(50 ug/ml). 0.1% SDS, 10% , 42
 42 0.2×SSC 0.1% SDS .
 ' (moderately) 가 ' Sambrook et al., supra 가
 (: , %SDS) 가
 20% , 5×SSC(150 mM NaCl, 15 mM), 50 mM 가
 , 10% DNA(20 ug/ml) (pH 7.6), 5×
 1×SSC 37-50 , 가 37
 ,
 ' (Abs)' ' (Igs)' 가 가
 ,
 .
 ' 150,000 2 (L)(light)
 2 (H)(heavy) 1
 , 가 가 가 (variable
) (V_H) (constant) 가 가
 (V_L) ; 가
 , 가
 가 (Clothia et al., J. Mol. Bio
 l., 186:651-663[1985]; Novontny and Habor, Proc. Natl. Acad. Sci. USA, 82:4592-4596[1985]).
 '가 ' 가
 가 가 , 가 가
 . 가 (complimentar

ity determining region)(CDR) 가 (hypervariable) 3 가 .
 가 (FR) .
 4 FR β - , CDR FR
 β - 3 CDR CDR (Kabat
 et al., Sequences of Proteins of Immunological Interest, National Institute of Health, Bethesda, MD[1987]).

가 'Fab' 2 , 2
 가 'Fc' .
 가 F(ab')₂ .
 'Fv'
 V_H - V_L 가 3 CDRs , 6 CDR
 Fv) 가 (3 CDR 가 .
 Fab (CH1) . Fab'
 CH1 Fab 가 가
 Fab'-SH 가 Fab'
 F(ab')₂ 가 Fab'
 () ' ' , (λ)

IgA, IgD, IgE, IgG IgM , () 가 5
 : IgG-1, IgG-2, IgG-3 IgG-4; IgA-1 IgA-2). (

가 (:Fab, F(ab')₂ Fv) .

() () , ()
 가 가 , (:Fab, F(ab')₂ Fv) .
 256:495(1975)] DNA [4.816.567 Cabilly et al]] [Nature

() , ()
 가 () , 가
 [4.816.567 Cabilly et al; Morrison et al., Proc.Natl. Acad. Sci. USA 81:685
 1-6855[1984]].

(:) ' '
 (:Fv, Fab, Fab', F(ab')₂) . , ,
 (CDR) 가 , ,
 () CDR Fv

CDR
가 ,
CDR 가 ,
FR (Fc), [John
et al., Naure 321:522-525[1986]; Reoghman et al., Nature, 332:323-329[1988] Presta, Curr. Op. Struct.
Biol. 2:593-596[1992]]

II

IL-3 Ba/F3 DNA ³H- mpl 가 , mpl P
(TPO) 가 mpl ()
()
가 mpl () mp
I () mpl hML ¹⁵³ hTPO ¹⁵³ hML
, hML ²⁴⁵ hTPO ²⁴⁵ hML hML, hML ³³² hTPO ³³² 1 hML
(SEQ ID NO:1) 가 'EPO- hML
(R153A, R154A)

hML2, hML3, hML4, mML, mML2, mML3, pML pML2
mpl

D NO:12 amp; 13] mpl (1:[SEQ ID NO:1]), mpl (16:[SEQ I
mpl (19:[SEQ ID NO:18])
% , 70% , 75% , 80% , 85
% , 90% , 가 , 95% , 가
mpl ()

mpl 가 :

- (1): PBS, 0.1% SDS PBS SDS 4M MgCl₂ PBS
60000-70000 Mr ;
- (2): ;
- (3): pH(2.5), 0.1% SDS 2M ;
- (4): , ;
- (5): 25000-35000 Mr SDS-PAGE 1
8000-22000 60000 Mr ;
- (6): SDS-PAGE 28000 31000 Mr (doublet)
;
- (7): 18000-22000, 28000 31000 SPAPPACDPRLLNKLLRDDHVLH
GR(SEQ ID NO:29) ;
- (8):

CM ,

MONO-Q,

MONO-S,

- ,

WGA - ,

Con A - ,

650 m (toyopearl),

650 m ,

650 m ,

.

mpl 1(SEQ ID NO:1) 가 cDNA

.

mpl -mpl , -mpl

, mpl , mpl

.

mpl 가 . mpl 70% ,

75% ,

95%

mpl

80% ,

85 ,

90%

, 가

mpl

).

N-
hML EPO
hML

hML (

hML

153

'EPO-

가

(: , , , Gly, Pro)

hML C-

ML₃₃₂ (R153A, R154A)

PPQ)가

Arg

153

154가 Ala

hML

111

114(QLPP

h

(AGAG)

hML₃₃₂

hML₁₅₃

4hML₃₃₂

4hML₁₅₃

.

mpl

()

, hML₁₅₃ IgG

IL-3, G-CSF

EPO

가 가 .

mpl

10(SEQ ID NO:7)

EPO hML

N-

153

157 hML

'ML-EPO

, hML

EPO

Q ID NO:6)

hML

가

, 가

153

166

. hML N-

(EPO) 24-27, 38-40

83-85

N-

; (EPO) 9-22, 59-76, 90-107

132-152

4

α-

N-

C-

(epo) 44-52

[Wen wt al., blood, 82:1507-1516[1993]

Biossel et al., J. Biol. Chem., 268(21):15983

-15993[1993]

] 'ML-EPO

'가

-

(TEPO)

가

mpl

mpl

(14,

24)

mpl

10, 15, 20, 25, 30

40

가

17, 229

245(1-X

mpl

1(SEQ ID NO:1)

mpl

ML[1-X]

X가 153, 191, 205, 2

가

mpl

mpl

mpl

mpl

mpl

mpl

가

Blood. Cells 15:123-133[1989]; Gordon et al., Blood, 80:302-307[0992]). 가 , meg-CSF

. 1960

meg-CSF

가 [Odell et al., Proc. Soc. Exp. Biol. Med., 108:428-431[1961]; [Nakeff et al., Acta Haematol. 54:340-344[1975]; [Specter, Proc. Soc. Exp. Biol. 108:146-149[1961]; [Schreiner et al., J. Clin. Invest. 49:1709-1713[1970]; Ebbe, Blood, 44:605-608[1974]; Hoffman et al., N. Engl. H. Med., 305:553[1981]; Straneva et al., Exp. Hematol. 17:1122-1127[1988]; Mazur et al., Exp. Hematol. 13:1164[1974]; Mazur et al., J.Clin,Invest. 68:733-741[1981]; Sceiner et al., Blood, 56:183-188[1980]; Hill et al., Exp. Hematol., 20:354-360 [1992]; Heygi et al., Int. J. Cell Cloning, 8:236-244[1990].

[Hill R.J. et al., Blood 80:346(1992); Ericks on-Miller C.L.et al., Brit, J, Heamatol., 84:197-203(1993); Straneva J.E. et al., Exp. Hematol. 20:4750(1992): Tsukada J. et al., Blood 81:866-867[1993]). , meg-CSF

APP) 가 APP mpl (ML) APP c-mpl (ML cDNA) 가 meg-CSF

1. mpl

가 , (APP) 2 . A . APP가 mpl P(Ba/F3-mpl) Ba/F3 3 H- Ba/F3 (: mpl P APP가) . APP 가 mpl-IgG APP Ba/F3 . APP , DTT APP pH(2 pH 2.5) . 가 mpl-IgG APP . APP 1 2 , mpl (HIC), 4 mpl 1 . mpl- (F6) 9.8 x 10⁶ /mg (specific act 83 x 10⁶ - 가 (250 gms 3 µg) 4 x 10⁶ (0.8 /mg 3.3 x 10⁶ /mg) mpl 3x10⁶ units/mg .

[1]

	(ml)	mg/ml	/ml		/mg	%	
APP	5000	50	40	200,000	0.8	-	1
	4700	0.8	40	200,000	50	94	62
-	640	0.93	400	256,000	430	128	538
mpl(µl)	12	5x10 ⁻⁴	1666	20,000	3,300,000	10	4,100,000

. mpl 5 7 SDS-
. 1 Ba/F3-mpl 50%
SDS-PAGE(4 20%, Novex) mpl
(5). 가 66000, 55000, 30000, 2800
0 18000-22000 Mr . Ba/F3-mpl
가 , 2
, 가 Mr 28000 32000
가 18000-22000 (6). 가
Mr 30000, 28000 18000-22000 . (: 30, 28 18-22 kDa
) , 3 3 PVDF
2 .

[2]

30 kDa 1 5 10 15 20 25 (S)PAPPA(C)DPRLLNKLLRDD(H/S)VLH(G)RL	(SEQ ID NO:30)
28 kDa 1 5 10 15 20 25 (S)PAPPAXDPRLLNKLLRDD(H)VL(H)GR	(SEQ ID NO:31)
18-22 kDa 1 5 10 XPAPPAXDPRLX(N)(K)	(SEQ ID NO:32)

18-22 kDa , 30 kDa, 28 kDa
가 SDS-PAGE 4-20% (28000-32000) () mpl
가 17000 30000 Mr
mpl RNA CD 34 + 가
(Methia et al., supra). mpl 가
APP mpl APP
APP 4
(PSC) mpl-IgG APP
GPII b III a 125 I- -II b III a (7). 7
, 10% APP 3 , mpl 가 APP Ba/F3-mpl
가 , 가 mpl-IgG 10% APP 0, 2 4 가
APP (8). mpl

2. mpl

30 kDa, 28 kDa 18-22 kDa , 2

DNA PCR PCR 가 69 bp DNA

pGEMT PCR (PRLNKLRL[SEQ ID NO:33])

5 (28 30 kDa 9-17

). PCR DNA pR45

45 가 : PCR

5'GCC-GTG-AAG-GAC-GTG-GTC-GTC-ACG-AAG-CAG-TTT-ATT-TAG-GAG-TCG-3'

(SEQ ID NO:34)

6 가 λ gem12 DNA

45 390 bp EcoRI-XbaI pBluescript SK-DNA가 D

NA mpl 9(SEQ ID NO:3 amp; 4)

DNA (' 3')

3' (6) 3' 5' cDNA

2 PCR 140 bp . 12% PCR PCR

DNA cDNA , 293 cDNA

DR2 cDNA (7×10⁶) 가

45-mer PCR 1.8 kb 가

7 mpl (hML)

1(SEQ ID NO:1 amp; 2)

3, mpl (hML)

mpl (hML) cDNA (1[SEQ ID NO:2]) 1774 (A)

215 5' 498 3'

(216-218) 가 1059 220 353

N- (von Heijne et al., Eur. J. Biochem., 133:17-21[1983]) 21 22

가 332 가 mpl

332 38 kDa . 6 N- 332

4 가

mpl (Genbank) mpl

153 가 23% (10:[SEQ ID NO:6 amp; 7]).

, hML (hEPO) 50% . hEPO hML

4 . 4 3 () hML

(Wang F.F.et al., Endocrinology 116:2286-2292[1983]). 가 , hML

hML N- hML

hEPO 가 , hML mRNA AAUAAA , 3'

mRNA (Shawet et al., Cell, 46:659-667[1986]). AUUUA 가 1.8 kb hML RNA 가 (Jacobs et al., Nature, 313:804-809[1985] Bondurant et al., Molec. Cell. Biol., 6:2731-2733[1986]).

hML C- . N- 6 , hML 60000 Mr C- hML 가 (Tak euchi et al., J. Biol. Chem., 265:12127-12130[1990]; Narhi et al., J. Biol. Chem., 266:23022-23026[1991] Spivak et al., Blood, 7:90-99[1989]). hML C- 2 [153-154 245-246 Arg-Arg] A PP 154 ML 30, 28 18-22 kDa , Arg 153 -Arg ML

4. mpl

mpl PCR , hML 10 , hML2, hML3 hML4 11 RNA RT-PCR . hML 3 가 4 (SEQ ID NO:6, 8, 9 amp; 10). hML3 700 116 139 cDNA 가 265 hML4 hML3 61 8 hML 12 () 116 bp (hML2 , hML4) (619) 12 bp () , hML Arg 153 -Arg 154 2 hML(R153A, R154A) , Arg 153 -Arg 154 hML 'EPO 10 PCR 'EPO , hML 153 Arg153 PCR

5. (293) mpl (rhML)

cDNA가 mpl , pRK5-hML 153 293 Ba/F3 293 3 H- pRK 293 mpl-IgG 가 (cDNA가 가 ML(hML) . 'EPO- mpl , hML, rhML 153 293 hML(12a) c-mpl , ML C-

6. mpl

rhML hML 가 rhML 153 가 (12B). , IL-3 , IL-11, IL-6, IL-1, , G-CSF, IL-9, LIF, (KL), M-CSF, OSM GM-CSF ML 가 , (ML)

(McDonald, Proc. Soc. Exp. Biol. Med., 14:1006-1001[1973] MecDonald et al., Scand. J. haematol., 16 326-334[1976]).

가 . 가

(McDonald, et al., J. Lab. Clin. Med., 77:134-143[1971]). rML

35 S . rML 64000 32000 rhML .
가 가 ,
가 20% 가 (p=0.0005 0.0001) 35 S 가 40% 가
(12c). IL-6 (ML
) . rML 16000 가 .

293 hML Ba/F3-mpl (13)
. hML2 hML3 가 , hML(R153A, R154A)
hML hML 153 Arg 153 -Arg 154

7. mpl

(Williams et al., J. Cell Physiol., 110:101-104[1982] Williams et al., Blood Cells, 15:123-133[1989]).

ML , 가 . ML
. , APP
mpl-IgG (7 8). , c-mpl
(Methia et al., EMBO, 12:2645-2653[1993]) c-mpl
(Skoda et., EMBO, 12:2645-2653[1993] Vigon et al., Oncogene, 8:2607-2615
[1993]) ML c-mpl (Methi
a et al., Blood, 82:1395-1401[1993]) ML
ML 가 ML 가 .

8. mpl (TPO)

TPO DNA pR45 가 λ -Gem12 mpl
cDNA 3' 가 가
. 35 kb 2 TPO 2
(BamH1 EcoRI) (14a, 14b 14c).
7 kb DNA 6 /
(Shapiro, M. B. et al., Nucl. Acids Res. 15:7155[1987]). 1
2 5' 4
26 3 50
3' 6
4 6 5' . hML-2(hTPO-2)
DNA TPO
(FISH) 3q27-28 .

9. 293 TPO

293 ML TPO 19
cDNA pRK5-hmpl 1 PCR . PCR , TPO
pRK5tkneo(Clal Xbal pRK5tkneo.ORF(pRK5)
) .

EPO , PCR p
 RK5-tkneoEPO-D .

CaPO₄ 가 . ML₁₅₃ ML₃₃₂ Ba/F3-mpl

rhML₃₃₂ 19 , 293-rhML₃₃₂ -
 () 가 2M 2M 1 M Na
 Cl 1 M NaCl 10 WGA- 가 2M
 . WGA- 0.5 M N- -D-
 . SDS-PAGE C4-HPLC (Synchrom, Inc.) 가
 (15). 293-rhML₃₃₂ 68-80 kDa

rhML₁₅₃ 19 , 293-rhML₃₃₂
 . mpl 가
 . RhML₁₅₃ rhML₃₃₂ C4-
 . SDS-PAGE . rhML₁₅₃ Mr 18000-
 (15). HPLC 22000 2 2

10. mpl

mpl DNA PCR 32 P-dATP
 32 P-dCTP λ GT10 , cDNA 10⁶
 . 1443 (16:[SEQ ID NO:12 amp; 13])
 . 138-141
 (Kozak, M. J. Cell Biol., 108:229-241[1989]). 1056
 352 . 5' 137
 3' 247 가 . 3' (A)
 N-
 (von Heijne, G. Eur. J. Biochem. 133:17-21[
 1983]) 21 22 가 m
 ML₃₃₁ (mML2) 331 (35 kDa) 가
 . 4 () 7 N- (5 가
) . hML 가 C-

ML , ML 'EPO'
) , ML
 () cDNA 가 (618 12
 가 111-114 . , 가 ML
 . LPLQ mML 335 mML
 . 17(SEQ ID NO:14 amp; 15) 1443 . mML
 (A) 1068 bp 가 138-140
 134 5' 241 3' 356 21
 . hML3
 116 가 mML3 .
 18(SEQ ID NO: 9 amp; 16)

ML(19 [SEQ ID NO: 6 amp; 16] 72%
 . 'EPO' (1-153 1-149
) (62 %) (86%) . 'EPO'
 , hML
 (153-154) 가
 'EPO'
 ML 가
 , Arg₁₅₃ -Arg₁₅₄ hML

mML (mpl) (mpl) mpl 1 Ba/F3 293 3 H- ML dDNA가 ML

11. mpl

ML(pML)cDNA 13 RACE PCR . 1342 bp PCR cDNA
332 가 mpl 가 20(SEQ ID NO: 18 amp; 19) pML(pML 332)

4 가 pML2 (228) (21(SEQ ID NO:21)). pML pML2 11-114 QLPP가 ML c
DNA 4 (22 [SEQ ID NO:18 amp; 21]).

ML (19[SEQ ID NO: 6, 17 amp; 18]), 72 %, 68% 73 %
80 84 %가 ML(EPO) () 57 67 %가
3 (19[SEQ ID NO: 6, 17 amp; 18]). 245 246
ML N- 4 가, N-
ML 6 N- 가 , 5 7 N-

12. (CHO) TPO

CHO O-D(TPO 153) pSV15.ID.LL.MLORF(TPO 332), pSV15.ID.LL.MLEP 23 24
20 , TPO cDNA PCR
pSV15.ID.LL.MLORF . EPO pSV15.ID.LL 2 (ClaI SalI) (EPOD.Sal)
pSV15.ID.LL.MLEPO-D . TPO EPO

NotI (CHO-DP12)
(1989 3 15 307,247). 10 7 [Andreason, G.L. J. Tissue Cult.
Meth. 15,56[1993]] 10, 25 50 mg DNA BRL (350 , 33
0 mF,) DHFR (DMEM-F12
50:50, 2 mM , 2-5%) . 10 15 96
ML 153 ML 332 Ba/F3-mpl
가 (1).

CHO (HCCF) TPO 20
3 5 100 L () 가
TPO 2.0 M 2.0 M 3 5
1.0 M NaCl 3 5

TPO (Wheat Germ Lectin)
가 () 8 16 ml 2 5
TPO 2.0 M 0.5 M N- -D-

TPO C₁₂E₈ 가 0.04%가 가

0.1% TFA, 0.04 C₁₂E₈ (load) 가 SDS-PAGE C₄ 0.1% TFA, 0.04 C₁₂E₈ 0.2 0.5 mg 2 가 Amicon YM 가

C4 6 10000 30000 가 Tween-80 가 0.01%가

2 5% / 0.01% Tween-80

TPO S-300 HR SDS-PAGE () 가 (Pooling) 2-8

13. TPO TPO ,

E.coli TPO 21 , pMP21, pMP151, pMP41, pM P57 pMP202 TPO 155 pMP210-1, T8, -21, -22, -24, -25

TPO 153 TPO 6 가 pMP210-1 pMP251 TPO 2 , E.coli TPO

(Yansura, D. G. et al., Methods in Enzymology(Goeddel, D.V., Ed.)185:54-60, Academic Press, San Diego[1990]). pMP1 pMP172 TPO

TPO CaCl₂ E.coli [Mandel, M. et al., J. Mol. Biol., 53:159-162[1970]] 21 ,

(600 nm)가 2 3 가 15 ,

2 23 TPO N C TPO 2

11,502 ; Jones , 4,512,922 , Olson , ; Builder et al., 4,518,526 E.coli Builder 4,5

4,620,948 .

A. TPO

TPO E.coli TPO가 , 100 g (Polytorn) , , ,

(: 10 mM Tris, 5 mM EDTA, pH 8) 10 가 ,

30 5000×g

가 10 LH (LH Incelt (Microfluidics International) . ,

ech, Inc.) TPO 30 5000×g ,

(: -70).

B. TPO 가

TPO 가 가 가

pH -HCl, 가 TPO .

8.0-9.0 가 4 9 M, 8.0 6 8 M . 가 pH pH -HCl 7.5-9.5, TPO . 가

(DTE), (DTT), (GSH), (DTT), (: GSH/GSSG) TPO TPO-S- TPO 가 H 8, 6-8 M TPO 25 mM DTT) 5 가 (20 mM Tris, pH 4 TPO 가 (6 8M) 1 3 30 30000×g TPO (2 ml/ 200 (, 2.6×60 cm) 10 mM DTT pH 6.0 20 mM Na TPO 160 200 ml C4 (2×20 cm VYDAC) 5 ml/ TPO 가 30 % 0.1 % TFA(60 %) 가 50% TPO

C. TPO

TPO 가 가 , TPO (Ba/F3 3 pg/ml TPO 가 , (>10%). 10% , 30-50%, 가 50% Troton X-100, 가 , CHAPS, CHAPSO, SDS, Tween 20 Tween 80, Zwittergent 3-14 가 , 가 CHAPS (CHAPS CHAPSO) CHAPS 1% EDTA(1 5 mM)가 0.1 M 0.5 M () 15% 가 , (RSH) (GSH), (GSSG) , pH 7.5 9가 TPO 가 pH 가 (: , 가 , 4 TPO

40-60 % TPO (TPO TPO (: 200 C4

TPO 4 , 3 가 .

1: 1-4 2-3

2: 1-2 3-4

3: 1-3 2-4

, TPO 가 C4 Ba/F3 가 .

가
TPO 10 20%
TPO 1-4
2-3 가
D. TPO
TPO 가 , Ba/F3 , TPO(Met
-1, 1-153) Ba/F3 가 3.3 pg(0.3 pM) . mpl
ELISA , 1.9 ng/ml(120 pM) X
(30 ng/ml , TPO(Met -1, 1-153)
(25, 26 28). TPO

14,
1 Ba/F3 mpl ,
(CMK) (-GPII b III a) (Sat
o , Brit. J. Haematol., 72:184-190[1989])(4)
(DAMI) (Ogura , Blood, 72(1):49-50[1988])
-DNA 가
가 , (GPII b III a) , (: mpl)가
, CMK DAMI , CMK
(4) GPII b III a . DAMI (1
5) 가 가 2N, 4N, 8
N, 16N, 32N 가 (16) (mpl
mpl)
2 가 TPO 가 mpl mpl-Rse
mpl mpl CHO mpl-Rse , Rse
ELISA IgG ELISA 가 mpl ELISA
ELISA . mpl (TPO 155) 18
mpl

15. TPO
TPO (CHO) , E.coli (293)
, CHO 3 TPO가 가 TPO가
가

(a) E.coli-rhTPO(Met -1, 153)

E.coli EPO 'Met' (TPO 153 -1 Met가) 25A, 25B
25C C57 B6 E.coli
2 가
26A, 26B 26C (137 Cs) C57 B6

(b) CHO-rhTPO 332

TPO CHO 27A, 27B 27C C57 B6
5

가 .

(c) CHO-rhTPO₃₃₂ ; E.coli-rhTPO(Met⁻¹, 153); 293-rhTPO₃₃₂ E.coli-rhTPO₁₅₅

28 (CHO-rhTPO₃₃₂ ; E.coli-rhTPO(Met⁻¹, 153); 293-rhTPO₃₃₂
E.coli-rhTPO₁₅₅) rhTPO
가 , CHO 가 가

(d) CHO-rhTPO₁₅₃ , CHO-rhTPO^{'clipped'} CHO-rhTPO₃₃₂

29 CHO(CHO-rhTPO₁₅₃ , CHO-rhTPO^{'clipped'} CHO-rhTPO₃₃₂)
rhTPO
가 , CHO 가 가 .

16. mpl

mpl mpl ()
mpl mpl 가 mpl DNA
mpl / , DNA
mpl mpl DNA
mpl DNA 가
mpl mpl
가 mpl
가 mpl
mpl

A. mpl DNA

mpl DNA mpl mRNA 가 mpl 가 DNA
cDNA

. cDNA 가 . cDNA mpl , m
pl cDNA () 가 20 , 80 cDNA
DNA () DN
A , cDNA cD
NA Sambrook et al., Supra 10 12

mpl Sambrook et al., Supra 14 PCR 가
mpl DNA

() cDNA , ,

cDNA

가

() mpl

DNA

ATP(: γ 32 P) 5'

mpl mpl mpl 가

cDNA

B. mpl

mpl mpl DNA mpl mpl

mpl mpl DNA 가

mpl

mpl

(1)

(2) 1 3 (3)

mpl

[Cunningham Wells, Science, 244:1081-1085[1989]]

(: arg, asp, his, lys glu

가

가

, ala

mpl

2 mpl ()가 (

mpl , mpl DNA 가

DNA mpl

1 30 , 1 10

mpl

가 mpl 가

mpl mpl 가

mpl mpl 3 (:

)

가 100 ()
(: mpl 1 10 , mpl
1 5 , 가 1 3 . N- 가
mpl , mpl N- N-
mpl
gD E.coli STII lpp가 ,
mpl mpl N- C- (: 가 (: 가
mpl (: E.coli trp locus
(1989 4 6 89/0
2922). 가 C- 가
가 가 mpl
가 () mpl
가 () mpl
3 () mpl 가
3 가
가 3 가

[3]

Ala(A)	Val; Leu:Ile	Val
Arg(R)	Lys; Gln; Asn	Lys
Asn(N)	Gln; His; Lys; Arg	Gln
Asp(D)	Glu	Glu
Cys(C)	Ser	Ser
Gln(Q)	Asn	Asn
Gly(I)	Asp	Asp
His(H)	Asp; Gln; Lys; Arg	Arg
Ile(I)	Leu; Val; Met; Ala; Phe	Leu
Leu(L)	; Ile; Val; Met; Ala; Phe	Ile
Lys(K)	Arg; Gln; Asn	Arg
Met(M)	Leu; Val; Ile; Ala	Leu
Phe(F)	Leu; Val; Ile; Ala	Leu
Pro(P)	Gly	Gly
Ser(S)	Thr	Thr
Thr(T)	Ser	Ser

Trp(W)	Tyr	Tyr
Tyr(Y)	Trp; Phe; Thr; Ser	Phe
Val(V)	Ile; Leu; Met; Phe; Ala;	Leu

mpl (a) (:
, (b) , (c)

•

•

- (1) : , Met, Ala, Val, Leu, Ile;
- (2) : Cys, Ser, Thr;
- (3) : Asp, Glu;
- (4) : Asn, Gln, His, Lys, Arg;
- (5) : Gly, Pro;
- (6) : Trp, Tyr, Phe

$$\text{C-} \quad \text{N-} \quad 3 \quad (\quad 3$$

mpl (異常) 가 . , epo
o . , epo .

mpl () , PCR (mpl ())

mpl DNA , ,
[DNA, 2:183[1983]] DNA (mpl , m
mpl DNA
DNA)
, DNA 가 mpl DNA

, 가 25

12 15 .

가 DNA Crea
[Proc. Natl. Acad. Sci. USA, 75:5765[1978]]

DNA Viera [Meth. Enzymol., 153:3[1987]] M13 (M13mp18 M13mp19가)
Sambrook [Molecular Cloning: A Laboratory Manual (Cold Spring Harbor Laboratory Press, NY 1989)] 4.21-4.41

DNA
DNA (DNA , DNA I 가
가 DNA mpl (, E.coli JM101 32-)
DNA
가
3 P) ((dATP), (dGTP) (dTTP 가)
dCTP-(aS) - 가 DNA 가 , DNA dCTP
, dCTP-(aS) DNA 가 가
가 ExoIII 가 , 가 DNA DNA 4
, ATP DNA 가 DNA E.coli JM101
가 mpl DNA 가
가
0),
DNA 가 DNA
DNA 2 ()
DNA DNA 2
가 A 가 DNA DN
PCR mpl RNA PCR DNA
[Erlich, supra, R. Higudhi, p, 61-70): DNA PCR , DNA

DNA . DNA 가

A DNA 200 DNA DN PCR

DNA 가

DNA PCR , DNA 가 .

PCR 2 PCR 3 () 2

PCR , DNA(1 μ g) DNA 100 ng PCR (P

가 PCR (4 GeneAmp () (P

erkin-Elmer Cetus, Norwalk, CT Emerymille, CA) ,

25 pmole 가 50 μ l) 가 . 35 μ l 가 .

100 5 , 1 μ l *Thermus aquaticus*(Taq) DNA (5

/ul, Perkin-Elmer Cetus) 가 .

DNA (Perkin-Elmer Cetus) 가 .

2 , 55

30 , 72

19 :

30 , 94

30 , 55

30 , 72 .

50) , DNA / (50:

Wells [Gene, 34:315[1985]]

mpl DNA (

) . mpl DNA 가 .

가 mpl DNA 가

mpl DNA 가

3' 5' 가

C. 가

mpl (: cDNA DNA) (DNA

) DNA 가 가 , (1) DNA

(DNA , (2) , (3)

DNA)

(i)

mpl
N-가
가 mpl DNA
(:) . mpl
, lpp, II
(1990 4 4 362,179) , 1990 11 15
90/13646 (: mpl
mpl gD) mpl
mpl , mpl

(ii)

DNA 가
DNA
pBR322 (SV40, , 2 μ BPV)
V40 (S
).
가 가
E.coli

DNA

DNA

DNA

mpl

DNA가

, mpl

DNA

가

mpl

DNA

가

(iii)

(가)

(a)

, (b)

(c)

(

D-

)

가

(Southern et al., J. Molec. Appl. Genet., 1:327[1982]),

(Mulli

gan et al., Science, 209:1422[1980])

(Sudgen et al., Mol. Cell. Biol., 5:410-413[1985])

가

G418

(

), xgpt(),

가

(DHFR)

mpl

가 mpl DNA가 가
가 DNA mpl 가
가
가 ,DHFR (Mtx) DHFR
가 DHFR
Urlaub Chasin [Proc. Natl. Acad.Sci. USA, 77:4216[1980]]
가 , DHFR (CHO) 가 Mtx
가 DHFR DNA(mpl
DNA) 가 , Mtx 가 DHFR 가
CL61 CHO-K1) (117,060) (: ATCC No. C
3' (APH) mpl , DHFR
(G418 DHFR 가
4,965,199].

YRp7 trp1 [Stinchcomb et al., Nature, 282:39[1979]; Kingsman et al., Gene, 7:141[1979]; Tschemper et al., Gene, 10:157[1980]]. trp1
(: ATCC No.44076 PEP4-1)
(Jones, Genetics, 85:12[1977]).
trp1 가 , Leu-2 (ATCC No
.20,622 38,626) Leu2 가
(iv)

mpl 가
가 mpl
(100 1000bp) (5')
2가) , DNA 가 (:
) ,
가 ,
mpl DNA 가 mpl
mpl DNA () m
pl mpl DNA mpl
pl

β - (Chang et al., Nature, 275:6
15[1978]; Goeddel et al., Nature, 281:544[1979]),
nucleic Acids Res., 8:4057[1980] 36,776) tac (Goeddel, N
Proc. Natl. Sci. USA, 80:21-25[1983])가 (deBoer et al.,
가
mpl DNA mpl
o(S.D.) (Siebenlist et al., Cell, 20:269[1980]).
DNA 가 Shine-Dalgan

가 25
30 AT- 70 80
X가 CXCAAT 3'
A 가 AATAAA 3'

I. Chem 255:2073[1980]) 3- (Hitzeaman et al., J.Bio
-3-
-6- , 3-
(Hess et al., J. Adv. Enzyme Reg., 7:149[1968] Holland, Biochemistry, 17:4900[1978])가

2, C, 가 , 가 , , -3-
가 [Hitzman et al., 73,657] .
mpl (1989 7
5 2,211,504), (2), , 40(S
V40) , -B 가
mpl , ,
SV40 SV40 SV40
[Fiers et al., Nature, 273:113[1978]; Mulligan and Berg, Science, 209:1422-1427[1980]; Pavlakis et al., Proc. Natl. Acad.Sci.USA, 78:7398-7402[1981]. HindIII E
[Greenaway et al., Gene, 18:355-360[1982]].
DNA 4,419,446 .
4,601,978 cDNA
[Gray et al., 295:503-508[1982],
β - cDNA [Reyes et al.,
Nature, 297:598-601[1982]], β 1
Canaani and Berg, Proc. Natl. Acad. Sci. USA, 79:5166-5170[1982]]
CV-1 , HeLa
NIH-3T3 CAT [Gorman et al., Proc. Natl. Acad.
Sci. USA, 79:6777-6781[1982]
(v)
mpl DNA
가 가 10 300 bp DNA -
(Osborne et al., Mol. Cell Bio., 4:1293[1984]) [Bane
rji et al., Cell, 33:729[1983] 5' (Laimins et al., Proc. Natl. Acad. Sci. USA, 78:993[198
1] 3'[Luski et al., Mol. Cell Bio., 3:1108[1983])
(, a-)
가 SV40 (100-270 bp),
[Yaniv et al., Nature, 297:17-18[1982]]
mpl 3' 5' 5'
(vi)
(, , , ,)
mRNA
DNA cDNA 5' 3' mpl
mRNA 가
(vii)
DNA ,
E.coli K12 29
4(ATCC No. 31,446)
() Messing [Nucleic Acids Res., 9:309[1981]
[Methods in Enzymology, 65:499[1980]] Mexam

(viii)

mpl DNA 가
 가 [Sambrook et al., supra pp16.17-16.22].
 DNA
 가 mpl
 가 mpl

(ix)

mpl [Gething et al., Nature, 293:620-625[1981]; Mantei et al., Nature, 281:40-46[1979]; Levinson et al., 117,060 ; 117,058]
 mpl
 pRK5(307,247 , 5,258.287) pSV16B(PCT 91/08291)

D. _____

(: E.coli, B. (subtilis)
 (Bacilli), P. (aeruginosa) (Pseudomonas) , (Salmonella t
 ynphimurium) (Serratia marcescans)가 . E.coli B, E.coli X1776(ATCC No. 31,5
 36) E.coli W3110(ATCC No. 27,325) E.coli가 E.coli
 E.coli 294(ATCC No. 31,446)

, PCR

mpl
 (Saccharomyces cerevisiae) 가
 가
 Schizosaccharomyces pombe(Beach and Nurse, Nature, 290:140[1981]; 1985 5 2 1
 39,383), K. lactis(Louvencourt et al., J.Bacteriol., 737[1983]), K. fragillis. K.bulgaricus, K.therm
 otoleurns K. marxianus Kluyveromyces (4,943,529), yarrowia[
 402,226], Pichia pastoris(183,070 ; Sreekrina et al., J. Basic Microbiol.,28:265-278[1988])
 , Candida, Trichoderma reesia(244,234), Neurespora crassa(Case et al., Proc. Natl. Acad. Sci.
 USA, 76:5259-5263[1979]),Neurospora, Penicillin, Tolypocalidium(1991 1 10 91
 /00357), A. nidulans(Balland et al., Biochem. Biophys. Res. Commun. 112:284-289[1983]; Tilburn et a
 l., Gene, 26:205-221[1983]; Yelton et al., Proc. Natl. Acad. Sci. USA, 81:1470-1474[1984]) A. niger(Kell
 y Hynes, EMBO J., 4:475-479[1985]) Aspergillus 가

mpl
 가
 가
 가 Spodoptera frugiperda()
 , Aedes aegypti(), Aedes aldopictus(), Drosophila melanogaster() Bombyx mori
 가 Luckow et al., Bi
 o/Technology, 6:47-55[1988]; Miler et al., Genetic Engineering, Setlow et al., eds., Vol.8(Plenum Publishing
 , 1986) pp. 277-279; Nature, 315:592-594[1985]
 (: Autigrapha californica NPV L-1 Bombyx mori NPV Bm-5)
 , Spodoptera frugiperda

mpl DNA Agarobacterium tumefaciens
 A. tumefaciens mpl DNA가
 가 mpl DNA가
 (:) (Depoker et al., J.Mol. A

ppl. Gen., 1:561[1982]). T-DNA 780 DNA DNA
가 가 (1989 6 21
321,196).
()
(Tissue Culture, Academic Press, Kruse and Patterson, editors[1973]).
SV40(COS-7, ATCC CRL 1651) CV1 ; ()
293)(Graham et al., J.Gen Viol., 36:59[1977]);
(BHK, ARCC CCL 10); /-DHFR(CHO)(Urlaub Chasin, Proc. Natl
. Sci. USA, 77:4216[1980]); (TM4, Mather, Biol. Reprod., 23:243-251[1980];
(CV1 ATCC CCL 70); (VERO-76, ATCC CRL-1587);
(HELA, ATCC CCL 2); (MDCK ATCC CCL 34); (BRL 3A ATCC C
RL 1442); (W138, ATCC CCL 75); (Hep G2, HB 8065); (MMT 0605
62, ATCC CCL51); TRI (Mather et al., Annals N.Y. Acad. Sci., 383:44-68[1982]); MRC 5 ; FS4 :
(Hep G2)가 .

가 , CaPO₄ .
DNA DNA가 가
, Sambrook et al., supra
가 가 . Agrobacterium tumfa
cience Shaw [Gene, 23:315[1983] 1991 1 10 89/05859]
m van der Eb, Virology, 52:456-457] , [Graha
1983 8 16 Axel 4,399,216
Van Solingen et al., J.Bact., 130:946[1977] Hsiao et al., Proc. Natl. Acad. Sci.(USA), 76:3829[19
78] DNA

E. _____

mpl Sambrook et al., supra
mpl . Ham's F10(Si
gma), Minimal Essential ([MEM], Sigma), RPMI-1640(Sigma) Dulbecco's Modified Medium([DMEM],
Sigma) , [Ham and Wallace, Meth. Enz., 5
8:44[1979], Barns and Sato, Anal. Biochem.,102:255[1980]; 4,767,704 ; 4,657,866 ;
4,927,762 ; 4,560,655 ; 90/03430; 78/00195 ; 30,985
1990 10 3 07/592,107 07/592,141 ()
() 가
() () , ()
(HEPES), () , ()
, pH
가 .

F. _____ / _____

()

01-5205[1980]) , mRNA (Thomas, Proc. Natl. Acad. Sci. USA, 77:52
³²P (: , ,
) (DNA , RNA ,
 DNA-RNA DNA- 가 , 가 ,
 가
 ,
 , (, , ,
 가)
 [Hsu et al., Am. J. Clin. Path, m 75:734-738[1980]

()

mpl

DNA

G. mpl

mpl
 mpl 가 가 가 , mpl
 가 (:Amicon Millipore Pellicon ultrafiltration units). mpl mpl 가
 가
 , 가 , (: -hmpl
 Mab), (: mpl-IgG A), (:
 Con A- , - (: DEAE IL-2 RP-HPLC G-75), (RP-H
 PLC)([1984])가 IL-2 RP-HPLC Urdal et al., J.Chromatog, 296:171
 SDS-PAGE

mpl

mpl
) mplmpl
 , mpl
)

(PMSF)

mpl-IgG

Affi-Gel 10(Bio-Rad, ,) (

mpl

가 mpl

H. *mpl*

mpl *mpl* *mpl* 가
 mpl 40 mpl *mpl*
 . *mpl*

mpl

N- C- .

α - (),

, α - β - (5-) , N- , 3- -2-

-7- , -2- -1,3- , p- , 2- -4- ,

pH 5.5-7.0

pH 6.0 0.1M .

; O- ; 2,4- ; ; ; ;

1,2- 1 , pKa가 , 2,3- ,

. ,

. 가 , N-

O- 125 | 131 | 3- T

() [R-N=C=N-R' (, R R')],

1- -3-(2- -4-) 가, 1- -3-(4- -4,4-)

- *mpl*

1,1- *mpl* 가 , 가

()-2- , N- , 4-

(3,3'- (: -N- (-1,8-)) -3-[(p

-)]

3969287

α - (T.E. Creighton, Proteins: Structure and Molecular Properties, W.H. Freeman amp; Co., San Francisco, pp. 79-86, 1983), N- C-

가 .

mpl

mpl 1 mpl 1 , (

) mpl 1

N- O- . N- -X- -X-

(, X)

. ,

5- . O-) N- (, , 5- 가

mpl
1 (N-) 가

1 (O-) *mpl* 1 DNA

, *mpl* DNA . DAN ' *mpl*

mpl 가

N- O-

, (b) , (c) (: , (d) , (a) (: ,), (f) 87/05330 (1987 9 11)

[Wriston, CRC Crit. Rev. Biochem., pp 259-306 (1981)]

mpl

, (N- N-)

(Hakimuddin) [Arch. Biochem. Biophys., 259:52, 1987] (Edge) [Anal. Biochem., 118:131, 1981]

(Thotakura) [Meth. Enzymol., 138:350, 1987]

가 - -

(Duskin) [J. Biol. Chem., 257:3105, 1982]

-N-

mpl 4640835 , 4496689 , 4301144 , 4670

417 , 4791192 , 4179337 *mpl*

(pegylated) *mpl*

mpl () 가 *mpl*

, *mpl* , *mpl*

가 .

17. *mpl*

(1)

mpl (sc) (ip) . *mpl* (keyhole) (limpet) , , (

R¹ N=C=NR (, N- (, R R¹) , , SOCl₂

(,) 1 μ g 3 ,
 1 , mpl , 1/5 1/10
 (boosting) . 7 14 , , mpl 가
 . 가가 , , mpl
 , 가 , .

(ii)

(,) 가
 .

, *mpl* [Kohler amp; Milstein, Nature, 256:495 (1975)]
 DNA (4816567 , Cabilly
) .

,
 ,
 , . (Goding, Monoclonal Antibodies : Principles and Practic
 e, pp. 59 - 103 [Academic Press, 1986]).

(parent) 1
 , 가
 (HGPRT HPRT) 가 ,
 (HGPRT) (HAT).

, HAT
 MPC-11 (Salk Institute Cell Distribution Center, MOPC-21
 , SP-2 (American Type Culture Collection,
) .
 [Kozbor, J. Immunol., 133:3001 (1984); Brodeur , Monoclonal Antibody Production Techniqu
 es and Application, pp. 51-63, Marcel Dekker, Inc., New York, 1987].

가 mpl
 (, RIA) (ELISA) .

[Scatchard analysis; Munson amp; Pollard, Anal. Bio
 chem., 107:220 (1980)] .

, ()
 , (Goding)
 RPMI-1640 . ,
 .

, A- ,
 , ,
 .

DNA , (:
)
 DNA , COS ,
 DNA , DNA

(Cabilly , Morrison Proc. Nat. Acad. Sci., 81:6851 (1984)),

가 mpl 가

가

-4-

가 가 3

H, ¹⁴C, ³²P, ³⁵S, ¹²⁵I, ¹²⁵I, ³²P, ¹⁴C, ³H

가 [Hunter , Nature, 144: 945 (1962); David , Biochemistry, 13:1014 (1974); Pain , J. Immunol. Meth., 40:219(1981); Nygren, Hyst ochem. and Cytochem., 30:407 (1982)]

(Zola, Monoclonal Antibodies: A Manual of Techniques. pp 147-158 (CRC Press, Inc., 1987)).

(mpl) mpl

(mpl)

(mpl) 1

2 가 3 (David amp; Greene

4,376,110). 2 가 ()

가 (:)

가 ELISA , 가

(iii)

1 (import)'

가 (Winter) (Jones , Nature, 321: 522-525 (1986); Riechmann , Nature, 332:323-327 (1988); Verhoeyen , Science, 239:1534-1536 (1988))

CDR CDR

(Cabilly), (intact) 가 CDR

가 FR 가

가 (best-fit)' 가 가

가 가 (FR) (Sims , J. Immunol. 151:2296 (1993); Chothia Lesk, J. Mol. Biol. 196:901 (1987)).

가 가 (Carter , Proc. Natl. Acad. Sci. USA, 89:4285 (1992); Presta , J. Immol., 151:2623 (1993)).

가
가
가
가
가 () , FR
가 , CDR
1992 8 21
07/934,373 (1991 6 14
07/715272
(
(:)
(J H)
(: Jakobovits , Proc. Natl. Acad. Sci. USA, 90:2551-255 (1993); Jakobovits Nature, 362:255-258 (1993); Bruggermann , Year in Immuno., 7:33 (1993)).
(Hoogenboom and Winter, J. Mol. Biol. 227, 381 (1991); Marks , J. Mol. Biol. 222, 581 (1991)).

(iv)
2
(Millstein Cuello, Nature, 305:537-539(1983)).
(; quadroma) 10 (1
가)
93/08829 (1993 5 13
) [Trauneker , EMBO, 10:3655-3659 (1991)]
가 (-)
, CH2 CH3
1 (CH1)
DNA가
3 , 3
1 2 3
가 (arm)
1 (2)
가
07/931811 (1992 8 17
)
[Suresh Methods in Enzymology 121:
210 (1986)]

(v)
(91/00360 , 92/00373 , 103089) 4676980 , HIV
가 4676980

IV. mpl

가 , 가 (TPO) mpl
 (HIV- ITP HIV- ITP), (DIC),
 가 가
 (TPO)
 (a) (f)

IL-3, (EPO), , IL-6 IL-11 G-CSF, GM-CSF, LIF, M-CSF, IL-1,
 , pH,
 가
 (10)
 ; EDTA
 () (Tween), (Pluronics)
 0.5
 500 mg

ger , J. Biomed. Mater. Res., 15:167-277, 1981 Langer, Chem. Tech., 12:98-105, 1982 [: Lan
) ()], (3773919 , 58,48
 1), L- -L- (Sidman , Biopolymers, 22:547-556, 1983),
 (Lupron Depot TM ; (: TM
 -D-(-)-3- (133988)
 100 가
 37

가 . S-S , 가 , (entrapped) 3218121 ; Epstein , Proc. Natl. Acad. Sci. USA, 82:3688-3692, 1985; Hwang , Proc. Natl. Acad. Sci. USA, 77:4030-4034, 1980; 52322 ; 36676 ; 88046 ; 143,949 ; 14 2641 ; 83-118008 ; 4485045 4544545 ; 10232 4 . 30 % (200 800) ,

가 , 1 0.1 100 μ g/kg , 0.1 50 μ g/kg , 1 5 μ g/kg/ , G-CSF, GM-CSF EPO ,

가

1

mpl

900 cGy 4mEV 가 6-8 , 1800 $\times$ g 30 6 NaCl 4M , 30 (Sorvall) RC3B 3800 rpm 4M N aCl 10 mM NaPO₄ 가 (Phenyl-Toyopearl) (220 M ℓ) , dH₂O dH₂ O A₂₈₀ 0.05 가 , PBS (Blue-Sepharose) (240 M ℓ) 15 mS , PBS PBS NaPO₄ (pH 7.4) . 2M 5 2M 1M NaCl NaPO₄ (pH 7.4) (Pefabloc : Boehinger 0.01 % (n- β -D-) 1M EDTA [Nature, 337:525-531 (1989)] Mannheim) , CD4-IgG ((Capon, D.J.) () . CD) mpl-IgG (Ultralink : Pierce) 10 PBS 2M NaCl PBS 4-IgG (2 M ℓ) , mpl-IgG (4 M ℓ) 1/10 1M -HCl (pH 8.0) , 0.1M -HCl (pH 2.25) .

가 SDS-PAGE (4-20 %, Novex gel) mpl- 66,000, 55,000, 30,000, 28,000 14,000 (5) . Ba/F3- mpl

2

PBS 10-20 mg mpl-IgG CD4-IgG 0.5 g (Pierce) .

mpl - IgG

mpl (1-491) IgG1 Fc 293
mpl 1-491 cDNA CMK cDNA
 PCR , Clal 5' BstEII 3' BstEII
mpl DNA 2 BstEII PCR BstEII
 , Clal BstEII Bluescript IgG1 Fc *mpl*
mpl PCR 3' BstEII Fc *mpl*
 Clal Xbal pRK5tkneo ,
 293 0.4 mg/MØ G418 ,
 1-2 mg/MØ *mpl* -IgG Fc ELISA
 가

Ba/F3 mpl P

8
n-Strep
FACS

Ba/F3 mpl

mpI
 $37^\circ C$
 $5\% CO_2$
 $IL-3$
 $50,000$
 96-
 $20\ \mu\ell$
 GF/C
(Packard Top Count counter)
 $40\ \mu\ell$
 2

5×10^{-5}
 $1Me$
 mpI
 mpI P Ba/F3
 $200\ \mu\ell$
 24
 $6-8$
 $가$
 5
(Microscint 20)
 2

mpl

12 2 Biorad 422 12-14K

1. 50 mM + 0.05 % SDS (pH 7.8) . 1 ℓ
 4-6 4-6 10 ma/ (40 v
 4
)
 etman)
 SDS 50 μℓ (Pip
 300-500
 μℓ 10 mm (Spectrapor) 4 12-14K
 6 600 Mℓ (PBS 4 mM) 4-6
 2.5
 1 가 3 14 K rpm
 SDS 가 4 1
 - 70

3

mpl

mpl - IgG 6 (2.6 Mℓ) (Microcon)-10 (Amicon)
 mpl 가 1 % SDS , 5 μℓ 10 % SDS 6 가
 (20 μℓ) , 2X (20 μℓ) #6 가 , (40 μℓ) 4-20 %
 , 10 % () 10 mM 3-() -1- (CAPS) (pH 11.0)
 5 (Immobilon)-PSQ (Millipore)
 BioRad Trans-Blot (32) 250 mA 45 PVDF 40 %
 0.1 % (Coomassie Blue) R-250, 0.1 % 1 , 50 %
 10 % 2-3 18,000-35,000 가
 30,000, 28,000 22,000

30, 28 22 kDa PTH 가
 470A Applied Biosystem 80-90 % (A 가
 (Rodriguez) [J. Chromatogr., 350:217-225 (1985)]). (~ 12 μℓ/ ℓ) Nelson Analyt
 UV Blott
 ical 970 Justice Innovation VAX 5900
 ((Henzel) [J. Chromatogr., 404 :41-52 (1987)]). N- ()
 1) () 2

< 2>

30 kDa [1.8 pmol] 1 5 10 15 20 25 (S)PAPPA(C)DPRLLNKLLRDD(H/S)VLH(G)RL	(: 30)
28 kDa [0.5 pmol] 1 5 10 15 20 25 (S)PAPPAXDPRLLNKLLRDD(H)VL(H)GR	(: 31)
18-22 kDa [0.5 pmol] 1 5 10 XPAPPAXDPRLX(N)(K)	(: 32)

4

(PSC) () IMDM (Gibco) 5 , 800×g 1
5 , 800×g 30 IMDM , 60 % (Percoll : 1.077 gm/Mℓ)
, 24- , 30 (Costar) 30 % FBS IMDM (1 Mℓ) 1-2×10⁶
/Mℓ . APP APP가 mpl 10 % 가 , 37 5 % CO₂
12-14 . , 0, 2 4 0.5 μg mpl -IgG 가
10 % APP . mpl - IgG APP mpl

(Dr. Nichols, Mayo Clinic) (Solberg) , GPIIb/IIIa
100 μg HP1-1D ((Grant, B.) [Blood 69:1334-1339 (1987)])
Enzymobeads (Biorad) 1mCi Na¹²⁵I
HP1-1D 0.01 % - PBS - 70
1-2×10⁶ cpm/μg (12.5 % 95 %)

3 . 12-14 , 1 Mℓ 1.5 Mℓ
(eppendorf) , 10 800×g , 0.02 % E
DTA 20 % 100 μℓ PBS . 50 μℓ 10 ng¹²⁵
I-HP1-1D 가 , (RT) 60
RT 10 800×g , 2 (gamm
a counter : Packard) 1 HP1-1D 가 1 μg
HP1-1D 60 가 HP1-1D
¹²⁵I-HP1-1D

5

PCR

30 kDa, 28 kDa 18-22 kDa - ,
(PCR) (4). 2-8 (2
mpl/ 1) 20-mer 18-24 (mpl/ 2)
1-mer 2

[4]

mpl 1 : 5' CCN GCN CCN CCN GCN TGY GA 3' (2,048)	(: 35)
mpl 2 : 5' NCC RTG NAR NAC RTG RTC RTC 3' (2,048)	(: 36)

DNA PCR . 50 μℓ 10 mM
-HCl (pH 8.3), 50 mM KCl, 3 mM MgCl₂ , 100 μg/Mℓ BSA, 400 μ M dNTPs, 1 μ M
2.5 Taq 0.8 μg DNA 94 8 ,
94 45 , 55 1 , 72 1 35 . 72 10
PCR 12 % ,
가 . - PCR 69
bp . 3 5 DNA , pGEMT (Promega)

[5]

gem T3
5' <u>CCAGCGCCGC CAGCCTGTGA</u> CCCCCGACTC CTAAATAAAC TGCCTCGTGA
3' GGTCGCGGCG GTCGGACACT GGGGGCTGAG GATTTATTTG ACGGAGCA <u>CT</u>
TGACCACGTT CAGCACGGC [69 bp] (: 37)
<u>ACTGGTGCAA GTCGTGCCG</u> (: 38)
gem T7
5' <u>CCAGCACCTC CGGCATGTGA</u> CCCCCGACTC CTAAATAAAC TGCTTCGTGA
3' GGTCGTGGAG GCCGTACACT GGGGGCTGAG GATTTATTTG ACGAAGCA <u>CT</u>
CGACCACGTC CATCACGGC [69 bp] (: 39)
<u>GCTGGTGCA GTAGTGCCG</u> (: 40)
gem T9
P R L L N K L L R
(: 32)
5' <u>CCAGCACCGCCGGCATGTGA</u> CCCCCGACTCCTAAATAAACTGCTTCGTGACG
3' GGTCGTGGCGGCCGTACACTGGGGGCTGAGGATTTATTTGACGAAGCA <u>CTGC</u>
ATCATGTCTATCACGGT 3' (: 41)
<u>TAGTACAGATAGTGCCA</u> 5' (: 42)

PCR				30 kDa, 28 kDa	18-22 kDa
9-17	N-	,		DNA	
6					
mpl					
5	, pR45	45-mer			
	. 45-mer	가 :			
5' GCC-GTG-AAG-GAC-GTG-GTC-GTC-ACG-AAG-CAG-TTT-ATT-TAG-GAG-TCG 3'					
(SEQ ID NO : 28)					
	(γ ³² P)-ATP	T4		³² P	
	λ gem12	DNA	(7).		
			#4	가	
45-mer	2.8 kb BamHI-XbaI	pBluescript SK-		DNA	
	mpl	DNA			
b BamHI-XbaI	390 bp EcoRI-XbaI	DNA가	EcoRI	2.8 k	
		, pBluescript SK-			
		DNA			
			9 (SEQ ID NO : 3	4)	
			(' 3')		

() 가 mpl 1
mpl 68
3' 196 42
16 26 mpl
7
mpl cDNA
' 3' (6) , ' 3' 3' 5' 2
(6).

[6]

Fwd :	
5' GCT AGC TCT AGA AAT TGC TCC TCG TGG TCA TGC TTC T 3'	(: 43)
Rvs :	
5' CAG TCT GCC GTG AAG GAC ATG G 3'	(: 44)

2 5 cDNA DNA
1 ng Quick Clone cDNA (Clonotech) PCR
140 bp PCR 12 %
DNA , 293 cDNA
cDNA (Clonotech cat. #7171-1)
λ DR2 cDNA (Clonotech cat. #HL1151x) T4
45-mer (γ ³²P)-ATP 2
, 42 20 % , 5xSSC, 10xDenhardt's, 0.05 M (pH 6.5), 0.1
% , 50 μg/Ml DNA
2xSSC , 42 0.5xSSC, 0.1 % SDS 1 (Kodak) X-
1) BamHI-XbaI PCR λ DR2 (Clonotech cat. #6475-
94 7 5 μl
72 1.5) 72 15 , 30 (94 1 , 52 1
FL2b 1.8 kb 가
λ DR2 (arm) pDR2 (Clonotech , λ DR2 amp; pDR2 cloning and Expression S
ystem Library Protocol Handbook, p 42) (Clonotech ,
λ DR2 amp; pDR2 cloning and Expression System Library Protocol Handbook, p 29-30). BamHI XbaI
pDR2-FL2b 650 BamHI 가
BamHI-XbaI 2 (0.65 kb 1.15 kb) . DN
A pDR2-FL2b 3
DNA DNA (-
) AB1373 ((Sanger) [Proc. Natl.
Acad. Sci. USA, 74 : 5463-5467 (1977)] (Smith) [Nature, 321 : 674-679 (1986)]).
AB1373 M13 Janus ((Burland) [Nucl. Acids Res., 21 : 3385-3390 (1993)]).
DNASTAR, Inc.) (

BamHI-XbaI (1.15 kb) BamHI (0.65 kb) pDR2-FL2b
 T4 DNA , M13 Janus SmaI
 M13
 (Sanger)
 [Proc. Natl. Acad. Sci. USA, 74 : 5463-5467 (1977)], ³³P α-dATP (Sequenase)
 se : United States Biochemical Corp.) M13 DNA
 ion) . DNA (Sequencher) V2.1b12 (Gene Codes Corporat
 1 (SEQ ID NO :1)

8

mpl (TPO)

mpl cDNA 3' (BamHI 3') TPO
 DNA (7)
 pR45 λ -Gem 12 TPO 2
 (BamHI . 35 kb 2
 EcoRI)
 DNA 7kb 6 (14A, B C).
 (Shapiro, M. B.)
 [Nucl. Acids Res., 15 : 7155 (1987)] . 1 2 5'
 4 26 3
 3'
 6 . hML-2 (hTPO-2) 4 50 6 5'

9

mpl (hML)

pDR2-FL2b . 1.8 kb DNA , XbaI , BamHI
 (cytomegalovirus)
 pRK5 (pRK5-h *mpl* I) (pRK5
 5,258,287). pRK5-h *mpl* I DNA PEG , F-12 , 2
 0 mM (Hepes : pH 7.4) 10 % (Dulbecco) (Eagle) (
 DMEM) 293 (Gorman) DNA Cloning :
 A Practical Approach (Glover, D.M.)) II , pp 143-190, IRL Press, Washington, D.C.)
 36 , 293 Ba/F3 Ba/F3-
mpl (12a). pRK5-h *mpl* I Ba/F3
 , Ba/F3-*mpl* (12a), cDNA가
mpl

10

mpl : hML2, hML3, hML4

hML (splicing) , hML
 RNA RT-PCR
 () . PCR
 cDNA (1 SEQ ID
 NO : 1). , EPO- (PCR) C- 가
 7 cDNA PCR .

phmplIcdna.3e 1 : 5' TGTGGACTTTAGCTTGGGAGAATG 3'	(: 45)
pbx4.f2 : 5' GGTCCAGGGACCTGGAGGTTTG 3'	(: 46)

PCR M13 hML (hML₃₃₂) 가 , 3 ML
 . 가 (hML) 가 (hML-4) 4 *mpl*
 11 (SEQ ID NO : 6, 8, 9 10) .

11

mpl

hML2, hML2, hML (R153A, R154A)

hML2 hML3, hML (R153A, R154A) (Russell Higuchi) [PCR Protocols, A guide to Methods and Application, Acad. Press, M.A. Innis, D.H. Gelfand, J.J. Sninsky amp; T.J. White Editors]
 PCR hML .
 , ' ' 8 , ' ' 9 .

[8]

Cla.FL.F2 : 5' ATC GAT ATC GAT AGC CAG ACA CCC CGG CCA G 3'	(: 47)
HMPLL-R : 5' GCT AGC TCT AGA CAG GGA AGG GAG CTG TAC ATG AGA 3'	(: 48)

[9]

hML-2 : MLΔ4.F : 5' CTC CTT GGA ACC CAG GGC AGG ACC 3' MLΔ4.R : 5' GGT CCT GCC CTG GGT TCC AAG GAG 3'	(: 49) (: 50)
hML-3 : hMLΔ116+ : 5' CTG CTC CGA GGA AAG GAC TTC TGG ATT 3' hMLΔ116- : 5' AAT CCA GAA GTC CTT TCC TCG GAG CAG 3'	(: 51) (: 52)
hML (R153A, R154A) : RR-KO-F : 5' CCC TCT GCG TCG CGG CGG CCC CAC CCA C 3'	(: 53)

RR-KO-R :

5' GTG GGT GGG GCC GCC GCG ACG CAG AGG G 3'

(: 54)

PCR

Pfu DNA

(Stratagene)

:

94 7 , 94 1 , 55 1 , 72 1.5 30 .
 72 10 . PCR Clal-XbaI ,
 , pRK5tkneo . 293 , Ba/F3- *mp*
 / . hML-2 hML-3 , hML (R1
 53A, R154A) hML , 가
 (13).

12

mpl cDNA : mML, mML-2 mML-3

mML cDNA

mpl DNA PCR , , ³²P-dATP ³²
 P-dCTP (priming) . λ GT10 (Clontech cat# ML3001
 a) cDNA 10⁶ 2 35 %
 , 5xSSC, 10xDenhardt's, 0.1 % SDS, 0.05 M (pH 6.5), 0.1 % , 100 μg/Ml
 DNA 2xSSC , 42 0.5xSSC, 0
 .1 % SDS 1 . , cDNA Bluescript SK- Eco
 RI . 1.5 kb 'LD' , ML c
 DNA LD 14 (SEQ ID
 NO : 1 11) ML 331 , m
 ML 331 (mML-2) .
 ML EPO () () cDNA ML
 , 12 가 가 ML 618
 LPLQ 335 111-114 가
 ML , mML mML 335 . mML 'L2' hML3
 16 (SEQ ID NO : 12 13) 가 , mML-3 2
 116 가
 16 .

mML

ML 8 . mML mML-2
 CMV SV40 mMLpRKtkneo mML2pRKtkneo pRK5t
 kneo 3 . , 5 . 10 %
 DMEM .

Ba/F3

mpl (mmpl)

c- *mpl* 1 *mpl* m *mpl* pRKtkneo
 45-2653 (1993)]) , *mpl* ((Skoda, R.C.) [EMBO J. 12 : 26
 Ba/F3 , 2 mg/Ml G418 (20 μg :) (5×10⁶ , 250 , 960 μF)
 - *mpl* - IgG . Ba/F3 IL-3 WE
 HI -3B RPMI 1640 . mML mML-2 293
 1 m *mpl* h *mpl* BaF3 .

13

mpl cDNA : pML pML-2

ML (pML) cDNA RACE PCR ML dT ML 2
 cDNA . 1342 bp PCR cDNA
 (). cDNA가 18 (SEQ ID NO : 9 16)
 332 (pML 332)

:

pML cDNA

ML EMBL3 (Clontech Inc.) pR45
 7
 ML ML cDNA RACE PCR
 2 ML
 mRNA BamdT : cDNA
 mRNA

(BamdT : 5' GACTCGAGGATCCATCGATTTTTTTTTTTTTTTTTTTT 3')

(SEQ ID NO : 55)

PCR (95 60 , 58 60 , 72 90 28) 1 ML
 h-forward-1 BAMAD 100 M (50 mM KCl, 1.5 mM MgCl₂, 10 mM
 (pH 8.0), 0.2 mM dNTPs 0.05 U/Ml Amplitaq [Perkin Elmer Inc.])

(h-forward-1 : 5' GCTAGCTCTAGAAATTGCTCCTCGTGGTCATGCTTCT 3')

(SEQ ID NO : 43)

(BAMAD : 5' GACTCGAGGATCCATCG 3')

(SEQ ID NO : 56)

, PCR Cla 1 (1:1), Cla
 1 Kpn 1 0.1 mg Bluescript SK- (Stratagene inc.) 2
 , 1/4 2 ML forward-1 T3-21 (Bluescript SK-
) PCR (22) 2
 가 .

(forward-1 : 5' CGTAGCTCTAGAAGCCCGGCTCCTCCTGCCTG 3')

(SEQ ID NO : 57)

(T3-21 : 5' CGAAATTAACCCTCACTAAAG 3')

(SEQ ID NO : 58)

PCR XbaI ClaI , Bluescript SK- PCR

4 pML-2 2 (21 [SEQ I
 D NO :21]). pML pML-2 , pML-2가 111-114
 QLPP가 (22 [SEQ ID NO : 18 21]). ML cDNA

4

14

GPII_b III_a (TPO) CMK

CMK 10 % 10 mM RMPI 1640 (Sigma)

GIF 5 × 10⁵ /Mℓ 5 mg/ℓ 10 mg/ℓ 1 × 10⁶ TPO

100 μℓ 37 5 % CO₂ 48 100 μℓ CMK 100 μℓ 가

1000 rpm 1 200 μℓ 0.1 % BSA-PBS 1000 rpm GPII_b III_a 2D2

가 4 1 0.1 % BSA-PBS FASCA

3 1

N

15

96-AMI DAMI (TPO) D

DAMI 10 mM 100 ng/Mℓ G 50 μg/Mℓ IMDM + 10 %

(Gibco) 1 × 10⁶ /Mℓ 96- 100 μℓ TPO

DAMI 가 37 5 % CO₂ 48

1000 rpm Sorvall 6000B 200 μℓ 70 % -PBS 가

200 μℓ PBS-0.1 % BSA 15 0.05 % -20 150 μℓ 1 mg/Mℓ RNase

0.1 mg/Mℓ 37 1 DNA

TPO : (>G2+M %/<G2+M %)

(NPR) = -----;

: (>G2+M %/<G2+M %)

16

(TPO)

((反跳))

³⁵S

1 C57BL6 (Charles River) 1 Mℓ (6 amps)

0.1 Mℓ 30 μCi Na₂³⁵SO₄ PBS 2 7

% (眼窩後)

17

mpl-Rse.gD

(TPO) KIRA ELISA

(Vigon) [PNAS, USA 89 : 5640-5644 (1992)] *mpl* *mpl*
(ECD) (TM) Rse (ICD) (Mark) [J. of Biol. Chem.
269 (14) : 10720-10728 (1994)] (, Rse.gD) (, Rse.gD)
KIRA ELISA (30 31).

(a)

gD (5B6) (Herpes simplex) D
((Paborsky) [Protein Engineering 3(6) : 547-553 (1990)]).
(PBS : pH 7.4) 3.0 mg/Mℓ , 1.0 Mℓ -20 .

(b) -

- (4G10) UBI () , - (long-arm)
-N- (Biotin-X-NHS, Research Organics, Cleveland, OH) .

(c)

mpl . *mpl* 4

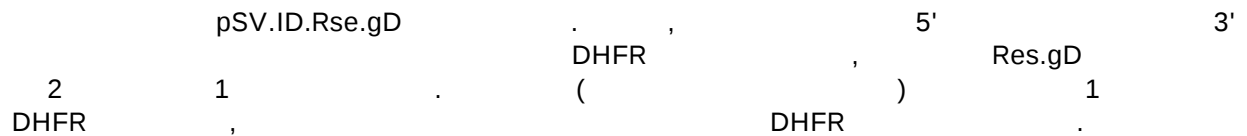
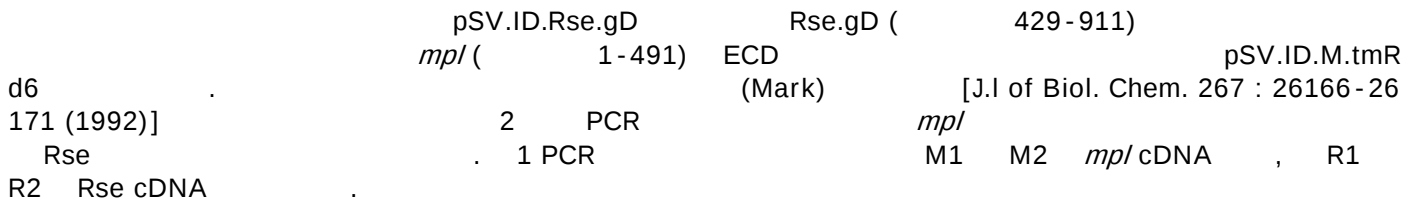
(d) Rse.gD

5B6 Rse C- 10 (880-890)
21 가 가 . 10

[10]

5'- TGCAGCAAGGGCTACTGCCACACTCGAGCTGCGCAGATGCTAGCCTCAAGATGGCTGATCCAAATCGATTCCGCGGCAAAGATCTTCCGGTCCTGTAGAAGCT -3'	(: 59)
5'- AGCTTCTACAGGACCGGAAGATCTTTGCCGCGGAATCGATTTGGATCAGCCATCTTGAGGCTAGCATCTGCGCAGCTCGAGTGTGGCAGTAGCCCTTGCTGCA -3'	(: 60)

DNA Rse cDNA ((Mark) [Journal of Biological Chemistry 269 (14) : 10
720-10728 (1994)]) 2644 PstI pSV17.ID.LL (32A-L
SEQ ID NO : 22) HindIII Rse 1-880 cDNA

(e) *mpl*-Rse.gD

(M1 : 5'-TCTCGCTACCGTTTACAG-3')

(SEQ ID NO : 61)

(M2 : 5'-CAGGTACCCACCAGGCGGTCTCGGT-3')

(SEQ ID NO : 62)

(R1 : 5'-GGGCCATGACACTGTCAA-3')

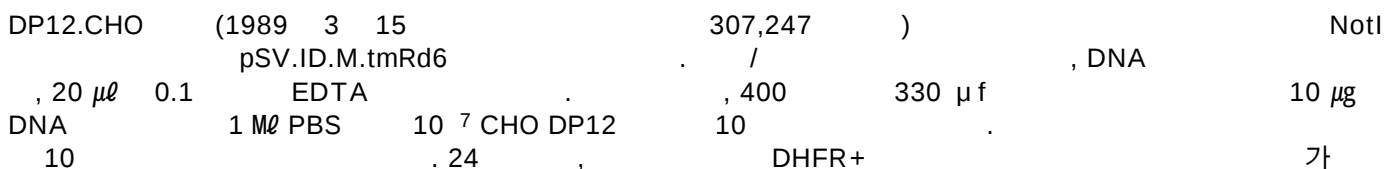
(SEQ ID NO : 63)

(R2 : 5'-GACCGCCACCGAGACCGCCTGGTGGGTACCTGTGGTCCTT-3')

(SEQ ID NO : 64)

PvuII-SmaI

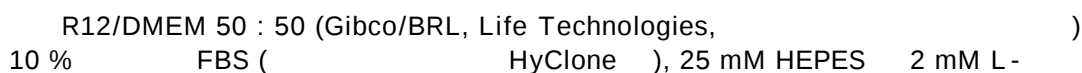
(f)



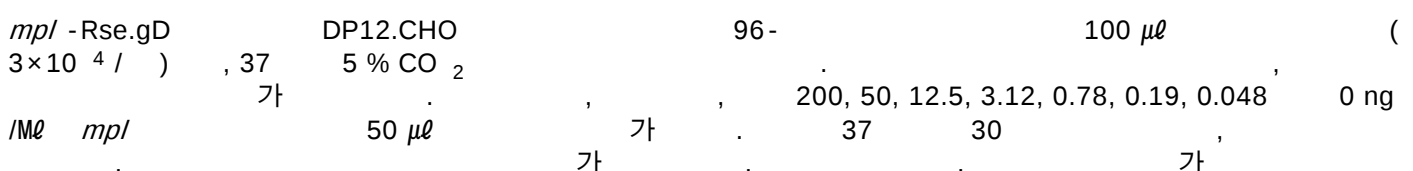
(g) KIRA ELISA



(h)



(i) KIRA ELISA



, 100 μ l 가 . 50 mM HEPES 150 mM NaCl (Gibco), 0
 .5 % Triton-X 100 (Gibco), 0.01 % , 30 KIU/Ml (ICN Bioche
 micals), 1 mM 4-(2-)- HCl (AEBSF : ICN Biochemicals), 50 μ M
 (ICN Biochemicals) 2 mM (NaVO : Sigma Chemic
 al Co : pH 7.5) , ()
 Bellco Instruments) 60 .

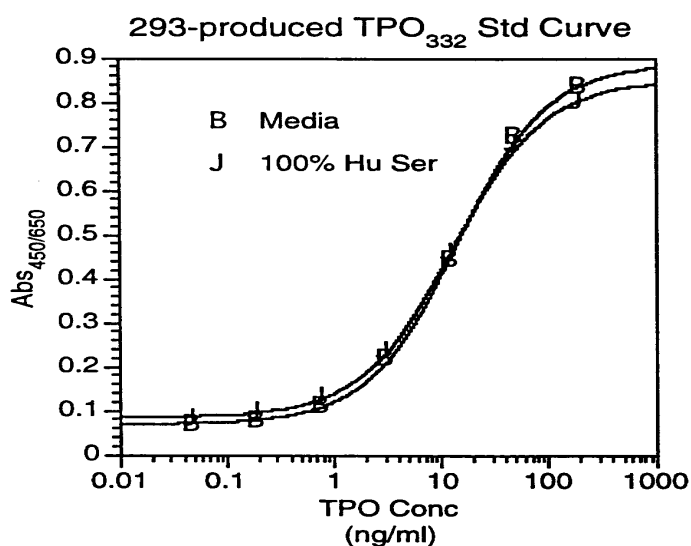
가 , 5B6 -gD (50 mM 5.0 μ g/Ml, pH 9.6, 100 μ l/)
 4 ELISA (Nunc Maxisorp, Inter Med, Denmark) ,
 60 150 μ l/ Block Buffer [0.5 % BSA ()
 Interger Company) 0.01 % PBS] . 60 ,
 (Skatron Instruments, Inc ScanWasher 300) -gD
 5B6 (0.05 % -20 0.01 % PBS) 6 .

- 가 MPL/Rse.gD -gD 5B6 ,
 ELISA , 2 *mpl* -Rse.gD
 (0.5 % BSA, 0.05 % -20, 5 mM EDTA, 0.01 %
 PBS) 1:18000 100 μ l 4G10 (-) (, 56 ng/Ml) 가 . 2
 (HRPO)- (, 1:60000 100 μ l
 Zymed Laboratories, S.) 가 , 100
 μ l (30 [TMB] ; 2- ; 가 Kirk
 egaard and Perry) 가 10 , 100 μ l/ 1.0 M H₃PO₄ 가
 . Macintosh Centris 650 (Apple Computers) DeltaSoft
 (BioMetallics, Inc) vmax ()
 Molecular Devices) 450 nm 650 nm (ABS_{450/650})

dp12.trkA,B C.gD 200, 50, 12.5, 3.12, 0.78, 0.19, 0.048 0 ng/Ml *mpl*
 , DeltaSoft ng/Ml TPO ABS_{450/650} $\pm$ sd
 , ng/Ml TPO .

mpl 가 *mpl* -Rse.gD
 () 100 % pK *mpl* -Rse.gD KIRA ELISA 100 %
 ()

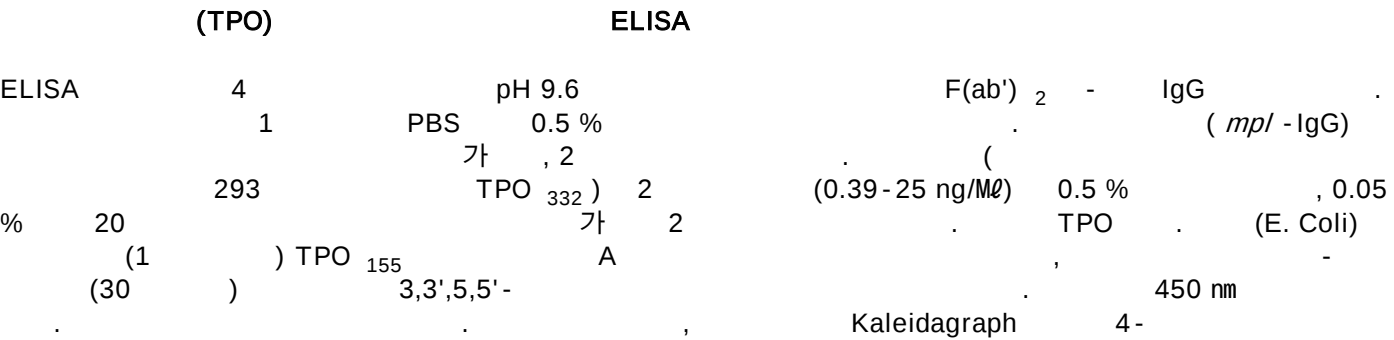
293- TPO₃₃₂



TPO EC50

TPO ()	EC 50 (/)	EC50 ()
TPO 332 (293)	2.56 ng/Mℓ	67.4 pM
TPO 332 (293)	3.69 ng/Mℓ	97.1 pM
TPO 153 (293)	~41ng/Mℓ	~1.08 nM
TPO 155 (.)	0.44 ng/Mℓ	11.6 pM
TPO 153met (.)	0.829 ng/Mℓ	21.8 pM

18



19

293 TPO

1. 293

TPO cDNA PCR

[11]

Cla.FL.F : 5' ATC GAT ATC GAT CAG CCA GAC ACC CCG GCC AG 3'	(: 65)
hmpII - R : 5' GCT AGC TCT AGA CAG GGA AGG GAG CTG TAC ATG AGA 3'	(: 48)

pfu DNA (Stratagene) PRK5 - h mpI I (6)

94 7 25 (94 1 , 55 1 72 1)

72 15 . PCR pRK5tkneo ()

pRK5tkneo. ORF . EPO pRK5) ClaI XbaI

forward Cla.FL.F :

Arg.STOP.Xba :

5' TCT AGA TCT AGA TCA CCT GAC GCA GAG GGT GGA CC 3'

(SEQ ID NO : 66)

pRK5-tkneoEPO-D . 2 7 .

2.

2 9 CaPO₄ 0.4 mg/ML G418.10 . 10
15 24 , 96- , Ba/F3- mp
/ (1) ML₁₅₃ ML₃₃₂

3. rhML₃₃₂

293-rhML₃₃₂ 10 mM (pH 7.4 : A) Blue-Sepharose (Pharmacia
) 가 , 10 A 2 M A
2 M 1 M NaCl A , Blue-Sepharose
A WGA-Sepharose 가 , WGA-Sepharose 10
2 M 1 M NaCl A , 0.5 M N-D-
WGA-Sepharose 0.1 % TFA C4-HPLC (Synchrom, Inc.
) 가 . C4-HPLC (0-25 %, 25-35 %, 35-70 %)
rhML₃₃₂ 28-30 % . SDS-PAGE rhML
332 68-80 kDa (15).

4. rhML₁₅₃

293-rhML₁₅₃ rhML₃₃₂ Blue-Sepharose . Blue-Sep
harose - 가 . mpI - rhML₁₅₃
rhML₃₃₂ C4-HPLC . SDS-P
AGE rhML₁₅₃ ~18,000-21,000 2 2 (15).

20

CHO TPO

1. CHO

:

pSV15.ID.LL.MLORF (hTPO₃₃₂),

pSV15.ID.LL.MLEPO-D (hTPO₁₅₃)

23 24 .

2. CHO

hTPO cDNA 12 PCR

[12]

Cla.FL.F2 : 5' ATC GAT ATC GAT AGC CAG ACA CCC CGG CCA G 3'	(: 47)
--	---------

ORF.Sal : 5' AGT CGA CGT CGA CGT CGG CAG TGT CTG AGA ACC 3'	(: 67)
--	---------

pfu DNA (Stratagene) PRK5-h *mpI* (7 9)
94 7 25 (94 1 , 55 1 72 1)
LL Clal Sal1 72 15 PCR pSV15.ID.LL.MLORF pSV15.ID.
2 forward Cla.FL.F2 EPO
:

EPOD.Sal :
5' AGT CGA CGT CGA CTC ACC TGA CGC AGA GGG TGG ACC 3'
(SEQ ID NO : 68)

pSV15.ID.LL.MLEPO-D . 2 7 9
SV40 / (enhancer) CHO pSV15.ID.LL
SV40 DHFR cDNA
(TPO)

3. TPO₃₃₂ TPO₁₅₃ CHO

a. CHO
TPO (1989 3 15) CHO (Chinese Hamster Ovary) CHO-DP12
(Dr. L. Chasin 307,247).
CHO-K1 DUX-B11(DHFR-)-) Stanford University Dr. Frand Lee
가
DHFR- (,)
DHFR cDNA CHO

b. ()
TPO₃₃₂ TPO₁₅₃ DP12 pSV15.ID.LL.MLORF
pSV15.ID.LL.MLEPO-D . 3
NOTI 10 µg, 25 µg 50 µg
3' , TPO (23). 10
0 µl 37 1 DNA 2mM 15 (50:49:1)
MEM-F12 1:1 50 µl Ham's D
DP12 , DNA 1 750
µl 10⁷ (750 µl) DNA 330 µF
1 350 , BRL BRL 5
가 10 CHO (1×GHT,
2 mM 5 % 가 DMEM-F12 50 : 50) 5 Ml
60 mm , 5 % CO₂

c.

2 % 5 %
 am's DMEM-F12, 1 : 1) 150 mm 60 mm
 5/150 mm 37 /5 % CO₂ 10 15 (1) 96- 4-5 5
 0 Mℓ 3-5) 2 (DMSO 5
 50 μℓ 10 % FCS TPO 3 Ba/F
 가 150 mm T- 2

d.

가
 CHO 2 3가 (105, 5×10⁵ 106 /) 4가
 (, 50 nM, 100 nM, 200 nM 400nM) 10 cm
 96- 37 /5 % CO (, 600 nM, 8
 00 nM, 1000 nM 1200 nM) 가 , 96-

4. CHO TPO₃₃₂ TPO₁₅₃

5 % O₂ , 25-40 , p
 H TPO가

5. CHO TPO

(HCCF) 100 ℓ HCCF/ ℓ 300 Mℓ/ /cm² 0.01 M
 (pH 7.4), 0.15 M NaCl Blue Sepharose 6 Fast Flow (Pharmacia) 가
 3 5 , 3 5 0.01 M
 (pH 7.4), 2.0 M , TPO 3 5 0.01 M (pH 7.
 4), 2.0 M , 1.0 M NaCl

TPO Blue Sepharose Pool 8 16 Mℓ Blue Sepharose Pool/ Mℓ 50 Mℓ/ /cm²
 0.01 M (pH 7.4), 2.0 M 1.0 M NaCl Wheat Germ Lectin Sepharose
 6MB (Pharmacia) 가 , 2 3
 TPO 2 5 0.01 M (pH 7.4), 2.0 M 0.5 M N- -D-

Wheat Germ Lectin Pool 0.04 % C₁₂E₈ 0.1 % (TFA)
 0.2 0.5 mg / Mℓ 157 Mℓ/ /cm² 0.1 % TFA,
 0.04 % C₁₂E₈ C₄ (Vydac 214TP1022) 가
 0.1 % TFA, 0.04 % C₁₂E₈ 2 1 15
 0 30 % . 2 60 30 60 %
 . TPO 50 % SDS-PAGE

C₄ Pool 2 0.01 M (pH 7.4), 0.15 M NaCl , 10,000
 30,000 Amicon YM 6 0.01 M (pH 7.4), 0.15 M
 NaCl / 0.0
 1 % -80

NaCl, 0.01 % 2 5 % / 0.01 M (pH 7.4), 0.15 M
-80 Sephacryl D-300 HR (Pharmacia) 가 , 17 M² /cm²
TPO SDS-PAGE
0.22 μ , Millex-GV , 2-8

21

TPO

1. TPO

pMP21, pMP151, pMP41, pMP57 pMP202 TPO
 155
 pMP210-1, T8, -21, -22, -24, -25 TPO 153
 , TPO 6 , pMP251 TP
 O 2 pMP210-1
 TPO ((Yansura, D.G.) [
 Methods in Enzymology (Goeddel, D.V., Ed) 185 : 54-60, Academic Press, San Diego (1990)]).
 pMP1 pMP172 TPO .

(a) pMP1

pMP1 TPO 155 1 Mul-BamHI pPho21 pPho21
 phoA , Mul 20-21 STII
 pHGH1 (Chang, C.N. [Gene 55 : 189-196 (1987)])
 2 TPO 19-103 pRK5-h *mpl* (9) DNA 258
 Hinfl-PstI , 1-18 DNA T4-DNA 가 , PstI

5' CGCGTATGCCAGCCC GGCTCCTCCTGCTTGTGACCTCCGAGTCCTCAGTAAACTTCGTG
ATACGGTCGGGCCGAGGAGGACGAACACTGGAGGCTCAGGAGTCATTTGACGAAGCACTGA-5'
(SEQ ID NO :69)

(SEQ ID NO :70)

4 TPO 104-155 pRKhmpII 152 PstI-HaeIII .
pdh108 412 StuI-BamHI
(Scholtissek, S. [NAR 15 : 3185 (1987)]).

(b) pMP21

1 pMP21 STII 13 34 3 DNA TPO 155
1 XbaI - SphI pVEG31 pVEG31
pHGH207 - 1 (de Boer, H.A. [in Promoter Structure and Function (Rodriguez, R.L. Chamberlain, M.J. Ed.) 462, Praeger, New York (1982)])

2 DNA :

5'-CTAGAATTATGAAAAAGAATATCGCATTCTTCTTAA

TTAATACTTTTTCTTATAGCGTAAAGAAGAATTGCGC-5'

(SEQ ID NO : 71)

(SEQ ID NO : 72)

TPO 155 pMP1 1072 MluI - SphI .

(c) pMP151

pMP151 STII 7 , 8 , Xa TP

O 155 . 35 , pMP151 3 D

NA , 1 XbaI - SphI pVEG31 . 2

DNA :

5'-CTAGAATTATGAAAAAGAATATCGCATTTTCATCACCATCACCATCACCATC

ACATCGAAGGTCGTAGCC

TTAATACTTTTTCTTATAGCGTAAAGTAGTGGTAGTGGTAGTGGTAG

TGTAGCTTCCAGCAT -5'

(SEQ ID NO : 73)

(SEQ ID NO : 74)

TPO 154 pMP11 1064 BglI - SphI .

pMP11 STII pMP1 (pMP1

). .

(d) pMP202

pMP202 Xa 가 pMP151

. 36 , pMP202 3 DNA

1 XbaI - SphI pVEG31 . 2 DNA

5'-CTAGAATTATGAAAAAGAATATCGCATTTTCATCACCATCACCATCACCATCACATCGAACCACGTAGCC

TTAATACTTTTTCTTATAGCGTAAAGTAGTGGTAGTGGTAGTGGTAGTGGTAGCTTGGTGCAT -5'

(SEQ ID NO : 75)

(SEQ ID NO : 76)

pMP11 1064 BglI - SphI .

(e) pMP172

pMP172 TPO 153 , pMP210 . 37

, pMP172 3 DNA , 1

pLS32lamB . 2 EcoRI - HindIII

DNA : EcoRI - HgaI

5' - TCCACCCTCTGCGTCAGGT (SEQ ID NO : 77)

GGACGCAGTCCATCGA -5' (SEQ ID NO : 78)

(f) pMP210

pMP210 TPO 6 3 DNA 153 3 XbaI-SphI
8 pVEG31 2 DNA (Klenow) , XbaI HinfI
DNA TPO 6 :

5'-GCAGCAGTTCTAGAATTATGTCNCCNGCNCCNCCNGCNTGTGACCTCCGA

GTTCTCAGTAAA (SEQ ID NO : 79)

AACTGGAGGCT

CAAGAGTCATTTGACGAAGCACTGAGGGTACAGGAAG-5' (SEQ ID NO : 80)

3 TPO 19-153 pMP172 890 HinfI-SphI
3700 pMP210 (50
(Yansura, D.G. [Methods:A Companion to Methods in Enz
ymology 4 : 151-158 (1992)]). 8 TPO
가 5 DNA , 39 (SEQ ID NO : 23, 24, 25, 26,
27 28).

(g) pMP41

pMP41 STII 7 Xa
TPO 155 40 3 DN
A , 1 XbaI-SphI pVEG31 2
DNA :

5'-CTAGAATTATGAAAAAGAATATCGCATTTATCGAAGGTCGTAGCC

(SEQ ID NO : 81)

TTAATACTTTTTCTTATAGCGTAAATAGCTTCCAGCAT-5'

(SEQ ID NO : 82)

pMP11 1064 BglI-SphI

(h) pMP57

pMP57 STII 9 2 Lys-Arg TPO
155 2 ArgC
41 3 DNA 1
XbaI-SphI pVEG31 2 DNA :

5'-CTAGAATTATGAAAAAGAATATCGCATTTCTTCTTAAACGTAGCC

(SEQ ID NO : 83)

TTAATACTTTTTCTTATAGCGTAAAGAAGAATTTGCAT-5'

(SEQ ID NO : 84)

pMP11 1064 BglI-SphI

(i) pMP251

pMP251 TPO 2 가
 2 XbaI - ApaI , pMP21 2 DNA , 1 4
 pal pMP210-1 316 XbaI - A

2. TPO

TPO CaCl₂ 44C6 (w3110 tonA Δ rpoH_{ts} lon
 Δ clpP Δ galE) (600 nm)가 2-3 3
 7 50 μ g/M ℓ LB , LB 0.49 w/v%
 50 μ g/M ℓ M9 20 $\times$. 30 1
 , -3- 50 μ g/M ℓ 가 , 30 1
 5

22

TPO (Met⁻¹ 1-153)

TPO , TPO (Met⁻¹ 1-153) N C
 가 (23).

A. TPO (Met⁻¹ 1-153)

pMP210-1 TPO (Met⁻¹ 1-153)
 , 100 g Polytron homogenizer 1 ℓ , 5
 000 $\times$ g 30 Polytron homogenizer 1 ℓ
 rofluidizer (Microfluidics International) LH Cell Disrupter (LH Inceltech, Inc.) Mic
 , 2 R (refractile body) 5,000g 30 ,
 - 70

B. TPO (Met⁻¹ 1-153) 가

6-8 M 25 mM DTT () 5 () 20 mM
 , 4 1-3 TPO 가 , (6-8 M)
 TPO 30,000 $\times$ g 30 ,
 Superdex 200 (Pharmacia , 2.6 $\times$ 60 cm) , 20 mM (p
 H 6.0) 160 200 M ℓ TPO 10 mM DTT 5
 M ℓ / . TPO C4 (2 $\times$ 20cm VYDAC)
 0.1 % TFA () 30 % 가 .
 (60 30-60 %) 50 %
 TPO

C. TPO (Met⁻¹ 1-153)

40 M ℓ 0.1 % TFA/50 % 20 mg TPO
 360 M ℓ :

50 mM

0.3 M NaCl

5 mM EDTA

2 % CHAPS

25 %

5 mM

1 mM

pH 8.3

, 4 12-48 TPO -
 (). TFA 가 0.2 % , 0.45
 0.22 , 1/10 C4
 TPO (Met⁻¹ 1-153)
 TPO 45 % . TPO -
 TPO (Met⁻¹ 1-153) SDS C4
 95 % 가 , C4
 150 mM NaCl 0.01 % 80 (10 mM (pH 5.5), 1
 (pH 5.5) 10 mM (pH 7.4))가 .
 0 mM
 Ba/F3 TPO (3 pg/M ℓ),
 (<10 %) , 10 % ,
 30-50 %, 가 50 5 (X-100, -
 , CHAPS, CHAPSO, SDS, 20 80, Zwittergent 3-14)
 가 CHAPS (CHAPS CHAPSO)
 가 0.1 M 0.5 M NaCl CHAPS
 A (1-5 mM) () . 15 % . EDT
 가
 9 pH TPO (, , 7.5) 10-15
 % 가 4 TPO
 40-60 % (TPO TPO) C4
 TPO . TPO (, Superdex 200 R
)
 TPO (Met⁻¹ 1-153)가 4 , 3
 :
 1 : 1-4 2-3
 2 : 1-2 3-4
 3 : 1-3 2-4
 , TPO C4
 1 Ba/F3 가 .
 TPO 10-20 % .
 , 1). C4 (5-10 nmole) TPO 1-4 2-3 (= 1 :
 25). DTT 가 가 .
 , TPO 가 가 .
 TPO 1

-4 2-3

D. TPO (met 1-153)

TPO (Met⁻¹ 1-153) 3.3 pg/M $\varnothing$ (0.3 pM) . Ba/F3 , B
a/F3 , 1.9 ng/M $\varnothing$ (120 pM) . , . *mpl* ELISA
, TPO (Met⁻¹ 1-153) X-
(30 ng/).

23

TPO

3 TPO
(1) MLF - STII 13 TPO N- (1-155)
, C C Cys⁷ Cys¹⁵¹
:

MKKNIAFLLNAYA SPAPPAC CVRRA (SEQ ID NO : 85)

TPO 가
(2) H8MLF - STII 7 , 8 Xa IEGR TPO
N- (1-155) ,
Cys⁷ Cys¹⁵¹ : , C C

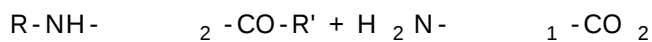
MKKNIAFH8HHHHHHHIEGRSPAPPAC CVRRA (SEQ ID NO : 86)

IEGR Xa
N- 155 TPO
(3) T-H8MLF - IEPR TPO N- (2)
, C C Cys⁷ Cys¹⁵¹
:

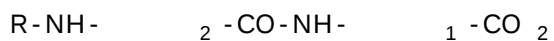
MKKNIAFH8HHHHHHHIEPRSPAPPAC CVRRA (SEQ ID NO : 87)

155 TPO N-
A. TPO (1), (2) (3) , 가
R TPO (Met⁻¹ 1-153) 22 22
TPO (Met⁻¹ 1-153) , 가 22
TPO (0.1 % TFA C4 , TPO ,
M () Ba/F3 , 2-5 p
B. (2) (3) N- TPO (1-155)
TPO (2) (3) TPO N- 가
(2) (3) C4 , 2
Xa

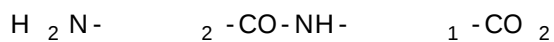
TPO (2), 1 M (pH 8), NaCl, CaCl₂ 0.1 M, 2 mM, 가, 50 mM Xa (New England Biolabs), pH 8, 1 : 25, 1 : 100, SDS, C4, (2), N-SPAPP, B-N-가, TTAHKDP (SEQ ID NO : 88), 118, 17000, 1, 가, Xa, 12000, 5000, 2, 1, 4, 가, TPO (1-155), N-, -4 pmole, 가, (3), 1 : 25, 1 : 50, TPO, 50 mM (pH 8), 2% CHAPS, 0.3 M NaCl, 5 mM EDTA, (Calbiochem), SDS, C4, 90 %, TPO, Xa, N- (5 %), TPO, Xa, TPO, Ba/F3, 0.2-0.4 pmole, ELISA, 2-4 ng/M $\emptyset$, 27, (120-240 pmole), HPLC, 10 mM, (pH 5.5), 10 mM, 150 mM NaCl, 0.01 % (pH 7.4), 80, 10 mM, (pH 5.5), HPLC, SDS, PLC, N-, TPO, 30 ng/, 24, mpl, mpl, (hML)가, 가, hML, BPN, 가, (S221C/P225A), Biochem. 30 : 4151-4159 (1991)], A), (Jackson DNA), [Science (1994)], 가, hML₁₅₃, N-, C-, HPLC, 가, N-, C-, N-, C->N, 가, 50, 가, 1, hML



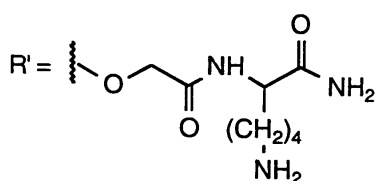
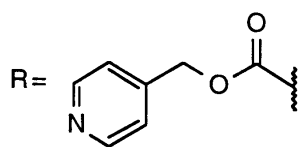
↓ 1) 가



↓ 2) Zn/CH₃CO₂H



↓ 3) 1+2



가 hML 153 18-25 'EPO- 7 13
18-25mer . . .

[13]

	(glc-K-NH ₂)	-NH ₂	% 가	%
1 (23/24)	HVLH (: 89)	SRLS (: 90)	92	08
(22/23)	SHVL (: 91)	HSRL (: 92)	48	52
2 (46/47)	AVDF (: 93)	SLGE (: 94)	22	78
3 (69/70)	AVTL (: 95)	LLEG (: 96)	53	47
4 (89/90)	LSSL (: 97)	LGQL (: 98)	95	05
(88/89)	C(acm)LSS (: 99)	LLGQ (: 100)	00	00
(90/91)	SLL (: 101)	GQLS (: 102)	45	55
(88/89)	CLSS (: 103)	LLGQ (: 100)	90	10
5 (107/108)	LQSL (: 104)	LGTQ (: 105)	99	01
(106/107)	ALQS (: 106)	LLGT (: 107)	70	30
6 (128/129)			60	40

	NAIF (: 108)	LSFQ (: 109)		
--	------------------	------------------	--	--

14 가
N- 가
, HF (iNOC) (Veber [J. Org. Chem. 42 : 3286-3289 (1977)]). (Zn/CH₃CO₂H) N- 가 (glc-K-NH₂) C- (Abrahmsen [Biochem. 30 : 4151-4159 (1991)]). iNOC , glc-K-NH₂ 2 . EPO , 7 151 28 85 . HPLC , (acm) 7 151 28 85 , acm , 7 151 가 28 85 acm , 7 151 28 85 Cys .

[14]

<i>I</i>
1 (SEQ ID NO : 110) iNOC-HN-SPAPPACDLRVLSKLLRDSHVL-glc-K-NH ₂ (1-22)
2 (SEQ ID NO : 111) iNOC-HN-HSRLSQCPEVHPLPTPVLLPAVDF-glc-K-NH ₂ (23-46)
3 (SEQ ID NO : 112) iNOC-HN-SLGEWKTQMEETKAQDILGAVTL-glc-K-NH ₂ (47-69)
4 (SEQ ID NO : 113) iNOC-HN-LLEGVMAARGQLGPTCLSSLL-glc-K-NH ₂ (70-90)
5 (SEQ ID NO : 114) iNOC-HN-GQLSGQVRLLLGALQS-glc-K-NH ₂ (90-106)
6 (SEQ ID NO : 115) iNOC-HN-LLGTQLPPQGRTTAHKDPNAIF-glc-K-NH ₂ (107-128)
7 (SEQ ID NO : 116) H ₂ N-LSFQHLLRGKVRFLMLVGGSTLCVR-CO ₂ (129-153)

25 100 mM (pH 8 : 5 μM 가)
, C- (2-5 mM)
(100 mM 1 mg/Mø, pH 8) 가 ~ 5 μM , 가 10×
NH₂ 가 3-5 glc-K-
PLC (0.1 % TFA CH₃CN/H₂O) 25 . HPLC C18 H
, . HCl (iN
OC) . hML 153 hML 154-332

hML

hML

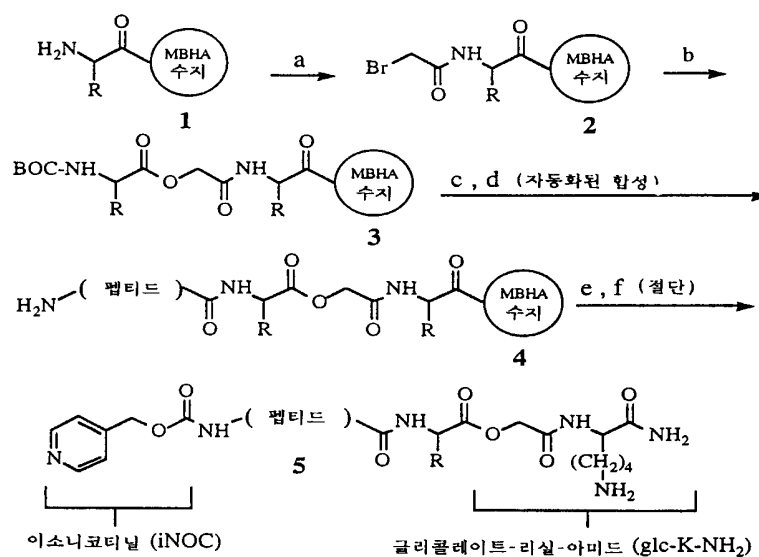
hML

가

(14)

2

반응도 2. 단편 결합을 위한 펩티드 단편의 고체상 합성



- a) (DMA) (MBHA) 1 (0.63 meq./qm., Advanced ChemTech) 1 25
(5 eq.) (5 eq.)
- b) DMA , Boc (3 eq., Bachem) 24 50
(DMF) (6 eq.)
3 DMF (3×) (CH₂Cl₂:
3×) 3 (Appl
ied Biosystems 430 A)
- c) N- α -Boc CH₂Cl₂ 45 %
- d) Boc (5 eq.) DMA -1- - - - ()
(BOP, 4 eq.) N- (NMM, 10 eq.) , 1-2
- e) N- α -Boc (TFA/CH₂Cl₂) 4 , (iNOC) 24 25
DMA 4- -2,4- (3 eq.) NMM (6 eq.) (4)
- f) 1 0 HF (5 % /5 %) iN
OC - - 5 , C18 HPLC (0.1 % TFA
CH₃CN/H₂O)

American Type Culture Collection

Escherichia coli, DH10B-pBSK-h *mpI* 4.8 : ATCC CRL 69575, 1994 2 24 .

, pSV15.ID.LL.MLORF : ATCC CRL 75958, 1994 12 2 .

CHO DP-12 , ML 1/50 MCB (#1594) : ATCC CRL 11770, 1994 12 6 .

(ATCC). 30
ATCC

(TPO), TPO DNA, TPO
TPO가

(v) 컴퓨터 판독 형태:

(A) 미디엄 타입: 5.25 인치, 360 kb 플로피 디스크

(B) 컴퓨터: IBM PC compatible

(C) 운영 체제: PC-DOS/MS-DOS

(D) 소프트웨어: patin (Genentech)

(vi) 현재 출원 데이터:

(A) 출원 번호:

(B) 출원일:

(C) 분류:

(vii) 선행 출원 데이터:

(A) 출원 번호: 08/176553

(B) 출원일: 1994. 1. 3

(vii) 선행 출원 데이터:

(A) 출원 번호: 08/348657

(B) 출원일: 1994. 12. 2

(vii) 선행 출원 데이터:

(A) 출원 번호: 08/185607

(B) 출원일: 1994. 1. 21

(vii) 선행 출원 데이터:

(A) 출원 번호: 08/348658

서열 목록

(1) 종합 정보:

(i) 출원인: 제넨테크, 인크.

이튼, 단 엘.

드 소바지, 프레데릭 제이.

(ii) 발명의 명칭: 트롬보포이에틴

(iii) 서열의 개수: 144

(iv) 주소:

(A) 명칭: 제넨테크, 인크.

(B) 가: 포인트 산 브루노 불리바드 460

(C) 도시: 사우쓰 샌프란시스코

(D) 주: 캘리포니아

(E) 국가: 미합중국

(F) 우편 번호 (ZIP): 94080

(B) 출원일: 1994. 12. 2

(vii) 선행 출원 데이터:

(A) 출원 번호: 08/196689

(B) 출원일: 1994. 2. 15

(vii) 선행 출원 데이터:

(A) 출원 번호: 08/223263

(B) 출원일: 1994. 4. 4

(vii) 선행 출원 데이터:

(A) 출원 번호: 08/249376

(B) 출원일: 1994. 5. 25

(viii) 변호사/대리인 정보:

(A) 이름: 윈터, 다릴 비.

(B) 등록 번호: 32,637

(C) 참고/부전 번호: 871P5PCT

(ix) 통신 정보:

(A) 전화 번호: 415/225-1249

(B) 텔레팩스: 415/952-9881

(C) 텔렉스: 910/371-7168

(2) SEQ ID NO:1에 대한 정보:

(i) 서열 특성:

(A) 길이: 353 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:1

```

Met Glu Leu Thr Glu Leu Leu Leu Val Val Met Leu Leu Leu Thr
-21 -20          -15          -10
Ala Arg Leu Thr Leu Ser Ser Pro Ala Pro Pro Ala Cys Asp Leu
  -5          1          5
Arg Val Leu Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser
 10          15          20
Arg Leu Ser Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val
 25          30          35
Leu Leu Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln
 40          45          50
Met Glu Glu Thr Lys Ala Gln Asp Ile Leu Gly Ala Val Thr Leu
 55          60          65
Leu Leu Glu Gly Val Met Ala Ala Arg Gly Gln Leu Gly Pro Thr
 70          75          80
Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln Val Arg Leu
 85          90          95
Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr Gln Leu Pro Pro
100          105          110
Gln Gly Arg Thr Thr Ala His Lys Asp Pro Asn Ala Ile Phe Leu
115          120          125
Ser Phe Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu
130          135          140
Val Gly Gly Ser Thr Leu Cys Val Arg Arg Ala Pro Pro Thr Thr
145          150          155
Ala Val Pro Ser Arg Thr Ser Leu Val Leu Thr Leu Asn Glu Leu
160          165          170
Pro Asn Arg Thr Ser Gly Leu Leu Glu Thr Asn Phe Thr Ala Ser
175          180          185
Ala Arg Thr Thr Gly Ser Gly Leu Leu Lys Trp Gln Gln Gly Phe
190          195          200

```

Arg Ala Lys Ile Pro Gly Leu Leu Asn Gln Thr Ser Arg Ser Leu
 205 210 215
 Asp Gln Ile Pro Gly Tyr Leu Asn Arg Ile His Glu Leu Leu Asn
 220 225 230
 Gly Thr Arg Gly Leu Phe Pro Gly Pro Ser Arg Arg Thr Leu Gly
 235 240 245
 Ala Pro Asp Ile Ser Ser Gly Thr Ser Asp Thr Gly Ser Leu Pro
 250 255 260
 Pro Asn Leu Gln Pro Gly Tyr Ser Pro Ser Pro Thr His Pro Pro
 265 270 275
 Thr Gly Gln Tyr Thr Leu Phe Pro Leu Pro Pro Thr Leu Pro Thr
 280 285 290
 Pro Val Val Gln Leu His Pro Leu Leu Pro Asp Pro Ser Ala Pro
 295 300 305
 Thr Pro Thr Pro Thr Ser Pro Leu Leu Asn Thr Ser Tyr Thr His
 310 315 320
 Ser Gln Asn Leu Ser Gln Glu Gly
 325 330 332

(2) SEQ ID NO:2에 대한 정보:

(i) 서열 특성:

(A) 길이: 1795 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:2

TCTTCCTACC CATCTGCTCC CCAGAGGGCT GCCTGCTGTG CACTTGGGTC 50
 CTGGAGCCCT TCTCCACCCG GATAGATTCC TCACCCCTTG CCCGCCTTTG 100
 CCCCACCCTA CTCTGCCCAG AAGTGCAAGA GCCTAAGCCG CCTCCATGGC 150
 CCCAGGAAGG ATTCAGGGGA GAGGCCCCAA ACAGGGAGCC ACGCCAGCCA 200

GACACCCCGG CCAGA										ATG GAG CTG ACT TTG CTC CTC				239
										Met Glu Leu Thr Glu Leu Leu Leu				
										-21 -20 -15				
GTG GTC ATG CTT CTC CTA ACT GCA AGG CTA ACG CTG TCC	278													
Val Val Met Leu Leu Leu Thr Ala Arg Leu Thr Leu Ser														
										-10 -5				
AGC CCG GCT CCT CCT GCT TGT GAC CTC CGA GTC CTC AGT	317													
Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser														
										1 5 10				
AAA CTG CTT CGT GAC TCC CAT GTC CTT CAC AGC AGA CTG	356													
Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu														
										15 20 25				
AGC CAG TGC CCA GAG GTT CAC CCT TTG CCT ACA CCT GTC	395													
Ser Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val														
										30 35				
CTG CTG CCT GCT GTG GAC TTT AGC TTG GGA GAA TGG AAA	434													
Leu Leu Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys														
										40 45 50				
ACC CAG ATG GAG GAG ACC AAG GCA CAG GAC ATT CTG GGA	473													
Thr Gln Met Glu Glu Thr Lys Ala Gln Asp Ile Leu Gly														
										55 60 65				
GCA GTG ACC CTT CTG CTG GAG GGA GTG ATG GCA GCA CGG	512													
Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala Ala Arg														
										70 75				
GGA CAA CTG GGA CCC ACT TGC CTC TCA TCC CTC CTG GGG	551													
Gly Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly														
										80 85 90				
CAG CTT TCT GGA CAG GTC CGT CTC CTC CTT GGG GCC CTG	590													
Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu														
										95 100				
CAG AGC CTC CTT GGA ACC CAG CTT CCT CCA CAG GGC AGG	629													
Gln Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg														
										105 110 115				
ACC ACA GCT CAC AAG GAT CCC AAT GCC ATC TTC CTG AGC	668													
Thr Thr Ala His Lys Asp Pro Asn Ala Ile Phe Leu Ser														
										120 125 130				
TTC CAA CAC CTG CTC CGA GGA AAG GTG CGT TTC CTG ATG	707													

Phe Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu Met
 135 140
 CTT GTA GGA GGG TCC ACC CTC TGC GTC AGG CGG GCC CCA 746
 Leu Val Gly Gly Ser Thr Leu Cys Val Arg Arg Ala Pro
 145 150 155
 CCC ACC ACA GCT GTC CCC AGC AGA ACC TCT CTA GTC CTC 785
 Pro Thr Thr Ala Val Pro Ser Arg Thr Ser Leu Val Leu
 160 165
 ACA CTG AAC GAG CTC CCA AAC AGG ACT TCT GGA TTG TTG 824
 Thr Leu Asn Glu Leu Pro Asn Arg Thr Ser Gly Leu Leu
 170 175 180
 GAG ACA AAC TTC ACT GCC TCA GCC AGA ACT ACT GGC TCT 863
 Glu Thr Asn Phe Thr Ala Ser Ala Arg Thr Thr Gly Ser
 185 190 195
 GGG CTT CTG AAG TGG CAG CAG GGA TTC AGA GCC AAG ATT 902
 Gly Leu Leu Lys Trp Gln Gln Gly Phe Arg Ala Lys Ile
 200 205
 CCT GGT CTG CTG AAC CAA ACC TCC AGG TCC CTG GAC CAA 941
 Pro Gly Leu Leu Asn Gln Thr Ser Arg Ser Leu Asp Gln
 210 215 220
 ATC CCC GGA TAC CTG AAC AGG ATA CAC GAA CTC TTG AAT 980
 Ile Pro Gly Tyr Leu Asn Arg Ile His Glu Leu Leu Asn
 225 230
 GGA ACT CGT GGA CTC TTT CCT GGA CCC TCA CGC AGG ACC 1019
 Gly Thr Arg Gly Leu Phe Thr Pro Gly Pro Ser Arg Arg Thr
 235 240 245
 CTA GGA GCC CCG GAC ATT TCC TCA GGA ACA TCA GAC ACA 1058
 Leu Gly Ala Pro Asp Ile Ser Ser Gly Thr Ser Asp Thr
 250 255 260
 GGC TCC CTG CCA CCC AAC CTC CAG CCT GGA TAT TCT CCT 1097
 Gly Ser Leu Pro Pro Asn Leu Gln Pro Gly Tyr Ser Pro
 265 270
 TCC CCA ACC CAT CCT CCT ACT GGA CAG TAT ACG CTC TTC 1136
 Ser Pro Thr His Pro Pro Thr Gly Gln Tyr Thr Leu Phe
 275 280 285
 CCT CTT CCA CCC ACC TTG CCC ACC CCT GTG GTC CAG CTC 1175
 Pro Leu Pro Pro Thr Leu Pro Thr Pro Val Val Gln Leu
 290 295
 CAC CCC CTG CTT CCT GAC CCT TCT GCT CCA ACG CCC ACC 1214
 His Pro Leu Leu Pro Asp Pro Ser Ala Pro Thr Pro Thr
 300 305 310

CCT ACC AGC CCT CTT CTA AAC ACA TCC TAC ACC CAC TCC 1253
 Pro Thr Ser Pro Leu Leu Asn Thr Ser Tyr Thr His Ser
 315 320 325

CAG AAT CTG TCT CAG GAA GGG T AAGGT TCTCAGACAC 1290
 Gln Asn Leu Ser Gln Glu Gly
 330 332

TGCCGACATC AGCATTGTCT CATGTACAGC TCCCTTCCCT GCAGGGCGCC 1340
 CCTGGGAGAC AACTGGACAA GATTTCTCTAC TTTCTCCTGA AACCCAAAGC 1390
 CCTGGTAAAA GGGATACACA GGACTGAAAA GGGAATCATT TTTCACTGTA 1440
 CATTATAAAC CTTTCTGAGC TATTTTTTTTA AGCTATCAGC AATACTCATC 1490
 AGAGCAGCTA GCTCTTTGGT CTATTTTCTG CAGAAATTG CAACTCACTG 1540
 ATTCTCTACA TGCTCTTTTT CTGTGATAAC TCTGCAAAGG CCTGGGCTGG 1590
 CCTGGCAGTT GAACAGAGGG AGAGACTAAC CTTGAGTCAG AAAACAGAGA 1640
 AAGGGTAATT TCCTTTGCTT CAAATTCAAG GCCTTCCAAC GCCCCCATCC 1690
 CCTTACTAT CATTCTCAGT GGGACTCTGA TCCCATATTC TTAACAGATC 1740
 TTACTCTTG AGAAATGAAT AAGCTTTCTC TCAGAAAAAA AAAAAAAAAA 1790
 AAAAA 1795

(2) SEQ ID NO:3에 대한 정보:

(i) 서열 특성:

(A) 길이: 42 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:3

Leu Leu Leu Val Val Met Leu Leu Leu Thr Ala Arg Leu Thr Leu
 -16 -15 -10 -5

Ser Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys
 1 5 10

Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu
 15 20 25 26

(2) SEQ ID NO:4에 대한 정보:

(i) 서열 특성:

(A) 길이: 390 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:4

```

GAATTCCTGG AATACCAGCT GACAATGATT TCCTCCTCAT CTTTCAACCT 50
CACCTCTCCT CATCTAAGAA   TTG CTC CTC GTG GTC ATG CTT 91
                        Leu Leu Leu Val Val Met Leu
                        -16 -15                      -10

CTC CTA ACT GCA AGG CTA ACG CTG TCC AGC CCG GCT CCT 130
Leu Leu Thr Ala Arg Leu Thr Leu Ser Ser Pro Ala Pro
                        -5                      1

CCT GCT TGT GAC CTC CGA GTC CTC AGT AAA CTG CTT CGT 169
Pro Ala Cys Asp Leu Arg Val Leu Ser Lys Leu Leu Arg
  5                10                15

GAC TCC CAT GTC CTT CAC AGC AGA CTG GTGA GAACTCCCAA 210
Asp Ser His Val Leu His Ser Arg Leu
  20                25  26

CATTATCCCC TTTATCCGCG TAACTGGTAA GACACCCATA CTCCCAGGAA 260
GACACCATCA CTTCTCTTAA CTCCTTGACC CAATGACTAT TCTTCCCAT 310
TTGTCCCCAC CTACTGATCA CACTCTCTGA CAAGAATTAT TCTTCACAAT 360
ACAGCCCGCA TTTAAAAGCT CTCGTCTAGA 390

```

(2) SEQ ID NO:5에 대한 정보:

(i) 서열 특성:

- (A) 길이: 390 염기
- (B) 타입: 핵산
- (C) 나선 구조: 단일나선
- (D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:5

```
TCTAGACGAG AGCTTTTAAA TGCGGGCTGT ATTGTGAAGA ATAATTCTTG 50
TCAGAGAGTG TGATCAGTAG GTGGGGACAA TATGGGAAGA ATAGTCATTG 100
GGTCAAGGAG TTAGAGGAAG TGATGGTGTC TTCCTGGGAG TATGGGTGTC 150
TTACCAGTTA CGCGGATAAA GGGGATAATG TTGGGAGTTC TCACCAGTCT 200
GCTGTGAAGG ACATGGGAGT CACGAAGCAG TTTACTGAGG ACTCGGAGGT 250
CACGAAGCAGG AGGAGCCGGG CTGGACAGCG TTAGCCTTGC AGTTAGGAGA 300
AGCATGACCA CGAGGAGCAA TTCTTAGATG AGGAGAGGTG AGGTTGAAAG 350
ATGAGGAGGA AATCATTGTC AGCTGGTATT CCAGGAATTC 390
```

(2) SEQ ID NO:6에 대한 정보:

(i) 서열 특성:

- (A) 길이: 332 아미노산
- (B) 타입: 아미노산
- (D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:6

```
Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys Leu
 1              5              10              15
Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro
                20              25              30
```

Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp
 35 40 45
 Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala
 50 55 60
 Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met
 65 70 75
 Ala Ala Arg Gly Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu
 80 85 90
 Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
 95 100 105
 Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala
 110 115 120
 His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu
 125 130 135
 Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu
 140 145 150
 Cys Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr
 155 160 165
 Ser Leu Val Leu Thr Leu Asn Glu Leu Pro Asn Arg Thr Ser Gly
 170 175 180
 Leu Leu Glu Thr Asn Phe Thr Ala Ser Ala Arg Thr Thr Gly Ser
 185 190 195
 Gly Leu Leu Lys Trp Gln Gln Gly Phe Arg Ala Lys Ile Pro Gly
 200 205 210
 Leu Leu Asn Gln Thr Ser Arg Ser Leu Asp Gln Ile Pro Gly Tyr
 215 220 225
 Leu Asn Arg Ile His Glu Leu Leu Asn Gly Thr Arg Gly Leu Phe
 230 235 240
 Pro Gly Pro Ser Arg Arg Thr Leu Gly Ala Pro Asp Ile Ser Ser
 245 250 255
 Gly Thr Ser Asp Thr Gly Ser Leu Pro Pro Asn Leu Gln Pro Gly
 260 265 270
 Tyr Ser Pro Ser Pro Thr His Pro Pro Thr Gly Gln Tyr Thr Leu
 275 280 285
 Phe Pro Leu Pro Pro Thr Leu Pro Thr Pro Val Val Gln Leu His
 290 295 300
 Pro Leu Leu Pro Asp Pro Ser Ala Pro Thr Pro Thr Pro Thr Ser
 305 310 315

Pro Leu Leu Asn Thr Ser Tyr Thr His Ser Gln Asn Leu Ser Gln
 320 325 330
 Glu Gly
 332

(2) SEQ ID NO:7에 대한 정보:

(i) 서열 특성:

(A) 길이: 166 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:7

Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr
 1 5 10 15
 Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala
 20 25 30
 Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala
 50 55 60
 Val Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu
 65 70 75
 Arg Gly Gln Ala Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro
 80 85 90
 Leu Gln Leu His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu
 95 100 105
 Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser
 110 115 120
 Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala
 125 130 135
 Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg
 140 145 150

Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp
 155 160 165
 Arg
 166

(2) SEQ ID NO:8에 대한 정보:

(i) 서열 특성:

(A) 길이: 328 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:8

Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys Leu
 1 5 10 15
 Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro
 20 25 30
 Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp
 35 40 45
 Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala
 50 55 60
 Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met
 65 70 75
 Ala Ala Arg Gly Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu
 80 85 90
 Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
 95 100 105
 Ser Leu Leu Gly Thr Gln Gly Arg Thr Thr Ala His Lys Asp Pro
 110 115 120
 Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val
 125 130 135
 Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg Arg
 140 145 150

```

Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser Leu Val Leu
      155                      160                      165

Thr Leu Asn Glu Leu Pro Asn Arg Thr Ser Gly Leu Leu Glu Thr
      170                      175                      180

Asn Phe Thr Ala Ser Ala Arg Thr Thr Gly Ser Gly Leu Leu Lys
      185                      190                      195

Trp Gln Gln Gly Phe Arg Ala Lys Ile Pro Gly Leu Leu Asn Gln
      200                      205                      210

Thr Ser Arg Ser Leu Asp Gln Ile Pro Gly Tyr Leu Asn Arg Ile
      215                      220                      225

His Glu Leu Leu Asn Gly Thr Arg Gly Leu Phe Pro Gly Pro Ser
      230                      235                      240

Arg Arg Thr Leu Gly Ala Pro Asp Ile Ser Ser Gly Thr Ser Asp
      245                      250                      255

Thr Gly Ser Leu Pro Pro Asn Leu Gln Pro Gly Tyr Ser Pro Ser
      260                      265                      270

Pro Thr His Pro Pro Thr Gly Gln Tyr Thr Leu Phe Pro Leu Pro
      275                      280                      285

Pro Thr Leu Pro Thr Pro Val Val Gln Leu His Pro Leu Leu Pro
      290                      295                      300

Asp Pro Ser Ala Pro Thr Pro Thr Pro Thr Ser Pro Leu Leu Asn
      305                      310                      315

Thr Ser Tyr Thr His Ser Gln Asn Leu Ser Gln Glu Gly
      320                      325                      328

```

(2) SEQ ID NO:9에 대한 정보:

(i) 서열 특성:

(A) 길이: 265 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:9

```

Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys Leu
 1           5           10           15
Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro
          20           25           30
Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp
          35           40           45
Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala
          50           55           60
Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met
          65           70           75
Ala Ala Arg Gly Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu
          80           85           90
Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
          95          100          105
Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala
          110          115          120
His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu
          125          130          135
Arg Gly Lys Asp Phe Trp Ile Val Gly Asp Lys Leu His Cys Leu
          140          145          150
Ser Gln Asn Tyr Trp Leu Trp Ala Ser Glu Val Ala Ala Gly Ile
          155          160          165
Gln Ser Gln Asp Ser Trp Ser Ala Glu Pro Asn Leu Gln Val Pro
          170          175          180
Gly Pro Asn Pro Arg Ile Pro Glu Gln Asp Thr Arg Thr Leu Glu
          185          190          195
Trp Asn Ser Trp Thr Leu Ser Trp Thr Leu Thr Gln Asp Pro Arg
          200          205          210
Ser Pro Gly His Phe Leu Arg Asn Ile Arg His Arg Leu Pro Ala
          215          220          225
Thr Gln Pro Pro Ala Trp Ile Phe Ser Phe Pro Asn Pro Ser Ser
          230          235          240
Tyr Trp Thr Val Tyr Ala Leu Pro Ser Ser Thr His Leu Ala His
          245          250          255
Pro Cys Gly Pro Ala Pro Pro Pro Ala Ser
          260          265

```

(2) SEQ ID NO:10에 대한 정보:

(i) 서열 특성:

(A) 길이: 261 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:10

```

Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys Leu
 1          5          10          15
Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro
          20          25          30
Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp
          35          40          45
Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala
          50          55          60
Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met
          65          70          75
Ala Ala Arg Gly Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu
          80          85          90
Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
          95          100          105
Ser Leu Leu Gly Thr Gln Gly Arg Thr Thr Ala His Lys Asp Pro
          110          115          120
Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Asp
          125          130          135
Phe Trp Ile Val Gly Asp Lys Leu His Cys Leu Ser Gln Asn Tyr
          140          145          150
Trp Leu Trp Ala Ser Glu Val Ala Ala Gly Ile Gln Ser Gln Asp
          155          160          165
Ser Trp Ser Ala Glu Pro Asn Leu Gln Val Pro Gly Pro Asn Pro
          170          175          180
Arg Ile Pro Glu Gln Asp Thr Arg Thr Leu Glu Trp Asn Ser Trp
          185          190          195

```

Thr Leu Ser Trp Thr Leu Thr Gln Asp Pro Arg Ser Pro Gly His
 200 205 210
 Phe Leu Arg Asn Ile Arg His Arg Leu Pro Ala Thr Gln Pro Pro
 215 220 225
 Ala Trp Ile Phe Ser Phe Pro Asn Pro Ser Ser Tyr Trp Thr Val
 230 235 240
 Tyr Ala Leu Pro Ser Ser Thr His Leu Ala His Pro Cys Gly Pro
 245 250 255
 Ala Pro Pro Pro Ala Ser
 260 261

(2) SEQ ID NO:11에 대한 정보:

(i) 서열 특성:

(A) 길이: 7849 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:11

CCCAGCCTCC TTTCTCTTGT TCCCTGGTCA TGCCTGCCTC CCTGTCTCCT 50
 GTCTCTCCCT CCCACACACA CCCACTATCC TCCCAGCTAT CCCTACACCC 100
 TCCTTCCTAA TCTTGGGAGA CATCTCGTCT GGCTGGACGG GAAAATTCCA 150
 GGATCTAGGC CACACTTCTC AGCAGACATG CCCATCCTTG GGGAGGAGGA 200
 ACAGGAGAGA GCCTGAGGAA GTTCTGGGGG ACAGGGGGAT GATGGGATCA 250
 AGGTCAGGCC AGGAAGCCCC TGAGGACAGA GACTGTGGGG AGACTGGGAC 300
 TGGGAAGAAA GCAAAGGAGC TAGAGCCAGG GCCAAAGGAA AAGGGGGGCC 350
 AGCAGGGAGG TATTTGCGGG GGAGGTCCAG CAGCTGTCTT TCCTAAGACA 400
 GGGACACATG GGCCTGGTTA TTCCTCTTGT CACATGTGGA ACGGTAGGAG 450

ATGGAAGACG GAGACAGAAC AAGCAAAGGA GGGCCCTGGG CACAGAGGTC 500
 TGTGTGTGTA GCCATCCAAG CCACTGGACC CCAGCAGACG AGCACCTAAG 550
 CTCAGGCTTA ACCCAGTGCA CGTGTGCGCA CATACTGTG CCCCACACCT 600
 GACAGTCCAC TCAACCCGTC CAAACCCTTT CCCCATAACA CCAACCCATA 650
 ACAGGAGATT TCTCTCATGT GGGCAATATC CGTGTTCCTA CTTGCGAAAG 700
 GGGAAATGACA AGATAGGACT CCCTAGGGGA TTACAGAAAG AAAAGCAGGA 750
 AAGCAAGCAT CCTGTTGGAT TTCAGCAGCA GGTATGATGT CCAGGGAAAA 800
 GAAATTTGGA TAGCCAGGGA GTGAAAACCC CACCAATCTT AAACAAGACC 850
 TCTGTGCTTC TTCCCCAGCA ACACAAATGT CCTGCCAGAT TCCTCCTGGA 900
 AAAAAACTTC TGCTCCTGTC CCCCTCCAGG TCCCAGGTG CCCATGTCCA 950
 GGAAAAGATG GATCCCCCTA TCCAAATCTT CTCCGTGGTG TGTGTGGGTG 1000
 GAGGAGTGGA CCCTGGTCCA GGCAGGGGCT CCAGGGAAGA GAAGGCGTCA 1050
 CTTCCGGGGG CCTTCACCAG TGTCTGGTGG CTCCCTTCTC TGATTGGGCA 1100
 GAAGTGGCCC AGGCAGGCGT ATGACCTGCT GCTGTGGAGG GGCTGTGCCC 1150
 CACCGCCACA TGTCTTCTA CCCATCTGCT CCCCAGAGGG CTGCCTGCTG 1200
 TGCACTTGGG TCCTGGAGCC CTTCTCCACC CGGTGAGTGG CCAGCAGGGT 1250
 GTGGGGTTAT GTGAGGGTAG AAAGGACAGC AAAGAGAAAT GGGCTCCCAG 1300
 CTGGGGGAGG GGCAGGCAAA CTGGAACCTA CAGGCACTGA CCTTTGTCTA 1350
 GAAGAGTGTA GCCTTCCCAG AATGGGAGGA GCAGGGCAGA GCAGGGGTAG 1400
 GGGGTGGGGT GCTGTTTCTT GAGGGACTGA TCACTTACTT GGTGGAATAC 1450
 AGCACAGCCC TGGCTGGCCC TAAGGAAAGG GGACATGAGC CCAGGGAGAA 1500
 AATAAGAGAG GGAGCTGCAC TTAGGGCTTA GCAAACACAG TAGTAAGATG 1550
 GACACAGCCC CAATCCCCAT TCTTAGCTGG TCATTCTCTG TTAGCTTAAG 1600
 GTTCTGAATC TGGTGTGGG GAAGCTGGGC CAGGCAAGCC AGGGCGCAAG 1650
 GAGAGGGTAA TGGGAGGAGG GCCCACTCAT GTTGACAGAC CTACAGGAAA 1700
 TCCCAATATT GAATCAGGTG CAAGCCTCTT TGCACAACTT GTGAAAGGAG 1750
 GAGGAAGCCA TGTGGGGGGT CCTGTGAAGG AACCGGAAGG GGTCTGCCA 1800
 AGGGGGCAGG GAGGCAGGTG TGAGCTATGA GACAGATATG TTAGTGGGCG 1850

CCTAAGACAA GGTAAGCCCC TAAGGTGGGC ATCACCAGC AGGTGCCCCGT 1900
 TCCTGGGCAG CTGGTCTCAG GAAGGAAGTC CCAGAACTGT TAGCCCATCT 1950
 CTTGGCCTCA GATAATGGAG TATTTCAGGA CTTGGAGTCC AAAGAAAAGC 2000
 TCCAGTGGCT TTATGTGTGG GGGTAGATAG GGAAAGAATA GAGGTTAATT 2050
 TCTCCCATAC CGCCTTTTAA TCCTGACCTC TAGTGGTCCC AGTTACAGCT 2100
 TTGTGCAGTT CCCCTCCCCA GCCCCACTCC CCACCGCAGA AGTTACCCCT 2150
 CAACATATTG CGCCCCGTTG CCAGTTCCTC ACCCAGGCCC TGCATCCCAT 2200
 TTTCCACTCT CTTCTCCAGG CTGAAGCCAC AATACTTTCC TTCTCTATCC 2250
 CCATCCCAGA TTTTCTCTGA CCTAACACC AAGGTTGCTC AGAATTTAAG 2300
 GCTAATTAAG ATATGTGTGT ATACATATCA TGTCTGCTG CTCTCAGCAG 2350
 GGGTAGGTGG CACCAAATCC GTGTCCGATT CACTGAGGAG TCCTGACAAA 2400
 AAGGAGACAC CATATGCTTT CTTGCTTTCT TTCTTTCTTT CTTTCTTTT 2450
 TTTTTTTTGA GACGGAGTTT CACTCTTATT GCCCAGGCTG GAGTGCAATG 2500
 GTGCGATCTC GGCTCACCAC AAACCTCCGC CTCCCAGGTA CAAGCGATTC 2550
 TCCTGTCTCA GCCTCCCAAG TAGCTTGGAT TACAGGCATG AGCCACCACA 2600
 CCCTGCTAGT TTTTTTGTAT TTCGTAGAGC CGGGGTTTCA CCATGTTAGT 2650
 GAGGCTGGTG GCGAACTCCT GACCTCAGGT GATCCACCCG CCTTGGAATC 2700
 CCAAAGTGCT GGGATTACAG GCATGAGCCA CTGCACCCGG CACACCATAT 2750
 GCTTTCATCA CAAGAAAATG TGAGAGAATT CAGGGCTTTG GCAGTTCAG 2800
 GCTGGTCAGC ATCTCAAGCC CTCCCAGCA TCTGTTCAAC CTGCCAGGCA 2850
 GTCTCTTCTT AGAACTTGG TTAAATGTTT ACTCTTCTTG CTAATTTAG 2900
 GATAGATTCC TCACCTTGG CCCGCCTTTG CCCCACCCTA CTCTGCCAG 2950
 AAGTGCAAGA GCCTAAGCCG CCTCCATGGC CCCAGGAAGG ATTCAGGGGA 3000
 GAGGCCCAA ACAGGGAGCC ACGCCAGCCA GACACCCCG CCAGAATGGA 3050
 GCTGACTGGT GAGAACACAC CTGAGGGGCT AGGGCCATAT GGAAACATGA 3100
 CAGAAGGGGA GAGAGAAAGG AGACACGCTG CAAGGGGCAG GAAGCTGGGG 3150
 GAACCATTC TCCCAAAAT AAGGGGTCTG AGGGGTGGAT TCCCTGGGT 3200
 TCAGGTCTGG GTCCTGAATG GGAATTCCTG GAATACCAGC TGACAATGAT 3250

TTCTCTCTCA TCTTTCAACC TCACCTCTCC TCATCTAAGA ATTGCTCCTC 3300
 GTGGTCATGC TTCTCCTAAC TGCAAGGCTA ACGCTGTCCA GCCCGGCTC 3350
 TCCTGCTTGT GACCTCCGAG TCCTCAGTAA ACTGCTTCGT GACTCCCATG 3400
 TCCTTCACAG CAGACTGGTG AGAACTCCCA ACATTATCCC CTTTATCCGC 3450
 GTAACGGTA AGACACCCAT ACTCCCAGGA AGACACCATC ACTTCCTCTA 3500
 ACTCCTTGAC CCAATGACTA TTCTTCCCAT ATTGTCCCCA CCTACTGATC 3550
 AACTCTCTG ACAAGAATTA TTCTTCACAA TACAGCCCGC ATTTAAAAGC 3600
 TCTCGTCTAG AGATAGTACT CATGGAGGAC TAGCCTGCTT ATTAGGCTAC 3650
 CATAGCTCTC TCTATTTTCA CTCCCTTCTC CCCCCACCA TCTTTTTC 3700
 CAGAGCCAGT GCCCAGAGGT TCACCCCTTG CCTACACCTG TCCTGCTGCC 3750
 TGCTGTGGAC TTTAGCTTGG GAGAATGGAA AACCCAGATG GTAAGAAAGC 3800
 CATCCCTAAC CTTGGCTTCC CTAAGTCCTG TCTTCAGTTT CCCACTGCTT 3850
 CCCATGGATT CTCCAACATT CTGAGCTTT TTAATAATAT CTCACCTTCA 3900
 GCTTGGCCAC CCTAACCCAA TCTACATTCA CCTATGATGA TAGCCTGTGG 3950
 ATAAGATGAT GGCTTGCAGG TCCAATATGT GAATAGATT GAAGCTGAAC 4000
 ACCATGAAAA GCTGGAGAGA AATCGCTCAT GGCCATGCCT TTGACCTATT 4050
 CCYGTTCAGT CTTCTTAAAT TGGCATGAAG AAGCAAGACT CATATGTCAT 4100
 CCACAGATGA CACAAAGCTG GGAAGTACCA CTAAAATAAC AAAAGACTGA 4150
 ATCAAGATTC AAATCACTGA AAGACTAGGT CAAAACAAG GTGAAACAAC 4200
 AGAGATATAA ACTTCTACAT GTGGGCCGGG GGCTCACGCC TGTAATCCCA 4250
 GCACTTTGGG AGGCCGAGGC AGGCAGATCA CCTGAGGGCA GGAGTTTGAG 4300
 AGCAGCCTGG CCAACATGGC GAAACCCGT CTCTACTAAG AATACAAAAT 4350
 TAGCCGGGCA TGCTAGTGCA TGCCTGTAAT CCCAGCTACT TGAAGGCTG 4400
 AAGCAGGAGA ATCCCTTGAA CCCAGGAGGT GGAGGTTGTA GTGAGCTGAG 4450
 ATCATGCCAA TGCACTCCAG CCTGGGTGAC AAGAGCAAAA CTCCGTCTCA 4500
 AAAAGAAAAA AAAATTCTAC ATGTGTAAAT TAATGAGTAA AGTCCTATTC 4550
 CAGCTTTCAG GCCACAATGC CCTGCTTCCA TCATTAAAGC CTCTGGCCCT 4600
 AGCACTTCCT ACGAAAAGGA TCTGAGAGAA TTAAATTGCC CCCAACTTA 4650

CCATGTAACA TTACTGAAGC TGCTATTCTT AAAGCTAGTA ATTCTTGTCT 4700
 GTTTGATGTT TAGCATCCCC ATTGTGGAAA TGCTCGTACA GAACTCTA⁺TT 4750
 CCGAGTGGAC TACACTTAAA TATACTGGCC TGAACACCGG ACATCCCCCT 4800
 GAAGACATAT GCTAATTTAT TAAGAGGGAC CATATTAAAC TAACATGTGT 4850
 CTAGAAAGCA GCAGCCTGAA CAGAAAGAGA CTAGAAGCAT GTTTTATGGG 4900
 CAATAGTTTA AAAA⁺ACTAAA ATCTATCCTC AAGAACCCTA GCGTCCCTTC 4950
 TTCCTTCAGG ACTGAGTCAG GGAAGAAGGG CAGTTCCTAT GGGTCCCTTC 5000
 TAGTCCTTTC TTTTCATCCT TATGATCATT ATGGTAGAGT CTCATACCTA 5050
 CATTAGTTT ATTTATTATT ATTATTTGAG ACGGAGTCTC ACTCTATCCC 5100
 CCAGGCTGGA GTGCAGTGGC ATGATCTCAA CTCACTGCAA CCTCAGCCTC 5150
 CCGGATTCAA GCGATTCTCC TGCCTCAGTC TCCCAAGTAG CTGGGATTAC 5200
 AGGTGCCCCA CACCATGCCC AGCTAATTTT TGTATTTT⁺TG GTAGAGATGG 5250
 GGTTTCACCA TGTTGGCCAG GCTGATCTTG AACTCCTGAC CTCAGGTGAT 5300
 CCACCTGCCT CAGCCTCCCA AAGTGCTGGG ATTACAGGCG TGAGCCACTG 5350
 CACCCAGCCT TCATTCA⁺GTT TAAAAATCAA ATGATCCTAA GGTTT⁺TGCAG 5400
 CAGAAAGAGT AAATTTGCAG CACTAGAACC AAGAGGTA⁺AA AGCTGTAACA 5450
 GGGCAGATTT CAGCAACGTA AGAAAAAGG AGCTCTTCTC ACTGAAACCA 5500
 AGTGTAAGAC CAGGCTGGAC TAGAGGACAC GGGAGTTTTT GAAGCAGAGG 5550
 CTGATGACCA GCTGTGGGA GACTGTGAAG GAATTCCTGC CCTGGGTGGG 5600
 ACCTTGGTCC TGTCCAGTTC TCAGCCTGTA TGATTC⁺ACTC TGCTGGCTAC 5650
 TCCTAAGGCT CCCCACCCGC TTTTAGTGTG CCCTTTGAGG CAGTGC⁺GCTT 5700
 CTCTCTCCA TCTCTTCTC AGGAGGAGAC CAAGGCACAG GACATTCTGG 5750
 GAGCAGTGAC CCTTCTGCTG GAGGGAGTGA TGGCAGCACG GGGACA⁺ACTG 5800
 GGACCACTT GCCTCTCATC CCTCCTGGGG CAGCTTTCTG GACAGGTCCG 5850
 TCTCCTCCTT GGGGCCCTGC AGAGCCTCCT TGGAA⁺CCCAG GTAAGTCCCC 5900
 AGTCAAGGGA TCTGTAGAAA CTGTTCTTTT CTGACTCAGT CCCACTAGAA 5950
 GACCTGAGGG AAGAAGGGCT CTTCCAGGGA GCTCAAGGGC AGAAGAGCTG 6000
 ATCTACTAAG AGTGCTCCCT GCCAGCCACA ATGCCTGGGT ACTGGCATCC 6050

TGTCTTTCCT ACTTAGACAA GGGAGGCCTG AGATCTGGCC CTGGTGTGTTG 6100
 GCCTCAGGAC CATCCTCTGC CCTCAGCTTC CTCCACAGGG CAGGACCACA 6150
 GCTCACAAGG ATCCCAATGC CATCTTCCTG AGTTTCCAAC ACCTGCTCCG 6200
 AGGAAAGGTG CGTTTCCTGA TGCTTGTAGG AGGGTCCACC CTCTGCGTCA 6250
 GCGGGGCCCC ACCCACCACA GCTGTCCCCA GCAGAACCTC TCTAGTCCTC 6300
 ACACTGAACG AGCTCCCAAA CAGGACTTCT GGATTGTTGG AGACAAACTT 6350
 CACTGCCTCA GCCAGAATA CTGGCTCTGG GCTTCTGAAG TGGCAGCAGG 6400
 GATTGAGAGC CAAGATTCCT GGTCTGCTGA ACCAAACCTC CAGGTCCCTG 6450
 GACCAAATCC CCGGATACCT GAACAGGATA CACGAACTCT TGAATGGAAC 6500
 TCGTGGACTC TTTCTGGAC CCTCAGCAG GACCCTAGGA GCGCCGACA 6550
 TTTCTCAGG AACATCAGAC ACAGGCTCCC TGCCACCCAA CCTCCAGCCT 6600
 GGATATTCTC CTTCCCCAAC CCATCCTCCT ACTGGACAGT ATACGCTCTT 6650
 CCCTCTTCCA CCCACCTTGC CCACCCCTGT GGTCCAGCTC CACCCCTGC 6700
 TTCCTGACCC TTCTGCTCCA ACGCCACCC CTACCAGCCC TCTTCTAAAC 6750
 ACATCTACA CCCACTCCA GAATCTGTCT CAGGAAGGGT AAGGTTCTCA 6800
 GACTGCGG ACATCAGCAT TGTCTCATGT ACAGCTCCCT TCCCTGCAGG 6850
 GCGCCCCTGG GAGACAACTG GACAAGATT CTACTTTCT CCTGAAACCC 6900
 AAAGCCCTGG TAAAAGGGAT ACACAGGACT GAAAAGGGAA TCATTTTCA 6950
 CTGTACATTA TAAACCTTCA GAAGCTATTT TTTAAGCTA TCAGCAATAC 7000
 TCATCAGAGC AGCTAGCTCT TTGGTCTATT TTCTGCAGAA ATTTGCAACT 7050
 CACTGATTCT CTACATGCTC TTTTCTGTG ATAACCTGCTC AAAGGCCTGG 7100
 GCTGGCCTGG CAGTTGAACA GAGGGAGAGA CTAACCTGA GTCAGAAAAC 7150
 AGAGAAAGGG TAATTTCTT TGCTTCAAAT TCAAGGCCTT CCAACGCCCC 7200
 CATCCCCTTT ACTATCATTC TCAGTGGGAC TCTGATCCA TATTCTTAAC 7250
 AGATCTTTAC TCTTGAGAAA TGAATAAGCT TTCTCTCAGA AATGCTGTCC 7300
 CTATACACTA GACAAAAGTG AGCCTGTATA AGGAATAAAT GGGAGCGCCG 7350
 AAAAGCTCCC TAAAAGCAA GGGAAAGATG TTCTTCGAGG GTGGCAATAG 7400
 ATCCCCCTCA CCCTGCCACC CCAAACAAA AAGCTAACAG GAAGCCTTGG 7450

AGAGCCTCAC	ACCCACAGGTA	AGGCTGTGTA	GACAGTTCAG	TAAAGACAGG	7500
ACCTGGATGT	GACAGCTGAG	CAAACAGCTA	GAGCTTTGGC	AGCTCAGCAG	7550
GAGGCTTTGC	CAGGCATGGA	CGCTGCCTC	CCTCCTGTGG	AGGTCAGGAG	7600
GAAGTGCAGG	AAGTGGCATG	AGTCAGGCTC	CTTGAGCTCA	CACAGCAGGA	7650
GAACAAGTAC	AAGTCAAGTA	CAAGTTGAAG	GCTCATTTCC	CAGTTCCCGC	7700
AAATGCATCT	AAAAAGCAGC	TCTGTGTGAC	CACCATAAAC	TCTGCTAGGG	7750
GATCTCTAAA	AAGGAGTCAG	GCTTATGGGG	CTTTGCAAAT	AAGTGCTGCC	7800
TTGGTGCTCA	GGAAAAAGGTT	TGTGTTGCAC	AAAACACAAA	TTCCACTGCG	7849

(2) SEQ ID NO:12에 대한 정보:

(i) 서열 특성:

- (A) 길이: 1443 염기
(B) 타입: 핵산
(C) 나선 구조: 단일나선
(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:12

GAGTCTCTGG	CCCACCTCTC	TCCCACCCGA	CTCTGCCGAA	AGAAGCACAG	50
AAGCTCAAGC	CGCCTCCATG	GCCCCAGGAA	AGATTCAGGG	GAGAGGCCCC	100
ATACAGGGAG	CCACTTCAGT	TAGACACCT	GGCCAGA	ATG GAG	143
				Met Glu	
				-21 -20	
CTG ACT GAT TTG CTC CTG GCG GCC ATG CTT CTT GCA GTG	182				
Leu Thr Asp Leu Leu Leu Ala Ala Met Leu Leu Ala Val					
	-15			-10	
GCA AGA CTA ACT CTG TCC AGC CCC GTA GCT CCT GCC TGT	221				
Ala Arg Leu Thr Leu Ser Ser Pro Val Ala Pro Ala Cys					
	-5		1		5
GAC CCC AGA CTC CTA AAT AAA CTG CTG CGT GAC TCC CAC	260				
Asp Pro Arg Leu Leu Asn Lys Leu Leu Arg Asp Ser His					
	10			15	20

CTC CTT CAC AGC CGA CTG AGT CAG TGT CCC GAC GTC GAC 299
 Leu Leu His Ser Arg Leu Ser Gln Cys Pro Asp Val Asp
 25 30

CCT TTG TCT ATC CCT GTT CTG CTG CCT GCT GTG GAC TTT 338
 Pro Leu Ser Ile Pro Val Leu Leu Pro Ala Val Asp Phe
 35 40 45

AGC CTG GGA GAA TGG AAA ACC CAG ACG GAA CAG AGC AAG 377
 Ser Leu Gly Glu Trp Lys Thr Gln Thr Glu Gln Ser Lys ;
 50 55

GCA CAG GAC ATT CTA GGG GCA GTG TCC CTT CTA CTG GAG 416
 Ala Gln Asp Ile Leu Gly Ala Val Ser Leu Leu Leu Glu
 60 65 70

GGA GTG ATG GCA GCA CGA GGA CAG TTG GAA CCC TCC TGC 455
 Gly Val Met Ala Ala Arg Gly Gln Leu Glu Pro Ser Cys
 75 80 85

CTC TCA TCC CTC CTG GGA CAG CTT TCT GGG CAG GTT CGC 494
 Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln Val Arg
 90 95

CTC CTC TTG GGG GCC CTG CAG GGC CTC CTA GGA ACC CAG 533
 Leu Leu Leu Gly Ala Leu Gln Gly Leu Leu Gly Thr Gln
 100 105 110

GGC AGG ACC ACA GCT CAC AAG GAC CCC AAT GCC CTC TTC 572
 Gly Arg Thr Thr Ala His Lys Asp Pro Asn Ala Leu Phe
 115 120

TTG AGC TTG CAA CAA CTG CTT CGG GGA AAG GTG CGC TTC 611
 Leu Ser Leu Gln Gln Leu Leu Arg Gly Lys Val Arg Phe
 125 130 135

CTG CTT CTG GTA GAA GGT CCC ACC CTC TGT GTC AGA CGG 650
 Leu Leu Leu Val Glu Gly Pro Thr Leu Cys Val Arg Arg
 140 145 150

ACC CTG CCA ACC ACA GCT GTC CCA AGC AGT ACT TCT CAA 689
 Thr Leu Pro Thr Thr Ala Val Pro Ser Ser Thr Ser Gln
 155 160

CTC CTC ACA CTA AAC AAG TTC CCA AAC AGG ACT TCT GGA 728
 Leu Leu Thr Leu Asn Lys Phe Pro Asn Arg Thr Ser Gly
 165 170 175

TTG TTG GAG ACG AAC TTC AGT GTC ACA GCC AGA ACT GCT 767
 Leu Leu Glu Thr Asn Phe Ser Val Thr Ala Arg Thr Ala
 180 185

GGC CCT GGA CTT CTG AGC AGG CTT CAG GGA TTC AGA GTC 806
 Gly Pro Gly Leu Leu Ser Arg Leu Gln Gly Phe Arg Val
 190 195 200

AAG ATT ACT CCT GGT CAG CTA AAT CAA ACC TCC AGG TCC 845
 Lys Ile Thr Pro Gly Gln Leu Asn Gln Thr Ser Arg Ser
 205 210 215
 CCA GTC CAA ATC TCT GGA TAC CTG AAC AGG ACA CAC GGA 884
 Pro Val Gln Ile Ser Gly Tyr Leu Asn Arg Thr His Gly
 220 225
 CCT GTG AAT GGA ACT CAT GGG CTC TTT GCT GGA ACC TCA 923
 Pro Val Asn Gly Thr His Gly Leu Phe Ala Gly Thr Ser
 230 235 240
 CTT CAG ACC CTG GAA GCC TCA GAC ATC TCG CCC GGA GCT 962
 Leu Gln Thr Leu Glu Ala Ser Asp Ile Ser Pro Gly Ala
 245 250
 TTC AAC AAA GGC TCC CTG GCA TTC AAC CTC CAG GGT GGA 1001
 Phe Asn Lys Gly Ser Leu Ala Phe Asn Leu Gln Gly Gly
 255 260 265
 CTT CCT CCT TCT CCA AGC CTT GCT CCT GAT GGA CAC ACA 1040
 Leu Pro Pro Ser Pro Ser Leu Ala Pro Asp Gly His Thr
 270 275 280
 CCC TTC CCT CCT TCA CCT GCC TTG CCC ACC ACC CAT GGA 1079
 Pro Phe Pro Pro Ser Pro Ala Leu Pro Thr Thr His Gly
 285 290
 TCT CCA CCC CAG CTC CAC CCC CTG TTT CCT GAC CCT TCC 1118
 Ser Pro Pro Gln Leu His Pro Leu Phe Pro Asp Pro Ser
 295 300 305
 ACC ACC ATG CCT AAC TCT ACC GCC CCT CAT CCA GTC ACA 1157
 Thr Thr Met Pro Asn Ser Thr Ala Pro His Pro Val Thr
 310 315
 ATG TAC CCT CAT CCC AGG AAT TTG TCT CAG GAA ACA TAGCGC 1199
 Met Tyr Pro His Pro Arg Asn Leu Ser Gln Glu Thr
 320 325 330 331
 G GGCACTGGCC CAGTGAGCGT CTGCAGCTTC TCTCGGGGAC 1240
 AAGCTTCCCC AGGAAGGCTG AGAGGCAGCT GCATCTGCTC CAGATGTTCT 1290
 GCTTTCACCT AAAAGGCCCT GGGGAAGGGA TACACAGCAC TGGAGATTGT 1340
 AAAATTTTAG GAGCTATTTT TTTTAACTT ATCAGCAATA TTCATCAGAG 1390
 CAGCTAGCGA TCTTTGTCT ATTTTCGGTA TAAATTTGAA AATCACTAAT 1440
 TCT 1443

(2) SEQ ID NO:13에 대한 정보:

(i) 서열 특성:

(A) 길이: 352 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:13

```

Met Glu Leu Thr Asp Leu Leu Leu Ala Ala Met Leu Leu Ala Val
-21 -20                -15                -10
Ala Arg Leu Thr Leu Ser Ser Pro Val Ala Pro Ala Cys Asp Pro
  -5                1                5
Arg Leu Leu Asn Lys Leu Leu Arg Asp Ser His Leu Leu His Ser
 10                15                20
Arg Leu Ser Gln Cys Pro Asp Val Asp Pro Leu Ser Ile Pro Val
 25                30                35
Leu Leu Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln
 40                45                50
Thr Glu Gln Ser Lys Ala Gln Asp Ile Leu Gly Ala Val Ser Leu
 55                60                65
Leu Leu Glu Gly Val Met Ala Ala Arg Gly Gln Leu Glu Pro Ser
 70                75                80
Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln Val Arg Leu
 85                90                95
Leu Leu Gly Ala Leu Gln Gly Leu Leu Gly Thr Gln Gly Arg Thr
100                105                110
Thr Ala His Lys Asp Pro Asn Ala Leu Phe Leu Ser Leu Gln Gln
115                120                125
Leu Leu Arg Gly Lys Val Arg Phe Leu Leu Leu Val Glu Gly Pro
130                135                140
Thr Leu Cys Val Arg Arg Thr Leu Pro Thr Thr Ala Val Pro Ser
145                150                155
Ser Thr Ser Gln Leu Leu Thr Leu Asn Lys Phe Pro Asn Arg Thr
160                165                170

```

```

Ser Gly Leu Leu Glu Thr Asn Phe Ser Val Thr Ala Arg Thr Ala
175                      180                      185

Gly Pro Gly Leu Leu Ser Arg Leu Gln Gly Phe Arg Val Lys Ile
190                      195                      200

Thr Pro Gly Gln Leu Asn Gln Thr Ser Arg Ser Pro Val Gln Ile
205                      210                      215

Ser Gly Tyr Leu Asn Arg Thr His Gly Pro Val Asn Gly Thr His
220                      225                      230

Gly Leu Phe Ala Gly Thr Ser Leu Gln Thr Leu Glu Ala Ser Asp
235                      240                      245

Ile Ser Pro Gly Ala Phe Asn Lys Gly Ser Leu Ala Phe Asn Leu
250                      255                      260

Gln Gly Gly Leu Pro Pro Ser Pro Ser Leu Ala Pro Asp Gly His
265                      270                      275

Thr Pro Phe Pro Pro Ser Pro Ala Leu Pro Thr Thr His Gly Ser
280                      285                      290

Pro Pro Gln Leu His Pro Leu Phe Pro Asp Pro Ser Thr Thr Met
295                      300                      305

Pro Asn Ser Thr Ala Pro His Pro Val Thr Met Tyr Pro His Pro
310                      315                      320

Arg Asn Leu Ser Gln Glu Thr
325                      330 331

```

(2) SEQ ID NO:14에 대한 정보:

(i) 서열 특성:

(A) 길이: 1536 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:14

GAGTCTTGG CCCACTCTC TCCCACCGA CTCTGCCGAA AGAAGCACAG 50
AAGCTCAAGC CGCCTCCATG GCCCCAGGAA AGATTGAGG GAGAGGCCCC 100
ATACAGGGAG CCACTTCAGT TAGACACCCT GGCCAGA ATG GAG 143
Met Glu
-21 -20

CTG ACT GAT TTG CTC CTG GCG GCC ATG CTT CTT GCA GTG 182
Leu Thr Asp Leu Leu Leu Ala Ala Met Leu Leu Ala Val
-15 -10

GCA AGA CTA ACT CTG TCC AGC CCC GTA GCT CCT GCC TGT 221
Ala Arg Leu Thr Leu Ser Ser Pro Val Ala Pro Ala Cys
-5 1 5

GAC CCC AGA CTC CTA AAT AAA CTG CTG CGT GAC TCC CAC 260
Asp Pro Arg Leu Leu Asn Lys Leu Leu Arg Asp Ser His
10 15 20

CTC CTT CAC AGC CGA CTG AGT CAG TGT CCC GAC GTC GAC 299
Leu Leu His Ser Arg Leu Ser Gln Cys Pro Asp Val Asp
25 30

CCT TTG TCT ATC CCT GTT CTG CTG CCT GCT GTG GAC TTT 338
Pro Leu Ser Ile Pro Val Leu Leu Pro Ala Val Asp Phe
35 40 45

AGC CTG GGA GAA TGG AAA ACC CAG ACG GAA CAG AGC AAG 377
Ser Leu Gly Glu Trp Lys Thr Gln Thr Glu Gln Ser Lys
50 55

GCA CAG GAC ATT CTA GGG GCA GTG TCC CTT CTA CTG GAG 416
Ala Gln Asp Ile Leu Gly Ala Val Ser Leu Leu Leu Glu
60 65 70

GGA GTG ATG GCA GCA CGA GGA CAG TTG GAA CCC TCC TGC 455
Gly Val Met Ala Ala Arg Gly Gln Leu Glu Pro Ser Cys
75 80 85

CTC TCA TCC CTC CTG GGA CAG CTT TCT GGG CAG GTT CGC 494
Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln Val Arg
90 95

CTC CTC TTG GGG GCC CTG CAG GGC CTC CTA GGA ACC CAG 533
Leu Leu Leu Gly Ala Leu Gln Gly Leu Leu Gly Thr Gln
100 105 110

CTT CCT CTA CAG GGC AGG ACC ACA GCT CAC AAG GAC CCC 572
Leu Pro Leu Gln Gly Arg Thr Thr Ala His Lys Asp Pro
115 120

AAT GCC CTC TTC TTG AGC TTG CAA CAA CTG CTT CGG GGA 611
Asn Ala Leu Phe Leu Ser Leu Gln Gln Leu Leu Arg Gly
125 130 135

AAG GTG CGC TTC CTG CTT CTG GTA GAA GGT CCC ACC CTC 650
 Lys Val Arg Phe Leu Leu Leu Val Glu Gly Pro Thr Leu
 140 145 150

TGT GTC AGA CGG ACC CTG CCA ACC ACA GCT GTC CCA AGC 689
 Cys Val Arg Arg Thr Leu Pro Thr Thr Ala Val Pro Ser
 155 160

AGT ACT TCT CAA CTC CTC ACA CTA AAC AAG TTC CCA AAC 728
 Ser Thr Ser Gln Leu Leu Thr Leu Asn Lys Phe Pro Asn
 165 170 175

AGG ACT TCT GGA TTG TTG GAG ACG AAC TTC AGT GTC ACA 767
 Arg Thr Ser Gly Leu Leu Glu Thr Asn Phe Ser Val Thr
 180 185

GCC AGA ACT GCT GGC CCT GGA CTT CTG AGC AGG CTT CAG 806
 Ala Arg Thr Ala Gly Pro Gly Leu Leu Ser Arg Leu Gln
 190 195 200

GGA TTC AGA GTC AAG ATT ACT CCT GGT CAG CTA AAT CAA 845
 Gly Phe Arg Val Lys Ile Thr Pro Gly Gln Leu Asn Gln
 205 210 215

ACC TCC AGG TCC CCA GTC CAA ATC TCT GGA TAC CTG AAC 884
 Thr Ser Arg Ser Pro Val Gln Ile Ser Gly Tyr Leu Asn
 220 225

AGG ACA CAC GGA CCT GTG AAT GGA ACT CAT GGG CTC TTT 923
 Arg Thr His Gly Pro Val Asn Gly Thr His Gly Leu Phe
 230 235 240

GCT GGA ACC TCA CTT CAG ACC CTG GAA GCC TCA GAC ATC 962
 Ala Gly Thr Ser Leu Gln Thr Leu Glu Ala Ser Asp Ile
 245 250

TCG CCC GGA GCT TTC AAC AAA GGC TCC CTG GCA TTC AAC 1001
 Ser Pro Gly Ala Phe Asn Lys Gly Ser Leu Ala Phe Asn
 255 260 265

CTC CAG GGT GGA CTT CCT CCT TCT CCA AGC CTT GCT CCT 1040
 Leu Gln Gly Gly Leu Pro Pro Ser Pro Ser Leu Ala Pro
 270 275 280

GAT GGA CAC ACA CCC TTC CCT CCT TCA CCT GCC TTG CCC 1079
 Asp Gly His Thr Pro Phe Pro Pro Ser Pro Ala Leu Pro
 285 290

ACC ACC CAT GGA TCT CCA CCC CAG CTC CAC CCC CTG TTT 1118
 Thr Thr His Gly Ser Pro Pro Gln Leu His Pro Leu Phe
 295 300 305

CCT GAC CCT TCC ACC ACC ATG CCT AAC TCT ACC GCC CCT 1157
 Pro Asp Pro Ser Thr Thr Met Pro Asn Ser Thr Ala Pro
 310 315

CAT CCA GTC ACA ATG TAC CCT CAT CCC AGG AAT TTG TCT 1196
 His Pro Val Thr Met Tyr Pro His Pro Arg Asn Leu Ser
 320 325 330

CAG GAA ACA TAGCG CGGGCACTGG CCCAGTGAGC GTCTGCAGCT 1240
 Gln Glu Thr
 335

TCTCTCGGGG ACAAGCTTCC CCAGGAAGGC TGAGAGGCAG CTGCATCTGC 1290

TCCAGATGTT CTGCTTTTCAC CTAAAAGGCC CTGGGGAAGG GATACACAGC 1340

ACTGGAGATT GTAAAATTTT AGGAGCTATT TTTTITTAAC CTATCAGCAA 1390

TATTCATCAG AGCAGCTAGC GATCTTTGGT CTATTTTCGG TATAAATTG 1440

AAAATCACTA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 1490

AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAA 1536

(2) SEQ ID NO:15에 대한 정보:

(i) 서열 특성:

(A) 길이: 356 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:15

Met Glu Leu Thr Asp Leu Leu Leu Ala Ala Met Leu Leu Ala Val
 -21 -20 -15 -10

Ala Arg Leu Thr Leu Ser Ser Pro Val Ala Pro Ala Cys Asp Pro
 -5 1 5

Arg Leu Leu Asn Lys Leu Leu Arg Asp Ser His Leu Leu His Ser
 10 15 20

Arg Leu Ser Gln Cys Pro Asp Val Asp Pro Leu Ser Ile Pro Val
 25 30 35

Leu Leu Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln
 40 45 50

Thr Glu Gln Ser Lys Ala Gln Asp Ile Leu Gly Ala Val Ser Leu
 55 60 65

Leu Leu Glu Gly Val Met Ala Ala Arg Gly Gln Leu Glu Pro Ser
 70 75 80
 Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln Val Arg Leu
 85 90 95
 Leu Leu Gly Ala Leu Gln Gly Leu Leu Gly Thr Gln Leu Pro Leu
 100 105 110
 Gln Gly Arg Thr Thr Ala His Lys Asp Pro Asn Ala Leu Phe Leu
 115 120 125
 Ser Leu Gln Gln Leu Leu Arg Gly Lys Val Arg Phe Leu Leu Leu
 130 135 140
 Val Glu Gly Pro Thr Leu Cys Val Arg Arg Thr Leu Pro Thr Thr
 145 150 155
 Ala Val Pro Ser Ser Thr Ser Gln Leu Leu Thr Leu Asn Lys Phe
 160 165 170
 Pro Asn Arg Thr Ser Gly Leu Leu Glu Thr Asn Phe Ser Val Thr
 175 180 185
 Ala Arg Thr Ala Gly Pro Gly Leu Leu Ser Arg Leu Gln Gly Phe
 190 195 200
 Arg Val Lys Ile Thr Pro Gly Gln Leu Asn Gln Thr Ser Arg Ser
 205 210 215
 Pro Val Gln Ile Ser Gly Tyr Leu Asn Arg Thr His Gly Pro Val
 220 225 230
 Asn Gly Thr His Gly Leu Phe Ala Gly Thr Ser Leu Gln Thr Leu
 235 240 245
 Glu Ala Ser Asp Ile Ser Pro Gly Ala Phe Asn Lys Gly Ser Leu
 250 255 260
 Ala Phe Asn Leu Gln Gly Gly Leu Pro Pro Ser Pro Ser Leu Ala
 265 270 275
 Pro Asp Gly His Thr Pro Phe Pro Pro Ser Pro Ala Leu Pro Thr
 280 285 290
 Thr His Gly Ser Pro Pro Gln Leu His Pro Leu Phe Pro Asp Pro
 295 300 305
 Ser Thr Thr Met Pro Asn Ser Thr Ala Pro His Pro Val Thr Met
 310 315 320
 Tyr Pro His Pro Arg Asn Leu Ser Gln Glu Thr
 325 330 335

(2) SEQ ID NO:16에 대한 정보:

(i) 서열 특성:

(A) 길이: 241 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:16

```

Ser Pro Val Ala Pro Ala Cys Asp Pro Arg Leu Leu Asn Lys Leu
 1          5          10          15
Leu Arg Asp Ser His Leu Leu His Ser Arg Leu Ser Gln Cys Pro
          20          25          30
Asp Val Asp Pro Leu Ser Ile Pro Val Leu Leu Pro Ala Val Asp
          35          40          45
Phe Ser Leu Gly Glu Trp Lys Thr Gln Thr Glu Gln Ser Lys Ala
          50          55          60
Gln Asp Ile Leu Gly Ala Val Ser Leu Leu Leu Glu Gly Val Met
          65          70          75
Ala Ala Arg Gly Gln Leu Glu Pro Ser Cys Leu Ser Ser Leu Leu
          80          85          90
Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
          95          100          105
Gly Leu Leu Gly Thr Gln Leu Pro Leu Gln Gly Arg Thr Thr Ala
          110          115          120
His Lys Asp Pro Asn Ala Leu Phe Leu Ser Leu Gln Gln Leu Leu
          125          130          135
Arg Gly Lys Asp Phe Trp Ile Val Gly Asp Glu Leu Gln Cys His
          140          145          150
Ser Gln Asn Cys Trp Pro Trp Thr Ser Glu Gln Ala Ser Gly Ile
          155          160          165
Gln Ser Gln Asp Tyr Ser Trp Ser Ala Lys Ser Asn Leu Gln Val
          170          175          180
Pro Ser Pro Asn Leu Trp Ile Pro Glu Gln Asp Thr Arg Thr Cys
          185          190          195

```

Glu	Trp	Asn	Ser	Trp	Ala	Leu	Cys	Trp	Asn	Leu	Thr	Ser	Asp	Pro	200	205	210
Gly	Ser	Leu	Arg	His	Leu	Ala	Arg	Ser	Phe	Gln	Gln	Arg	Leu	Pro	215	220	225
Gly	Ile	Gln	Pro	Pro	Gly	Trp	Thr	Ser	Ser	Phe	Ser	Lys	Pro	Cys	230	235	240

(2) SEQ ID NO:17에 대한 정보:

(i) 서열 특성;

(A) 길이: 335 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:17

Ser	Pro	Val	Ala	Pro	Ala	Cys	Asp	Pro	Arg	Leu	Leu	Asn	Lys	Leu	1	5	10	15
Leu	Arg	Asp	Ser	His	Leu	Leu	His	Ser	Arg	Leu	Ser	Gln	Cys	Pro	20	25	30	
Asp	Val	Asp	Pro	Leu	Ser	Ile	Pro	Val	Leu	Leu	Pro	Ala	Val	Asp	35	40	45	
Phe	Ser	Leu	Gly	Glu	Trp	Lys	Thr	Gln	Thr	Glu	Gln	Ser	Lys	Ala	50	55	60	
Gln	Asp	Ile	Leu	Gly	Ala	Val	Ser	Leu	Leu	Leu	Glu	Gly	Val	Met	65	70	75	
Ala	Ala	Arg	Gly	Gln	Leu	Glu	Pro	Ser	Cys	Leu	Ser	Ser	Leu	Leu	80	85	90	
Gly	Gln	Leu	Ser	Gly	Gln	Val	Arg	Leu	Leu	Leu	Gly	Ala	Leu	Gln	95	100	105	
Gly	Leu	Leu	Gly	Thr	Gln	Leu	Pro	Leu	Gln	Gly	Arg	Thr	Thr	Ala	110	115	120	
His	Lys	Asp	Pro	Asn	Ala	Leu	Phe	Leu	Ser	Leu	Gln	Gln	Leu	Leu	125	130	135	
Arg	Gly	Lys	Val	Arg	Phe	Leu	Leu	Leu	Val	Glu	Gly	Pro	Thr	Leu	140	145	150	

```

Cys Val Arg Arg Thr Leu Pro Thr Thr Ala Val Pro Ser Ser Thr
155                               160                               165

Ser Gln Leu Leu Thr Leu Asn Lys Phe Pro Asn Arg Thr Ser Gly
170                               175                               180

Leu Leu Glu Thr Asn Phe Ser Val Thr Ala Arg Thr Ala Gly Pro
185                               190                               195

Gly Leu Leu Ser Arg Leu Gln Gly Phe Arg Val Lys Ile Thr Pro
200                               205                               210

Gly Gln Leu Asn Gln Thr Ser Arg Ser Pro Val Gln Ile Ser Gly
215                               220                               225

Tyr Leu Asn Arg Thr His Gly Pro Val Asn Gly Thr His Gly Leu
230                               235                               240

Phe Ala Gly Thr Ser Leu Gln Thr Leu Glu Ala Ser Asp Ile Ser
245                               250                               255

Pro Gly Ala Phe Asn Lys Gly Ser Leu Ala Phe Asn Leu Gln Gly
260                               265                               270

Gly Leu Pro Pro Ser Pro Ser Leu Ala Pro Asp Gly His Thr Pro
275                               280                               285

Phe Pro Pro Ser Pro Ala Leu Pro Thr Thr His Gly Ser Pro Pro
290                               295                               300

Gln Leu His Pro Leu Phe Pro Asp Pro Ser Thr Thr Met Pro Asn
305                               310                               315

Ser Thr Ala Pro His Pro Val Thr Met Tyr Pro His Pro Arg Asn
320                               325                               330

Leu Ser Gln Glu Thr
335

```

(2) SEQ ID NO:18에 대한 정보:

(i) 서열 특성:

(A) 길이: 332 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:18

```

Ser Pro Ala Pro Pro Ala Cys Asp Pro Arg Leu Leu Asn Lys Leu
 1          5          10          15
Leu Arg Asp Ser His Val Leu His Gly Arg Leu Ser Gln Cys Pro
          20          25          30
Asp Ile Asn Pro Leu Ser Thr Pro Val Leu Leu Pro Ala Val Asp
          35          40          45
Phe Thr Leu Gly Glu Trp Lys Thr Gln Thr Glu Gln Thr Lys Ala
          50          55          60
Gln Asp Val Leu Gly Ala Thr Thr Leu Leu Leu Glu Ala Val Met
          65          70          75
Thr Ala Arg Gly Gln Val Gly Pro Pro Cys Leu Ser Ser Leu Leu
          80          85          90
Val Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
          95          100          105
Asp Leu Leu Gly Met Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala
          110          115          120
His Lys Asp Pro Ser Ala Ile Phe Leu Asn Phe Gln Gln Leu Leu
          125          130          135
Arg Gly Lys Val Arg Phe Leu Leu Leu Val Val Gly Pro Ser Leu
          140          145          150
Cys Ala Lys Arg Ala Pro Pro Ala Ile Ala Val Pro Ser Ser Thr
          155          160          165
Ser Pro Phe His Thr Leu Asn Lys Leu Pro Asn Arg Thr Ser Gly
          170          175          180
Leu Leu Glu Thr Asn Ser Ser Ile Ser Ala Arg Thr Thr Gly Ser
          185          190          195
Gly Phe Leu Lys Arg Leu Gln Ala Phe Arg Ala Lys Ile Pro Gly
          200          205          210
Leu Leu Asn Gln Thr Ser Arg Ser Leu Asp Gln Ile Pro Gly His
          215          220          225
Gln Asn Gly Thr His Gly Pro Leu Ser Gly Ile His Gly Leu Phe
          230          235          240
Pro Gly Pro Gln Pro Gly Ala Leu Gly Ala Pro Asp Ile Pro Pro
          245          250          255
Ala Thr Ser Gly Met Gly Ser Arg Pro Thr Tyr Leu Gln Pro Gly
          260          265          270

```

```

Glu Ser Pro Ser Pro Ala His Pro Ser Pro Gly Arg Tyr Thr Leu
275                               280                               285

Phe Ser Pro Ser Pro Thr Ser Pro Ser Pro Thr Val Gln Leu Gln
290                               295                               300

Pro Leu Leu Pro Asp Pro Ser Ala Ile Thr Pro Asn Ser Thr Ser
305                               310                               315

Pro Leu Leu Phe Ala Ala His Pro His Phe Gln Asn Leu Ser Gln
320                               325                               330

```

(2) SEQ ID NO:19에 대한 정보:

(i) 서열 특성:

(A) 길이: 1026 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:19

```

AGC CCG GCT CCT CCT GCC TGT GAC CCC CGA CTC CTA 36
Ser Pro Ala Pro Pro Ala Cys Asp Pro Arg Leu Leu
1                               5                               10

AAT AAA CTG CTT CGT GAC TCC CAT GTC CTT CAC GGC AGA 75
Asn Lys Leu Leu Arg Asp Ser His Val Leu His Gly Arg
15                               20                               25

CTG AGC CAG TGC CCA GAC ATT AAC CCT TTG TCC ACA CCT 114
Leu Ser Gln Cys Pro Asp Ile Asn Pro Leu Ser Thr Pro
30                               35

GTC CTG CTG CCT GCT GTG GAC TTC ACC TTG GGA GAA TGG 153
Val Leu Leu Pro Ala Val Asp Phe Thr Leu Gly Glu Trp
40                               45                               50

AAA ACC CAG ACG GAG CAG ACA AAG GCA CAG GAT GTC CTG 192
Lys Thr Gln Thr Glu Gln Thr Lys Ala Gln Asp Val Leu
55                               60

GGA GCC ACA ACC CTT CTG CTG GAG GCA GTG ATG ACA GCA 231
Gly Ala Thr Thr Leu Leu Leu Glu Ala Val Met Thr Ala
65                               70                               75

```

CGG GGA CAA GTG GGA CCC CCT TGC CTC TCA TCC CTG CTG 270
 Arg Gly Gln Val Gly Pro Pro Cys Leu Ser Ser Leu Leu
 80 85 90

GTG CAG CTT TCT GGA CAG GTT CGC CTC CTC CTC GGG GCC 309
 Val Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala
 95 100

CTG CAG GAC CTC CTT GGA ATG CAG CTT CCT CCA CAG GGA 348
 Leu Gln Asp Leu Leu Gly Met Gln Leu Pro Pro Gln Gly
 105 110 115

AGG ACC ACA GCT CAC AAG GAT CCC AGT GCC ATC TTC CTG 387
 Arg Thr Thr Ala His Lys Asp Pro Ser Ala Ile Phe Leu
 120 125

AAC TTC CAA CAA CTG CTC CGA GGA AAG GTG CGT TTC CTG 426
 Asn Phe Gln Gln Leu Leu Arg Gly Lys Val Arg Phe Leu
 130 135 140

CTC CTT GTA GTG GGG CCC TCC CTC TGT GCC AAG AGG GCC 465
 Leu Leu Val Val Gly Pro Ser Leu Cys Ala Lys Arg Ala
 145 150 155

CCA CCC GCC ATA GCT GTC CCG AGC AGC ACC TCT CCA TTC 504
 Pro Pro Ala Ile Ala Val Pro Ser Ser Thr Ser Pro Phe
 160 165

CAC ACA CTG AAC AAG CTC CCA AAC AGG ACC TCT GGA TTG 543
 His Thr Leu Asn Lys Leu Pro Asn Arg Thr Ser Gly Leu
 170 175 180

TTG GAG ACA AAC TCC AGT ATC TCA GCC AGA ACT ACT GGC 582
 Leu Glu Thr Asn Ser Ser Ile Ser Ala Arg Thr Thr Gly
 185 190

TCT GGA TTT CTC AAG AGG CTG CAG GCA TTC AGA GCC AAG 621
 Ser Gly Phe Leu Lys Arg Leu Gln Ala Phe Arg Ala Lys
 195 200 205

ATT CCT GGT CTG CTG AAC CAA ACC TCC AGG TCC CTA GAC 660
 Ile Pro Gly Leu Leu Asn Gln Thr Ser Arg Ser Leu Asp
 210 215 220

CAA ATC CCT GGA CAC CAG AAT GGG ACA CAC GGA CCC TTG 699
 Gln Ile Pro Gly His Gln Asn Gly Thr His Gly Pro Leu
 225 230

AGT GGA ATT CAT GGA CTC TTT CCT GGA CCC CAA CCC GGG 738
 Ser Gly Ile His Gly Leu Phe Pro Gly Pro Gln Pro Gly
 235 240 245

GCC CTC GGA GCT CCA GAC ATT CCT CCA GCA ACT TCA GGC 777
 Ala Leu Gly Ala Pro Asp Ile Pro Pro Ala Thr Ser Gly
 250 255

```

ATG GGC TCC CGG CCA ACC TAC CTC CAG CCT GGA GAG TCT 816
Met Gly Ser Arg Pro Thr Tyr Leu Gln Pro Gly Glu Ser
260                265                270

CCT TCC CCA GCT CAC CCT TCT CCT GGA CGA TAC ACT CTC 855
Pro Ser Pro Ala His Pro Ser Pro Gly Arg Tyr Thr Leu
275                280                285

TTC TCT CCT TCA CCC ACC TCG CCC TCC CCC ACA GTC CAG 894
Phe Ser Pro Ser Pro Thr Ser Pro Ser Pro Thr Val Gln
290                295

CTC CAG CCT CTG CTT CCT GAC CCC TCT GCG ATC ACA CCC 933
Leu Gln Pro Leu Leu Pro Asp Pro Ser Ala Ile Thr Pro
300                305                310

AAC TCT ACC AGT CCT CTT CTA TTT GCA GCT CAC CCT CAT 972
Asn Ser Thr Ser Pro Leu Leu Phe Ala Ala His Pro His
315                320

TTC CAG AAC CTG TCT CAG GAA GAG TAAG GTGCTCAGAC 1010
Phe Gln Asn Leu Ser Gln Glu Glu
325                330                332

CCTGCCAACT TCAGCA 1026

```

(2) SEQ ID NO:20에 대한 정보:

(i) 서열 특성:

(A) 길이: 1014 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:20

```

AGC CCG GCT CCT CCT GCC TGT GAC CCC CGA CTC CTA 36
Ser Pro Ala Pro Pro Ala Cys Asp Pro Arg Leu Leu

```

```

      1              5              10
AAT AAA CTG CTT CGT GAC TCC CAT GTC CTT CAC GGC AGA 75
Asn Lys Leu Leu Arg Asp Ser His Val Leu His Gly Arg
      15              20              25

CTG AGC CAG TGC CCA GAC ATT AAC CCT TTG TCC ACA CCT 114
Leu Ser Gln Cys Pro Asp Ile Asn Pro Leu Ser Thr Pro
      30              35

GTC CTG CTG CCT GCT GTG GAC TTC ACC TTG GGA GAA TGG 153
Val Leu Leu Pro Ala Val Asp Phe Thr Leu Gly Glu Trp
      40              45              50

AAA ACC CAG ACG GAG CAG ACA AAG GCA CAG GAT GTC CTG 192
Lys Thr Gln Thr Glu Gln Thr Lys Ala Gln Asp Val Leu
      55              60

GGA GCC ACA ACC CTT CTG CTG GAG GCA GTG ATG ACA GCA 231
Gly Ala Thr Thr Leu Leu Leu Glu Ala Val Met Thr Ala
      65              70              75

CGG GGA CAA GTG GGA CCC CCT TGC CTC TCA TCC CTG CTG 270
Arg Gly Gln Val Gly Pro Pro Cys Leu Ser Ser Leu Leu :
      80              85              90

GTG CAG CTT TCT GGA CAG GTT CGC CTC CTC CTC GGG GCC 309
Val Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala
      95              100

CTG CAG GAC CTC CTT GGA ATG CAG GGA AGG ACC ACA GCT 348
Leu Gln Asp Leu Leu Gly Met Gln Gly Arg Thr Thr Ala
      105              110              115

CAC AAG GAT CCC AGT GCC ATC TTC CTG AAC TTC CAA CAA 387
His Lys Asp Pro Ser Ala Ile Phe Leu Asn Phe Gln Gln
      120              125

CTG CTC CGA GGA AAG GTG CGT TTC CTG CTC CTT GTA GTG 426
Leu Leu Arg Gly Lys Val Arg Phe Leu Leu Leu Val Val
      130              135              140

GGG CCC TCC CTC TGT GCC AAG AGG GCC CCA CCC GCC ATA 465
Gly Pro Ser Leu Cys Ala Lys Arg Ala Pro Pro Ala Ile
      145              150              155

GCT GTC CCG AGC AGC ACC TCT CCA TTC CAC ACA CTG AAC 504
Ala Val Pro Ser Ser Thr Ser Pro Phe His Thr Leu Asn
      160              165

AAG CTC CCA AAC AGG ACC TCT GGA TFG TTG GAG ACA AAC 543
Lys Leu Pro Asn Arg Thr Ser Gly Leu Leu Glu Thr Asn
      170              175              180

TCC AGT ATC TCA GCC AGA ACT ACT GGC TCT GGA TTT CTC 582

```

```

Ser Ser Ile Ser Ala Arg Thr Thr Gly Ser Gly Phe Leu
      185                      190

AAG AGG CTG CAG GCA TTC AGA GCC AAG ATT CCT GGT CTG 621
Lys Arg Leu Gln Ala Phe Arg Ala Lys Ile Pro Gly Leu
195                      200                      205

CTG AAC CAA ACC TCC AGG TCC CTA GAC CAA ATC CCT GGA 660
Leu Asn Gln Thr Ser Arg Ser Leu Asp Gln Ile Pro Gly
      210                      215                      220

CAC CAG AAT GGG ACA CAC GGA CCC TTG AGT GGA ATT CAT 699
His Gln Asn Gly Thr His Gly Pro Leu Ser Gly Ile His
      225                      230

GGA CTC TTT CCT GGA CCC CAA CCC GGG GCC CTC GGA GCT 738
Gly Leu Phe Pro Gly Pro Gln Pro Gly Ala Leu Gly Ala
      235                      240                      245

CCA GAC ATT CCT CCA GCA ACT TCA GGC ATG GGC TCC CGG 777
Pro Asp Ile Pro Pro Ala Thr Ser Gly Met Gly Ser Arg
      250                      255

CCA ACC TAC CTC CAG CCT GGA GAG TCT CCT TCC CCA GCT 816
Pro Thr Tyr Leu Gln Pro Gly Glu Ser Pro Ser Pro Ala -
      260                      265                      270

CAC CCT TCT CCT GGA CGA TAC ACT CTC TTC TCT CCT TCA 855
His Pro Ser Pro Gly Arg Tyr Thr Leu Phe Ser Pro Ser
      275                      280                      285

CCC ACC TCG CCC TCC CCC ACA GTC CAG CTC CAG CCT CTG 894
Pro Thr Ser Pro Ser Pro Thr Val Gln Leu Gln Pro Leu
      290                      295

CTT CCT GAC CCC TCT GCG ATC ACA CCC AAC TCT ACC AGT 933
Leu Pro Asp Pro Ser Ala Ile Thr Pro Asn Ser Thr Ser
      300                      305                      310

CCT CTT CTA TTT GCA GCT CAC CCT CAT TTC CAG AAC CTG 972
Pro Leu Leu Phe Ala Ala His Pro His Phe Gln Asn Leu
      315                      320

TCT CAG GAA GAG TAAGGT GCTCAGACCC TGCCAACTTC 1010
Ser Gln Glu Glu
325                      328

AGCA 1014

```

(2) SEQ ID NO:21에 대한 정보:

(i) 서열 특성:

(A) 길이: 328 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:21

```

Ser Pro Ala Pro Pro Ala Cys Asp Pro Arg Leu Leu Asn Lys Leu
 1          5          10          15
Leu Arg Asp Ser His Val Leu His Gly Arg Leu Ser Gln Cys Pro
          20          25          30
Asp Ile Asn Pro Leu Ser Thr Pro Val Leu Leu Pro Ala Val Asp
          35          40          45
Phe Thr Leu Gly Glu Trp Lys Thr Gln Thr Glu Gln Thr Lys Ala
          50          55          60
Gln Asp Val Leu Gly Ala Thr Thr Leu Leu Leu Glu Ala Val Met
          65          70          75
Thr Ala Arg Gly Gln Val Gly Pro Pro Cys Leu Ser Ser Leu Leu
          80          85          90
Val Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
          95          100          105
Asp Leu Leu Gly Met Gln Gly Arg Thr Thr Ala His Lys Asp Pro
          110          115          120
Ser Ala Ile Phe Leu Asn Phe Gln Gln Leu Leu Arg Gly Lys Val
          125          130          135
Arg Phe Leu Leu Leu Val Val Gly Pro Ser Leu Cys Ala Lys Arg
          140          145          150
Ala Pro Pro Ala Ile Ala Val Pro Ser Ser Thr Ser Pro Phe His
          155          160          165
Thr Leu Asn Lys Leu Pro Asn Arg Thr Ser Gly Leu Leu Glu Thr
          170          175          180
Asn Ser Ser Ile Ser Ala Arg Thr Thr Gly Ser Gly Phe Leu Lys
          185          190          195
Arg Leu Gln Ala Phe Arg Ala Lys Ile Pro Gly Leu Leu Asn Gln
          200          205          210
Thr Ser Arg Ser Leu Asp Gln Ile Pro Gly His Gln Asn Gly Thr
          215          220          225

```

His	Gly	Pro	Leu	Ser	Gly	Ile	His	Gly	Leu	Phe	Pro	Gly	Pro	Gln
				230					235					240
Pro	Gly	Ala	Leu	Gly	Ala	Pro	Asp	Ile	Pro	Pro	Ala	Thr	Ser	Gly
				245					250					255
Met	Gly	Ser	Arg	Pro	Thr	Tyr	Leu	Gln	Pro	Gly	Glu	Ser	Pro	Ser
				260					265					270
Pro	Ala	His	Pro	Ser	Pro	Gly	Arg	Tyr	Thr	Leu	Phe	Ser	Pro	Ser
				275					280					285
Pro	Thr	Ser	Pro	Ser	Pro	Thr	Val	Gln	Leu	Gln	Pro	Leu	Leu	Pro
				290					295					300
Asp	Pro	Ser	Ala	Ile	Thr	Pro	Asn	Ser	Thr	Ser	Pro	Leu	Leu	Phe
				305					310					315
Ala	Ala	His	Pro	His	Phe	Gln	Asn	Leu	Ser	Gln	Glu	Glu		
				320					325			328		

(2) SEQ ID NO:22에 대한 정보:

(i) 서열 특성:

(A) 길이: 5141 염기

(B) 타입: 핵산

(C) 나선 구조: 이중나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:22

```

TTCGAGCTCG CCCGACATTG ATTATTGACT AGAGTCGATC GACAGCTGTG 50
GAATGTGTGT CAGTTAGGGT GTGGAAAGTC CCCAGGCTCC CCAGCAGGCA 100
GAAGTATGCA AAGCATGCAT CTCAATTAGT CAGCAACCAG GTGTGGAAAG 150
TCCCCAGGCT CCCCAGCAGG CAGAAGTATG CAAAGCATGC ATCTCAATTA 200
GTCAGCAACC ATAGTCCCGC CCCTAACTCC GCCCATCCCG CCCCTAACTC 250

```

CGCCCAGTTC CGCCCATCT CCGCCCCATG GCTGACTAAT TTTTTTTATT 300
TATGCAGAGG CCGAGGCCGC CTCGGCCTCT GAGCTATTCC AGAAGTAGTG 350
AGGAGGCTTT TTTGGAGGCC TAGGCTTTTG CAAAAAGCTA GCTTATCCGG 400
CCGGGAACGG TGCATTGGAA CGCGGATTCC CCGTGCCAAG AGTGACGTAA 450
GTACCGCCTA TAGAGCGATA AGAGGATTTT ATCCCCGCTG CCATCATGGT 500
TCGACCATTG AACTGCATCG TCGCCGTGTC CCAAAATATG GGGATTGGCA 550
AGAACGGAGA CCTACCCTGG CCTCCGCTCA GGAACGAGTT CAAGTACTTC 600
CAAAGAATGA CCACAACCTC TTCAGTGGAA GGTAACAGA ATCTGGTGAT 650
TATGGGTAGG AAAACCTGGT TCTCCATTCC TGAGAAGAAT CGACCTTTAA 700
AGGACAGAAT TAATATAGTT CTCAGTAGAG AACTCAAAGA ACCACCACGA 750
GGAGCTCATT TTCTTGCCAA AAGTTTGGAT GATGCCTTAA GACTTATTGA 800
ACAACCGGAA TTGGCAAGTA AAGTAGACAT GGTTTGGATA GTCGGAGGCA 850
GTTCTGTTTA CCAGGAAGCC ATGAATCAAC CAGGCCACCT TAGACTCTTT 900
GTGACAAGGA TCATGCAGGA ATTTGAAAGT GACACGTTTT TCCCAGAAAT 950
TGATTTGGGG AAATATAAAC CTCTCCCAGA ATACCCAGGC GTCCTCTCTG 1000
AGGTCCAGGA GGAAAAAGGC ATCAAGTATA AGTTTGAAGT CTACGAGAAG 1050
AAAGACTAAC AGGAAGATGC TTTCAAGTTC TCTGCTCCCC TCCTAAAGCT 1100
ATGCATTTTT ATAAGACCAT GGGACTTTTG CTGGCTTTAG ATCCCCTTGG 1150
CTTCGTTAGA ACGCGCTAC AATTAATACA TAACCTTATG TATCATAAC 1200
ATACGATTTA GGTGACACTA TAGATAACAT CCACTTTGCC TTTCTCTCCA 1250
CAGGTGTCCA CTCCCAGGTC CAACTGCACC TCGGTTCTAA GCTTCTGCAG 1300
GTCGACTCTA GAGGATCCCC GGGGAATTCA ATCGATGGCC GCCATGGCCC 1350
AACTTGTTTA TTGCAGCTTA TAATGGTTAC AAATAAAGCA ATAGCATCAC 1400
AAATTTACA AATAAAGCAT TTTTTCACT GCATTCTAGT TGTGGTTTGT 1450
CCAACTCAT CAATGTATCT TATCATGTCT GGATCGATCG GGAATTAATT 1500
CGGCGCAGCA CCATGGCCTG AAATAACCTC TGAAAGAGGA ACTTGGTTAG 1550
GTACCTTCTG AGGCGGAAAG AACCAGCTGT GGAATGTGTG TCAGTTAGGG 1600
TGTGGAAAGT CCCCAGGCTC CCCAGCAGGC AGAAGTATGC AAAGCATGCA 1650
TCTCAATTAG TCAGCAACCA GGTGTGGAAG GTCCCCAGGC TCCCAGCAG 1700

GCAGAAGTAT GCAAAGCATG CATCTCAATT AGTCAGCAAC CATAGTCCCG 1750
 CCCCTAATC CGCCCATCCC GCCCCTAACT CCGCCCAGTT CCGCCCATTC 1800
 TCCGCCCCAT GGCTGACTAA TTTTTTTTAT TTATGCAGAG GCCGAGGCCG 1850
 CCTCGGCCTC TGAGCTATTC CAGAAGTAGT GAGGAGGCTT TTTTGGAGGC 1900
 CTAGGCTTTT GCAAAAAGCT GTTACCTCGA GCGGCCGCTT AATTAAGGCG 1950
 CGCCATTTAA ATCCTGCAGG TAACAGCTTG GCACTGGCCG TCGTTTTACA 2000
 ACGTCGTGAC TGGGAAAACC CTGGCGTTAC CCAACTTAAT CGCCTTGCG 2050
 CACATCCCCC CTTCGCCAGC TGGCGTAATA GCGAAGAGGC CCGCACCGAT 2100
 CGCCCTTCCC AACAGTTGCG TAGCCTGAAT GCGAATGGC GCCTGATGCG 2150
 GTATTTTCTC CTTACGCATC TGTGCGGTAT TTCACACCGC ATACGTCAA 2200
 GCAACCATAG TACGCGCCCT GTAGCGGCGC ATTAAGCGCG GCGGGTGTGG 2250
 TGGTTACGCG CAGCGTGACC GCTACACTTG CCAGCGCCCT AGCGCCCGCT 2300
 CCTTTCGCTT TCTTCCCTTC CTTTCTCGCC ACGTTCGCCG GCTTTCCCG 2350
 TCAAGCTCTA AATCGGGGGC TCCCTTTAGG GTTCCGATTT AGTGCTTTAC 2400
 GGCACCTCGA CCCCAAAAAA CTTGATTTGG GTGATGGTTC ACGTAGTGGG 2450
 CCATCGCCCT GATAGACGGT TTTTCGCCCT TTGACGTTGG AGTCCACGTT 2500
 CTTTAATAGT GGACTCTTGT TCCAACTGG AACAACTC AACCCATCT 2550
 CGGGCTATTC TTTTGATTTA TAAGGGATT TCGCGATTTC GGCCTATTGG 2600
 TTAAAAATG AGCTGATTTA AAAAAATTT AACGCGAATT TTAACAAAT 2650
 ATTAACGTTT ACAATTTTAT GGTGCACTCT CAGTACAATC TGCTCTGATG 2700
 CCGCATAGTT AAGCCAACTC CGCTATCGCT ACGTGAAGTG GTCATGGCTG 2750
 CGCCCCGACA CCCGCCAACA CCCGCTGACG CGCCCTGACG GGCTTGTCTG 2800
 CTCCCGGCAT CCGCTTACAG ACAAGCTGTG ACCGTCTCCG GGAGCTGCAT 2850
 GTGTCAGAGG TTTTCACCGT CATACCGAA ACGCGCGAGG CAGTATTCTT 2900
 GAAGACGAAA GGGCCTCGTG ATACGCCTAT TTTTATAGGT TAATGTCATG 2950
 ATAATAATGG TTTCTTAGAC GTCAGGTGGC ACTTTTCGGG GAAATGTGCG 3000
 CGGAACCCCT ATTTGTTTAT TTTTCTAAAT ACATTCAAAT ATGTATCCGC 3050
 TCATGAGACA ATAACCCTGA TAAATGCTTC AATAATATTG AAAAAGGAAG 3100

AGTATGAGTA TTCAACATTT CCGTGTGCGC CTTATTCCT TTTTTCGGC 3150
 ATTTTGCCTT CCTGTTTTTG CTCACCCAGA AACGCTGGTG AAAGTAAAAG 3200
 ATGCTGAAGA TCAGTTGGGT GCACGAGTGG GTTACATCGA ACTGGATCTC 3250
 AACAGCGGTA AGATCCTTGA GAGTTTTTCGC CCCGAAGAAC GTTTTCCAAT 3300
 GATGAGCACT TTAAAGTTC TGCTATGTGG CGCGGTATTA TCCCGTGATG 3350
 ACGCCGGGCA AGAGCAACTC GGTGCGCGCA TACACTATTC TCAGAATGAC 3400
 TTGGTTGAGT ACTCACCAGT CACAGAAAAG CATCTTACGG ATGGCATGAC 3450
 AGTAAGAGAA TTATGCAGTG CTGCCATAAC CATGAGTGAT AACACTGCGG 3500
 CCAACTTACT TCTGACAAAG ATCGGAGGAC CGAAGGAGCT AACCGCTTTT 3550
 TTGCACAACA TGGGGGATCA TGTAACTCGC CTTGATCGTT GGGAAACGGA 3600
 GCTGAATGAA GCCATACCAA ACGACGAGCG TGACACCACG ATGCCAGCAG 3650
 CAATGGCAAC AACGTTGCGC AAATATTAA CTGGCGAACT ACTTACTCTA 3700
 GCTTCCCGGC AACAAATTAAT AGACTGGATG GAGGCGGATA AAGTTGCAGG 3750
 ACCACTTCTG CGCTCGGCCC TTCCGGCTGG CTGGTTTATT GCTGATAAAT 3800
 CTGGAGCCGG TGAGCGTGGG TCTCGCGGTA TCATTGCAGC ACTGGGGCCA 3850
 GATGGTAAGC CCTCCCGTAT CGTAGTTATC TACACGACGG GGAGTCAGGC 3900
 AACTATGGAT GAACGAAATA GACAGATCGC TGAGATAGGT GCCTCACTGA 3950
 TTAAGCATTG GTAAGTGTCA GACCAAGTTT ACTCATATAT ACTTTAGATT 4000
 GATTTAAAAC TTCATTTTAA ATTTAAAAGG ATCTAGGTGA AGATCCTTTT 4050
 TGATAATCTC ATGACCAAAA TCCCTTAACG TGAGTTTTCG TTCCACTGAG 4100
 CGTCAGACCC CGTAGAAAAG ATCAAAGGAT CTTCTTGAGA TCCTTTTTTT 4150
 CTGCGCGTAA TCTGCTGCTT GCAAACAAA AAACCACCGC TACCAGCGGT 4200
 GGTTTGTTTG CCGGATCAAG AGCTACCAAC TCTTTTCCG AAGGTAAGT 4250
 GCTTCAGCAG AGCGCAGATA CCAAATACTG TCCTTCTAGT GTAGCCGTAG 4300
 TTAGGCCACC ACTTCAAGAA CTCTGTAGCA CCGCCTACAT ACCTCGCTCT 4350
 GCTAATCCTG TTACCAAGTG CTGCTGCCAG TGCGGATAAG TCGTGTCTTA 4400
 CCGGGTTGGA CTCAAGACGA TAGTTACCGG ATAAGGCGCA GCGGTCGGGC 4450
 TGAACGGGGG GTTCGTGCAC ACAGCCCAGC TTGGAGCGAA CGACCTACAC 4500

CGAACTGAGA TACCTACAGC GTGAGCATTG AGAAAGCGCC ACGCTTCCCG 4550
 AAGGGAGAAA GGCGGACAGG TATCCGGTAA GCGGCAGGGT CGGAACAGGA 4600
 GAGCGCACGA GGGAGCTTCC AGGGGGAAAC GCCTGGTATC TTTATAGTCC 4650
 TGTCGGGTTT CGCCACCTCT GACTTGAGCG TCGATTTTTC TGATGCTCGT 4700
 CAGGGGGGCG GAGCCTATGG AAAAACGCCA GCAACGCGGC CTTTTTACGG 4750
 TTCCTGGCCT TTTGCTGGCC TTTTGCTCAC ATGTTCTTTC CTGCGTTATC 4800
 CCCTGATTCT GTGATAACC GTATTACCGC CTTTGAGTGA GCTGATAACG 4850
 CTCGCCGAG CCGAACGACC GAGCGCAGCG AGTCAGTGAG CGAGGAAGCG 4900
 GAAGAGCGCC CAATACGCAA ACCGCCTCTC CCCGCGCGTT GGCCGATTCA 4950
 TTAATCCAGC TGGCACGACA GGTTCCTCCGA CTGGAAAGCG GGCAGTGAGC 5000
 GCAACGCAAT TAATGTGAGT TACCTCACTC ATTAGGCACC CCAGGCTTTA 5050
 CACTTTATGC TTCCGGCTCG TATGTTGTGT GGAATTGTGA GCGGATAACA 5100
 ATTTACACA GGAAACAGCT ATGACCATGA TTACGAATTA A 5141

(2) SEQ ID NO:23에 대한 정보:

(i) 서열 특성:

(A) 길이: 21 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:23

ATGTCNCCNG CNCCNCCNGC N 21

(2) SEQ ID NO:24에 대한 정보:

(i) 서열 특성:

(A) 길이: 21 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:24

ATGTCTCCAG CGCCGCCAGC G 21

(2) SEQ ID NO:25에 대한 정보:

(i) 서열 특성:

(A) 길이: 21 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:25

ATGTCGCCTG CTCCACCTGC T 21

(2) SEQ ID NO:26에 대한 정보:

(i) 서열 특성:

(A) 길이: 21 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:26

ATGTCGCCAG CGCCACCAGC C 21

(2) SEQ ID NO:27에 대한 정보:

(i) 서열 특성:

(A) 길이: 21 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:27

ATGTCCCCAG CCCACCCGC A 21

(2) SEQ ID NO:28에 대한 정보:

(i) 서열 특성:

(A) 길이: 21 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:28

ATGTCGCCAG CGCCGCCAGC G 21

(2) SEQ ID NO:29에 대한 정보:

(i) 서열 특성:

(A) 길이: 25 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:29

```

Ser Pro Ala Pro Pro Ala Cys Asp Pro Arg Leu Leu Asn Lys Leu
 1           5           10           15
Leu Arg Asp Asp His Val Leu His Gly Arg
                20           25

```

(2) SEQ ID NO:30에 대한 정보:

(i) 서열 특성:

(A) 길이: 26 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:30

```

Ser Pro Ala Pro Pro Ala Cys Asp Pro Arg Leu Leu Asn Lys Leu
 1           5           10           15
Leu Arg Asp Asp Xaa Val Leu His Gly Arg Leu
                20           25 26

```

(2) SEQ ID NO:31에 대한 정보:

(i) 서열 특성:

(A) 길이: 25 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:31

```
Ser Pro Ala Pro Pro Ala Xaa Asp Pro Arg Leu Leu Asn Lys Leu
 1           5           10           15
Leu Arg Asp Asp His Val Leu His Gly Arg
                20           25
```

(2) SEQ ID NO:32에 대한 정보:

(i) 서열 특성:

(A) 길이: 14 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:32

```
Xaa Pro Ala Pro Pro Ala Xaa Asp Pro Arg Leu Xaa Asn Lys
 1           5           10           14
```

(2) SEQ ID NO:33에 대한 정보:

(i) 서열 특성:

(A) 길이: 9 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:33

Pro Arg Leu Leu Asn Lys Leu Leu Arg
 1 5 9

(2) SEQ ID NO:34에 대한 정보:

(i) 서열 특성:

(A) 길이: 45 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:34

GCCGTGAAGG ACGTGGTCGT CACGAAGCAG TTTATTAGG AGTCG 45

(2) SEQ ID NO:35에 대한 정보:

(i) 서열 특성:

(A) 길이: 20 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:35

CCNGCNCNC CNGCNTGYGA 20

(2) SEQ ID NO:36에 대한 정보:

(i) 서열 특성:

(A) 길이: 21 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:36

NCCRTGNARN ACRTGRTCRT C 21

(2) SEQ ID NO:37에 대한 정보:

(i) 서열 특성:

(A) 길이: 69 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:37

CCAGCGCCGC CAGCCTGTGA CCCCCGACTC CTAAATAAAC TGCCTCGTGA 50
TGACCACGTT CAGCACGGC 69

(2) SEQ ID NO:38에 대한 정보:

(i) 서열 특성:

(A) 길이: 69 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:38

GCCGTGCTGA ACGTGGTCAT CACGAGGCAG TTTATTTAGG AGTCGGGGGT 50
CACAGGCTGG CGGCGCTGG 69

(2) SEQ ID NO:39에 대한 정보:

(i) 서열 특성:

(A) 길이: 69 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:39

CCAGCACCTC CGGCATGTGA CCCCCGACTC CTAAATAAAC TGCTTCGTGA 50
CGACCACGTC CATCACGGC 69

(2) SEQ ID NO:40에 대한 정보:

(i) 서열 특성:

(A) 길이: 69 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:40

GCCGTGATGG ACGTGTCGT CACGAAGCAG TTTATTTAGG AGTCGGGGGT 50
CACATGCCGG AGGTGCTGG 69

(2) SEQ ID NO:41에 대한 정보:

(i) 서열 특성:

(A) 길이: 69 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:41

CCAGCACCGC CGGCATGTGA CCCCCGACTC CTAAATAAAC TGCTTCGTGA 50
CGATCATGTC TATCACGGT 69

(2) SEQ ID NO:42에 대한 정보:

(i) 서열 특성:

(A) 길이: 69 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:42

ACCGTGATAG ACATGATCGT CACGAAGCAG TTTATTTAGG AGTCGGGGGT 50
CACATGCCGG CGGTGCTGG 69

(2) SEQ ID NO:43에 대한 정보:

(i) 서열 특성:

(A) 길이: 37 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:43

GCTAGCTCTA GAAATTGCTC CTCGTGGTCA TGCTTCT 37

(2) SEQ ID NO:44에 대한 정보:

(i) 서열 특성:

(A) 길이: 22 염기

- (B) 타입: 핵산
- (C) 나선 구조: 단일나선
- (D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:44

CAGTCTGCCG TGAAGGACAT. GG 22

(2) SEQ ID NO:45에 대한 정보:

(i) 서열 특성:

- (A) 길이: 24 염기
- (B) 타입: 핵산
- (C) 나선 구조: 단일나선
- (D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:45

TGTGGACTTT AGCTTGGGAG AATG 24

(2) SEQ ID NO:46에 대한 정보:

(i) 서열 특성:

- (A) 길이: 22 염기
- (B) 타입: 핵산
- (C) 나선 구조: 단일나선
- (D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:46

GGTCCAGGGA CCTGGAGGTT TG 22

(2) SEQ ID NO:47에 대한 정보:

(i) 서열 특성:

(A) 길이: 31 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:47

ATCGATATCG ATAGCCAGAC ACCCCGGCCA G 31

(2) SEQ ID NO:48에 대한 정보:

(i) 서열 특성:

(A) 길이: 36 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:48

GCTAGCTCTA GACAGGGAAG GGAGCTGTAC ATGAGA 36

(2) SEQ ID NO:49에 대한 정보:

(i) 서열 특성:

(A) 길이: 24 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:49

CTCCTTGGA CCCAGGGCAG GACC 24

(2) SEQ ID NO:50에 대한 정보:

(i) 서열 특성:

(A) 길이: 24 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:50

GGTCCTGCCC TGGGTTCCAA GGAG 24

(2) SEQ ID NO:51에 대한 정보:

(i) 서열 특성:

(A) 길이: 27 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:51

CTGCTCCGAG GAAAGGACTT CTGGATT 27

(2) SEQ ID NO:52에 대한 정보:

(i) 서열 특성:

(A) 길이: 27 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:52

AATCCAGAAG TCCTTTCCTC GGAGCAG 27

(2) SEQ ID NO:53에 대한 정보:

(i) 서열 특성:

(A) 길이: 28 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:53

CCCTCTGCGT CGCGGCGGCC CCACCCAC 28

(2) SEQ ID NO:54에 대한 정보:

(i) 서열 특성:

(A) 길이: 28 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:54

GTGGGTGGGG CCGCCGCGAC GCAGAGGG 28

(2) SEQ ID NO:55에 대한 정보:

(i) 서열 특성:

(A) 길이: 35 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:55

GACTCGAGGA TCCATCGATT TTTTTTTTTT TTTT 35

(2) SEQ ID NO:56에 대한 정보:

(i) 서열 특성:

(A) 길이: 17 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:56

GACTCGAGGA TCCATCG 17

(2) SEQ ID NO:57에 대한 정보:

(i) 서열 특성:

(A) 길이: 32 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:57

GCTAGCTCTA GAAGCCCGGC TCCTCCTGCC TG 32

(2) SEQ ID NO:58에 대한 정보:

(i) 서열 특성:

(A) 길이: 21 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:58

CGAAATTAAC CCTCACTAAA G 21

(2) SEQ ID NO:59에 대한 정보:

(i) 서열 특성:

(A) 길이: 103 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:59

```
TGCAGCAAGG GCTACTGCCA CACTCGAGCT GCGCAGATGC TAGCCTCAAG 50
ATGGCTGATC CAAATCGATT CCGCGGCAAA GATCTTCCGG TCCTGTAGAA 100
GCT 103
```

(2) SEQ ID NO:60에 대한 정보:

(i) 서열 특성:

(A) 길이: 103 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:60

```
AGCTTCTACA GGACCGGAAG ATCTTTGCCG CGGAATCGAT TTGGATCAGC 50
CATCTTGAGG CTAGCATCTG CGCAGCTCGA GTGTGGCAGT AGCCCTTGCT 100
GCA 103
```

(2) SEQ ID NO:61에 대한 정보:

(i) 서열 특성:

(A) 길이: 18 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:61

TCTCGCTACC GTTTACAG 18

(2) SEQ ID NO:62에 대한 정보:

(i) 서열 특성:

(A) 길이: 25 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:62

CAGGTACCCA CCAGGCGGTC TCGGT 25

(2) SEQ ID NO:63에 대한 정보:

(i) 서열 특성:

(A) 길이: 18 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:63

GGGCCCATGAC ACTGTCAA 18

(2) SEQ ID NO:64에 대한 정보:

(i) 서열 특성:

(A) 길이: 40 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:64

GACCGCCACC GAGACCGCCT GGTGGGTACC TGTGGTCCTT 40

(2) SEQ ID NO:65에 대한 정보:

(i) 서열 특성:

(A) 길이: 32 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:65

ATCGATATCG ATCAGCCAGA CACCCCGGCC AG 32

(2) SEQ ID NO:66에 대한 정보:

(i) 서열 특성:

(A) 길이: 35 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:66

TCTAGATCTA GATCACCTGA CGCAGAGGGT GGACC 35

(2) SEQ ID NO:67에 대한 정보:

(i) 서열 특성:

(A) 길이: 33 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:67

AGTCGACGTC GACGTCGGCA GTGTCTGAGA ACC 33

(2) SEQ ID NO:68에 대한 정보:

(i) 서열 특성:

(A) 길이: 36 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:68

AGTCGACGTC GACTCACCTG ACGCAGAGGG TGGACC 36

(2) SEQ ID NO:69에 대한 정보:

(i) 서열 특성:

(A) 길이: 62 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:69

CGCGTATGCC AGCCCGGCTC CTCCTGCTTG TGACCTCCGA GTCCTCAGTA 50
AACTGCTTCG TG 62

(2) SEQ ID NO:70에 대한 정보:

(i) 서열 특성:

(A) 길이: 61 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:70

AGTCACGAAG CAGTTTACTG AGGACTCGGA GGTCAACAAGC AGGAGGAGCC 50
GGGCTGGCAT A 61

(2) SEQ ID NO:71에 대한 정보:

(i) 서열 특성:

(A) 길이: 37 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:71

CTAGAATTAT GAAAAAGAAT ATCGCATTTC TTCTTAA 37

(2) SEQ ID NO:72에 대한 정보:

(i) 서열 특성:

(A) 길이: 37 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:72

CGCGTTAAGA AGAAATGCGA TATTCTTTTT CATAATT 37

(2) SEQ ID NO:73에 대한 정보:

(i) 서열 특성:

(A) 길이: 69 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:73

CTAGAATTAT GAAAAAGAAT ATCGCATTTC ATCACCATCA CCATCACCAT 50
CACATCGAAG GTCGTAGCC 69

(2) SEQ ID NO:74에 대한 정보:

(i) 서열 특성:

(A) 길이: 62 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:74

TACGACCTTC GATGTGATGG TGATGGTGAT GGTGATGAAA TCGCATATTC 50
TTTTTCATAA TT 62

(2) SEQ ID NO:75에 대한 정보:

(i) 서열 특성:

(A) 길이: 69 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:75

CTAGAATTAT GAAAAAGAAT ATCGCATTTC ATCACCATCA CCATCACCAT 50
CACATCGAAC CACGTAGCC 69

(2) SEQ ID NO:76에 대한 정보:

(i) 서열 특성:

(A) 길이: 62 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:76

TACGTGGTTC GATGTGATGG TGATGGTGAT GGTGATGAAA TCGATATTTC 50
TTTTTCATAA TT 62

(2) SEQ ID NO:77에 대한 정보:

(i) 서열 특성:

(A) 길이: 19 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:77

TCCACCCTCT GCGTCAGGT 19

(2) SEQ ID NO:78에 대한 정보:

(i) 서열 특성:

(A) 길이: 18 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:78

AGCTACCTGA CGCAGAGG 18

(2) SEQ ID NO:79에 대한 정보:

(i) 서열 특성:

(A) 길이: 62 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:79

GCAGCAGTTC TAGAATTATG TCNCCNGCNC CNCCNGCNTG TGACCTCCGA 50
GTTCTCAGTA AA 62

(2) SEQ ID NO:80에 대한 정보:

(i) 서열 특성:

(A) 길이: 49 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:80

GAAGGACATG GGAGTCACGA AGCAGTTTAC TGAGAACTCG GAGGTCACA 49

(2) SEQ ID NO:81에 대한 정보:

(i) 서열 특성:

(A) 길이: 45 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:81

CTAGAATTAT GAAAAAGAAT ATCGCATTTA TCGAAGGTCG TAGCC 45

(2) SEQ ID NO:82에 대한 정보:

(i) 서열 특성:

(A) 길이: 38 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:82

TACGACCTTC GATAAATGCG ATATTCTTTT TCATAATT 38

(2) SEQ ID NO:83에 대한 정보:

(i) 서열 특성:

(A) 길이: 45 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:83

CTAGAATTAT GAAAAAGAAT ATCGCATTTC TTCTTAAACG TAGCC 45

(2) SEQ ID NO:84에 대한 정보:

(i) 서열 특성:

(A) 길이: 38 염기

(B) 타입: 핵산

(C) 나선 구조: 단일나선

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:84

TACGTTTAAG AAGAAATGCG ATATTCTTTT TCATAATT 38

(2) SEQ ID NO:85에 대한 정보:

(i) 서열 특성:

(A) 길이: 25 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:85

Met	Lys	Lys	Asn	Ile	Ala	Phe	Leu	Leu	Asn	Ala	Tyr	Ala	Ser	Pro	1	5	10	15
Ala	Pro	Pro	Ala	Cys	Asp	Leu	Arg	Val	Leu	Ser	Lys	Leu	Leu	Arg	20	25	30	
Asp	Ser	His	Val	Leu	His	Ser	Arg	Leu	Ser	Gln	Cys	Pro	Glu	Val	35	40	45	
His	Pro	Leu	Pro	Thr	Pro	Val	Leu	Leu	Pro	Ala	Val	Asp	Phe	Ser	50	55	60	
Leu	Gly	Glu	Trp	Lys	Thr	Gln	Met	Glu	Glu	Thr	Lys	Ala	Gln	Asp	65	70	75	
Ile	Leu	Gly	Ala	Val	Thr	Leu	Leu	Leu	Glu	Gly	Val	Met	Ala	Ala	80	85	90	
Arg	Gly	Gln	Leu	Gly	Pro	Thr	Cys	Leu	Ser	Ser	Leu	Leu	Gly	Gln	95	100	105	
Leu	Ser	Gly	Gln	Val	Arg	Leu	Leu	Leu	Gly	Ala	Leu	Gln	Ser	Leu	110	115	120	
Leu	Gly	Thr	Gln	Leu	Pro	Pro	Gln	Gly	Arg	Thr	Thr	Ala	His	Lys	125	130	135	

```

Asp Pro Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly
      140              145              150
Lys Val Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val
      155              160              165
Arg Arg Ala
      168

```

(2) SEQ ID NO:86에 대한 정보:

(i) 서열 특성:

(A) 길이: 31 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:86

```

Met Lys Lys Asn Ile Ala Phe His His His His His His His
 1          5              10              15
Ile Glu Gly Arg Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val
      20              25              30
Leu Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu
      35              40              45
Ser Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu Leu
      50              55              60
Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu
      65              70              75
Glu Thr Lys Ala Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu
      80              85              90
Glu Gly Val Met Ala Ala Arg Gly Gln Leu Gly Pro Thr Cys Leu
      95              100             105
Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Leu
      110             115             120
Gly Ala Leu Gln Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly
      125             130             135
Arg Thr Thr Ala His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe
      140             145             150

```

Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly
 155 160 165
 Gly Ser Thr Leu Cys Val Arg Arg Ala
 170 174

(2) SEQ ID NO:87에 대한 정보:

(i) 서열 특성:

(A) 길이: 31 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:87

Met Lys Lys Asn Ile Ala Phe His His His His His His His His
 1 5 10 15
 Ile Glu Pro Arg Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val
 20 25 30
 Leu Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu
 35 40 45
 Ser Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu Leu
 50 55 60
 Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu
 65 70 75
 Glu Thr Lys Ala Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu
 80 85 90
 Glu Gly Val Met Ala Ala Arg Gly Gln Leu Gly Pro Thr Cys Leu
 95 100 105
 Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Leu
 110 115 120
 Gly Ala Leu Gln Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly
 125 130 135
 Arg Thr Thr Ala His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe
 140 145 150

Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly
 155 160 165
 Gly Ser Thr Leu Cys Val Arg Arg Ala
 170 174

(2) SEQ ID NO:88에 대한 정보:

(i) 서열 특성:

(A) 길이: 7 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:88

Thr Thr Ala His Lys Asp Pro
 1 5 7

(2) SEQ ID NO:89에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:89

His Val Leu His
 1 4

(2) SEQ ID NO:90에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:90

Ser Arg Leu Ser
1 4

(2) SEQ ID NO:91에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:91

Ser His Val Leu
1 4

(2) SEQ ID NO:92에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:92

His Ser Arg Leu
1 4

(2) SEQ ID NO:93에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:93

Ala Val Asp Phe
1 4

(2) SEQ ID NO:94에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:94

Ser Leu Gly Glu
1 4

(2) SEQ ID NO:95에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:95

Ala Val Thr Leu
1 4

(2) SEQ ID NO:96에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:96

Leu Leu Glu Gly
1 4

(2) SEQ ID NO:97에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:97

Leu Ser Ser Leu
1 4

(2) SEQ ID NO:98에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:98

Leu Gly Gln Leu
1 4

(2) SEQ ID NO:99에 대한 정보:

(i) 서열 특성:

(A) 길이: 5 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:99

Cys Xaa Leu Ser Ser
1 5

(2) SEQ ID NO:100에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:100

Leu Leu Gly Gln
1 4

(2) SEQ ID NO:101에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:101

Ser Ser Leu Leu
1 4

(2) SEQ ID NO:102에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:102

Gly Gln Leu Ser
1 4

(2) SEQ ID NO:103에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:103

Cys Leu Ser Ser
1 4

(2) SEQ ID NO:104에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:104

Leu Gln Ser Leu
1 4

(2) SEQ ID NO:105에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:105

Leu Gly Thr Gln
1 4

(2) SEQ ID NO:106에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:106

Ala Leu Gln Ser
1 4

(2) SEQ ID NO:107에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:107

Leu Leu Gly Thr
1 4

(2) SEQ ID NO:108에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:108

Asn Ala Ile Phe
1 4

(2) SEQ ID NO:109에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:109

Leu Ser Phe Gln
1 4

(2) SEQ ID NO:110에 대한 정보:

(i) 서열 특성:

(A) 길이: 22 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:110

```
Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys Leu
 1          5          10          15
Leu Arg Asp Ser His Val Leu
          20          22
```

(2) SEQ ID NO:111에 대한 정보:

(i) 서열 특성:

(A) 길이: 24 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:111

```
His Ser Arg Leu Ser Gln Cys Pro Glu Val His Pro Leu Pro Thr
 1          5          10          15
Pro Val Leu Leu Pro Ala Val Asp Phe
          20          24
```

(2) SEQ ID NO:112에 대한 정보:

(i) 서열 특성:

(A) 길이: 23 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:112

```

Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln
 1          5          10          15
Asp Ile Leu Gly Ala Val Thr Leu
          20          23

```

(2) SEQ ID NO:113에 대한 정보:

(i) 서열 특성:

(A) 길이: 21 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:113

```

Leu Leu Glu Gly Val Met Ala Ala Arg Gly Gln Leu Gly Pro Thr
 1          5          10          15
Cys Leu Ser Ser Leu Leu
          20          21

```

(2) SEQ ID NO:114에 대한 정보:

(i) 서열 특성:

(A) 길이: 16 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:114

Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
 1 5 10 15
 Ser
 16

(2) SEQ ID NO:115에 대한 정보:

(i) 서열 특성;

(A) 길이: 22 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:115

Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His
 1 5 10 15
 Lys Asp Pro Asn Ala Ile Phe
 20 22

(2) SEQ ID NO:116에 대한 정보:

(i) 서열 특성:

(A) 길이: 25 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:116

Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu Met
 1 5 10 15
 Leu Val Gly Gly Ser Thr Leu Cys Val Arg
 20 25

(2) SEQ ID NO:117에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:117

Met Pro Pro Ala
 1 4

(2) SEQ ID NO:118에 대한 정보:

(i) 서열 특성:

(A) 길이: 5 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:118

Met Ala Pro Pro Ala
 1 5

(2) SEQ ID NO:119에 대한 정보:

(i) 서열 특성:

(A) 길이: 6 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:119

```
Met Pro Ala Pro Pro Ala
  1             5  6
```

(2) SEQ ID NO:120에 대한 정보:

(i) 서열 특성:

(A) 길이: 7 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:120

```
Met Ser Pro Ala Pro Pro Ala
  1             5  7
```

(2) SEQ ID NO:121에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:121

Ala Pro Pro Ala
1 4

(2) SEQ ID NO:122에 대한 정보:

(i) 서열 특성:

(A) 길이: 5 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:122

Pro Ala Pro Pro Ala
1 5

(2) SEQ ID NO:123에 대한 정보:

(i) 서열 특성:

(A) 길이: 6 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:123

Ser Pro Ala Pro Pro Ala
1 5 6

(2) SEQ ID NO:124에 대한 정보:

(i) 서열 특성:

(A) 길이: 4 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:124

```
Val Arg Arg Ala
  1           4
```

(2) SEQ ID NO:125에 대한 정보:

(i) 서열 특성:

(A) 길이: 5 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:125

```
Val Arg Arg Ala Pro
  1           5
```

(2) SEQ ID NO:126에 대한 정보:

(i) 서열 특성:

(A) 길이: 6 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:126

Val	Arg	Arg	Ala	Pro	Pro
1				5	6

(2) SEQ ID NO:127에 대한 정보:

(i) 서열 특성:

(A) 길이: 7 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:127

Val	Arg	Arg	Ala	Pro	Pro	Thr
1				5		7

(2) SEQ ID NO:128에 대한 정보:

(i) 서열 특성:

(A) 길이: 8 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:128

Val	Arg	Arg	Ala	Pro	Pro	Thr	Thr
1				5			8

(2) SEQ ID NO:129에 대한 정보:

(i) 서열 특성:

(A) 길이: 9 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:129

```
Val Arg Arg Ala Pro Pro Thr Thr Ala
 1           5           9
```

(2) SEQ ID NO:130에 대한 정보:

(i) 서열 특성:

(A) 길이: 10 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:130

```
Val Arg Arg Ala Pro Pro Thr Thr Ala Val
 1           5           10
```

(2) SEQ ID NO:131에 대한 정보:

(i) 서열 특성:

(A) 길이: 11 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:131

Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro
 1 5 10 11

(2) SEQ ID NO:132에 대한 정보:

(i) 서열 특성:

(A) 길이: 12 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:132

Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser
 1 5 10 12

(2) SEQ ID NO:133에 대한 정보:

(i) 서열 특성:

(A) 길이: 13 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:133

Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg
 1 5 10 13

(2) SEQ ID NO:134에 대한 정보:

(i) 서열 특성:

(A) 길이: 14 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:134

```
Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr
 1          5          10          14
```

(2) SEQ ID NO:135에 대한 정보:

(i) 서열 특성:

(A) 길이: 15 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:135

```
Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser
 1          5          10          15
```

(2) SEQ ID NO:136에 대한 정보:

(i) 서열 특성:

(A) 길이: 16 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:136

```

Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser
 1          5          10          15
Leu
16

```

(2) SEQ ID NO:137에 대한 정보:

(i) 서열 특성:

(A) 길이: 17 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:137

```

Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser
 1          5          10          15
Leu Val
    17

```

(2) SEQ ID NO:138에 대한 정보:

(i) 서열 특성:

(A) 길이: 18 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:138

```

Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser
 1          5          10          15
Leu Val Leu
    18

```

(2) SEQ ID NO:139에 대한 정보:

(i) 서열 특성:

(A) 길이: 19 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:139

```
Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser
 1           5          10          15
Leu Val Leu Thr
          19
```

(2) SEQ ID NO:140에 대한 정보:

(i) 서열 특성:

(A) 길이: 20 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:140

```
Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser
 1           5          10          15
Leu Val Leu Thr Leu
          20
```

(2) SEQ ID NO:141에 대한 정보:

(i) 서열 특성:

(A) 길이: 21 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:141

```
Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser
 1           5          10          15
Leu Val Leu Thr Leu Asn
          20  21
```

(2) SEQ ID NO:142에 대한 정보:

(i) 서열 특성:

(A) 길이: 22 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:142

```
Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser
 1           5          10          15
Leu Val Leu Thr Leu Asn Glu
          20    22
```

(2) SEQ ID NO:143에 대한 정보:

(i) 서열 특성:

(A) 길이: 23 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:143

```
Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser
 1          5          10          15
Leu Val Leu Thr Leu Asn Glu Leu
          20          23
```

(2) SEQ ID NO:144에 대한 정보:

(i) 서열 특성:

(A) 길이: 24 아미노산

(B) 타입: 아미노산

(D) 토폴로지: 선형

(xi) 서열 설명: SEQ ID NO:144

```
Val Arg Arg Ala Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser
 1          5          10          15
Leu Val Leu Thr Leu Asn Glu Leu Pro
          20          24
```

(57)

1.

(a) mpl P IL-3 Ba/F3 DNA (³H-)

(b) , ³⁵S ,

(c) pH 2.5, 0.1% SDS 2M ,

(d) ,

(e)

SPAPPACDPRLNKLRRDDHVLHGR SPAPPACDLRVLSKLLRDSHVLHSRL
mpl .

2.

1 , mpl .

3.

1 70% mpl .

4.

mpl mpl , mpl 1 ,

5.

- 1 4 , mpl .
- 6.
- 1 4 , mpl .
- 7.
- 1 4 , mpl .
- 8.
- 1 4 .
- 9.
- 1 4 mpl mpl 가 DNA cDNA.
- 10.
- 가 8 .
- 11.
- 가 8 .
- 12.
- 8 mpl .
- 13.
- 8 mpl .
- 14.
- 13 , mpl 가 .
- 15.
- mpl / , DNA mpl .
- 16.
- 1 4 mpl 13 mpl .
- 가
- 17.
- 16 , , (colony) 가 .
- 18.
- 17 , 가 LIF, G-CSF, GM-CSF, M-CSF, Epo, IL-1, IL-2, IL-3, IL-5, IL-6, IL-7, IL-8, IL-9 IL-11 .
- 19.
- 9 DNA cDNA (pri ming)
- 20.
- 9 mpl .
- , mpl
- 21.

1 4 mpl 13 mpl
mpl .
22.
21 , 가 .
23.
21 가 .
24.
1 4 mpl .
25.
24 , .
26.
25 .
27.
1 4 ,
가 mpl .
28.
27 , 가 14 mpl 153-154 () 245-24
6 mpl .
29.
28 , 153-154 가 mpl .
30.
29 , 153-154 Arg-Arg 가 (Ala) mpl .
31.
4 mpl .
32.
4 31 , ()
mpl .
33.
32 , N- mpl .
34.
- 1 4 mpl .
35.
34 , 가 , mpl
.
36.
13 , 가 CHO .
37.
(heterologous polypeptide) , 1(SEQ ID NO:1) mpl SEQ ID NO:9 m
pl .

38.

37 , 1 (SEQ ID NO:1) mpl , 1 (SEQ ID NO:1) mpl

MPPA, (SEQ ID NO:117)

MAPPA, (SEQ ID NO:118)

MPAPPA, (SEQ ID NO:119)

MSPAPPA, (SEQ ID NO:120)

APPA, (SEQ ID NO:121)

PAPPA, (SEQ ID NO:122)

SPAPPA, (SEQ ID NO:123)

VRRA, (SEQ ID NO:124)

VRRAP, (SEQ ID NO:125)

VRRAPP, (SEQ ID NO:126)

VRRAPPT, (SEQ ID NO:127)

VRRAPPTT, (SEQ ID NO:128)

VRRAPPTTA, (SEQ ID NO:129)

VRRAPPTTAV, (SEQ ID NO:130)

VRRAPPTTAVP, (SEQ ID NO:131)

VRRAPPTTAVPS, (SEQ ID NO:132)

VRRAPPTTAVPSR, (SEQ ID NO:133)

VRRAPPTTAVPSRT, (SEQ ID NO:134)

VRRAPPTTAVPSRTS, (SEQ ID NO:135)

VRRAPPTTAVPSRTSL, (SEQ ID NO:136)

VRRAPPTTAVPSRTSLV, (SEQ ID NO:137)

VRRAPPTTAVPSRTSLVL, (SEQ ID NO:138)

VRRAPPTTAVPSRTSLVLT, (SEQ ID NO:139)

VRRAPPTTAVPSRTSLVLTL, (SEQ ID NO:140)

VRRAPPTTAVPSRTSLVLTLN, (SEQ ID NO:141)

VRRAPPTTAVPSRTSLVLTLNE, (SEQ ID NO:142)

VRRAPPTTAVPSRTSLVLTLNEL, (SEQ ID NO:143)

VRRAPPTTAVPSRTSLVLTNLNLP, (SEQ ID NO:144)

1 (SEQ ID NO:1) ML 176 332 ,

39.

37 , 1 (SEQ ID NO:1) mpl , 1 (SEQ ID NO:1) mpl

SPAPPACDLRVLSKLLRDSHVL, (SEQ ID NO:110)

HSRLSQCPEVHPLPTPVLLPAVDF, (SEQ ID NO:111)

SLGEWKTQMEETKAQDILGAVTL, (SEQ ID NO:112)

LLEGVMAARGQLGPTCLSSLL, (SEQ ID NO:113)

GQLSGQVRLLL GALQS, (SEQ ID NO:114)

LLGTQLPPQGRRTAHKDPNAIF, (SEQ ID NO:115)

LSFQHLLRGKVRFLMLVGGSTLCVR, (SEQ ID NO:116)

40.

37 , 1 (SEQ ID NO:1) mpl , 1 (SEQ ID NO:1) mpl

SEQ ID NO:1 1, 3-6, 9, 13-15, 17-28, 30, 32-34, 36-41, 43-50, 53-59, 61-68, 71, 73, 75-80, 82-88, 90-96, 98-99, 102-103, 105-107, 110, 112-113, 115-119, 121-130, 132-133, 135, 137-140, 143-150 152-156,

41.

37 , 1 (SEQ ID NO:1) mpl , 1 (SEQ ID NO:1) mpl

SEQ ID NO:1 7-8, 10-12, 16, 29, 31, 35, 42, 51-52, 60, 69, 72, 74, 81, 89, 97, 100-101, 104, 108-109, 111, 114, 120, 131, 134, 136, 141-142 151,

42.

37 , 1 (SEQ ID NO:1) mpl , 1 (SEQ ID NO:1) mpl

SEQ ID NO:1 111-114, 139-140, 142-144 147-150,

43.

37 , 1 (SEQ ID NO:1) mpl , 1 (SEQ ID NO:1) mpl

14a, 14b 14c (SEQ ID NO:1) 1, 2, 3, 4, 5 6,

44.

37 , 1 (SEQ ID NO:9) mpl , SEQ ID NO:9 mpl SEQ

ID NO:9 1-2, 5-8, 10, 12, 13-20, 22-30, 32, 34-35, 38-54, 56, 59-67, 69-81, 83, 85-105, 107-113, 115-126, 128-130, 132, 134-145, 147, 149 151-153,

45.

37 , 가

46.

45

가 IgG, IgM, IgA, IgD, IgE

47.

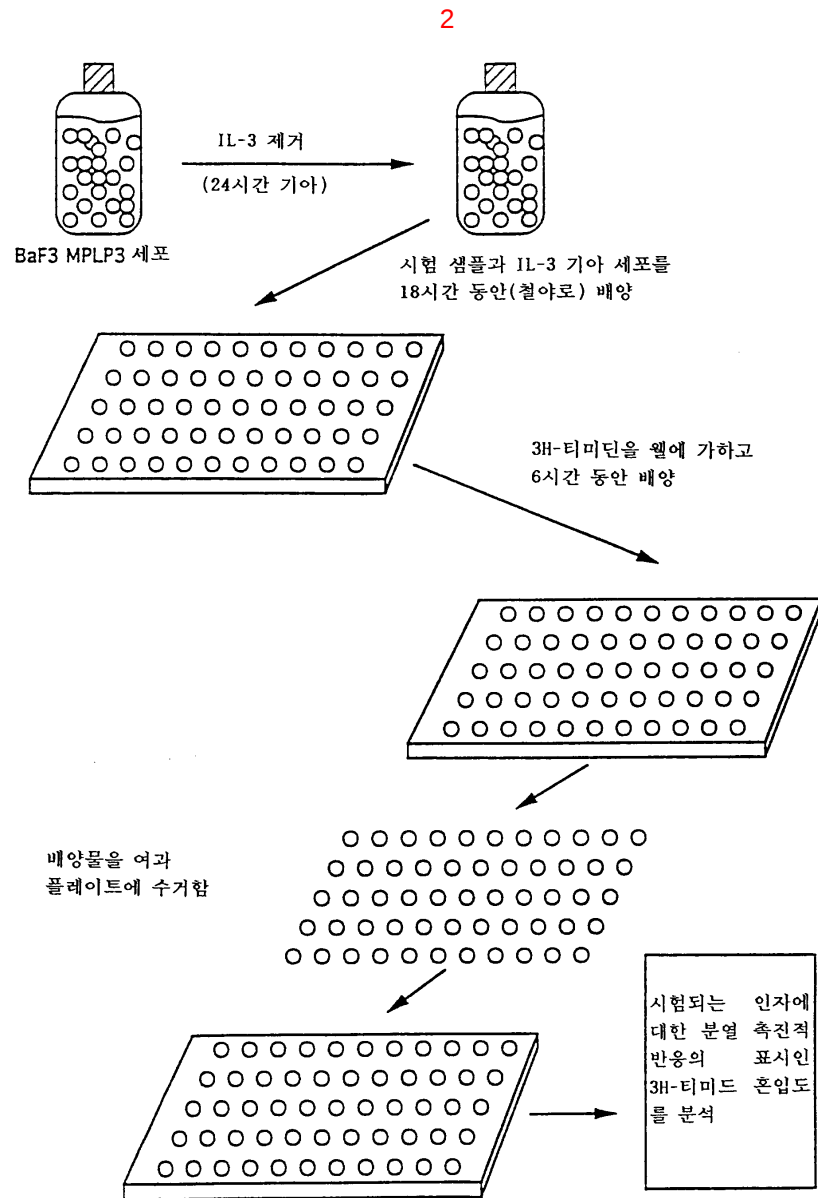
45

가 IgG1, IgG2, IgG3, IgG4

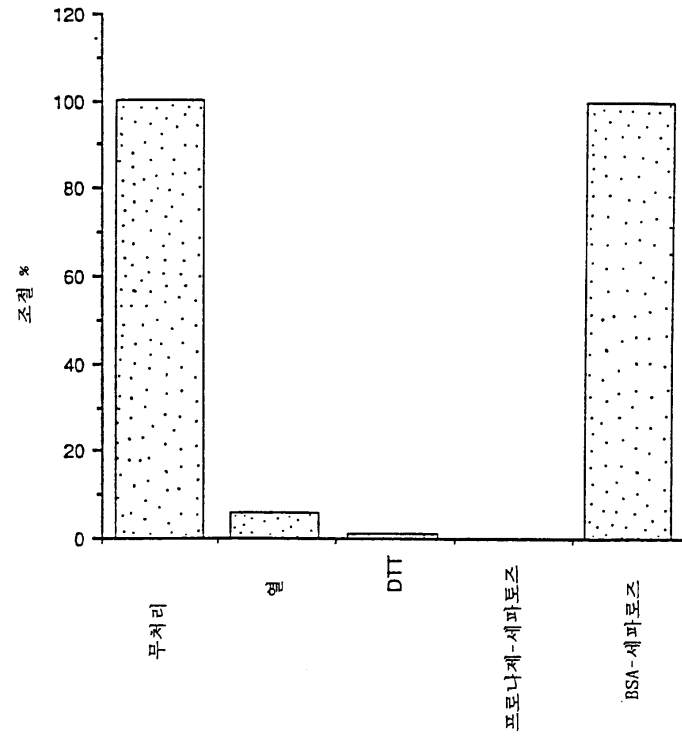
1 tcttccctaccatctgctcccccagaggctgctgctgctgcaacttgggtcccttgagcccttcccaaccgagatagatctctcaccttggcccgcttgg
101 ccccaacctactctgcccagaagtgcagaagcctaagccgctccatgccccaggaagatlcagggaagagccccaacagggagccagccagcca
-20
MetGluLeuThrGluLeuLeuValMetLeuLeuThrAlaArgLeuThrLeuSerSerProAlaProAlaCysAsp
201 gacaccccgccagaaTGAGAGCTGACTGAATTGCTCGTGGTCATGGCTTCTCTAACTGCAGAGCTGATCCAGCCGGCTCTGCTGCTG
10
LeuArgValLeuSerSerLeuLeuArgAspSerHisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuProThrProValLeuLeu
301 ACCTCCGAGTCCCTCAGTAACTGCTTCTGACTGCTTCACAGCAGACTGAGCCAGGCCAGAGTTCCACCCCTTGCTTACACCTGCTGCT
50
ProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGlnGluThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuLeuGlnGlyVal
401 GCCTGCTGTGGACTTTAGCTTTGGAGAAATGAAAAACCCAGATGAGAGAGACCAAGGCACAGACATTCTGGAGCAGTGACCCCTTCTGAGAGGAGTG
80
MetAlaAlaArgGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGlyValArgLeuLeuLeuGlyAlaLeuGlnSerLeuLeu
501 ATGGCAGCACGGGGACAACCTGGACCCACTTCCCTCAATCCCTCTGGGGCAGCTTCTGGACAGTCCGTCCTTCTGAGGCTTGGGGCCCTGCAGAGCCTCC
110
GlyThrGlnLeuProProGlnGlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHisLeuLeuArgGlyLysValArgPhe
601 TTGGAACCCAGCTTCTCCACAGGGCAGACACACTCCCAAGAGATCCCAATGCCATCTTCTGAGCTTCCAAACACCTGCCCGAGAAAGTGCGCTT
150
LeuMetLeuValGlyGlySerThrLeuCysValArgArgAlaProProThrThrAlaValProSerArgThrSerLeuValLeuThrLeuAsnGlnLeu
701 CCTGATGCTTGTAGGAGGATCCACCCTCTGCGTCAGGGGCCACCACCACACAGCTGTCCCGAGAGAACTCTTAGTCTCACACTGAACGAGCTC
180
ProAsnArgThrSerGlyLeuLeuGlnThrAsnPheThrAlaSerAlaArgThrThrGlySerGlyLeuLeuLysTrpGlnGlnGlyPheArgAlaLysIle
801 CCAACAGAGACTTCTGTGATTGTGGAGACAACCTCACTGCTCAGCCAGAACTACTGCTTGGGCTTGTGAAGTGGCAGCAGGAGATTCAAGACCAAGA

210
 ProGlyLeuLeuAsnGlnThiSerArgSerLeuAspGlnIleProGlyTyrLeuAsnArgIleHisGluLeuLeuAsnGlyTThiArgGlyLeuPhePro
 220
 230
 240
 901 TTCCTGGCTGCTGAACCAACCTCCAGTCCCTGGACCAAAATCCCGGATACCTGAACAGGATACAGAACTTGAATGGAACTCGTGGACTCTTTCC
 250
 260
 270
 GlyProSerArgArgThrLeuGlyAlaProAspIleSerSerGlyThrSerAspThrGlySerLeuProAsnLeuGlnProGlyTyrSerProSer
 1001 TGGACCCATCAGCCAGACCTTAGAGAGCCCGACATTTCTCAGGAACATCAGACACAGGCTCCCTGCCACCAACCTCCAGCTGGATTTCTCTTCC
 280
 290
 300
 ProThrHisProProThrGlyGlnTyrThrLeuPheProLeuProProThrLeuProThrProValGlnLeuHisProLeuLeuProAspProSerAla
 1101 CCAACCCATCCCTTACTGAGACAGTATACGCTTCTTCCCTTCCACCCACCTTGGTCCAGCTCCACCCCTCTTCCAGACCTTCTG
 310
 320
 330
 ProThrProThrProThrSerProLeuLeuAsnThrSerIYrThrHisSerGlnAsnLeuSerGlnGlnGly
 1201 CTCCAACGCCACCCCTACCAAGCCCTTTCTAAACATCTACACCCACTGCCAAGATCTGTCTCAGGAAGGATAGgtctcagacactgccgacatc
 1301 agcatltgtcatgtacagctcccttccctgcagggcgccccggagacaactgacaagatltccctactltctcctgaacccaagccctgtaaaa
 1401 gggatcacacaggaactgaaaagggaatcatlttctactgtacatataaaaccttcagaagctatlttllaagctatcagcaatcactcatcagagaagcta
 1501 gctccttggctcatlttctctgcagaatlttgcaactcactgactctacatgctcttctctgtgataactctgcaaggcctgggctggcctgagctc
 1601 gaacagaggagagactaaccttgagtcagaaaaacagagaaggtaatttcccttggcttcaaatccaaggcctccaacgcccccatcccttactat
 1701 catctcagtgaggactctgatcccatatltctaacagatccttactcttgagaatgaataagcttctctcagaaaaaataaaaaa

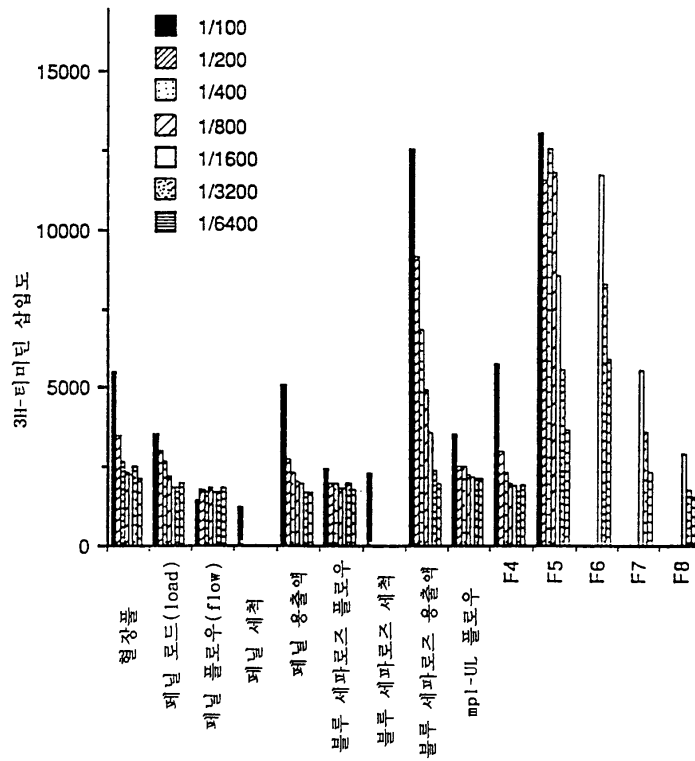
1b



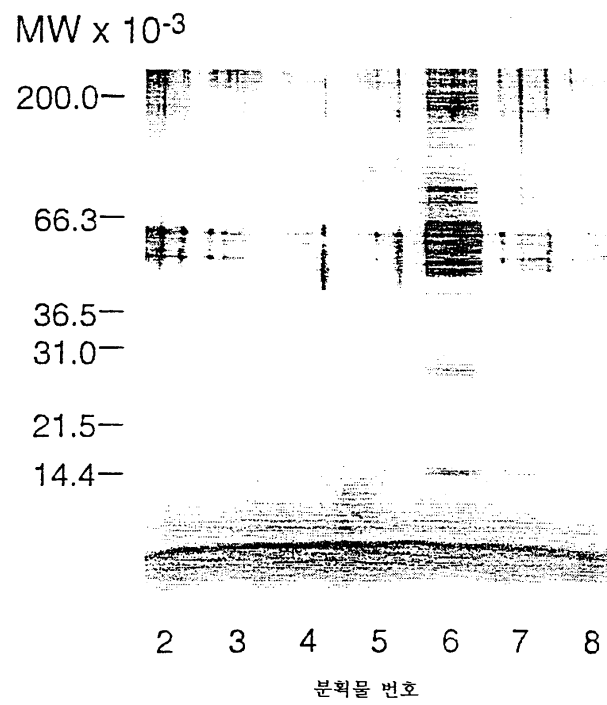
3



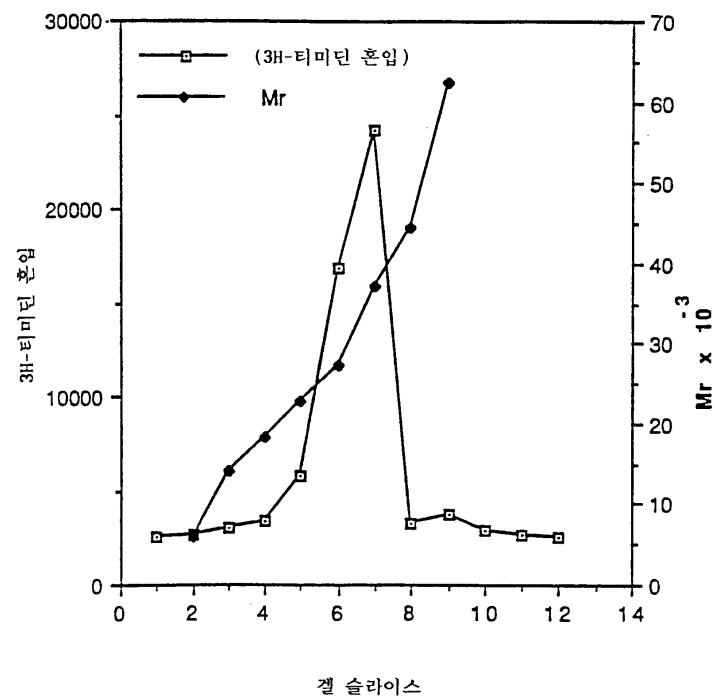
4



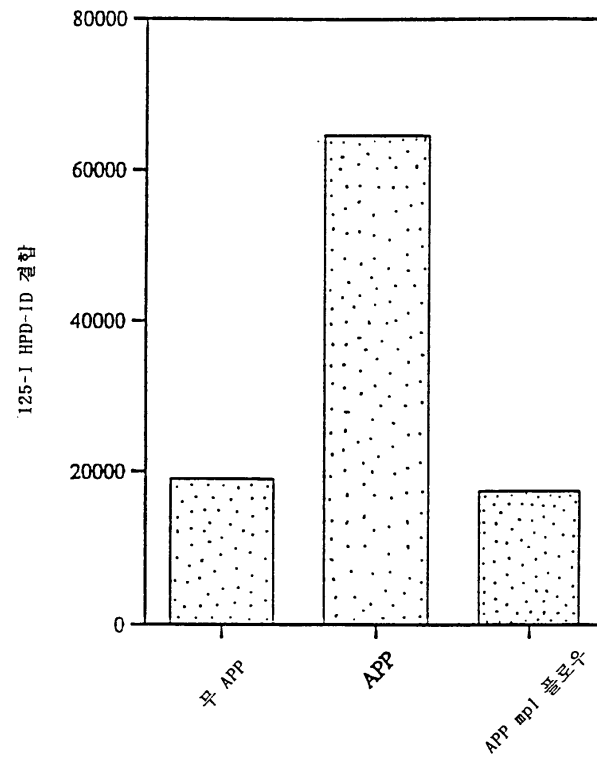
5



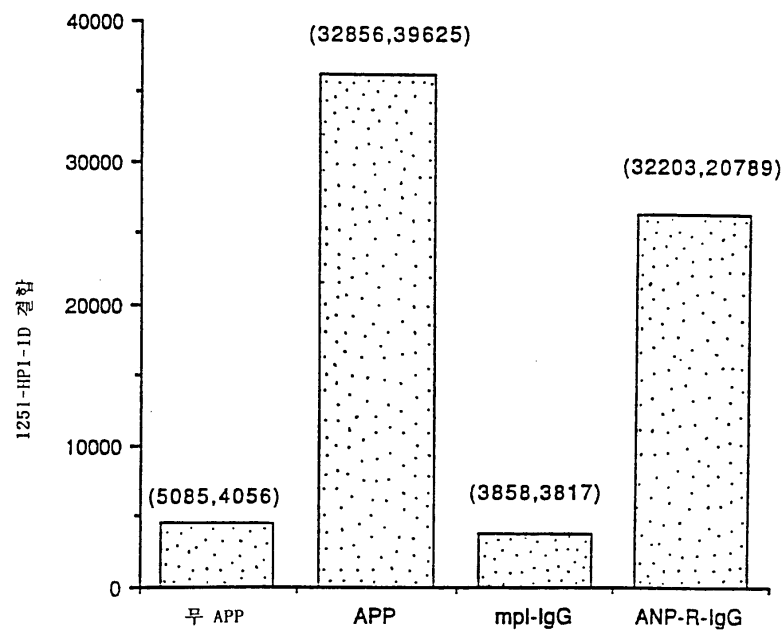
6



7



8



1 GAATTCCTGG AATACCACT GACAAATATT TCCTCCCAT CTTCAACCT CACCTCTCCT CATCTAAGAA TTGCTCTCTG TGGTCATGCT TCTCTAACT
 CTTAAGGACC TTATGTCGA CTGTTACTAA AGGAGAGTA GAAAGTTGGA GTGAGAGGA GTAGATTCTT AACGAGAGC ACCAGTAGA AGAGGATTGA
 A R L W L S S P A P P A C D L R V L S K L L R D S H V L H S R L
 101 GCAAGGCTAA GCTGTCTCAG CCCGGCTCCT CCTGCTTGAG ACCCTCGAGT CCTCAGTAA TGCTTCGAG ACTCCATGT CCTTCACAGC AGACTGTGA
 CGTTCGGATT GCGACAGGTC GGGCCGAGGA GACGAACAC TGGAGGCTCA GGAGTCATTT GACGAAGCAC TGAAGGTACA GAAAGTGTG TGTGACCACT
 20
 201 GAACGCCAA CATTATCCC TTTATCCGG TAACTGATA GACACCCATA CTCCAGGAA GACACCATCA CTTCCTCTAA CTCTTGACC CAATGACTAT
 CTTGAGGGTT GTAATAGGG AATATAGGCG ATTGACCAT CTGTGGGTAT GAGGTCTCTT CTGTGTAGT GAAGAGATT GAGGAACTGG GTTACTGATA
 301 TCTTCCCAT TTTGCCCCAC CTACTGATCA CACTCTGTGA CAAGAATTAT TCTTCACAT ACAGCCCGCA TTATAAAGCT CTGCTCTAGA
 AGAAGGTTAT AACAGGGGTG GATGACTAGT GTGAGAGACT GTTCTTAATA AGAAGTTTA TGTGGGGCGT AATTTTGA GAGCAGATCT

10

h-ML 1 S P A P P A C D L R V L S K L L R D S H V L H S R L S Q C P E V H P L P T P V L L P A V D F S L G E
h-epo 1 A P P R L I C D S R V L E R Y L L E A K E A E N I T T G C A E H C S L N E N I T V P D T K V N F Y A

h-ML 51 W K I Q M E E T K A Q D I L G A V T L L E G V M A A R G Q L G P T C L S - - S L L G Q L S G Q V R
h-epo 51 W K R M E V G Q Q A V E V W Q G L A L L S E A V L R G Q A L L V N S S Q P W E P L Q L H V D K A V S

h-ML 99 L L - - L G A L Q S L L G T Q - - L P P Q G R T T A H K K D P N A I F L S F Q H L L R G K V R F L L -
h-epo 101 G L R S L T T L L R A L G A Q K E A I S P P D A A S A A P L R T I T A D T F R K L F R V Y Y S N F L R

h-ML 143 - - M L V G G S T L C V R R A P P T T A V P S R T S L V L T L N E L P N R T S G L L E T N F T A S A
h-epo 151 G K L K L Y T G E A C R T G D R

h-ML 191 R T I G S G L L K M Q Q G F R A K I P G L L N Q T S R S L D Q I P G Y L N R I H E L L N G T R G L F

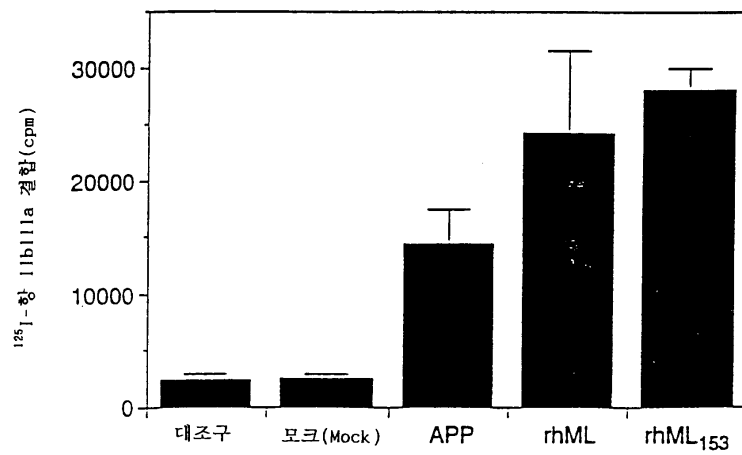
h-ML 241 P G P S R R T L G A P D I S S G T S D T G S L P P N L Q P G Y S P S P T H P P T G Q Y T L L F P L P P

h-ML 291 T L P T P V V Q L H P L L P D P S A P T P T P T S P L L N I S Y T H S O N L S Q E G

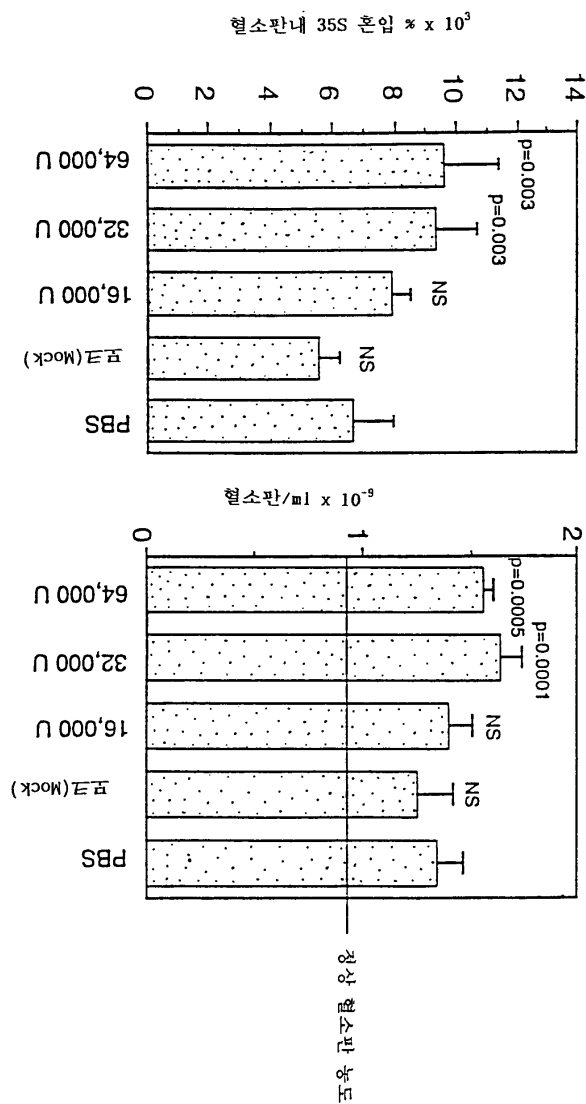
11a

hML	1	SPAPACDLRVL	SKLL	RDSHVL	HSRL	SQCP	EVHPL	PTPVLL	PAVDFSLGE
hML2	1	SPAPACDLRVL	SKLL	RDSHVL	HSRL	SQCP	EVHPL	PTPVLL	PAVDFSLGE
hML3	1	SPAPACDLRVL	SKLL	RDSHVL	HSRL	SQCP	EVHPL	PTPVLL	PAVDFSLGE
hML4	1	SPAPACDLRVL	SKLL	RDSHVL	HSRL	SQCP	EVHPL	PTPVLL	PAVDFSLGE
hML	51	WKTQMEETKA	QDILGAV	TLLLEGV	MAARG	QLGPTC	LSLLG	QLSGQVRLL	
hML2	51	WKTQMEETKA	QDILGAV	TLLLEGV	MAARG	QLGPTC	LSLLG	QLSGQVRLL	
hML3	51	WKTQMEETKA	QDILGAV	TLLLEGV	MAARG	QLGPTC	LSLLG	QLSGQVRLL	
hML4	51	WKTQMEETKA	QDILGAV	TLLLEGV	MAARG	QLGPTC	LSLLG	QLSGQVRLL	
hML	101	LGALQSL	LGTQLP	POGRTTA	HKDPNA	IFLSFQ	HLLRGK	VRFMLV	GGSTL
hML2	101	LGALQSL	LGT...	OGRTTA	HKDPNA	IFLSFQ	HLLRGK	VRFMLV	GGSTL
hML3	101	LGALQSL	LGTQLP	POGRTTA	HKDPNA	IFLSFQ	HLLRGK	DFW	IVGDKLH
hML4	101	LGALQSL	LGT...	OGRTTA	HKDPNA	IFLSFQ	HLLRGK	DFW	IVGDKLH
hML	151	CVRRAPPTTA	VP	SR	TS	SLVLT	LT	NELP	NR
hML2	147	CVRRAPPTTA	VP	SR	TS	SLVLT	LT	NELP	NR
hML3	149	CLS...	NYWL	...	WASE	VAAG	IQSD	SWSA	EPNLQ
hML4	145	CLS...	NYWL	...	WASE	VAAG	IQSD	SWSA	EPNLQ

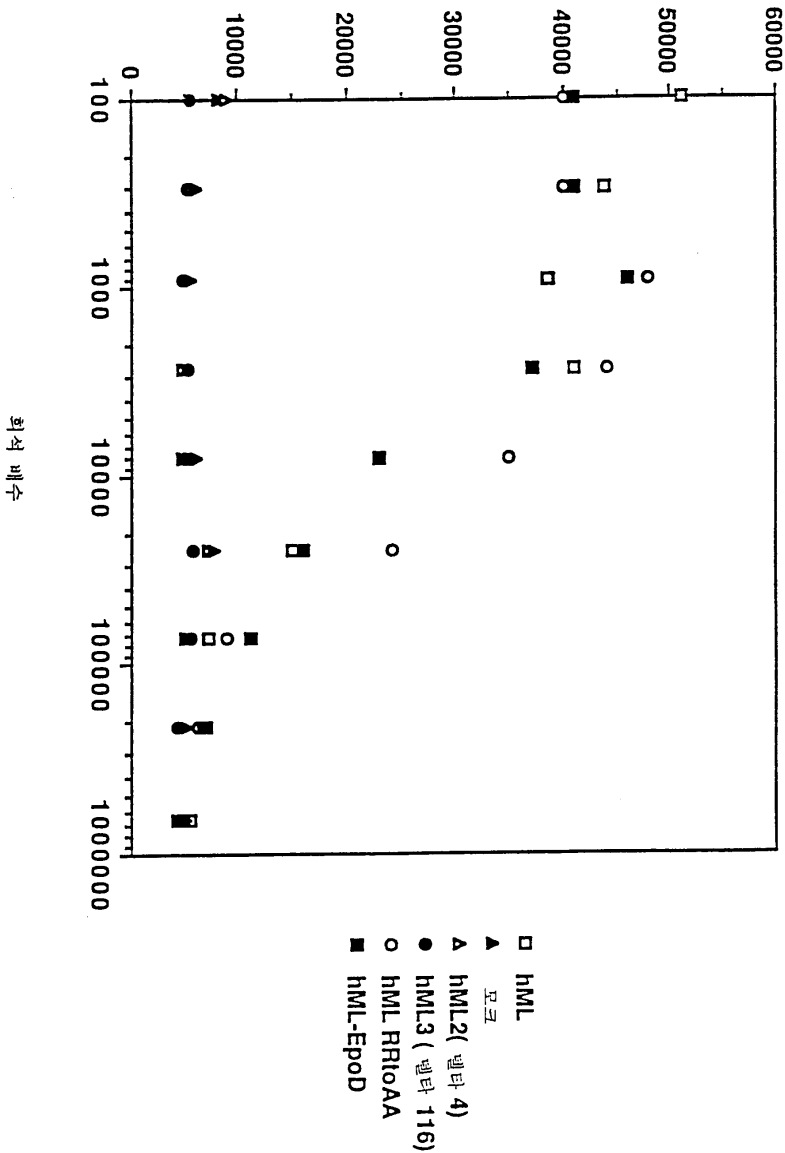
12b



12c



[3H]-티미딘 혼입



14a

1 cccagcctccttctctgttccctggtcagtcgctgcctccctgtctctctcctcccaacaaacccaactatcctccagctatccctacacccc
101 tccctccctaactcttggtggagacactctgcttctgtgacgaggaacaaatctccagatctagccaccacttctcagcagacatgccactccttggtggaggagaa
201 acgaggaaagagccctgtagagaaagtctctggggggaacaggggtgaatgcatgggtatcaaggtcagggccaggaagcccctgtagagacagggatctgtggggagatctggagac
301 tgggaagaagaacaaagagcctagagagccagggcccaaggaacaaagggggggccagccgggagatgattcttggggggaggtcccaagcagctgtccttccctaagacac
401 gggaacacatggggtgttatctcccttgtctacacatgtgtgaaacggttagagagatgggaagagcaggaacaaagcagaagggggggtccctgggacacaaaggtcc
501 tgtgtgtgtgagccatcccaagccacttggaccccagcagagcagagacactaaagctcagagcttaaacccagttgcacgtgtgtgcacatacatgtgcgccggacacct
601 gacaggtcccaactcaaacccgtcccaaacctcttccccaataaaccaaccatacagagagattctctcatalgtgggaaatccgtgtcccaacttcgaaagatg
701 gggaatgacaagatcagactcccttaagggtattacagaaagaaaagcaggaaagcagacatccctgttggaattccagcagcaggtatgaltgccagggaaa
801 gaatatgtgattagccagggagtggaaaaccccacccaactcttaaacaaagacctctgtgtcttctccccaagacaacaaatgtccctgcccagatctcctctgga
901 aaaaaaactctgtctctgtcccccctccaggtccccaagtgtgcccatgttccagggaaagatgatatcccccataccaaatctctccgtgtgtgtgtgtgtgtgt
1001 gagaggtggaaacctgtgtccagggcaggggtctccagggaaagaaagcgtcacttccggggggtctccacagtgctctgtgggtccctctcctctcgtatttgggaca

<cdna의 출발점 : 엑손 1>

<CDNA의 출발점 : 예순 1>

[illegible]

3403 LeuH1SerArgLeu
3401 TCTTTCACGACGACTGtgagaactccaacatltacccttltacgcgttaactcgttaagacacacatctccacgagagacaccatcaattccctta
3501 actctctgagcccaatgaactatcttccccaatcttgcccccaactactgatacaacatctctgacagaagaattatcttcccaatataagcccgcatcttaaaagc
3601 tctctctagagatagatctactctacatgagagactaagctctgtctatltagagctaacatagctctctctatltcagctccctctctcccccacccaattctttcaaa
<94/104>

48 SerGlnCysProGluValHisProLeuProThrProValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMet

3701 cagAGCCAGTGC^{CC}CAGAGTTCA^{CC}CTTTG^{CC}TACACCTGTCC^{TG}CTCCCTG^{CC}TGCTGACTTTAGCTTGGAGATG^{AAA}AA^{CC}CCAGATGgtaagaagc

3801 catccctaacccttgctccctaagtcctgtctctcagttccccaactgcttcccatgcatctcctccaacatctcttgagcttctttaaataatctcaccttca

3901 gctctggccacccttaaccocatctacatctcaacctatgatctagtcgctgtgataagatgatctgcttgccaggtcccaatctgtgaatagatttgaagcttgaaac
4001 accatgaaanaagctggagagaaatcgctcatctatgcccattgacctattccygttcagttctcttaaatctgcatlgaaagaagcaagatcatatgcat
4101 ccacagattgacacaaaagcttggggaagctacccttaaatatcaaaaagatctgaatctcaatctccatccgaaagactaagttcaaaaacaaagttgaaacac
4201 agagatataaactctacatctgctggccgggggtctcagcctctaatcccgaccactctgggagccgagcgagatccactgagggcaggaagttctgag
4301 agcagccttggcccaacttggcgaaaccccgctctctactaagaaatacaaaaataagccgggcatgtgtagtgcctgtaattccagctactctggaagcttg
4401 aagcagagagaatccctctgaaacccagagaagttggaaggtctgtaatgagctgagatcatatgccaatgcaatccagcctgggtgacaagaagcaaaactccgtctca
4501 aaaaagaaaaaaaattctcaatctgtcaaatctaaatgaagagtaaaagttccattccagctctccaggccacaatggccctgctccatcaattgaagcctctggccct
4601 agcactctctacgaaaaagagctctgagagaatlaaatctgccccaactctacatctgaacattacugaagctgtattctttaagctagtaattctgtctct
4701 gttctgattcttagcatcccatctgtggaatgctctgtacagaactctattccgaatggactacacttaaatatactctggccttgaaacacggacatcccccct
4801 gaagacatctatctaatcttaagagggaccactctaaactaacatgttctctgaaagccagcagcctgaacagaaagagactagaagcatcttataatggg

14d

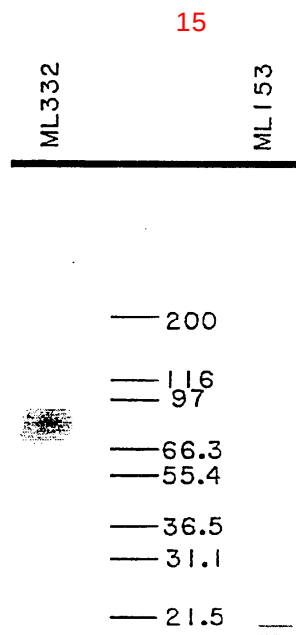
```

4901 caatagtttaaaaaactaaaatcctatccctcaagaaccctagcgtcccttctccctccagagctgagtcagggaagggaagctccatcgtgctcccttc
5001 taatcctcttcttctccctcttaagatcatatgctgtagagctcctaacctaacattagttatctatctatctatctatcttgagacggagctcctcatcc
5101 ccaggtctggagtgcaatgctgcatgctcctcaactcactgcgaacctcagcgtcccggtatctcaagcgatctcctcgctccagctcccaagtagctgggtac
5201 aggtgcccaaccaacatgcccagctaatcttgatcttctggtagagatgggtctccaccaagtctggccaggctgactcttgaaactcctgaacctcaggtgat
5301 ccacctgacctcagcctcccaaatgctgggattacagcgctgagccactgcaaccagccttcatctcaagttcaaaaaatcaatgatccctaaagttctgtag
5401 cagaaagagtaaatctgcagacactagaaccagaaggttaaaagctgttaacagggcagatctcagcaacgttaagaaaaaaggagctctctcactgaacc
5501 agtctaaagaccaggtcgtgactagaggaacagggagttcttgaaagcagaggtcgtgagagactgtaaggaactctcctgacctgggtgg
5601 accttgctctgtccagttctcagcctgtatgatctcactcgtcgtcactcctaaagctcccccacccgctttagtgcctcttgagcgagtgcgtc
    <예수 5>
77      GUGUThrLysAlaGlnAspIleuGlyAlaValThrLeuLeuGluGlyValMetAlaIArgGlyGlnLeu
5701 ctcctctccatctctctctcagGAGGAGACCAAGCCACAGGACATTTCTGGGAGGAGTGAACCTTCTGTGGAGGAGTGAAGCAGCAGCGGACACTG
103 G1YProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGlyGlnValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGln
5801 GGACCCACTTGCCCTCTCATCCCTCTGGGGCACTTTCTGACAGTCCGTCTCTCTGGGGCCCTGCAGAGCCTCTTGGAACCCAGtaagctcccc
5901 agtcaagggtatctgtgtaaaactgttcttctcgaactcagctcccaactagaagaccgtagggaaagggtctctccaggagctcgaaggcagaagagctg
6001 atcctaagagtgctccctgcagccacaatgcctgggtactgcatctcttctcacttagacaaggaggtcctgagatctgacctggtgtctg
    <예수 6>
133      LeuProGlnGlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHisLeuLeuArg
6101 GCCTCAGGACCATCCCTCTGCCCTTCAGCTTCCCTCCACAGGACCGCATGCCATGCCATCTCTCTGAGTTCCACACACTGCTCCG
    =====`포타는 스펀라이싱 부위`=====
158 GlyLysValArgPheLeuMetLeuValGlyLysThrLeuLysValArgAlaProProThrThrAlaValProSerArgThrSerLeuValLeu
6201 AGGAAGGTGCTTCTCTGTGTGTAGAGAGGTCACCTCTGTGCGTCAGCGGCCGCCACCCACAGCTGTGCCAGACAGACCTCTTACTCTTC
    ~ EP0 도메인의 끝
191 ThrLeuAsnGlyLeuProAsnArgThrSerGlyLeuLeuGlyLysThrAlaSerAlaArgThrThrGlySerGlyLeuLeuLysTrpGlnGly
6301 ACACGTGAACGAGCTCCCAACAGACTTCTGGATTGTGGAGACAACTTCACTGCTCAGCACTACTGAGCTTCTGAGCTTCTGAGCTGAGCAAG

```

14e

225 PheArgAlaIysIleProGlyLeuLeuAsnGlnThrSerArgSerLeuAspGlnIleProGlyTyrLeuAsnArgIleHisGluLeuLeuAsnGlyThr
 6401 GATTTCAGAGCCAAAGATTCTGGTCTGCTGAACCAACCTCAGGATCCCTGGAGCCAAATCCCGGATACCTTGAAACAGGATACACGAACTCTTGAATGGAAC
 258 ArgGlyLeuPhePheProGlyProSerArgArgThrLeuGlyAlaProAspIleSerSerGlyThrSerAspThrGlySerLeuProProAsnLeuGlnPro
 6501 TCGTGGACTCTTTCCTGGACCTCAGCAGGACCCCTAGAGCCCGGACATTTCTCAGGACATCAGACAGGCTCCCTGGCACCCAACTCCAGCTC
 291 GlyTyrSerProSerProThrHisProProThrGlyGlnTyrThrLeuPheProLeuProProThrLeuProThrProAlaIleGlnLeuHisProLeuLeu
 6601 GGATATTCTCTCCCAACCCATCTCTACGTGACAGATAGCTCTCCCTCTCCACCCACCTTGCCCACTGGGTGCTCCAGCTCCACCCCTGC
 325 ProAspProSerAlaProThrProThrProThrSerProLeuLeuAsnThrSerTyrThrHisSerGlnAsnLeuSerGlnGly:STOP
 6701 TTCCTGACCTTCTGCTCCAAAGCCCTCTCTTAACACATCTACACCCACTCCAGAACTGTCTCAGAAAGGATTAAGTTCTCA
 6801 GACACTGCCGACATCAGCAATTGTCTCATGTACAGCTCCCTCCCTGAGGGGCCCCCTGGAGACAACTGGAACAAGATTCTTCTTCCTGAAACCC
 6901 AAAGCCCTGGTAAAAAGGATACACAGACTGAAGAAATCAATTTTTCACCTGTACATTATTAACCTTCAGAACTATTTTAACTATCAGCAATAC
 7001 TCATCAGAGCAGCTAGCTTTTGGTCTATTTTCTGAGAAATTTGCAACTCACTGATTTCTCTACATGCTCTTTTCTGTGATTAATCTGCAAAAGCCCTGG
 7101 GCTGGCCCTGGCAGTTGAACAGAGGAGAGACTTAACCTTGAGTCAAGAAAAACAGAGAAAGGTAATTTCTTGCCTTCAAAATTCAGAGCCCTTCCAAAGCCCC
 7201 CATCCCTTTACTATCATTTCTCAGTGGGACTCTGATCCCATTTCTTAAAGATCTTTACTCTTGAGAAATGAATTAAGCTTTCTCTCAGAAATGctgtcc
 ~ 풀리A 부위
 7301 ctatacaactagacaaaactgagcctgltataaggaataaatgaggagcgcccgaaaagctcccttaaaaaagcaagggaagaagatgltccttcgagggtggaataag
 7401 atccccctcaaccctgccaaccccaaaaagaactaaacagaagccttggagaagccttcaacaccccaaggtaaagctgtgtgaacagltcaagtaagaacagag
 7501 accctgaltgtgacagctgagcaaacagctagagccttggcagctcagcaggaagccttggcaggcaatgagcgcctccctcctgtggaaggtcaggaag
 7601 gaagtgcaggaagtggcaatgagctcagagctccttgagctcaacacagcaggaagaacaagtacaagtlcaagtlgaaggtcattccagtlcccgag
 7701 aaatgcatctaaaaagcagctcgtgtgtgagccaccataaactcgtctaagggaatccttaaaaaggagtcaggtctatgaggccttgcacaataagtgctgtcc
 7801 ttggtgctcaggaagaagttcgtgtgtgcaacaacaacaattccactgac



16a

```

1 GAGTCTTGG CCCACTCTC TCCACCCGA CTCCTGCCGA AGAGCACAG AAGCTCAAG CGCTCCATG GCCCAGGAA AGATTCAAGG GAGAGCCCC
101 ATACAGGAG CCACTTCAGT TAGACACCTT GAGCAGATG GAGCTGACTG ATTGCTTCTT GGGGGCATG CTCTTGCGAG TGCCAGACT AACTCTGTC
Met GluLeuThra spleuleule uAlaAlaMet LeuLeuAlaV aAlaArgLe uThrLeuSer
201 AGCCCCGTAG CTCCTGCTG TGACCCAGA CTCCTAATA AACTGCTGCG TGACTCCAC CTCCTTCACA GCCACTGAG TCAGTGTCCC GACGTGACC
SerProVala lProAlaCy sAspProArg LeuLeuAsnL ySleuLeuAr gAspSerHis leuLeuHis eArgLeuSe rGlnCySPro AspValAspPro
401 CTTGTCAT CCCGTCTCTG TGGCTTCTG TGGACTTTCG CTGAGAGAA TGGAAACCC AGACGAAACA GAGCAGACA CAGGACATTG TAGGGGCGT
LeuSeril eProValleu LeuProAlaV alAspPheSe rLeuGlyGlu TrpLysThrG InThrGluG lNserLysAla GlnAspIleL euGlyAlaVal
70 SerLeuLeu LeuGluGlyV alMetAlaAl aArgGlyGln LeuGluProS erCySLeuSe rSerLeuLeu GlyGlnLeuS erGlyGlnVa lArgLeuLeu
401 GTCCCTTCTA CTGAGAGGAG TGATGGCAGC ACGAGGACAG TTGGAACCTT CTGCTCTCTC ATCCCTCTCTG GGACAGCTTT CTGGGCAAGT TCCGCTCTCTC
LeuGlyAlaLe uGlnGlyLe uLeuGlyThr GlnGlyArgT hrThrAlaHi sLysAspPro AsnAlaLeuP heLeuSerLe uGlnGlnLeu LeuArgGlyLys
501 TTGGGGGCCC TGCAGGGCCT CCTAGGAACC CAGGSCAGGA CCACAGCTCA CAAAGACCCC AATGCCCTCT TCTTGAGCTT GCAAACAATG CTTCGGGGA
ValArgPh eleuLeuLeu ValGluGlyP roThrLeuCy sValArgArg ThrLeuProT hrThrAlaVa lProSerSer ThrSerGlnL euLeuThrLeu
601 AGGTGCCCTT CCTGCTCTG GTAGAAAGTC CACCTCTCTG TGTCAAGCG ACCCTGCCAA CCACAGCTGT CCAAGCAGT ACTTCTCAAC TCCTCACACT

```

16b

```

170      AsnLysPhe ProAsnArgT HisSerGlyLe uLeuGluThr 180      AsnPheserV alThrAlaAr gThrAlaGly ProGlyLeuL euserArgLe uGInGlyPhe
701 AAACAAAGTTC CCAACACAGGA CTCTCTGATG GTTGGAGAGG AACTTCAGTG TCACAGCCAG AACTGCTGGC CCGAGACTTC TGAAGCAGGCT TCAGGGAATTC
      ArgValLysI leThrProG1 yGInLeuAsn GInThrSerA rSerProVa lGInIleSer GlyTyxLeuA snArgThrIi sGlyProVal AsnGlyThrHi's
801 AGAGTCACAG TTAATCCTGG TCAGCTAAAT CAATCCTCCA GATCCCAAGT CCAATCTCT GATTAACCTGA ACAGGACACA CGAAGCTGTG AATGGAACTC
      GlyLeuPh enIaGlyThr SerLeuGInT hrLeuGluA1 aSerAspIle SerProGlyA laphAsnLy sGlySerLeu AlaphAsnL eugInGlyGly
901 ATGGGCTCTT TGCTGGAACC TCACTTCAGA CCTGGAAGC CTCAGACATC TCAGCCCGAG CTTCAACAA AGGCTCCCTG GCATTCAACC TCCAGGGTGG
240      LeuProPro SerProSerL euAlaProAs pGlyHisThr 280      ProPherProP roSerProAl aleuProThr ThrHisGlyS erProProG1 nLeuHisPro
1001 ACTTCCCTCC TCTCCAAAGC TTGCTCCTGA TGGACACACA CCTTCCCTC CTTCACTGCG CTTGGCCACC ACCCATGGAT CTCCACCCCA GCTCCACCCC
310      LeuPherProA sPProSerTh rThrMetPro AsnSerThra lAProHisPr oValThrMet TyrProHisP roArgAsnLe uSerGInGlu Thr
1101 CTGTTTCTCG ACCCTTCAC CACCATGCTT AACTCTACCG CCCCCTATCC AGTCACAAATG TACCCTCATC CCAGGAATTT GTCTCAGGAA ACATAGCGCG
320      1201 GGCACTGGCC CAGTGAGCCT CTGCAAGCTT TCTCGGGGAC AAGCTTCCCC AGGAAGGCTG AGAGGACAGCT GCATCTGCTC CAGATGTTCT GCTTTCACCT
1301 AAAAGGCCCT GGGGAAGGGA TACACAGCAC TGGAGATGTG AAAATTTTAG GAGCTATTTT TTTTAACTT ATCAGCAATA TTCAATCAGAG CAGCTAGCGA
1401 TCTTTGTCTT ATTTTCGCTA TAAATTGAA AATCACTAAT TCT

```

- 202 -

801 LeuGlnGlyPheArgValIlySleThrProGlyGlnLeu²¹⁰AsnGlnThr²²⁰SerArgSerProValGlnIleSerGlyTyrLeu²³⁰AsnArgThr²⁴⁰IleGlyProVal
 901 AsnGlyThr²⁵⁰IleGlyLeuPheAlaGlyThrSerLeuGlnThrLeuGlnAlaSerAspIleSerProGlyAlaPheAsnIlysglySerLeuAlaPheAsn
 1001 LeuGlnGlyIlyLeuProProSerProSerLeuAlaProAspGlyHisThrProPheProProSerProAlaLeuProThrHisGlySerProPro
 1101 GlnLeuHisProLeuPheProAspProSerThrThrMetPro³¹⁰AsnSerThrAla³²⁰ProHisProVal³³⁰ThrMetTyrProHisProArg³⁴⁰AsnLeuSer³⁵⁰IleGln
 1201 ^{Thr}AAACATAGcgcggcactggccagtcgacgctctctcgcgggacaagcttccccagaagcctgagagcagctgcattcgtccagatgctt
 1301 ctgcttcaacctaaaaggccctggggaaggatcacacgcaactggagatbtgtaaatlttaaggactatttlttbaacctatcagcaatatcattcag
 1401 agcagctagcgatcttggctcatcttcggtataaatltgaaatccactaa
 1501 aa

17b

hML3 1 S P A P P A C D L R V L S K L L R D S H V L H S R L S Q C P E V H P L P T P V L L P A V D F S L G E
mML3 1 S P V A P A C D P R L L N K L L R D S H L L H S R L S Q C P D V D P L S I P V L L P A V D F S L G E

hML3 51 W K T Q M E E T K A O D I L G A V T L L L E G V M A A R G Q L G P T C L S S L L G Q L S G Q V R L L
mML3 51 W K T Q T E Q S K A O D I L G A V S L L L E G V M A A R G Q L E P S C L S S L L G Q L S G Q V R L L

hML3 101 L G A L Q S L L G T Q L P P Q G R T A H K D P N A I F L S F Q H L L R G K D F W I V G D K L H C L
mML3 101 L G A L Q G L L G T Q L P L Q G R T A H K D P N A L F L S L Q Q L L R G K D F W I V G D E L Q C H

18

hML3 151 S Q N Y W L W A S E V A A G I Q S Q D S W S A E P N L Q V P G P N P R I P E Q D T R T L E W H S W
mML3 151 S Q N C W P W T S E Q A S G I Q S Q D Y S W S A K S N L Q V P S P N L W I P E Q D T R T C E W H S W

hML3 200 T L S W T L T Q D P R S P G H F L R N I R H R L P A T Q P P A W I S F P N P S S Y W T V Y A L P S
mML3 201 A L C W N L T S D P G S L R H L A R S F Q Q R L P G I Q P P G W T S S F S K P C S

hML3 250 S T H L A H P C G P A P P A S

19

m-ML	1	S	P	V	A	P	A	C	D	P	R	L	N	K	L	R	D	S	H	L	H	S	R	L	S	O	C	P	D	V	D	P	L	S	I	L	P	V	L	L	P	A	V	D	F	S	L	G	E		
p-ML	1	S	P	A	P	A	C	D	P	R	L	N	K	L	R	D	S	H	V	L	H	G	R	L	S	O	C	P	D	I	N	P	L	S	T	P	V	L	L	P	A	V	D	F	I	L	G	E			
h-ML	1	S	P	A	P	A	C	D	L	R	V	L	S	K	L	R	D	S	H	V	L	H	S	R	L	S	O	C	P	E	V	H	P	L	P	I	P	V	L	L	P	A	V	D	F	S	L	G	E		
m-ML	51	W	K	T	O	T	E	O	S	K	A	O	D	I	L	G	A	V	S	L	L	E	G	V	M	A	R	G	O	L	E	P	S	C	L	S	S	L	L	G	O	L	S	G	O	V	R	L			
p-ML	51	W	K	T	O	T	E	O	T	K	A	O	D	I	L	G	A	V	T	L	L	E	E	A	V	M	T	A	R	G	O	V	P	P	C	L	S	S	L	L	V	O	L	S	G	O	V	R	L		
h-ML	51	W	K	T	O	M	E	I	T	K	A	O	D	I	L	G	A	V	T	L	L	E	G	V	M	A	R	G	O	L	G	P	I	C	L	S	S	L	L	G	O	L	S	G	O	V	R	L			
m-ML	101	L	G	A	L	O	G	L	L	G	I	O	L	P	L	O	G	R	T	A	H	K	D	P	N	A	L	F	L	S	L	O	Q	L	L	R	G	K	V	R	F	L	L	V	E	G	P	T	I	L	
p-ML	101	L	G	A	L	O	D	L	L	G	M	O	L	P	P	O	G	R	T	A	H	K	D	P	S	A	I	F	L	N	F	O	Q	L	L	R	G	K	V	R	F	L	L	V	G	P	S	L			
h-ML	101	L	G	A	L	O	S	L	L	G	I	Q	L	P	P	O	G	R	T	A	H	K	D	P	N	A	I	F	L	S	F	Q	H	L	L	R	G	K	V	R	F	L	M	L	V	G	S	T	I		
m-ML	151	C	V	R	R	I	L	P	T	T	A	V	P	S	S	T	S	O	L	T	L	N	K	L	F	P	N	S	G	L	L	E	T	F	S	V	T	A	R	T	A	G	P	G	L	L	S	R			
p-ML	151	C	A	K	R	A	P	P	A	I	A	V	P	S	S	T	S	P	F	H	I	L	N	K	L	P	N	S	G	L	L	E	T	F	S	I	S	A	R	T	I	G	S	G	F	L	K	R			
h-ML	151	C	V	R	R	A	P	P	T	T	A	V	P	S	R	I	S	L	V	T	L	H	E	L	P	N	S	G	L	L	E	T	F	E	T	I	A	S	A	R	T	I	G	S	G	L	L	K	H		
m-ML	201	L	O	G	F	R	V	K	I	T	P	G	O	L	L	S	R	S	P	V	Q	I	S	G	V	L	N	R	I	H	G	P	V	N	G	I	H	G	L	F	A	G	I	S	L	O	L	L	E		
p-ML	201	L	O	A	F	R	A	K	I	-	P	G	L	L	L	L	S	R	S	L	D	O	I	P	G	H	O	L	L	H	G	P	L	S	G	I	H	G	L	F	F	G	P	O	P	G	A	L	G		
h-ML	201	Q	O	G	F	R	A	K	I	-	P	G	L	L	L	L	S	R	S	L	D	O	I	P	G	V	L	N	R	I	H	E	L	L	N	G	I	R	G	L	F	P	G	P	S	R	I	L	G		
m-ML	251	A	S	D	I	S	P	G	A	F	N	K	G	S	L	A	F	N	L	Q	G	G	L	P	P	S	P	S	L	A	P	D	G	H	-	T	P	F	P	P	S	P	A	L	P	I	T	H	G	S	P
p-ML	250	A	P	D	I	P	L	A	T	S	G	M	G	S	R	P	I	Y	L	O	P	G	E	S	P	S	P	A	H	P	S	P	G	R	Y	T	L	F	S	P	S	P	S	-	-	P	T				
h-ML	250	A	P	D	I	S	S	G	T	S	D	T	G	S	L	P	P	N	L	O	P	G	Y	S	P	S	P	I	H	P	P	I	G	O	Y	T	L	F	P	L	P	I	P	T	-	-	P	V			
m-ML	300	P	O	L	H	P	L	F	P	D	P	S	I	T	M	P	N	S	I	A	P	N	P	V	I	M	Y	P	H	P	R	I	L	S	O	E	T														
p-ML	297	V	O	L	Q	P	L	L	P	D	P	S	A	I	T	P	N	S	I	S	P	L	L	F	A	A	H	P	H	I	F	O	L	L	S	O	E	E													
h-ML	297	V	O	L	H	P	L	L	P	D	P	S	A	I	T	P	I	T	S	P	L	L	N	T	S	Y	T	H	S	O	N	E	S	O	E	G															

20a

```

1000
101  SerProAlaProProAlaCysAspProArgLeuLeuAsnLysLeuLeuArgAspSerHisValLeuHisGlyArgLeuSerGlnCysProAspIleAsnPro
1  AGCCGGGCTCCTCCTGCTGCTGAGACCCCGACCTCTAATAAAGCTGCTGAGACTCCCATGTCTTCACGGCAGACTGAGCCAGTGCCCGACATTAAAC
400
101  LeuSerThrProValLeuLeuProAlaValAspPheThrLeuGlyGluTrpLysThrGlnThrGlnThrLysAlaGlnAspValLeuGlyAlaThr
101  CTTTGTCCACACCTGCTCCTGCTGCTGAGACTTCACCTTGGGAGATGAAACCCAGACGGAGCAGCAAGCAGATGTCCTGGAGGCCAC
70  80  90  100
201  ThrLeuLeuLeuGlnuAlaValMetThrAlaArgGlyGlnValGlyProProCysLeuSerSerLeuLeuValGlnLeuSerGlyGlnValArgLeuLeu
201  AACCTTCTGCTGAGGAGATGATGACACAGCAGGGGACAAAGTGAGACCCCTTGCTCTCATTCCTGCTGAGCAGCTTCTGACAGGTTGCGCTCTTC
110 120 130
101  LeuGlyAlaLeuGlnAspLeuLeuGlyMetGlnLeuProProGlnGlyArgThrThrAlaHisLysAspProSerAlaIlePheLeuAsnPheGlnGlnLeu
301  CTCGGGGCCCTGCAGGACCTCCTTGGAATGCAGCTTCCTCCACAGGGAAGACACAGCTCACAAGGATCCAGTGCCATCTTCTGAACTTCCACACAC
140 150 160
401  LeuArgGlyLysValArgPheLeuLeuValValGlyProSerLeuCysAlaLysArgAlaProProAlaIleAlaValProSerSerThrSerPro
401  TGCTCCGAGGAAAGGTGCGTTCCTGCTCTTGTAGTGGGCCCTCCCTCTGTGTCCAAGAGGGCCCGCCCATAGCTGTCCCGAGCAGCACCTCTCC

```

170 180 190 200
PheIleThrLeuAsnLysLeuProAsnArgThrSerGlyLeuLeuGluThrAsnSerSerLeSerAlaArgThrThrGlySerGlyPheLeuLysArg
501 ATTCCACACACTGAAACAAGCTCCCAACAGAGACTCTGGATTGTGGACAAACCTCCAGATCTCAGCCAGACTCTGAGATTTCTCAAGAGC
LeuGlnAlaPheArgAlaLysIleProGlyLeuLeuAsnGlnThrSerArgSerLeuAspGlnIleProGlyHisGlnAsnGlyThrHisGlyProLeuSer
601 CTGACAGGCACTTCAAGGCCAAGACTTCTGCTGCTGTGAACCAACCTCCAGGTGCTTACCAAAATGCTTGAGACACAGAAATGGACACACGGACCCCTGA
240 250 260
GlyIleHisGlyLeuPheProGlyProGlnProGlyAlaLeuGlyAlaProAspIleProProAlaThrSerGlyMetGlySerArgProThrTyrLeu
701 GTGGATTATGAGACTTCTTCTGGACCCCAACCCGGGGCCCTCGGAGGCTCCAGACATTTCTCCAGCAACTTCAGGATGGGCTCCGGGCCAACCTTACT
270 280 290 300
GlnProGlyGluSerProSerProAlaHisProSerProGlyArgTyrThrLeuPheSerProSerProThrSerProThrValGlnLeuGln
801 CCAGCTGGAGAGATGCTCTCTTCCGCCAGCTCAACCTTCTTCTGTCCTTCTTCTTCCACCCACACTCGGCCCTCCCCACAGTCCAGTCCAG
310 320 330
ProLeuLeuProAspProSerAlaIleThrProAsnSerThrSerProLeuLeuPheAlaAlaHisProHisPheGlnAsnLeuSerGlnGlu
901 CCTCTGCTTCTTCAACCCCTCTGGCAGTCACACCACTTACCAGTCTCTTCTTATTTGGACGTCACCTCATTTCCAGAACCTGTCTCAGGAAGAGTAAAG
1001 GTGCTCAGACCTGGCCAACTTCAGCA

21a

10 20 30

1 SerProAlaProProAlaCysAspProArgLeuLeuAsnLysLeuLeuAlaGAspSerHisValLeuHisGlyArgLeuSerGlnCysProAspIleAsnPro
AGCCCGGCTCTCTCCCTGTGTGACCCCGACTCTCTAAATAAACCTCTTGAGACTCCACATGTCCTTCACGCGACACTGAGCCAGTGCACAGACTTAAAC

40 50 60

101 LeuSerThrProValLeuLeuProAlaValAspPheThrLeuGlyGluTrpLysThrGlnThrGlnGlnThrLysLacInAspValLeuGlyAlaThr
CTTGTGTCCACACCTGTCTGTGCTGTGTGACTTACACTGTGGAGAAATGAAAACCCAGACGAGACAAAGGACACAGATGTCTGTGGAGGCCAC

70 80 90 100

201 ThrLeuLeuLeuGluValValMetThrAlaArgGlyGlnValGlyProProCysLeuSerSerLeuLeuValGlnLeuSerGlyGlnValAlaArgLeuLeu
AAACCTTCTGTGTGAGGACAGTATGATGACAGCACGAGGAGCAAGTGGAGCCCCCTTGCTCTTCATCTCTGTGTGAGAGCTTTCTGAGACAGGTTCCGCTCTTC

110 120 130

301 LeuGlyAlaLeuGlnAspLeuLeuGlyMetGlnGlyArgThrThrAlaHisLysAspProSerAlaIlePheLeuAsnPheGlnGlnLeuLeuArgGlyLys
CTCGGGGCGCTGTGACAGACTCTGTGGAATGACGAGGAAGACACAGCTCAAGATGCCAGTCCATCTTCTGAACTTCCACAACTGCTCCGAGAGA

140 150 160

401 ValArgPheLeuLeuLeuValValGlyProSerLeuCysAlaLysArgAlaProProAlaIleAlaValProSerSerThrSerProPheHisThrLeu
AGTGTGCGTTTCTGTGCTCTTGTGTAGTGGGCGCTCTCTCTGTGTGCCAAGAAGGCGCCACCGGCATAGCTGTGCCAGACGACACTTCTCCATTCCACACACT

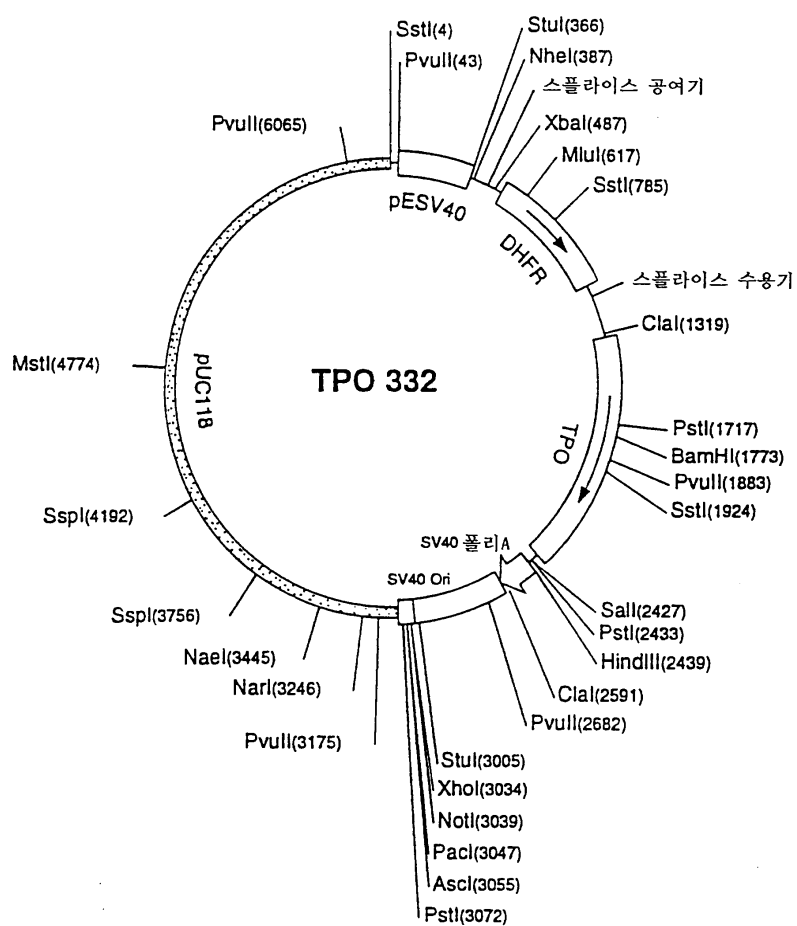
21b

170 AsnLysLeuProAsnArgThrSerGlyLeuLeuLutThrAsnSerSerIleSerAlaArgThrThrGlySerGlyPheLeuLysArgLeuGlnAlaPhe
 501 GAACAAGCTCCCAACAGGACCTCTGGATTGTTGGAGACAAACTCCAGTATCTCAGCCAGAACTACTGGCTGTGATTTCTCAAGAGCTGCAGGCATTC
 210 ArgAlaLysIleProGlyLeuLeuAsnGlnThrSerArgSerLeuAspGlnIleProGlyHisGlnAsnGlyThrHisGlyProLeuSerGlyIleHisGly
 601 AGAGCCAAGATTCTGTGCTGTAACCAACCTCCAGGTCCCTAGACCAAAATCCCTGGACACAGAAATGGACACACGAGACCCCTTGAAGTGAATTCTATG
 240 LeuPheProGlyProGlnProGlyValLeuGlyAlaProAspIleProProAlaThrSerGlyMetGlySerArgProThrTyrLeuGlnProGlyGlu
 701 GACTCTTTCCTGGACCCCAACCCGGGGCCCTCGAGCTCCAGACATTCTCCAGCACTTCAAGCAATGGGCTCCCGGCCAACCTTACCTCCAGCCTGGAGA
 270 SerProSerProAlaHisProSerProGlyArgTyrThrLeuPheSerProSerProThrSerProThrValGlnLeuGlnProLeuLeuPro
 801 GTCTCCTTCCCAAGCTCACCCCTTCTCTGACGATACACTCTCTCTCTCTCCACCCAGCTGCCCCCAAGTCCAGCTCCAGCCTCTGCTTCTCT
 310 AspProSerAlaIleThrProAsnSerThrSerProLeuLeuPheAlaAlaHisProHisPheGlnAsnLeuSerGlnGlnGlu
 901 GACCCCTCTGTGAGTACACCACTACAGTCTCTTCTATTTGAGCTCACCCCTCATTTCCAGAACTGTCTCAGGAAAGATAAGTGCTTCAGACCC
 1001 TGCCCACTTCAGCA

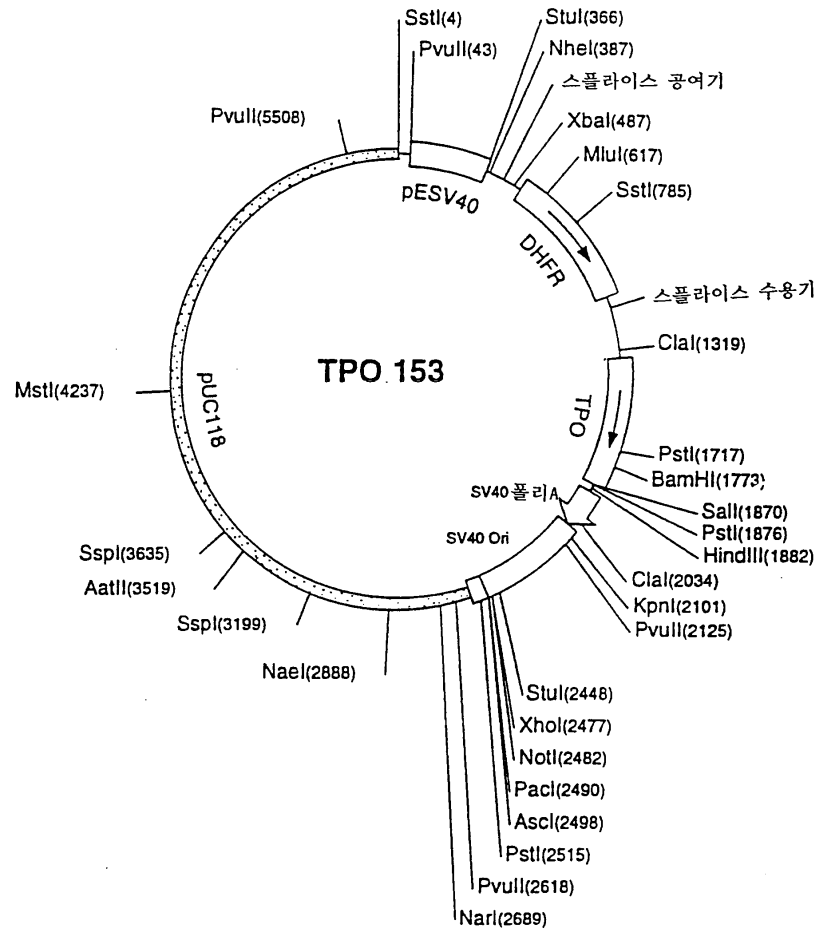
22

PML	1	S	P	A	P	A	C	D	P	R	L	L	N	K	L	R	D	S	H	V	L	H	G	R	L	S	O	C	P	D	I	N	P	L	S	T	P	V	L	L	P	A	V	D	F	T	L	G	E		
PML2	1	S	P	A	P	A	C	D	P	R	L	L	N	K	L	R	D	S	H	V	L	H	G	R	L	S	O	C	P	D	I	N	P	L	S	T	P	V	L	L	P	A	V	D	F	T	L	G	E		
PML	51	W	K	T	Q	T	E	Q	T	K	A	O	D	V	L	G	A	T	T	L	L	E	A	V	M	T	A	R	G	O	V	G	P	P	C	L	S	S	L	L	V	O	L	S	G	O	V	R	L	L	
PML2	51	W	K	T	Q	T	E	Q	T	K	A	O	D	V	L	G	A	T	T	L	L	E	A	V	M	T	A	R	G	O	V	G	P	P	C	L	S	S	L	L	V	O	L	S	G	O	V	R	L	L	
PML	101	L	G	A	L	Q	D	L	L	G	M	Q	L	P	P	Q	G	R	T	A	H	K	D	P	S	A	I	F	L	N	F	Q	Q	L	R	G	K	V	R	F	L	L	V	V	G	P	S	L			
PML2	101	L	G	A	L	Q	D	L	L	G	M	Q	L	P	P	Q	G	R	T	A	H	K	D	P	S	A	I	F	L	N	F	Q	Q	L	R	G	K	V	R	F	L	L	V	V	G	P	S	L			
PML	151	C	A	K	R	A	P	P	A	I	A	V	P	S	S	T	S	P	F	H	T	L	N	K	L	P	N	R	T	S	G	L	L	E	T	N	S	S	I	S	A	R	T	G	S	G	F	L	K	R	
PML2	147	C	A	K	R	A	P	P	A	I	A	V	P	S	S	T	S	P	F	H	T	L	N	K	L	P	N	R	T	S	G	L	L	E	T	N	S	S	I	S	A	R	T	G	S	G	F	L	K	R	
PML	201	L	Q	A	F	R	A	K	I	P	G	L	L	N	Q	T	S	R	S	L	D	Q	I	P	G	H	Q	N	G	T	H	G	P	L	S	G	I	H	G	L	F	P	G	P	O	P	G	A	L	G	A
PML2	197	L	Q	A	F	R	A	K	I	P	G	L	L	N	Q	T	S	R	S	L	D	Q	I	P	G	H	Q	N	G	T	H	G	P	L	S	G	I	H	G	L	F	P	G	P	O	P	G	A	L	G	A
PML	251	P	D	I	P	P	A	T	S	G	M	G	S	R	P	T	Y	L	Q	P	G	E	S	P	S	P	A	H	P	S	P	G	R	Y	T	L	F	S	P	S	P	T	S	P	S	P	T	V	O	L	O
PML2	247	P	D	I	P	P	A	T	S	G	M	G	S	R	P	T	Y	L	Q	P	G	E	S	P	S	P	A	H	P	S	P	G	R	Y	T	L	F	S	P	S	P	T	S	P	S	P	T	V	O	L	O
PML	301	P	L	L	P	D	P	S	A	I	T	P	N	S	T	S	P	L	L	F	A	A	H	P	H	F	Q	N	L	S	Q	E	E																		
PML2	297	P	L	L	P	D	P	S	A	I	T	P	N	S	T	S	P	L	L	F	A	A	H	P	H	F	Q	N	L	S	Q	E	E																		

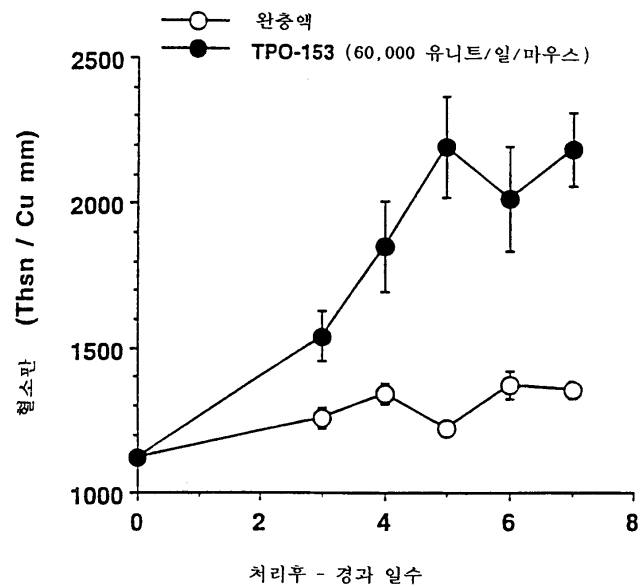
23



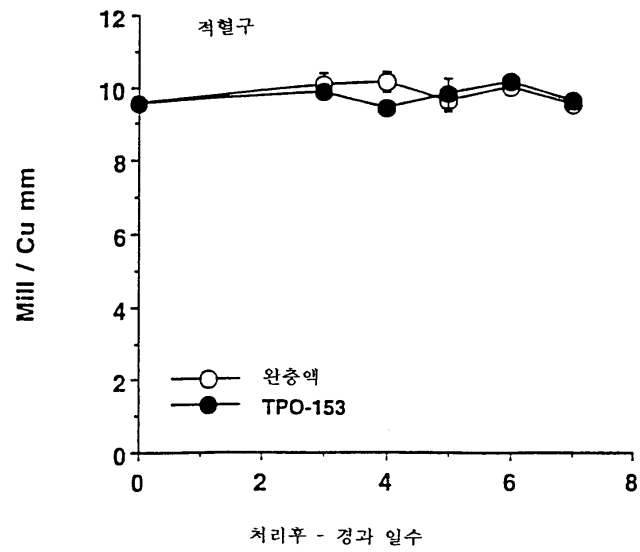
24



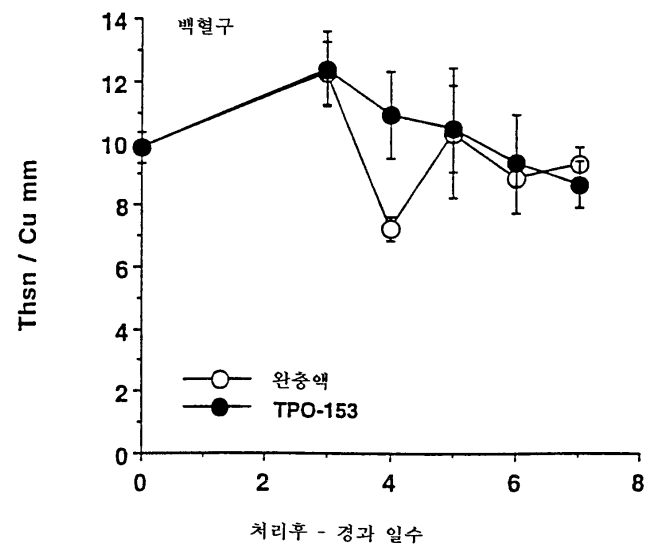
25a



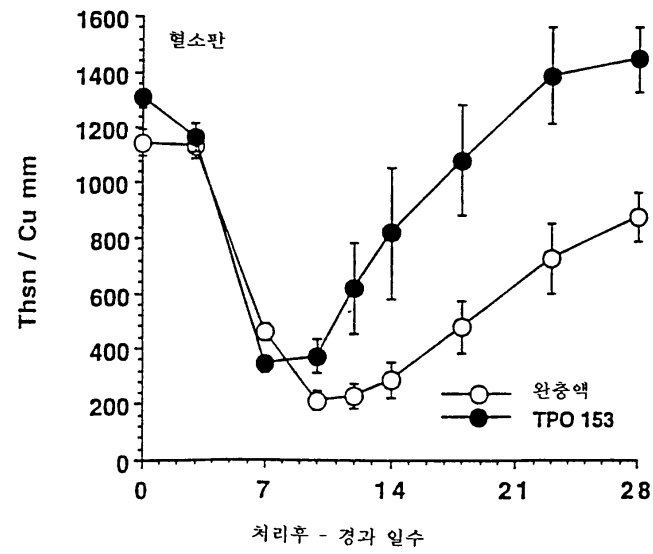
25b



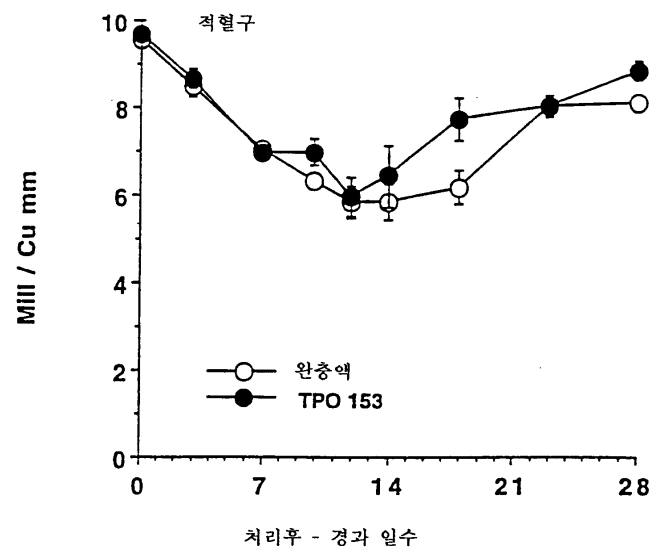
25c



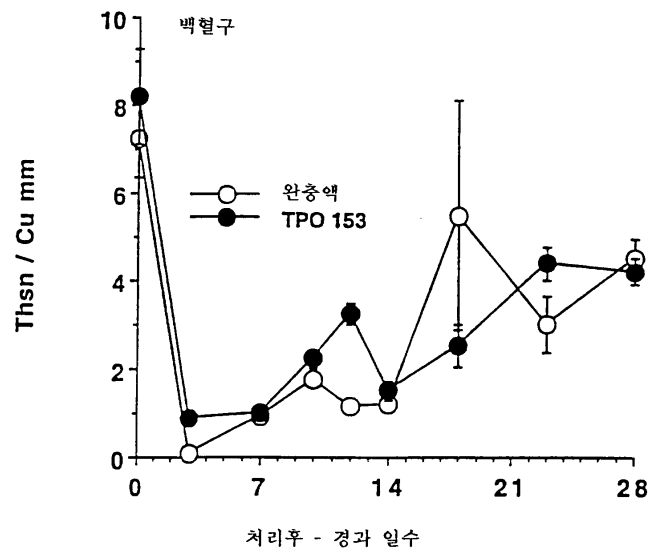
26a



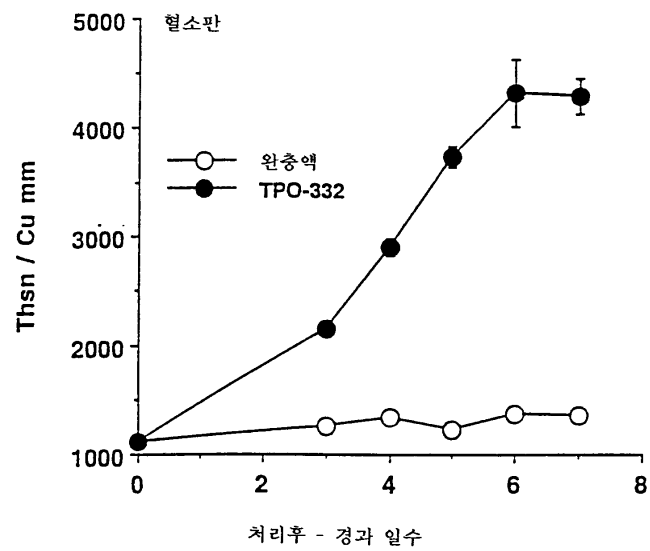
26b



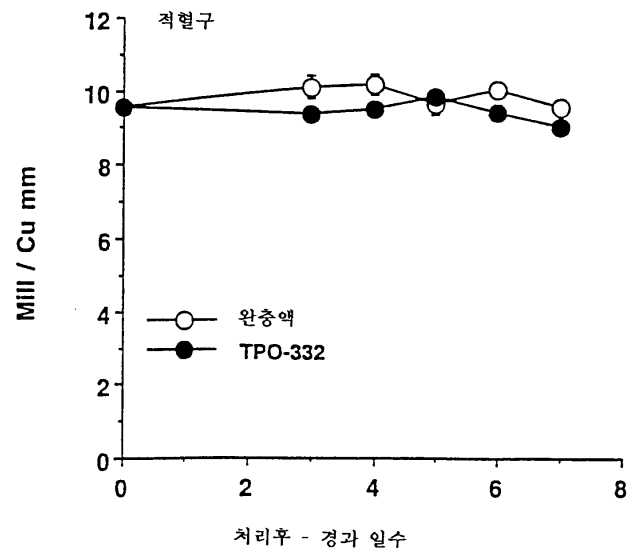
26c



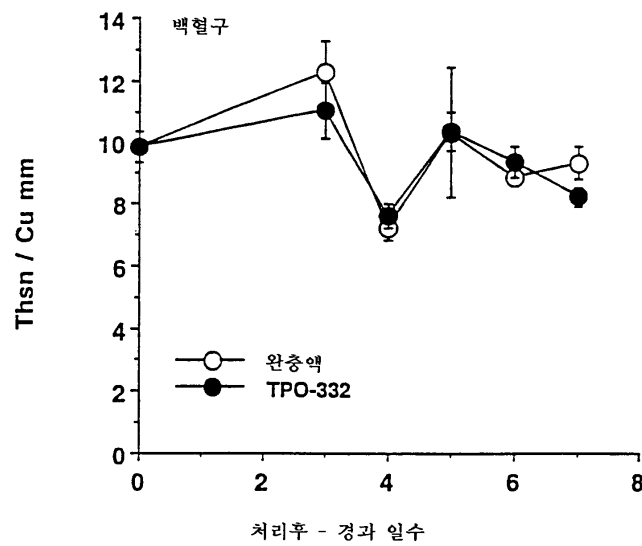
27a



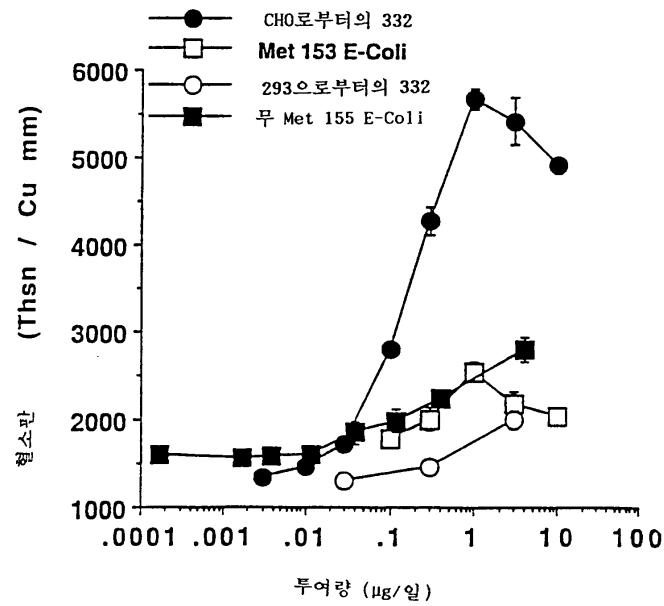
27b



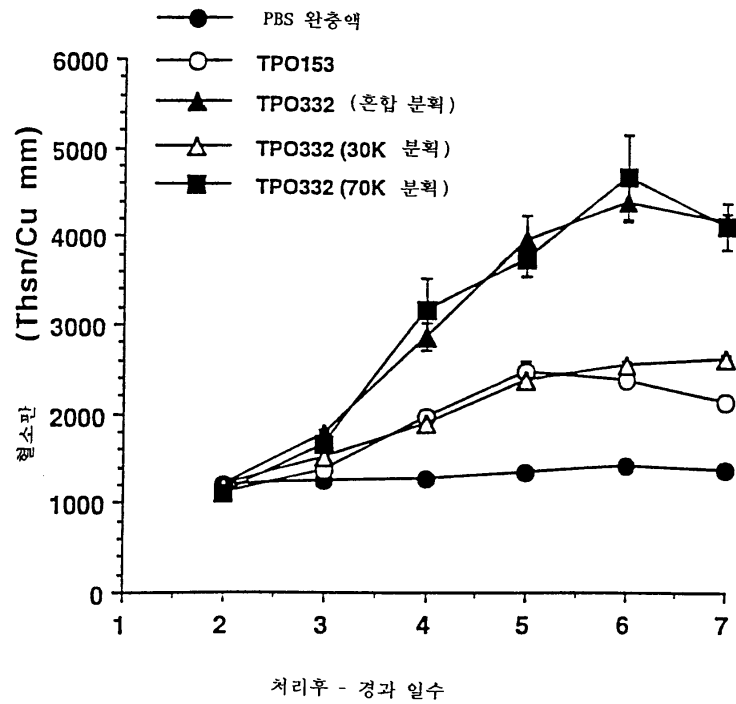
27c



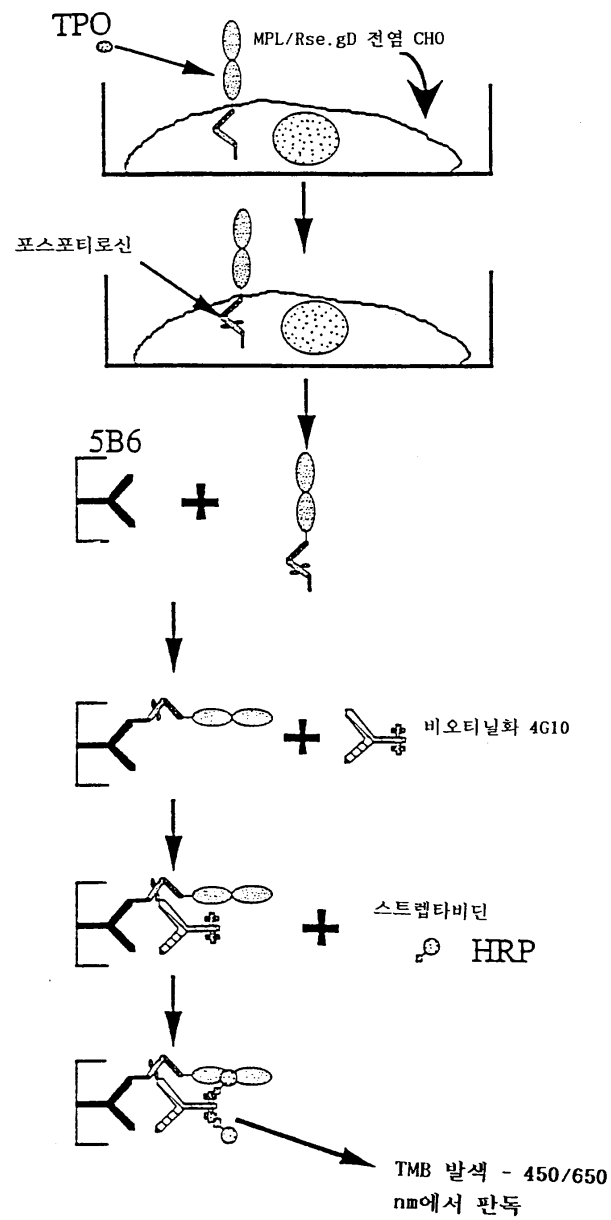
28



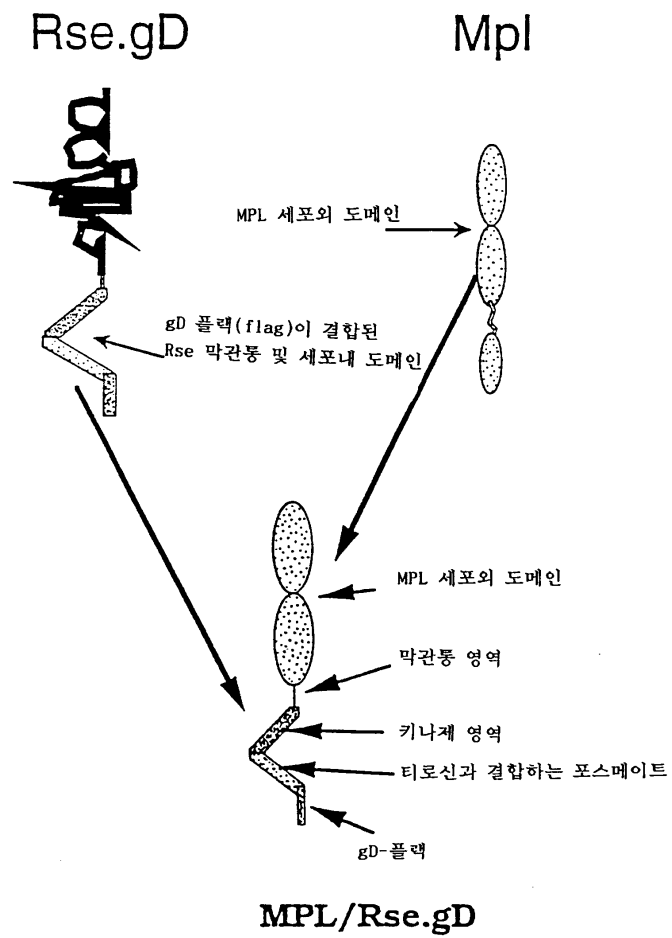
29



30a



30b



31

96웰 배양 플레이트(평평한 바닥)
에 웰당 5×10^4 MPL/Rse.gD 세포
를 가함



리간드로 30분간 자극

자극과정은 50 또는 100 μ l
중에서 수행될 수 있음



150 mM NaCl
0.5 % Triton-X 100
50 mM HEPES, pH 7.5
 Na_2VO_4 (포스파타제 억제제)

류펩틴, 아프로티닌
& AEBSF
(프로테아제 억제제):에 가용화



포획 항체, 5B6(항-gD 펩티드
mAb)으로 코팅된 ELISA 웰에
세포 용해물 85 μ l 가함



2시간 동안 진탕기 상에서 배양



플레이트를 세척하고 웰당 비오티닐화
4G10 400 Pg/ml, 100 μ l를 가함



Incub: 2시간 동안 배양



플레이트를 세척하고 웰당 지메드(Zymed) 스트렙타비딘/HRP
1:10K, 100 μ l를 가함



30분간 진탕기 상에서 배양



플레이트를 세척하고 Kirkegaard &
perry TMB 기질을 웰당 100 μ l씩 가함



10분간 발색



1M H_3PO_4 로 중지시키고 450/650 nm에서 판독

32a

```

                                aluI
                                sstI
                                sacI
                                hgiJII
                                hgiAI/aspHI
                                eci136II
                                bsp1286
                                bsiHKAII
                                bmyI
                                banII
                                rmaI
                                maeI
                                taqI
                                mcrI
                                nsbII
                                pleI
                                hinfi
                                puiI
                                mboI
                                sau3AI
                                aluI
                                pvuII
                                mboI/ndeII
                                dnuI
                                puiI/bspCI
                                pleI
                                dnuII
                                hinfi
                                taqI
                                mcrI
                                nsbII
                                maeI
                                taqI
                                nsbII
                                rmaI
                                bmyI
                                bsiHKAII
                                bsp1286
                                eci136II
                                hgiAI/aspHI
                                hgiJII
                                sacI
                                sstI
                                aluI

1  TTCGAGCTCG  CCCGACATG  ATTATGACT  AGAGTCGATC  GACAGCTGTG  GAATGTGTGT  CAGTTAGGGT
AAGCTCGAGC  GGGCTGTAAC  TAAATACTGA  TCTCAGCTAG  CTTCGACAC  CTTACACACA  GTCAATCCCA

                                nlaIV
                                scrFI
                                mvaI
                                ecorII
                                dsav
                                bstNI
                                apyI
                                bsajI
                                nspi
                                nsbII
                                sexAI

                                sfanI
                                ppulOI
                                nsiI/avaII
                                nlaIII
                                spnI
                                bstNI
                                apyI
                                nspi
                                nsbII
                                sexAI

71  GTGGAAGTC  CCCAGGCTCC  CCAGCAGGCA  GAAGTATGCA  AAGCATGCAT  CTCAATTAGT  CAGCAACCAG
CACCTTTCAG  GGGTCCGAGG  GGTGCTCCGT  CTTCAATACG  TTGTAACGTA  GAGTTAATCA  GTCGTTGGTC
```

32b

```

                                nlaIV
scrFI                               sfanI
                                mvaI
                                ecoRII
                                dsav
                                bstNI
                                apyI[dcm+]
                                bsaiI
141 GTGTGGAAG TCCCCAGGCT CCCCAGCAG CAGAAGTAG CAAGCATGC ATCTCAATTG GTCAGCAACC
CACACCTTTC AGGGTCCGA GGGGTCGTCC GTCTCATAC GTTTCGTACG TAGAGTTAAT CAGTCGTTGG

                                nsII/avaIII
                                nlaIII
                                sphi
                                nsPI
                                nsphi

[dcm+]
                                bstNI
                                apyI[dcm+]
                                bsaiI

                                nlaIII
                                styI
                                ncoI
                                bsII dsai
                                acII bsaiI
                                acII
                                acII foki
                                acII
                                fnu4HI
                                bglI
                                sfiI
                                haeIII/paiI
                                mliI mliI
                                haeIII/paiI
                                mliI mliI
                                ddeI
                                haeIII/paiI
                                mliI alui
                                haeIII/paiI
                                mliI
281 GCTGACTAAT TTTTATTAT TATGCAGAG CCGAGGCCGC CTCGGCCTCT GAGCTATTCC AGAAGTAGTG
CGACTGATTA AAAAAAATAA ATAGCTTCC GGTCCGGCG GAGCCGGAGA CTCGATAAAG TCTTCATCAC

```

32c

```

351 AGGAGGCTTT TTTGGAGGCC TAGGCTTTTG CAAAAGCTA GCTTATCCGG
TCTTCGAAA AAACCTCCGG ATCCGAAAC GTTTTCGAT CGAATAGGCC

      mluI      mluI maeI      aluI      maeI      mspI      hpaII
      haeIII/paI      rmaI      eaeI      eaeI/xmaII/ecoRI
      stuI      haeIII/paI      rmaI      maeI      cfrI
      haeI      mluI maeI      nheI      aluI      hpaII

401 CCGGGAACGG TGCATTGAA CGCGATTCC CCGTCCCAAG AGTGACGTA GTACCGCCTA TAGAGGATA
GGCCCTTCCC ACGTAACCTT GCGCTAAGG GGCACGGTTC TCACTGCATT CATGGCGGAT ATCTCGCTAT
      ^splice donor

      fnu4HI      bbvI      nspBII      nlaIII      taqI      sfanI      pfimI
      mluI      aciI      hinfI      hpaII      bstUI      maeII      rsaI      aciI
      nciI      mspI      tthI      fndII/mvnI      bsh1236I      maeIII      csp6I      scfI
      hpaII      dsav      cauII      bsh1236I      maeIII      csp6I      scfI
      dsav      cauII      bsh1236I      maeIII      csp6I      scfI

471 AGAGATTTT ATCCCCGCTG CCATCATGGT TCGACCAATG AACTGCATCG TCGCCGTGTC CCAAAATATG
TCTCTTAAAA TAGGGGCGAC GGTAGTACCA AGCTGGTAAC TTGACGTAGC AGCGGCACAG GGTTTTATAC
      DHER ATG^

```

32d

```

                                     haeIII/palI
                                     haeI
                                     scrFI
                                     mvaI      bsrBI
                                     ecorII
                                     dsav
                                     bstNI      aciI
                                     bsmAI      apyI(dcm+)
                                     bsai      bsajI mnlI ddeI xmnI      rsai
                                     CCTAACCGT TCTTGCCCTCT GGATGGGACC GAGGGCGAGT CCTTGCTCAA GTTCATGAAG GTTCTTACT
541 GGGATTGGCA AGAACGGAGA CCTACCCCTGG CCTCCGCTCA GGAACGAGTT CAAGTACTTC CAAAGAATGA
                                     asp700      scaI      csp6I
                                     mboII
                                     eco57I
                                     mvaI
                                     ecorII
                                     dsav
                                     bstNI
                                     apyI(dcm+)
                                     sexAI
                                     ddeI
611 CCACAACCTTC TTCAGTGAA GGTAAACAGA ATCTGGTGAT TATGGGTAGG AAAACCTGGT TCTCCATTCC
                                     mnlI      alwNI      hphI
                                     earI/ksp632I      hinfI
                                     mboII
                                     eco57I
                                     mvaI
                                     ecorII
                                     dsav
                                     bstNI
                                     apyI(dcm+)
                                     sexAI
                                     ddeI
GGTGTGGAG AAGTCACCTT CCATTGTCT TAGACCACTA ATACCCATCC TTTTGACCA AGAGGTAAG
                                     tflI      tru9I
                                     hinfI      msei
                                     mboII taqI      ahaII/draI      aseI/asnI/vspI      ddeI
681 TGAGAAGAAT CGACCTTTAA AGACAGAAT TAAATATAGT CTCAGTAGAG AACTCAAGA ACCACCACGA
                                     mboII taqI      ahaII/draI      aseI/asnI/vspI      ddeI
ACTCTTCTTA GCTGGAATTT TCCTGTCTTA ATTATATCAA GAGTCATCTC TTGAGTTTCT TGGTGGTGCT
                                     bslI mnlI

```

32e

```

sclI
sacI
hgiII
hgiAI/asphI
ecI136II
bspI286
bsiHKA1
bmyI
banII
aluI
bclXI
fokI
sfanI
mseI
afIII/bfrI
mspI
hpaiI
bswI
751 GGAGCTCAT TTCTTGCCAA AAGTTGGAT GATGCCCTTA GACTTATTGA ACAACCGGAA TTGGCAAGTA
CCTCGAGTAA AAGAACGGT TTCAAACTA CTACGGAAT CTGAATAACT TGTGGCCTT AACCGTTCAT
accI
nlaIII
mnlI
821 AAGTAGACAT GGTTCGATA GTCGAGGCA GTTCTGTTTA CCAGGAAGCC ATGAATCAAC CAGGCCACCT
TTCATCTGTA CCAACCTAT CAGCCTCCG CAAAGACAAT GGTCCCTCGG TACTTAGTTG GTCCGGTGGA
scrFI scrFI
mvaI mvaI
ecorII ecorII
dsav tflI dsav
bstNI nlaIII bstNI ddeI
apyI(dcm+) hinfI apyI(dcm+)
haeIII/paiI
haeI
```

32f

hgal
 hmlI/acyI
 ahaiI/bsaHI
 scrFI
 mvaI mmlI
 ecoRII
 dsav
 bstNI econI
 apyI[dcmt+] mmlI
 bsajI bsII ddei
 mmlI
 961 AAATATTAAC CTCTCCACAG ATACCACAGG GTCTCTCTG
 TTTAATATTTG GAGAGGCTCT TATGGGTCCG CAGAGAGAC

32g

```

                                SbfI
                                MvaI
                                EcoRII
                                DsaV
                                BstNI
                                ApyI[dcn+]
                                Sau96I
                                AuaI
                                AsuI      mnlI      SfiNI
1001 AGGTCCAGGA GGAAGGAGC ATCAAGTATA AGTTGAGT CTACGAGAAG AAAGACTAAC AGAAGATGC
TCCAGGTCTT CCTTTTCCG TAGTTCATAT TCAACTTCA GATGCTCTTC TTCTGATTG TCCTTCTACG
                                ^END DHER

                                SfiNI
                                MboII
                                AccI
                                MboII
                                Pvu10I
                                AuaI      mnlI
                                NsiI/avaII
                                BsaJI
                                DsaI
                                NlaIII
                                StyI
                                NcoI
                                Ppu10I
1071 TTTCAGTTC TCTGCTCCCC TCCTAAGCT ATGCAATTTT ATAGACCAAT GGGACTTTTG
AAAGTTCAGG AGACGAGGGG AGGATTTCGA TACGTAAAAA TATTCTGCTA CCTGAAAAC

```

32h

```

styI
bsaJI
sau3AI
mboI/ndeII(dam-)
dpuI(dam+)
dpuI(dam-)
alwI(dam-)
bstYI/xhoII
1131 CTGGCTTTAG ATCCCTTGG CTCGTTAGA ACGCGGTAC AATTATACA TAACCTTAG TATCATACAC
GACCGAAATC TAGGGAACC GAAGCAATCT TCGCGCGATG TTAATTATGT ATTGAATAC ATAGTATGTG
        bstYI
        bsh1236I
        bstUI
        fnu4HI
        aciI
        thai
        fnuDII/mvnI tru9I
        mseI
        aseI/asnI/vspI
        saug6I
        avaiI
        asuI
        scrFI
        mvaI
        ecorII
        dsav
        bstNI
        apyI(dcm+)
maeII
hphI   scfI   fokI
1201 ATACGATTTA GGTGACACTA TAGATACAT CCACTTTGCC TTTCTCTCCA CAGGTGTCCA CTCCAGGTC
TATGCTAAT CCACTGTGAT ATCTATTGTA GGTGAACGG AAAGAGAGT GTCCACAGGT GAGGTCACAG
        bsII
        bsaJI

```

32i

```

                                scrFI
                                nciI
                                mspI
                                hpaII
                                dsav
                                xmaI/pspAI
                                smaI
                                scrFI
                                nciI
                                dsav
                                caulI
                                bsaJI
                                avai
                                sau3AI
                                mboI/ndeII(dam-)
                                dpuI(dam+)
                                dpuI(dam-)
                                pleI
                                nlaIV caulI
                                bstYI/xhoII
                                taqI rmaI bamHI bsaJI
                                hinfI
                                salI maeI alwI(dam-)
                                hincII/hindII alwI(dam-)
                                accI xbaI mnlI bsaJI
                                GTCGACTCTA GAGGATCCCC
                                GTTGACGTGG AGCCAAGATT CGAAGACGTC
                                bsaJI ddeI bsgI
                                mnlI hindII bspMI
                                1271 CAAC TGCACC TCGGTTCTAA GCTTCTGCAG
                                GTTGACGTGG AGCCAAGATT CGAAGACGTC
```

32j

```

                                sau96I
                                acII  haeIII/palI
                                fnu4HI asuI
                                bglI  nlaIII
                                sfiI  styI
                                eaeI  ncoI
                                cfrI  dsai
ecorI    taqI haeIII/palI
apoi     clai/bsp106 bsajI
1321 GGGGAATTCA ATCGATGGCC GCCATGGCCC AACTGTGTTA TTGCAGCTTA TAATGGTTAC AAATAAAGCA
      CCCCTTAAGT TAGCTACCGG CGGTACCGGG TTGAACAAT AACGTCGAAT ATTACCAATG TTTATTTTCGT
      ^sv40 early poly A

                                aluI
                                fnu4HI
                                bvi
                                maeIII
                                rmaI
                                bsmI maeI
1391 ATAGCATCAC AAATTTCACA AATAAGCAT TTTTTCACCT GCATCTAGT TGTGGTTTGT CCAACTCAT
      TATCGTAGTG TTTAAGTGT TTATTCGTA AAAAAAGTGA CGTAAGATCA ACACCAACA GTTTGAGTA
```

32k

```

sau3AI
mboI/ndeII(dam-)
dpnI(dam+)
dpnII(dam-)
pvuI/bspcI
mcrI
taqI(dam-) tru9I
clai/bsp106(dam-)
sau3AI mseI
mboI/ndeII(dam-)
dpnI(dam+) xmnI
dpnII(dam-) aseI/asnI/vspI
alwi(dam-) asp700
nlaIII alwi(dam-) asp700
GTTACATGAG ATAGTACAGA CCTAGCTAGC CCTTAATTAA
sv40 origin^

1461 CAATGTATCT TATCATGTCT
GTTACATGAG ATAGTACAGA CCTAGCTAGC CCTTAATTAA

haeIII/palI
haeI
styI
fnu4HI ncoI
bvrI dsai
hinPI bsaiI
hhaI/cfoI nlaIII
mnlI mnlI
acc65I ddeI acil
rsal
csp6I
nlaIV
kpnI
hgiCI
banI
asp718
mnlI

1501 CGGCGGAGCA CCATGGCCTG AAATAACCTC TGAAGAGAGA ACTTGTTAG GTACCTTCTG AGGCGGAGAAG
GCCGCGTCTG GTTACCGGAC TTATTTGAG ACTTCTCTCT TGAACCAATC CATGGAAGAC TCCGCTTTTC

```

1571 AACCAAGCTGT GGAATGTGTG TCAGTTAGGG TGTTGAAAGT CCCAGAGCTC CCCAGCAGGC AGAAGTATGC
TTGGTCGACA CCTTACACAC AGTCATCC ACACCTTCA GGGTCCGAG GGGTCGTCG TCTTCATACG
alul
pvuII
nspBII
bsaJI
apyI[dcn+]
nlaIV
scrFI
mvaI
ecorII
dsav
bstNI

321
nsII/avaIII
nlaIII
sphi
nsPI
nspHI
sexAI
bstNI
apyI[dcn+]
bsaJI

1641 AAAGCATGCA TCTCAATTAG TCAGCAACCA GGTGTGAAA GTCCCCAGGC TCCCCAGCAG GCAGAAGTAT
TTTCGTACGT AGAGTTAATC AGTCGTTGGT CCACACCTTT CAGGGTCCG AGGGGTCGTC CGTCTTCATA
sfanI
ppu10I
nsII/avaIII
nlaIII
sphi
nsPI
nspHI
scrFI
mvaI
ecorII
dsav
bstNI
apyI[dcn+]
nlaIV

1711 GCAAGCATG CATCTCAATT AGTCAGCAAC CATAGTCCCG CCCCTAATC CGCCCATCCC GCCCCTACT
CGTTTCGTAC GTAGAGTTAA TCAGTCGTTG GTATCAGGCG GGGGATTGAG GCGGGTAGGG CCGGATTGA
sfanI
ppu10I
nsII/avaIII
nlaIII
sphi
nsPI
nspHI
acII
acII
fokI
acII

- 233 -

32n

```

1901 CTAGGCTTTT GCAAAAAGCT GTTACCTCGA GCGGCCGCTT AATTAGGCG CGCCATTAA ATCTGCAGG
GATCCGAAAA CGTTTTCGA CATGGAGCT CGCCGCGCAA TTAATTCCGC GCGGTAATT TAGGACGTCC
^start pUC18
^linearization linker inserted into hpaI site

          acII      hinfI
          haeIII/paI  hhaI/cfoI
          mcrI      tai
          eagI/xmaIII/ecI XI  fnuDII/mvuI
          taqI  eaeI      bstUI
          xhoI  notI      hinfI
          paeR7I cfrI  tru9I  hhaI/cfoI  tru9I  pstI
          avai  fnu4HI  pacI  ascI  ahaIII/draI
          mnlI  acII  mseI  tru9I  bsh1236I  mseI  bsgI
          rmaI
          maeI
          aluI  maeIII  bsrBI  fnu4HI  mseI  bssHI  swaI  sse8387I
1901 CTAGGCTTTT GCAAAAAGCT GTTACCTCGA GCGGCCGCTT AATTAGGCG CGCCATTAA ATCTGCAGG
GATCCGAAAA CGTTTTCGA CATGGAGCT CGCCGCGCAA TTAATTCCGC GCGGTAATT TAGGACGTCC
^start pUC18
^linearization linker inserted into hpaI site

          scriI
          mvaI
          ecorII
          dsav
          bstNI
          apyI[(dcm+)]
          tru9I
          maeIII  aluI  bsrI  maeII  bsrI  bsaiI  maeIII  mseI
          eaeI      haeIII/paI
          cfrI
          maeIII
1971 TAACAGCTTG GCACTGGCGG TCGTTTACA ACCTCGTGAC TGGGAAACC CTGGCGTTAC CCACTTAAT
ATTGTCGAAC CGTGACCGGC AGCAAAATGT TGCAGCACTG ACCCTTTTGG GACCGCAATG GGTGAATTA

```

320

```

                                sau3AI
                                sau96I    mboI/ndeII(dam-)
                                haeIII/paII
                                asuI      dpuI(dam+)
                                mnlI      dpuII(dam-)
                                mboII     acII   pvuI/bspcI
                                earI/ksp632I mcrI
2041 CGCCTTGCAG CACATCCCCC CTCGCCAGC TGGCGTATA GCGAAGAGGC CCGCACCGAT
      GCGGAACGTC GTGTAGGGGG GAAGCGGTCG ACCGCATTAT CGCTTCTCCG GCGGTGGCTA
                                hinPI
                                hhaI/cfoI
                                nlaIV
                                narI
                                kasi
                                hlnII/acyI
                                hgiCI
                                haeII
                                banI      sfaNI
                                bglI      ahaII/bsaHI
2101 CGCCCTTCCC AACAGTTGCG TAGCCTGAAT GCGGAATGGC GCCTGATGCG GTATTTCCTC CTACGCATC
      GCGGAAGGG  TTGTCAACGC ATCGACTTA  CCGCTTACCG CGGACTACGC CATAAAGAG  GAATGCGTAG
                                sfaNI

```

32p

2171 TGTGCGGTAT TTCACACCGC ATACGTCAAA GCAACCATAG TACGGCCCT GTAGCGGCGC
 ACACGCCATA AAGTGTGGCG TATGCAGTTT CGTGTATC ATGCGGGGA CATGCCGCG
 acII acII maeII
 rsal hhaI/cfoI fnu4HI
 csp6I bslI acII
 hinfI
 thai
 fnuDII/mvnI
 bstUI scfI
 bsh1236I
 2231 ATTAAGCGCG GCGGTGTGG TGGTACGCG CAGCGTACC GCTTACCTTG CCAGCGCCCT AGCGCCGCT
 TAATTGCGC CGCCACACACC ACCAATGCGC GTCGCACTGG CGATGTGAAC GGTCCGGGA TCGCGGCGA
 maeII bbvI maeII
 hhaI/cfoI
 fnu4HI
 hinfI
 fnuDII/mvnI
 bstUI
 bsh1236I
 acII
 hinfI haeII
 hhaI/cfoI bsrBI
 mseI bsh1236I
 tru9I acII
 hhaI/cfoI
 hinfI acII
 bstUI
 fnuDII/mvnI
 rmaI
 hinfI haeII
 hhaI/cfoI
 2301 CCTTTCGCTT TCTTCCCTTC CTTCCTGCC ACCTTCGCC GCTTCCCGG TCAAGCTCTA AATCGGGCGC
 GGAAGCGGA AGAAGGGAAG GAAAGGCGG TGCAAGCGGC CGAAGGGGC AGTCGAGAT TTAGCCCCC
 mboII
 mspI
 hpaII
 naeI
 maeII cfr10I
 aluI
 banII
 bmyI
 bsp1286
 nlaIV
 hgiIII
 bsp1286

2371 TCCCTTTAGG GTTCCGATT AGTCTTTAC GGCACCTCGA CCCCAGAAAA CTGTATTGG hphI
 AGGGAATCC CAAGCTAA TCACGAATG CCGTGAGCT GGGTTTTTT GAACATAACC
 nlaIV mnlI
 2401 GTGATGGTC ACGTAGTGG CCATCGCCCT GATAGACGGT TTTGCCCCCT TTGACGTTGG drdi hinfI maeII
 CACTACCAAG TGCATCACCC GGTAGCGGA CTATCTGCCA AAAAGCGGA AACTGCAACC TCAGTGCAA
 maeII haeIII/palI
 2501 CTTTAATAGT GGAATCTTGT TCCAACTGG AACACACTC AACCCATCT CCGGCTATT TTTGATTTA
 GAAATTATCA CCGAGACA AGTTTGACC TTGTTGTAG TTGGATAGA CCCCATAAG AAACTAAT
 tru9I pleI bslI
 msel hinfI bsrI bslI avai
 2571 TAAGGATT TCCCGATTG GGCCTATTG TTAATAATG AGCTGATT ACAAATAATT
 ATCCCTAAA ACGCTAAG CCGATAAC AATTTTAC TCGACTAAT TGTTTTAA
 haeIII/palI msel aluI msel apoI
 tru9I msel tru9I msel

32q

32r

thal
 fnuDII/mvni
 apoI
 bstUI
 bsh1236I
 AACGGCAATT
 TTGGCGCTTAA

maeII
 psp1406I
 tru9I
 mseI
 sspl mseI
 ATTAACGTTT
 TGAATGCAAA

hgiAI/aspHI
 bsp1286
 bsiHKA1
 bmyI
 ddeI
 apaLI/snoI
 alw44I/snoI
 csp6I
 rsal
 CCACGTGAGA
 GTCATGTTAG

bsrI
 maeIII
 hlnPI
 fnu4HI
 nlaIII
 hhaI/cfoI
 bsaAI
 tlh111I/aspI
 bbvI
 gtcATGGCTG
 CGCCCCGACA
 GCGGGGCTGT

fnu4HI
 sfanI
 bstUI
 mseI
 acil
 bsaAI
 tth111I/aspI
 bbvI
 gtcATGGCTG
 CGCCCCGACA
 GCGGGGCTGT

hlnPI
 hhaI/cfoI
 mspI
 hpaII
 scrFI
 nciI
 dsav
 foki
 cauII
 acil
 aluI
 maeIII

nsbII
 bsh1236I
 bstUI
 acil
 hgaI
 drdI
 ggcTTGTCTG
 CTCGCCGCAT
 CGCCTTACAG
 ACAAGCTGTG
 GGGCGGTTGT

acil
 hgaI
 drdI
 ggcTTGTCTG
 CTCGCCGCAT
 CGCCTTACAG
 ACAAGCTGTG
 GGGCGGTTGT

acil
 hgaI
 drdI
 ggcTTGTCTG
 CTCGCCGCAT
 CGCCTTACAG
 ACAAGCTGTG
 GGGCGGTTGT

32s

scriFI
 nciI
 mspI
 hpaII
 dsav
 nspi
 nspHI
 fnu4HI
 bsmAI
 bvi
 mli
 hphi
 hphi
 bsh1236I
 bstUI
 fnuDII/mvni
 hinpI
 hhai/cfoI
 thai mli
 fnuDII/mvni
 bstUI
 bsh1236I
 accgctcgcg ggaagctgcg GTGTCAGAGG TTTTCACCGT CATCACCGAA ACCGGCGAGG CAGTATTCTT
 TGGCAGAGGC CTCGACGTA CACAGTCTCC AAAAGTGGCA GTAGTGGCTT TGGCGGCTCC GTCATAGAA
 bslI caulI aluI nlaIII mli
 hphi
 bsh1236I
 bstUI
 fnuDII/mvni
 hinpI
 hhai/cfoI
 thai mli
 fnuDII/mvni
 bstUI
 bsh1236I
 accgctcgcg ggaagctgcg GTGTCAGAGG TTTTCACCGT CATCACCGAA ACCGGCGAGG CAGTATTCTT
 TGGCAGAGGC CTCGACGTA CACAGTCTCC AAAAGTGGCA GTAGTGGCTT TGGCGGCTCC GTCATAGAA
 mli
 .haeIII/palI
 mboII
 sau96I
 bpuAI
 asuI
 tru9I
 rcaI
 nlaIII
 mli
 hphi
 hphi
 bsh1236I
 bstUI
 fnuDII/mvni
 hinpI
 hhai/cfoI
 thai mli
 fnuDII/mvni
 bstUI
 bsh1236I
 accgctcgcg ggaagctgcg GTGTCAGAGG TTTTCACCGT CATCACCGAA ACCGGCGAGG CAGTATTCTT
 TGGCAGAGGC CTCGACGTA CACAGTCTCC AAAAGTGGCA GTAGTGGCTT TGGCGGCTCC GTCATAGAA
 ecoO109I/draII
 msel
 bspHI
 mli
 hphi
 hphi
 bsh1236I
 bstUI
 fnuDII/mvni
 hinpI
 hhai/cfoI
 thai mli
 fnuDII/mvni
 bstUI
 bsh1236I
 accgctcgcg ggaagctgcg GTGTCAGAGG TTTTCACCGT CATCACCGAA ACCGGCGAGG CAGTATTCTT
 TGGCAGAGGC CTCGACGTA CACAGTCTCC AAAAGTGGCA GTAGTGGCTT TGGCGGCTCC GTCATAGAA
 hiniI/acyI
 ahaII/bsaHI
 aatII
 ddeI
 maeII
 aciI
 thai
 fnuDII/mvni
 bstUI
 bsh1236I
 hinpI
 hhai/cfoI
 thai mli
 fnuDII/mvni
 bstUI
 bsh1236I
 accgctcgcg ggaagctgcg GTGTCAGAGG TTTTCACCGT CATCACCGAA ACCGGCGAGG CAGTATTCTT
 TGGCAGAGGC CTCGACGTA CACAGTCTCC AAAAGTGGCA GTAGTGGCTT TGGCGGCTCC GTCATAGAA
 ATATAATG TTTCTTAGAC GTCAGGTGGC ACTTTTCGGG GAAATGTGGC
 TATTATTACC AAAGAATCTG CAGTCCACCG TGAAGAAGCC CTTTACACGC

[illegible]

32u

```

sau3AI
mboI/ndelI|dam-|
dpuI|dam+|
dpuI|dam-|
alwI|dam-|
bstYI/xhoI
3261 AGATCCTTGA GAGTTTCCG CCCGAAGAC GTTTCACAT GATGAGCACT TTTAAGTTC
TCTAGGAAC CTCAAAAGCG GGGCTTCTTG CAAAAGTTA CTACTCGTGA AAATTTCAAG

maeII
pspI406I
xmnI
asp700
mboII
bmyI
ahaiII/draI

hgIAI/asphI
bsp1286
bsiHKA1
mseI

scrFI
nciI
mspi
hpaiI
dsav
hinII/acyI
hgaI cauiI
ahaiI/bsaHI
bcgI mcrI
fnu4HI
aciI

aciI
thai
fnuDII/mvnI
bstUI
bsh1236I
hinPI
hhaI/cfoI
3321 TGCTATGTGG CGCGGTATTA TCCCGTGATG ACGCCGGGCA AGAGCAACTC GGTCCGCCGA
ACGATACACC GCGCATTAAT AGGCACTAC TCGGCCCGT TCTCGTTGAG CCAGCGGCGT

rsal
csp6I bsrI
scaI hphI maeIII
sfanI
fokI
ddeI
3381 TACACTATTC TCAGAATGAC TTGGTTGAGT ACTCACCAGT CACAGAAAG CATCTTACGG
ATGTGATAG AGTCTTACTG AACCAACTCA TGAGTGGTCA GTGTCTTTTC GTAGAATGCC

```

32v

```

haeIII/palI
eaeI
cfrI
fnu4HI
nlaIII
fnu4HI
bvi
fnu4HI
nlaIII
3441 ATGGCATGAC AGTAGAGAA TTATGAGTG CTGCCATAC CATGAGTGA AACACTGCG CCACTTACT
TACCGTACTG TCATTCTCTT AATACGTAC GACGGTATG GTACTACTA TTGTGACGCC GGTGAATGA

sau96I
avaII
sau3AI
asui
mboI/ndeII(dam-)
dpnI(dam+)
dpnI(dam-)
pvuI/bspcI
mcrI mliI
aluI
acI
nlaIII alwI(dam-)
3511 TCTGACAACG ATCGAGGAC CGAAGGAGT AACCGCTTTT TTGCACACA TGGGGATCA TGTAACTCGC
AGACTGTTGC TAGCCTCCTG GCTTCCTCGA TTGGCGAAA AACGTGTTGT ACCCCCTAGT ACATTGAGCG

mspi
sau3AI nlaIV
mboI/ndeII(dam-) aluI
dpnI(dam+) hpaII
dpnI(dam-) bsaBI
maeIII
sfanI
bvi
fnu4HI
3581 CTTGATCGTT GGGAACCGGA GCTGAATGAA GCCATACCAA ACGACGAGCG TGACACACAG ATGCCAGCAG
GAACTAGCAA CCCTGGCCT CGACTTACTT CGGTATGTTT TGCTGCTCGC ACTGTGTTGC TACGTCGTC

```

32w

3651

CAATGGCAAC AACGTTGCCG AACCTATTAA CTGGCGAACT ACTTACTCTA GCTTCCCGG

GTTACCGTTG TTGCAACGCG TTGTGATTAAT GACCGCTTGA TGAATGAGAT CGAAGGGCCG

hinfI
hhaI/cfoI
mstI
avIII/fspI
maeII
pspI406I
trugI
mseI
bsrI
trugI
mseI
maeI
rmal
alul
dcaV
caulI

mspI
hpaII
scrFI
ncII
dsav

3711

AACAATTAAAT AGACTGATG GAGCGGATA AAGTTGCAGG ACCACTTCTG CGCTCGGCC TTCCGGCTGG

TTGTTAATTA TCTGACCTAC CTCCGCTTAT TTCACGCTCC TGGTGAAGAC GCGAGCCGGG AAGCCGACC

trugI
mseI
aseI/asnI/vspI
mnlI
aclI
sau96I
avaII
hinfI
haeIII/palI
mspI
hpaII

hinfI
hhaI/cfoI
maeI
bsrI
trugI
mseI
maeI
rmal
alul
dcaV
caulI

mspI
hpaII
scrFI
ncII
dsav

3781

CTGGTTTAT GCTGATAAAT CTGGAGCCGG TGAGCGTGGG TCTCGCGGTA TCATTGCAGC

GACCAATATA CGACTATTTA GACCTCGCC ACTCGACCC AGAGCGCAT AGTAACGTGC

mspI
hpaII
cfr10I
nlaIV hphI
gsul/bpmI
bsaI
bsmAI
bstuI
fndIII/mvnI
fnu4III
bbvI

hinfI
hhaI/cfoI
maeI
bsrI
trugI
mseI
maeI
rmal
alul
dcaV
caulI

mspI
hpaII
scrFI
ncII
dsav

- 243 -

32x

```

sau96I
asuI
nlaIV
bsrI haeIII/palI mnlI
ACTGGGGCCA GATGGTAAGC CCTCCCGTAT CGTAGTTATC TACACGACGG GGAGTCAGGC
3841 TGACCCCGGT CTACCATTCG GGAGGGCATG GCATCAATAG ATGTGCTGCC CCTCAGTCCG

dclI
sau3AI nlaIV
mboI/ndelI(dam-)
dpnI(dam+)
3901 AACTATGGAT GAACGAATA GACAGATCGC TGAGATAGGT GCCTCACTGA TTAAGCATTG
fokI
TTGATACCTA CTGCTTTAT CTGCTAGCG ACTCTATCCA CGAGTGACT AATTCGTAAC
tru9I
maeII mseI
3961 GTAACGTCA GACCAAGTTT ACTCATATAT ACTTTAGATT GATTAAAC TTCATTTTAA
maeII
CATTGACAGT CTGTTCAAA TGAATATATA TGAATCTAA CTAAATTTTG AAGTAAAAAT

rmaI
sau3AI hphI mboI/ndelI(dam-)
mboI/ndelI(dam-)
dpnI(dam+)
dpnI(dam-)
tru9I bstYI/xhoII alwI(dam-)
mseI alwI(dam-) bstYI/xhoII
nlaIII rcaI bspHI
4021 ATTTAAAGG ATCTAGGTGA AGATCCTTTT TGATTAATCTC ATGACCAAAA TCCCTTAACG TGAGTTTTCG
TAAATTTTCC TAGATCCACT TCTAGGAAAA ACTAATAGAG TACTGCTTTT AGGGAATTGC ACTCAAAAGC

```

32y

```

4091 TTCCACTGAG CGTCAGACCC CGTAGAAAG ATCAAGGAT CTCTTGAGA TCCTTTTTC
AAGTGACTC GCAGCTGGG GCATCTTTC TAGTTCTTA GAAGACTCT AGAAAAAAA

    ddeI          hgaI
    mboI/ndeII[dam-]
    dpnI[dam+]
    sau3AI
    bstYI/xhoII
    mboI/ndeII[dam-]
    dpnI[dam+]
    alwI[dam-]

4151 CTGCGCGTAA TCTGCTGCTT GCAACAATAA AAACACCGC TACCAGCGGT GATTGTTTG
GACGCGCATT AGACGACGAA CGTTGTTT TTTGTGGCG ATGTCGCCA CCAACAAC

    thal
    fnuDII/mynI
    bstUI
    bsh1236I
    hinPI          fnu4HI
    hhaI/cfoI      bbvI
    aciI          nspBII
    acI

    sau3AI
    mboI/ndeII[dam-]
    dpnI[dam+]
    dpnII[dam-]
    alwI[dam-]

    mspI
    hpaII          aluI
    CCGGATCAAG AGCTACCAAC TCTTTTCCG AAGTAAC TGCTCAGCAG AGCGACGATA CCAATACTG
GGCCTAGTTC TCGATGTTG AGAAAAAGC TTCCATTGAC CGAAGTCGTC TCGCGTCTAT GTTTATGAC

    bsrI          hlnPI
    maeIII        eco57I
    hhaI/cfoI

```

3221

```

4281 TCCTTCTAGT GTAGCCGTAG TTAGCCACC ACTTCAGAA CTCTGTAGCA CCGCCTACAT ACCTCGCTCT
      rmaI      maeI      bslI      haeI      haeIII/palI      scfI      aciI      mnlI
      AGGAGATCA CATCGGCATC AATCCGGTGG TGAAGTCTT GAGACATCGT GCGGATGTA TGAGCGAGA

4351 GCTAATCCTG TTACCAAGTGG CTGCTGCCAG TGGCGATPAG TCGTGTCTTA CCGGGTTGGA CTCAGACGA
      maeIII      bsrI      bsvI      bsrI      maeIII      alwNI      bsvI      fnu4HI
      CGATTAGGAC AATGGTCACC GACGACGGTC ACCGCTATTTC AGCACAGAAAT GGGCCAACCT GAGTTCTGCT

4421 TAGTTACCGG ATAAGGCGCA GCGTCGGGC TGAACGGGGG GTTCGTGCAC ACAGCCACGC TTGAGCGAA
      mspI      hpaII      bspBI      fnu4HI      nspBI      hglAI/aspHI
      bsaWI      hinfI      bspI      hpaII      bspI      bspI286
      maeIII      hhaI/cfoI      hinfI      aciI      bmyI      bspI      bspI286
      ATCAATGGCC TATTCGGCGT CGCAGCCCG ACTTGCCCC CAAGCACGTG TGTGGGTG AACCTCGCTT

4491 CGACCTACAC CGAAGTGAGA TACCTACAGC GTGAGCATTTG AGAAGCGCC ACGCTTCCCG AAGGAGAAA
      ddeI      scfI      hinfI      hhaI/cfoI
      GCTGGATGTG GCTTGACTCT ATGATGTG CACTCGTAC TCTTTCGGG TCGAAGGGC TTCCCTCTTT

```

32z2

[illegible]

	dsav	bstNI	apyl[dcml]	mli	drid	hgai	taqi	sfani
4631	GCCTGGTATC	TTTATAGTCC	TGTCGGGTTT	CGCCACTCT	GACTTGAGCG	TGCATTTTG	TGATGCTCGT	
	CGACCATAG	AAATATCAGG	ACAGCCCAA	GCGGTGAGCA	CTGAAGTCGC	AGCTAAAAAC	ACTACGAGCA	

4701 CAGGGGGGCG GAGCCTATG AAAACGCCA GCAACGGCG
GTCCCCCGC CTCGATACC TTTTGGCGT CGTTGGCGC

3223

```

                                haeIII/palI
                                scrFI
                                mvaI bslI
                                ecorII
                                dsav
                                bstNI
                                apyI(dcm+)
                                nlaIV haeI
                                haeIII/palI haeI
                                nspi
                                nlaIII
                                nspII
                                afIII
                                tflI
                                hinfI
4741 CTTTTCACGG TTCCTGGCCT TTGCTGGCC TTTGCTCAG ATGTTCTTC CTGCGTTATC CCCTGATTCT
      GAAAAATGCC AAGGACCGGA AAACGACCGG AAAACGAGTG TACAAGAAAG GACGCAATAG GGGACTAAGA
                                fnu4HI
                                bbvI
                                bsrBI
                                acII
                                mcrI
                                hinfI
4811 GTGATTAACC GTATTACCGC CTTTGAAGTA GCTGATACCG CTCGCCGCG AGCGGCGCTC GGCTTGCTGG
      CACCTATTGG CATTAATGGCG GAACTCACT CGACTATGCG GAGCGGCGTC
                                hinfI
                                haeII
                                sapI hhaI/cfoI
                                mboII
                                mcrI
                                hinfI
                                fnu4HI
                                bbvI pleI
                                hinfI hinfI
                                hhaI/cfoI
                                mnlI acII earI/ksp632I
                                acII
                                mnlI
4871 GAGCGGACCG AGTCAGTGG CGAGGAAGCG GAAGAGCGCC CAATACGCAA ACCGCCCTCTC
      CTCGCGTCGC TCAGTCACTC GCTCCTTCGC CTTCTCGCG GTTATGCGTT TGGCGGAGAG
```

32z4

```

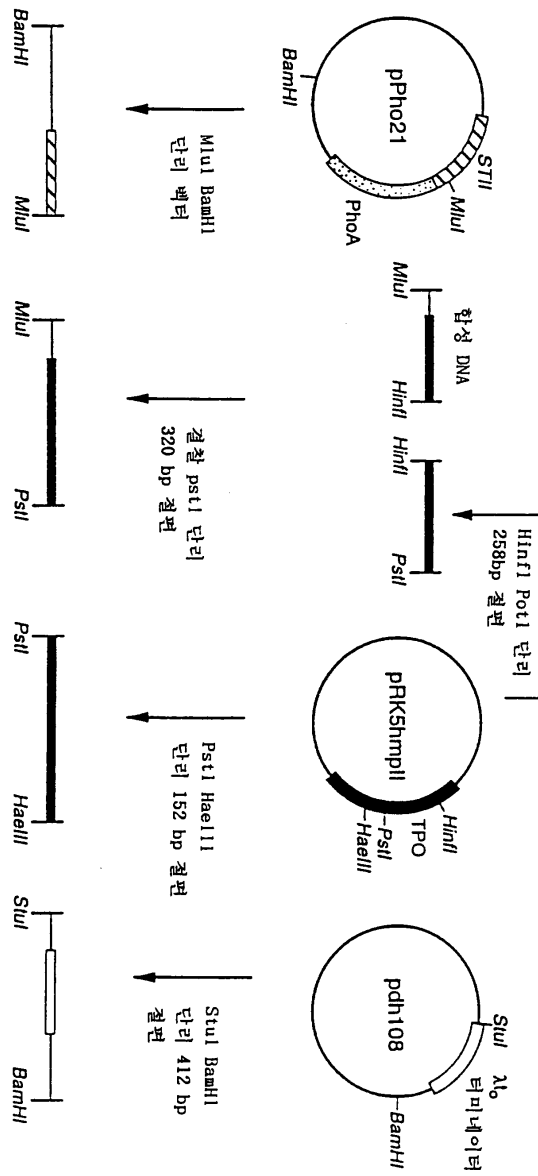
thai
fnuDII/mvni
bstUI
bsh1236I
hinPI
hhaI/cfoI
thai
fnuDII/mvni
bstUI
trugI aluI
bsh1236I haeIII/palI pvuII
bsII eaeI tfil asei/asni/vsPI
acII cfrI hinfl msel nspBII
4931 CCCGCGCGTT GGGCGATTCA TTAATCCAGC TGGCAGGACA GGTTCGCCGA CTGGAAGCG
GGGCGCGCAA CCGCTAAGT AATTAGTGC ACCGTGCTGT CCAAAGGCT GACCTTTCGC
bsrI acII

scrFI
mvaI
ecorII
dsav
nlaIV bstNI
hgiCI apyI(dcm+)
hinPI msel maeIII
hhaI/cfoI asei/asni/vsPI mnlI
banI bsaJI
4991 GGCAGTGAGC GCAACGCAAT TAATGTGAGT TACCTCACTC ATTAGGCACC CCAGGCTTTA CACTTATGC
CCGTCACTCG CGTTGCGTTA ATTACACTCA ATGGAGTGAG TAATCCGTGG GGTCCGAAAT GTGAATATACG
```

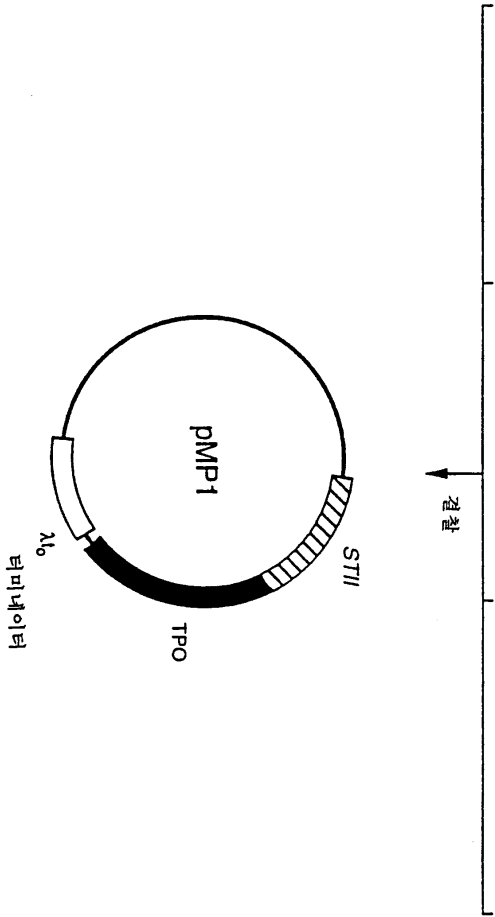
32z5

```
mspi  
hpaiI  
5061 TTCCGGCTCG TATGTTGTGT GGAATTGTGA GCGGATPACA ATTTCACACA GGAACAGCT ATGACCATGA  
AAGGCCGAGC ATACACACACA CCTTAACTACT CGCTATTGT TAAAGTGTGT CCTTGTGCA TACTGTACT  
lru9I  
msei  
aseI/asnI/vspi  
xmni  
asp700  
5131 TTACGAAATTA A  
AATGCTTAAT T  
>length: 5141
```

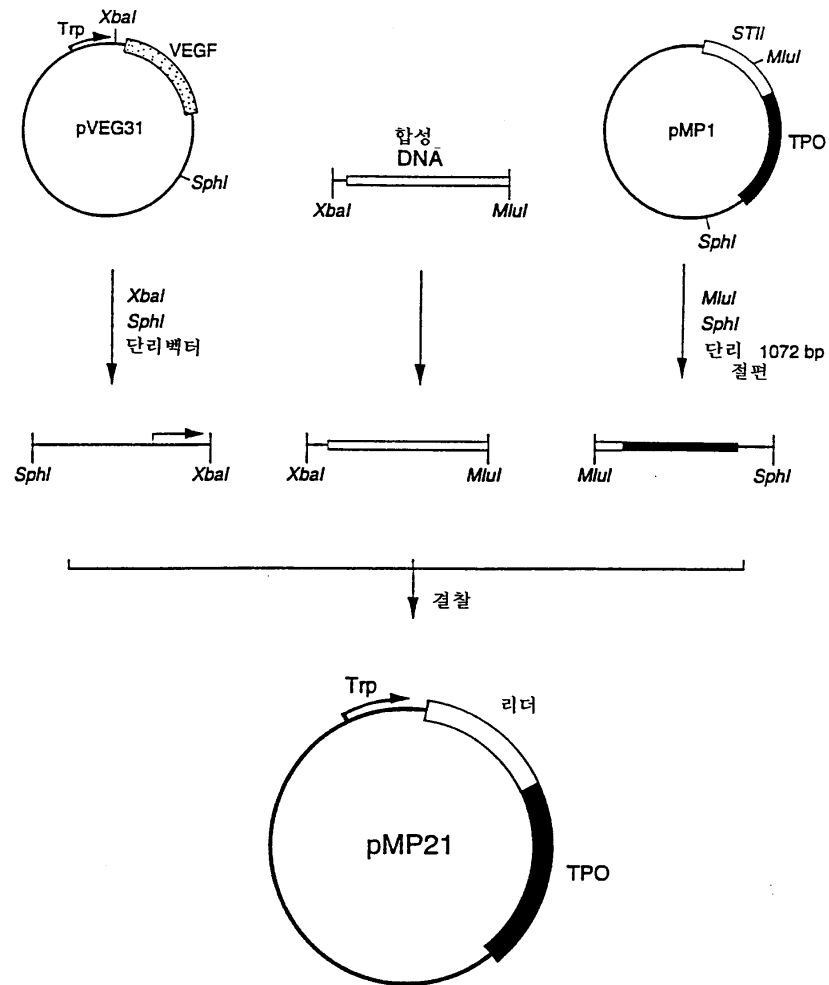
33a



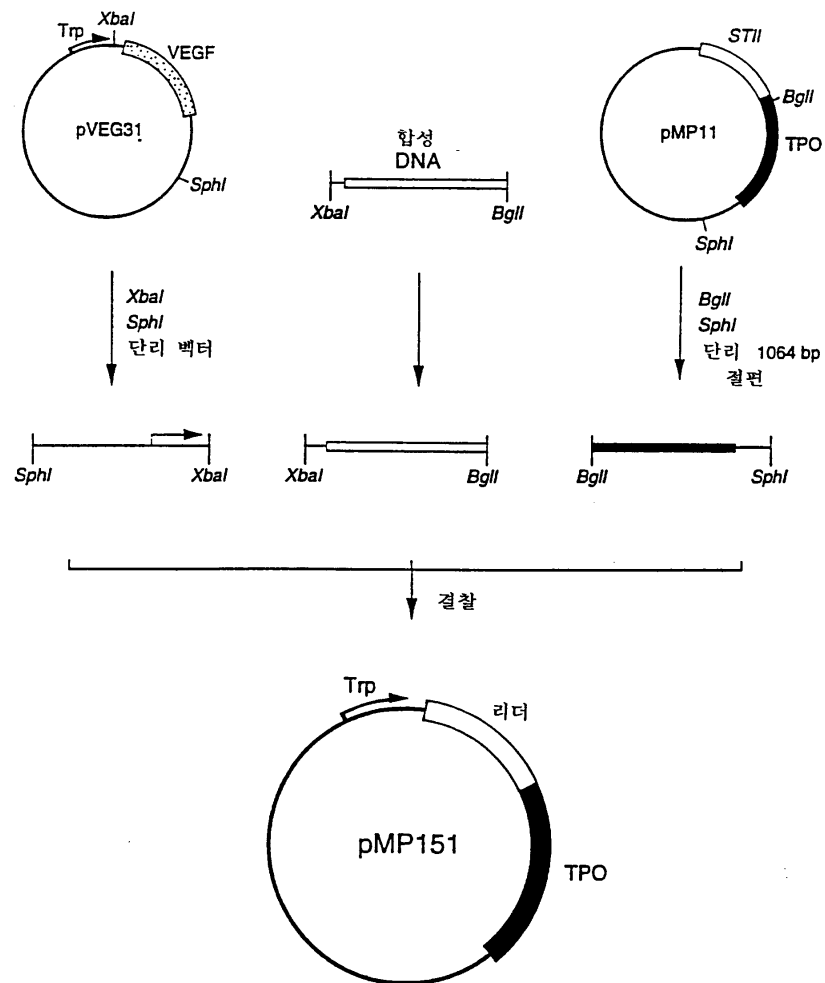
33b



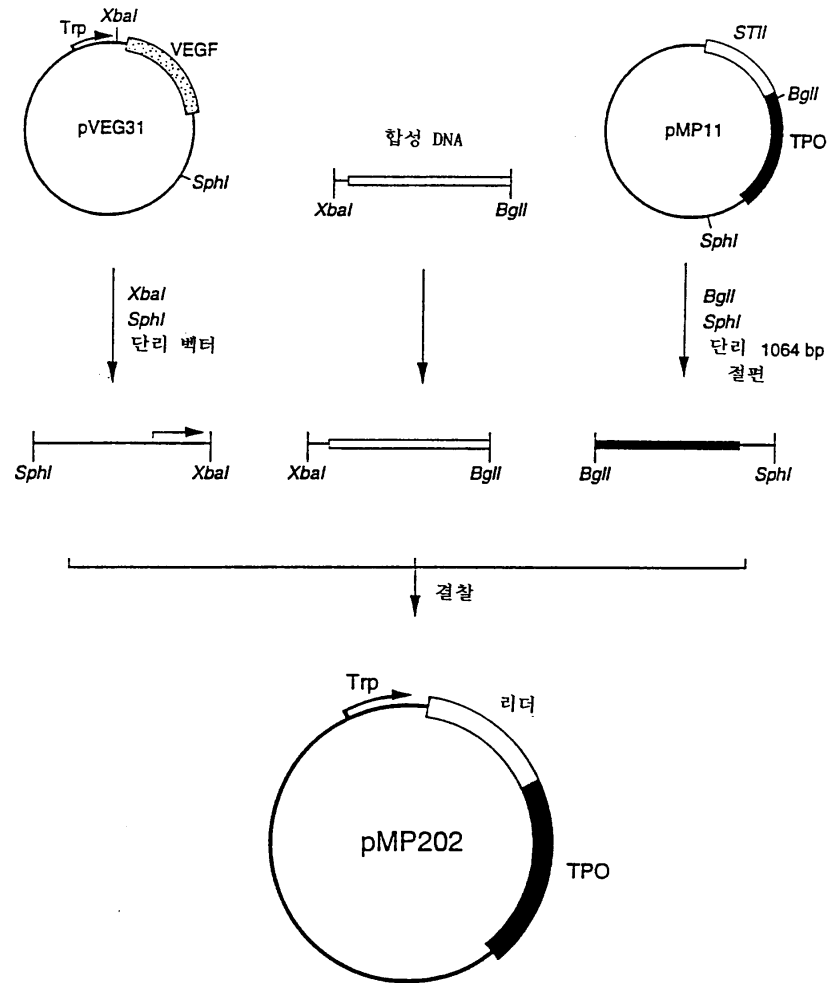
34

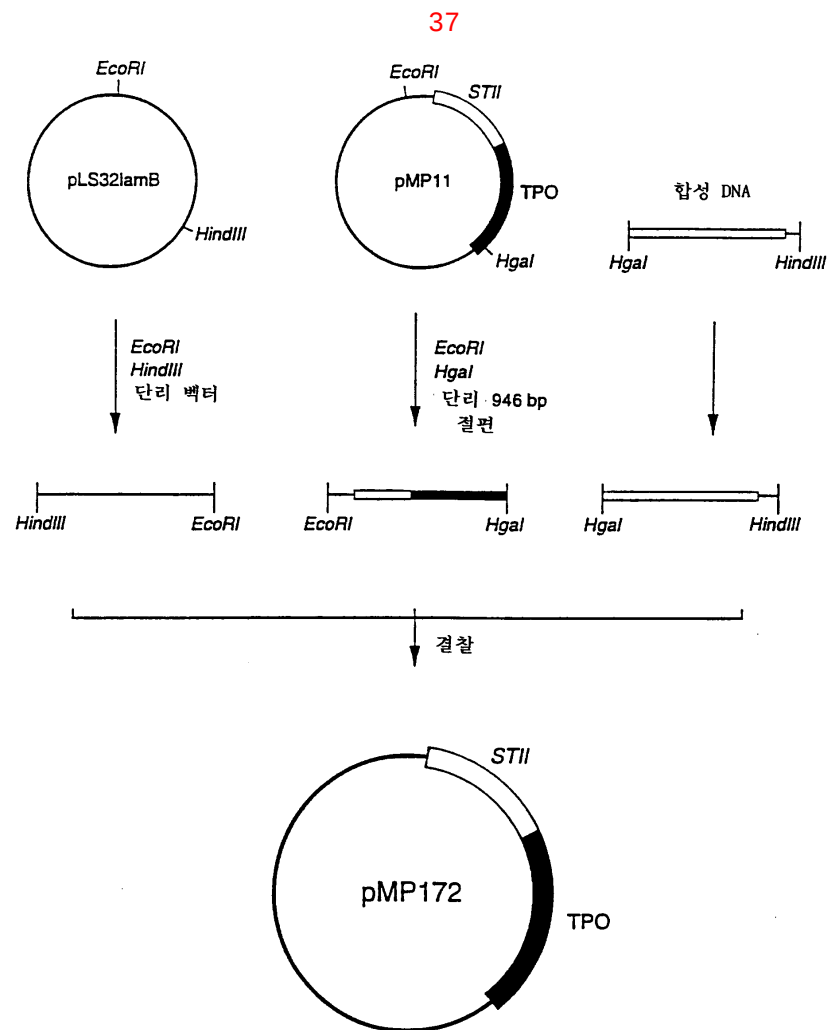


35

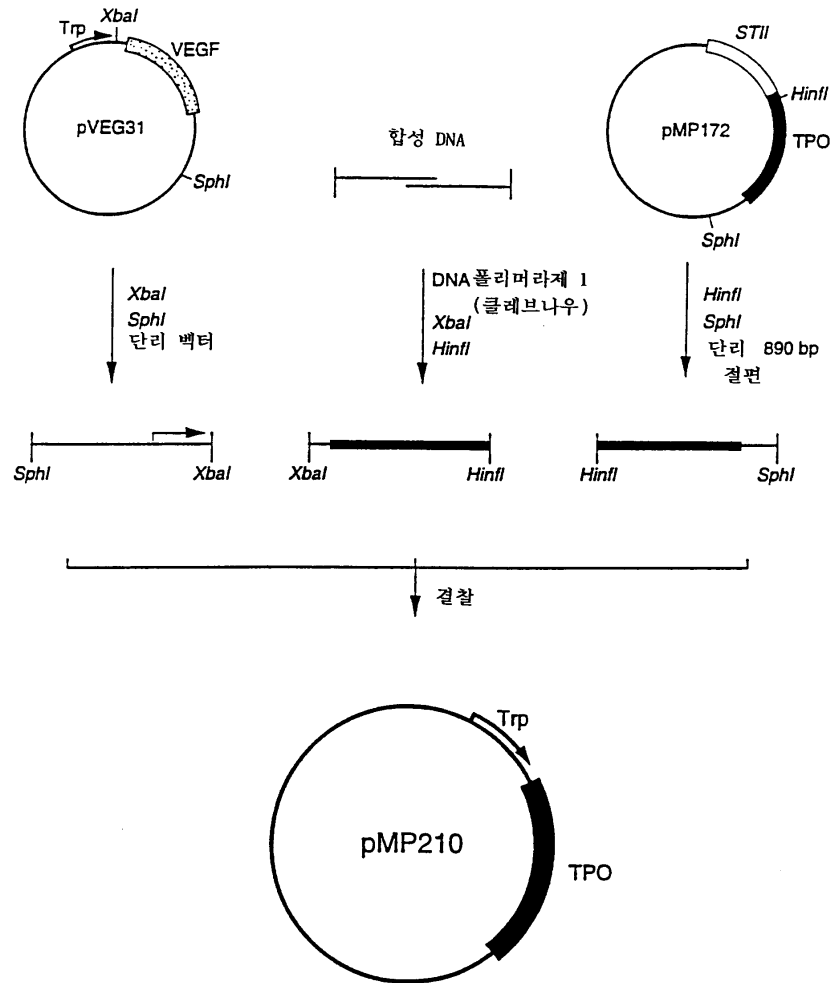


36





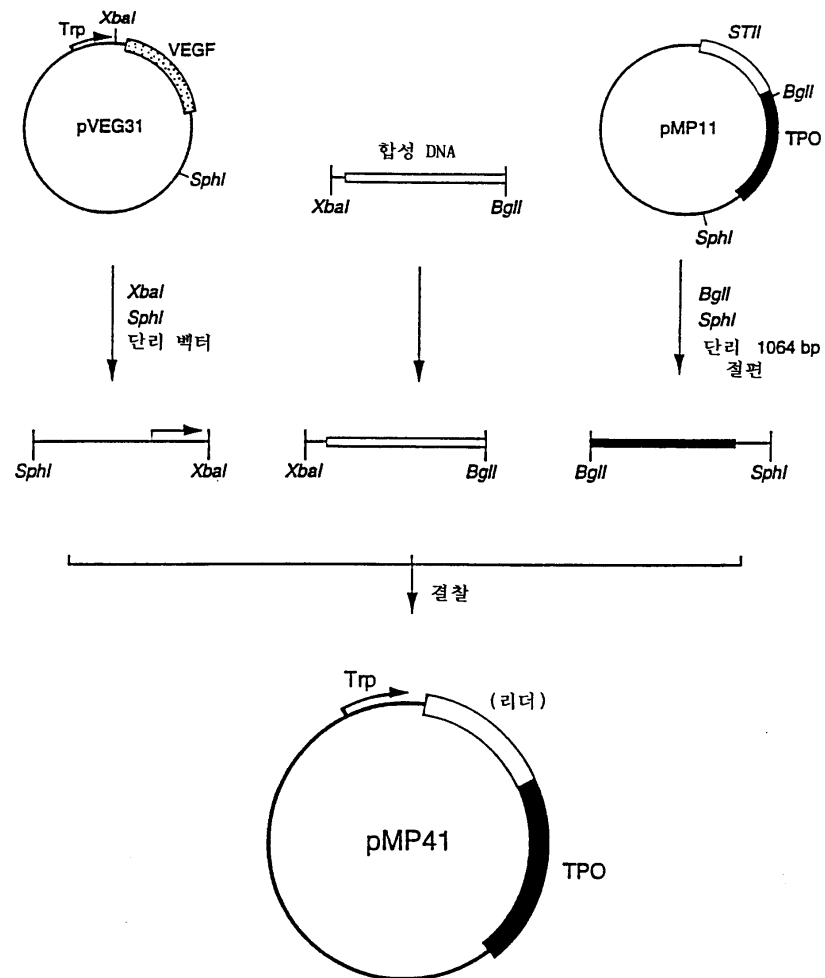
38



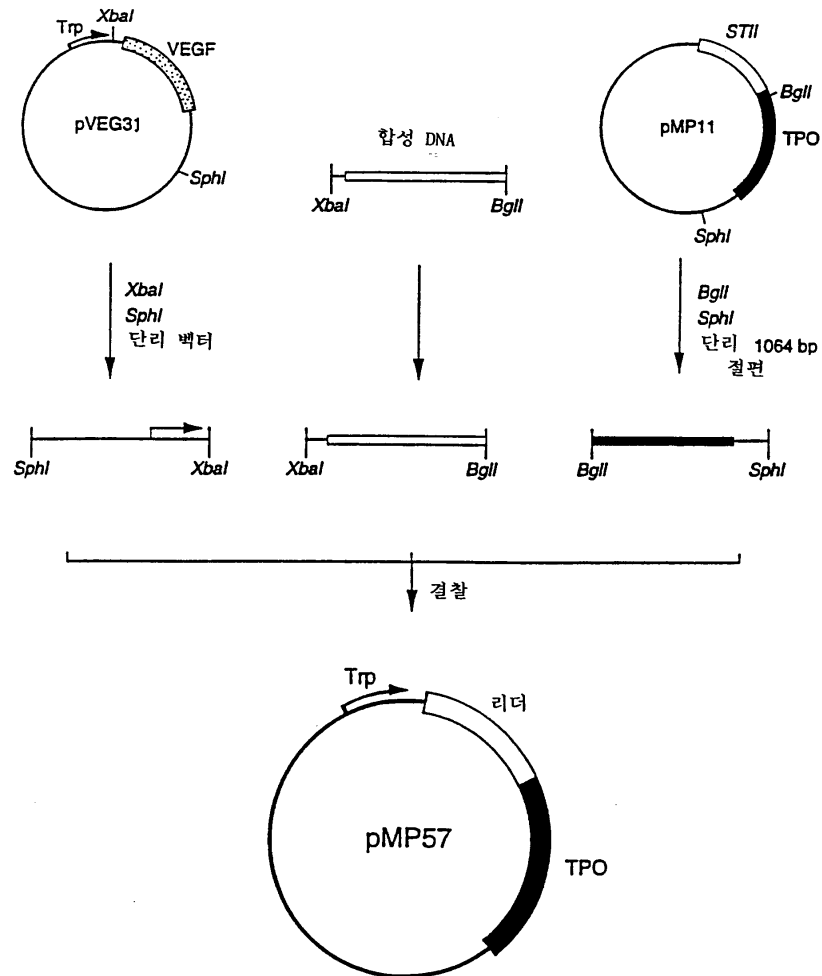
39

	Met	Ser	Pro	Ala	Pro	Pro	Ala
MP210 벡터	ATG	TCN	CCN	GCN	CCN	CCN	GCN
MP210-1	ATG	TCT	CCA	GCG	CCG	CCA	GCG
MP210-T8	ATG	TCG	CCT	GCT	CCA	CCT	GCT
MP210-21	ATG	TCG	CCA	GCG	CCA	CCA	GCC
MP210-24	ATG	TCC	CCA	GCC	CCA	CCC	GCA
MP210-25	ATG	TCG	CCA	GCG	CCG	CCA	GCG

40



41



42

