

(19) (KR)  
(12) (A)

(51) 。 Int. Cl.7

A61K 38/18

A61K 38/17

A61K 38/22

(11)

(43)

10-2004-0096592

2004 11 16

(21) 10-2004-7012978

(22) 2004 08 20

2004 08 20

(86) PCT/US2003/005150

(87)

WO 2003/072714

(86) 2003 02 21

(87)

2003 09 04

(30) 60/357,846 2002 02 21 (US)

60/434,645 2002 12 20 (US)

(71)

07940-0874

(72)

02143

157

16

02030

5

(74)

:

(54)

- 8 (GDF-8)

GDF-8

가가

4

2002 2 21  
60/434,645

가

60/357,846

2002 12 20

가

-8 (GDF-8), GDF-8

가가

(myostatin) -8 (GDF-8)

(Kingsley (1994) Genes Dev., 8: 133-46; Hoodless (1998) Curr. Topics Microbiol. Immunol., 228: 235-72). GDF-8

GDF-8 (McPherron (1997) Nature, 387: 83-90).

가가 GDF-8 (Ashmore (1974) Growth, 38: 501-507; Swatland and Kieffer (1994) J. Anim. Sci., 38: 752-757; McPherron and Lee (1997) Proc. Natl. Acad. Sci. U.S.A., 94: 12457-12461; Kambadur (1997) Genome Res., 7: 910-915).

HIV- GDF-8 가가 (Gonzalez-Cadavid (1998) Proc. Natl. Acad. Sci. U.S.A., 95: 14938-43). GDF-8 (WO 00/43781).

가

가

가

GDF-8 (Kim (2001) B.B.R.C. 281.: 902-906).

GDF-8 (McPherron and Lee, (1997) Proc. Nat. Acad. Sci. U.S.A., 94: 12457-12461).

GDF-8 (Miyazono (1998) J. Biol. Chem., 263: 6407-6415; Wakefield (1988) J. Biol. Chem., 263: 7646-7654; Brown (1990) Growth Factors, 3: 35-43). 2 GDF-8 가 GDF-8 (Thies (2001) Growth Factors, 18: 251-259).

(Gentry Nash (1990) Biochemistry, 29: 6851-6857; Derynck (1995) Nature, 316: 701-705; Massague (1990) Ann. Rev. Cell Biol., 12: 597-641). GDF-8

(Gamer (1999) Dev. Biol., 208: 222-232). GDF-8 가

GDF-8

GDF-8 가가

TGF-

(Bartholin (2001), Oncogene, 20: 5409-5419; Shibamura (1993) Eur. J. Biochem. 217: 13-19)

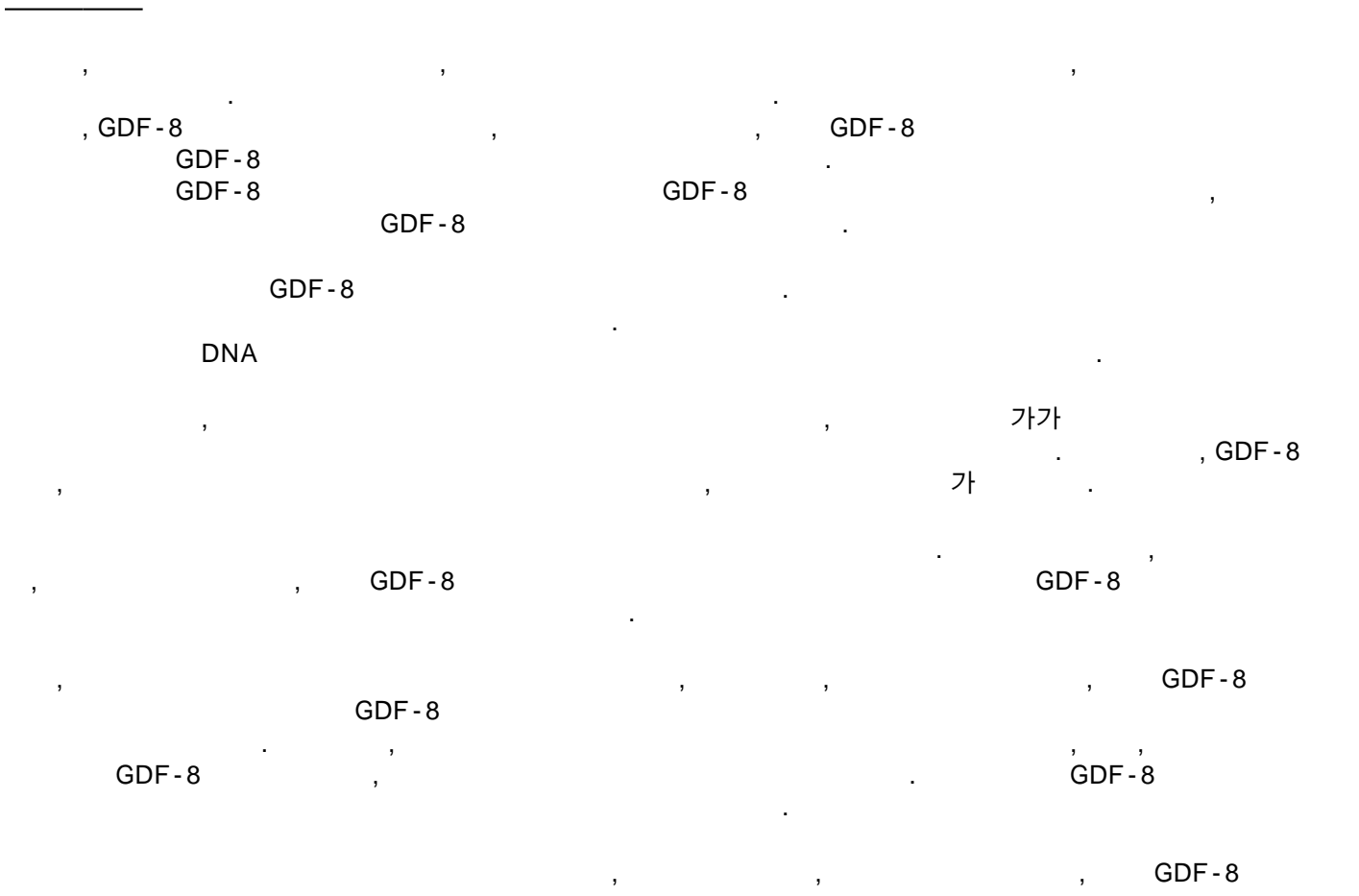
TGF- (Phillips and de Kretser (1998) Front. Neuroendocrin., 19: 287-322; Tsuchida (2000) J. Biol Chem., 275: 40788-40796; Patel (1996) Dev. Biol., 178: 327-342; Amthor (1996) Dev. Biol., 178: 343-362), TGF-

7 (IGFBP7, mac25) , IGFBP7 TGF- (Kato (2000) Mol. Med., 6: 126-135).

(agrin) 9 (Patthy (1993) Trends Neurosci., 16: 76-81).

(SPARC, BM40) (SCI, mast9, QR1) (Motamed (1999) Int. J. Biochem. Cell. Biol., 31: 1363-1366; Girard Springer (1996) J. Biol. Chem., 271: 4511-4517).

NCBI (National Center for Biotechnology Information, Bethesda, Maryland, USA) U198 78 (G01639, -1 (tomoregulin-1), T46914, GASP1 ( GDF- associated serum protein 1; ; 7), GASP2 (WFIKKK; Trexler (2001) Proc. Natl. Acad. Sci. U.S.A., 98: 3705-3709; 9), (testican; SPOCK) (Alliel (1993) Eur. J. Biochem., 214: 347-350) 가 GASP1 ( 6) GASP2 ( 8) Celera (Rockville, MD) (wobble codon) GASP1 Celera ( 13 ).



GDF-8

1 mock- ( ) JA16 GDF-8 (0) (mock ), SDS 가

2 N- 12 kDa (b ) C- (y ) GDF-8 ( : 19) MS/MS 가 y 2A GDF-8 가 가 2B GDF-8 GDF-8

3 F-8 GDF-8 : 30) ( 3C) 36 kDa MS/MS (FLRG) 가 GDF-8 ( : 23) ( 3A) FLRG ( 3B) GDF-8, GDF-8 GD

-- , 가 GDF-8 SDS 3D FLRG GDF-8

4 8 13 GDF-8 , FLRG, GDF-8 JA16 -LC-MS/MS GDF-8, GDF-8 FLRG ( GDF- associated serum protein 1, GASP1)

5 31 2 GASP1 ) 5B ( 33 MS/MS GDF-8 ) , 4 5A ( 3

6A GASP1 .2 6C 6A 6B 6B GASP1 가

7A GASP1 7B GASP1 7C 7D

8A GASP2 , 8B

9A GASP2 , 9B

10 GASP1 GASP1

A . GASP1 551 bp Clontech (Palo Alto, CA) 1 cDN  
 -3- (G3PDH)  
 . G3PDH . cDNA G3PDH  
 A2 S29

11 JA16 (0) mock P  
 BS , SDS , LS-  
 MS/MS . JA16  
 GDF-8 ( 16), GDF-8 . FLRG ( 11) GASP1 ( 4) . 11B GDF-  
 8 가 GDF-8 가

12 GDF-8 4, 11 16 ( 11) 1  
 . N- (b ) C- (y )  
 . GASP1 ( : 44) ( 12A), FLRG ( : 41) ( 12B), GDF-8  
 ( : 24) ( 12C), GDF-8 ( : 13) ( 12D)

13 GASP1 ( : 48) ( : 49) . J  
 A16 -

14A GASP1 . GASP1 29 /  
 , GASP1 2 Kunitz/BPTI , (Kazal  
 ) 14B  
 GASP1 GASP2 . GASP1 90% . GAS  
 P1 GASP2 54%

15 GASP1 GDF-8 GDF-8 . (A  
 ) JA16 , GDF-8 / 가 mock- GASP1-V5-His  
 COS GDF-8 -V5 ( ), -GDF-8 ( ),  
 - (B) GASP1 GDF-8 / 가  
 mock- GASP1-V5-His -V5 (A)

16 GASP1 TGF- GDF-8 BMP-11  
 . mock ( ) GASP1-V5-His ( )  
 (A) 10 ng/ml GDF-8, (B) 10 ng/ml BMP-11, (C) 10 ng/ml  
 A204 (A-C) RD (D) , (D) 0.5 ng/ml TGF-  
 가 가

17 GDF-8 GASP1 GASP1 RD (CAGA) 12 ( : 53)  
 20 ng/ml 가 ( ) . GDF-8

65-90 , 10  
 Kazal 가 , 5  
 , 1 2 . 7 8  
 (G,A)-(S,N)-(S,N,T)-(D,N)-(G,N) (T,S)-Y  
 가 . 9 10  
 2 ( V, I L)





1	6A	GASP1
2	6B	GASP1
3	6C	1 2 GASP1
4	7A	GASP1
5	7B	4 GASP1
6	7C	GASP1
7	7D	GASP1 6
8	8A	GASP2
9	8B	8 GASP2
10	9A	GASP2
11	9B	10 GASP2
12	2	
13-20	1, 5, 6	GDF-8
21-27	1, 5, 6	GDF-8
28-30	1, 5	FLRG
31-35	1, 5, 7	GASP1
36-37	1, 8	GDF-8
38-39	1, 8	GDF-8
40-42	1, 8	FLRG
43-45	1, 8,	GASP1
46	7	
47	7	
48	13	GASP1
49	13	48 GASP1
50	9	
51	9	
52	9	N-
53	11	





Sequence Analysis Software Package

Sequence Analysis Software Package, 'BLAST' (Altschul, 1990) (NCBI) ; 'FastA' (Lipman and Pearson, 1985; Pearson Lipman, 1988; Pearson Lipman, 1990) ; 'TfastA' (Pearson Lipman); 'FastX' (Pearson Lipman); 'TfastV' (Pearson Lipman) 가 ).

N- / C-

DNA

가 가

(hydropathic index) 가

(Kyte

Doolittle (1982) J. Mol. Biol, 157: 105-132).

2

DNA,

(+1.8), (+4.5), (+4.2), (+3.8), (+2.8), / (+2.5), (+1.9), (-1.3), (-1.6), (-3.2), (-0.4), (-0.7), (-0.8), (-0.9), (-3.5), (-3.5), (-3.5), (-3.9), (-4.5) 가 ±2, ±1, ±0.5 가 (Kyte Doolittle, 1982);

U. S. 4,554,101

U. S. 4,554,101 : (+3.0), (+3.0), (+3.0 ± 1), (+3.0 ± 1), (+0.3), (+0.2), (0), (-0.4), (-0.5 ± 1), (-0.5), (-0.5), (-1.0), (-1.3), (-1.5), (-1.8), (-1.8), (-2.3), (-2.5), (-3.4). +2, ±1, ±0.5 가

가

GDF

2 1 1 2  
2 ( )

U. S. 4,640,835 ; 4,496,689  
; 4,301,144 ; 4,670,417 ; 4,791,192 4,179,337

9,546 U. S. 4,766,106 ; 4,179,337 ; 4,495,285 ; 4,60

peg (PEG) peg  
peg GDF-8  
[Bhadra (2002) Pharmazie, 57: 5-29; Harris (2001) Clin. Pharmacokinet., 40: 539-551

IgG Fc IgG Fc Fc IgG Fc IgG1  
IgG4

) 가 가 ( /

N- 0- N- -X- ( , X  
)  
N- , 5- 5- , 가 . 0-

가 (N- )  
) 가 (0-

GDF a) (b) (c) (d) (f)  
(e) WO 87/05330, [Aplin and Wriston (1981) CRC Crit. Rev.  
Biochem., 22: 259-306]

) (N- N-

chem., 118: 131] [Hakimuddin (1987) Arch. Biochem. Biophys., 259: 52; Edge (1981) Anal. Biochem., 118: 131] . GDF [Thotakura (1987) Meth. Enzymol., 138: 350] - -

5,116,944

, U. S.

가

가

가

pH

가

any, NJ)

(PBS) 가

, Cremophor EL™ (BASF, Parsipp 가

Alza Cor

poration Nova Pharmaceuticals, Ind.

가

U. S. 4,522,811

DF),

( , BMP, TGF- , FGF, IGF), 가

( , C

X-

(ALS);

;가

( 1 )

( 2 )

( X), ( )

( ) /

D

2

(NIDDM)

3 가

: (1)

(3)

(DeFronzo (1997) Diabetes Rev. 5: 177-269).

2

가

( 가 ) /

가

GDF-8

, GDF-8

( GDF-8 )

GDF-8

GDF-8

50% , 60, 62, 64, 66, 68, 70, 72, 72, 76, 78, 80, 82, 84, 86, 94% , 95% 100%

88% , 90, 91, 92, 93,

GDF-8

가,

가,

(lean)

x-

85 mg, 30 mg  
1 1 , 1

70 mg,  
1 1

40 mg  
1

60 mg

5 mg

100 mg, 15 mg

GDF-8

) ED<sub>50</sub> (가 50% , LD<sub>50</sub> / ED<sub>50</sub> ) LD<sub>50</sub> ( 50% )

ED<sub>50</sub>

IC<sub>50</sub> ( , )

GDF-8 /

DNA

가 RNA 가 가 (HaMuSV), (MuMTV), (MoMuLV), (RSV). 가 가 GDF 가

가

LTR

PSI.2, PA317 PA12 가 (virion)

RNA

env

gag, pol

. RNA, DNA  
( , Fraley (1981) Trends Biochem. Sci., 6: 77 ).  
( , Mannino (1988) Biotechniques, 6: 682 ).

pH, 2 가

가 (egg)

GDF-8

GDF-8

GDF-8

, ELISA,

GDF-8

) 가 (

가

가 , 3,3',5,5'-

(TMB)

, IgG

A,

가

GDF-8

GDF-8

GDF-8

GDF-8

1: JA16

N- (4% 가 , Sigma H-8635, St Louis MO) MilliQ-H<sub>2</sub>O  
10 mg JA16/ ml -GDF-8 JA16 (100 mM MO  
PS, pH 7.5 3-4 µg/µl) 4 4 100 mM MOPS pH 7.5  
(PBS) (Ausubel (1999) Current Protocols in Molecular Biology, John Wiley amp; Sons)

PBS 4

JA16

2:

40  $\mu\ell$  , JA16  
 est Biologicals, Temecula CA) 30 ml  
 ~10 ml 1 % Triton X-100/PBS 2 , ~10 ml 0.1 % Triton  
 X-100/PBS 2 , ~1 ml PBS 2  
 'mock' ( , 100  $\mu\ell$  PBS 가 , 30 4  
 , 30  $\mu\ell$  4 xLDS (Invitrogen, Carlsbad CA)  
 ( , 100  $\mu\ell$  PBS 1  $\mu\text{g}/\mu\ell$  ( : DFGLDSDE  
 HSTESRSSRYPLTVDFEAFGWD-COOH ( : 12)) 가 , 30 4  
 4 xLDS (Invitrogen) 100  $\mu\ell$  PBS 가 , 10 80 가 , 30  $\mu\ell$   
 ).  
 12 36 kDa 2 1 가 1 JA16

3:

80 10 NuPage 10 x (Invitrogen) , 22 30 110  
 $\mu\text{M}$  MES 10% NuPage  
 -Tris (Invitrogen) 가 (Shevchenko  
 (1996) Anal. Chem., 68: 850-858). Abimed Digest Pro (Langenfeld, Germany) ProGest I  
 nvestigator (Genomics Solutions, Ann Arbor MI) (Promega, Madison WI)  
 , 1% ~20  $\mu\ell$   
 (5-10  $\mu\ell$ ) Picofrit (New Objectives, Woburn MA) 10 cm x75  $\mu\text{m}$  C 18  
 MS/MS LCQ Deca LCQ Deca XP (Finnigan, San Jose CA)  
 , Sequest (Finnigan) NCBI  
 , Sequest  
 X<sub>corr</sub> > 2.5 MS/MS

4:

0.45  $\mu\text{m}$  (Invitrogen) , 4 (Tris  
 (TBS: 10 mM Tris-Cl, pH 7.5, 150 mM NaCl) 5% )  
 1-3 1:1000 (probed), 5 x TBS ,  
 1-3 가 ,  
 . West Pico Substrate (Pierce)

5: GDF-8

GDF-8 GDF-8 12 kDa , 1  
 GDF-8 가  
 , LC-MS/MS MS/MS 2A 1 ,  
 6 GDF-8  
 1 JA16 GDF-8 ( : 13-20), GDF-8  
 ( : 21-27), FLRG ( : 28-30), GASP1 ( : 31-35) 가  
 Sequest (X<sub>corr</sub> , ) (z)



가 , 가 가 GDF-8 (43 kDa) 가 ,  
 ( 2B). 가 GDF-8 ,  
 8 ( ). , GDF-  
 JA16 가 GDF-8 BMP/GDF-11 ,  
 BMP-11

[ 1-1 ]

JA16 번역침전물에서 동정된 펩티드

		마우스 혈청	z	X <sub>corr</sub>
GDF-8 (성숙)	(K)	ANYCSGECEVFVLQK ( 서열번호 :13)	3+	4.63
	(K)	MSPINMLYFNGK ( 서열번호 :14)	2+	3.81
	(R)	DFGLDCDEHSTESR ( 서열번호 :15)	2+	3.47
	(K)	ANYCSGECEVFVLQK ( 서열번호 :16)	2+	3.31
	(K)	M*SPINMLYFNGK ( 서열번호 :17)	3+	2.95
	(R)	YPLTVDFEAFGWDWIIAPK ( 서열번호 :18)	2+	2.86
	(K)	M*SPINM*LYFNGK ( 서열번호 :19)	2+	2.51
	(R)	GSAGPCCTPTK ( 서열번호 :20)	2+	2.43
	GDF-8 (프로펩티드)	(K)	LDM*SPGTGIWQSIDVK ( 서열번호 :21)	2+
(K)		ALDENGHDLAVTFFPGGEDGLNPFLEVK ( 서열번호 :22)	3+	3.17
(K)		LDMSPGTGIWQSIDVK ( 서열번호 :23)	2+	2.98
(R)		ELIDQYDVQR ( 서열번호 :24)	2+	2.97
(K)		TPTTVFVQILR ( 서열번호 :25)	2+	2.91
(K)		AQLWIYLRPVK ( 서열번호 :26)	2+	2.77
(K)		EGLCNACAWR ( 서열번호 :27)	2+	2.75
폴리스타틴 유사	(R)	PQSCLVDTGSAHCWCR ( 서열번호 :28)	3+	3.34
관련 유전자 (FLRG)	(K)	DSCDGVCEGPGK ( 서열번호 :29)	2+	2.99
	(K)	SCAQVVCPR ( 서열번호 :30)	2+	2.59
신규 멀티도메인 프로테아제 저해제 (GASP1)	(R)	ECETDQECETYEK ( 서열번호 :31)	2+	2.98
	(R)	ADFPLSVVR ( 서열번호 :32)	2+	2.56
	(R)	EACEESCFFPR ( 서열번호 :33)	2+	2.95
	(R)	SDFVILGR ( 서열번호 :34)	2+	2.73
	(R)	VSELTEEQDSGR ( 서열번호 :35)	2+	3.88

M\* = 산화된 메티오닌

[ 1-2 ]

		인간 혈청	z	X <sub>corr</sub>
GDF-8 (성숙)	(K)	ANYCSGECEVFVLQK ( 서열번호 :36)	2+	4.21
	(R)	DFGLDCDEHSTESR ( 서열번호 :37)	3+	2.08
GDF-8 (프로펩티드)	(K)	ALDENGHDLAVTFFPGGEDGLNPFLEVK ( 서열번호 :38)	3+	3.71
	(R)	ELIDQYDVQR ( 서열번호 :39)	2+	3.01
폴리스타틴 유사	(R)	PQSCVVDQTGSAHCWCR ( 서열번호 :40)	3+	3.37
관련 유전자 (FLRG)	(R)	CECAPDCSGLPAR ( 서열번호 :41)	2+	3.21
	(R)	LQVCGSDGATYR ( 서열번호 :42)	2+	3.06
멀티도메인 프로테아제 저해제 (GASP1)	(R)	VSELTEEPDSGR ( 서열번호 :43)	2+	2.44
	(R)	CYMDAEACSK ( 서열번호 :44)	2+	2.69
	(K)	GITLAVVTCR ( 서열번호 :45)	2+	2.42

GDF-8 36 kDa  
 GDF-8, JA16  
 (follistatin-like related gene, FLRG) ( : 13-27). MS/MS  
 GDF-8 6 FLRG 3 가 GDF-8 FLR  
 3A 3C ( 3B 3D). GDF-8 G  
 DF-8 FLRG

7: GDF-8

GDF-8 GDF-8  
 가 가 GDF-8 JA16 GDF-8  
 PBS (mock ), JA16 GDF-8 JA16  
 A16 2 가 - GDF-8 12 kDa , GDF-8 ( 4). J  
 36 kDa SDS-PAGE ( 4). J  
 JA16 GDF-8 5  
 13 , 4 10 200 kDa  
 NCBI MS/MS LC-MS/MS  
 가 ( GDF-8, GDF-8 , 가 GDF-8  
 8, FLRG) ( 4). JA16  
 BMP-11/GDF-11 TGF- JA16  
 GDF-8 , JA16  
 -8 GDF-8/ ( ) GDF ActRIIB  
 GDF-8 GDF-8 (Lee and McPherron (2001) Proc.  
 Natl. Acad. Sci. U.S.A., 98: 9306-9311). GDF-8

MS/MS , Celera  
 가 13 MS/MS 가 4  
 1 (GASP1) JA16 GDF-  
 039 NCBI nr 가 gi 20914  
 GASP1 5 MS/MS ( 1 ( : 31-35);  
 5A B). GASP1 3 , 70-80 kDa  
 ( 4 ). 2.3 Sequest X<sub>corr</sub> 2 +  
 2 (junction) ( = ECETDQECETYEK ( : 31)) 가  
 Celera

GASP1 GASP1 ( 6). GASP1 63 kDa  
 571 N- 가 3  
 14 514 2 N- 가 Pfam BLAST ([Altschul (1990) J. Mol. Biol., 21  
 5: 403-410; Bateman (2002) Nucleic Acids Res., 30: 276-280] ) GASP1  
 GASP1 WAP /Kazal , 2 (tandem) Kunitz  
 , netrin ( 14A).  
 WAP 4 8  
 (Hennighausen and Sippel (1982) Nucleic Acids Res., 10: 2677-2684; Seemu  
 ller (1986) FEBS Lett., 199: 43-48). GDF-8 GASP1

GASP1, C- Kazal, FLRG, Kazal 가  
 Kunitz, netrin, GASP1 (Banyai and Patthy, 1999)  
 ; Mott 2000). GDF-8 가, GD  
 F-8 GDF-8 가

Celera BLAST, GASP1 > 50%  
 GASP2, GASP2, GASP1 가 (14B). GASP2 가 (multivale  
 nt) 2 JA16 GASP1 GASP2 가 GASP1 GASP2 가  
 가 GASP1 GASP2 가 ( > 90%  
 ). GASP1 gi 18652308 NCBI nr 가  
 GDF-8 가 (Hill (2002) J. Biol. Chem.,  
 277: 40735-40741), JA16 GASP1  
 3 (1). GASP1 GDF-8

GDF-8, GASP1 mRNA, GASP1 551 bp  
 1 cDNA (10). GASP1  
 Advantage cDNA PCR (Clontech) 1 cDNA (  
 Clontech, Palo Alto CA) ( : 5' TTGGCCACTGCCACCACAATCTCAACCACTT  
 3' ( : 46); : 5' TCTCAGCATGGCCATGCCGCCGTCGA 3' ( : 47)). GASP1

mRNA, GASP1 mRNA, GASP1  
 7 11 가, GASP1

8: GDF-8  
 GDF-8, GDF-8  
 가, GDF-8 JA16-  
 DF-8 /FLRG (11A). GDF-8, GDF-8 G  
 JA16 가 GDF-8 (11B).

GDF8, JA  
 16, LC-MS/MS, Sequest  
 FLRG, GASP1, JA16, GDF-8, GDF-8  
 36-45), MS/MS 12, GDF-8 1 ( :  
 9: GASP1

GASP1, GASP1, Celera  
 , GASP1 (fp: 5' CACCATGTGTGCCCCAGGGTATCATCGGTTCTGG 3' ( :  
 50); rp: 5' TTGCAAGCCCAGGAAGTCCTTGAGGAC 3' ( : 51)) PfuTurbo (St  
 ratagene) PCR QUICKCLONE cDNA (Clontech)  
 PCR 1% 가 1700 DNA p  
 cDNA3.1D/V5-His-TOPO (Invitrogen) TOPO, GASP1 C  
 - V5-His cDNA  
 13  
 ( , 288C:G; 294G:A; 615G:A; 738A:G; 768C:T; 1407A:G; 1419A:G; 1584C:G ( ,

) , Celera , ); 6A B  
 ) , Celera .  
 GASP1 N- 가 , C- V5-His GASP1 (GASP1-  
 V5-His) COS1 48  
 V5 (Sigma) Dulbecco's  
 Eagle's FuGENE 6 (Roche) GASP1-V5-His/pcDNA3.1D-V5-His-TOPO  
 COS1 48  
 80 kDa 가 , GASP1 ( 가  
 ). 10 ml His- ,  
 (Coomassie) SDS-PAGE GASP1  
 Edman N- L-P-P-I-R-Y-S-H-A-G-I ( : 52) , GASP1  
 1-29 가

**10: GDF-8**

**GDF-8**

**GASP1**

, GASP1 GDF-8 GASP1  
 6 (10 µl) 1.2 µg GDF-8 / GDF-8 GASP1- 400 µl  
 ) -V5 (30 µl) 가 가 (Thies 2001) . JA1  
 (PBS) 1% Triton 2 4 2  
 DTT 가 50 µl 1 xLDS . (Hill  
 2002).

GDF-8 GASP1 가 , GDF-8 GD  
 F-8 GASP1-V5-His COS1  
 . GDF-8 JA16 가 GASP1 ( 3) , GDF-8 ( 1) GD  
 GDF-8 ( 15A). GASP1 ( 3) GDF-8 ( 1) GD  
 F-8 , GDF-8 . GDF-8  
 GASP1 JA16 ( 4),  
 가 . 3 , GASP1 GDF-8 가 GDF-8  
 GASP1 가 3 GDF-8 가 ( 5). ,  
 GASP1 GDF-8 가 GDF-8  
 GASP1 GDF-8 가 , GDF-8 / GDF-8 , GASP  
 1 C- V5-His V5 (reverse) , 가 가 , GASP  
 , GDF-8 GASP1 ( 15B, 3 5),  
 ( 4), GDF-8 가 GASP1 GDF-8 GASP1  
 8 GDF-8 . , GASP1 GDF-8 GDF-  
 , FLRG (Hill (2002) J. Biol. Chem., 277: 40735-40741). GDF-8  
 가 가 GASP1  
 GASP1 GDF-8

**11: (Activin)**

**TGF- 1**

**GDF-8**

**BMP-11**

**GASP1**

A204 RD pGL3-(CAGA)<sub>12</sub> ( : 53) (Dennler (1998) EMBO J., 17: 3091-3100)  
 10 ng/ml GDF-8, 10 ng/ml BMP-11, 10 ng/ml rh GASP1  
 ng/ml rh TGF- 1 (R amp; D Systems) 37 30 A (R amp; D Systems), 0.5 [T  
 hies (2001) Growth Factors, 18: 251-259 Zimmers (2002) Science, 296: 1486-1488]  
 , A204 GDF-8, BMP-11, , TGF- 1  
 . RD GDF-8 TGF- 1 , GDF-8, BMP-11, GASP1  
 . GDF-8 A204 , TGF- GDF-8 RD  
 A204 , RD  
 (

). 가 가

FLRG (CAGA)<sub>12</sub> ( : 53)  
 GDF-8, BMP-11, TGF- $\beta$  1 GASP1 (C  
 AGA)<sub>12</sub> ( : 53)

V5-His GASP1 COS  
 GDF-8 (10 ng/ml), BMP-11 (10 ng/ml), (10 ng/ml), TGF- $\beta$  1 (0.5 ng/ml)  
 (CAGA)<sub>12</sub> ( : 53)  
 GASP1 GDF-8 ( 16A). GDF-8 BMP-11  
 11 , GASP1 B  
 MP-11 ( 16B). TGF- $\beta$  1 ( G  
 16C D), , GASP1 GDF-8  
 BMP-11

GDF-8 GASP1 GDF-8 IC50 가 .  
 GASP1-V5-His . G  
 ASP1 BioSepS3000 (Phenomenex) PBS  
 가 17 , GASP1 3 nM IC50 가 GDF-8

12:

GASP1 2 GDF-8  
 , 1 1  
 ,  
 GDF-8

[ 2 ]

1			25 mg	1 1	가
2	"	"	50 mg	"	"
3	"	"	50 mg	1 1	"
4	"	"	50 mg	1 1	"
5	"		25 mg	1 1	"
6		"	50 mg	"	
7	"	"	50 mg	1 1	"
8	"	"	50 mg	1 1	"
9	"		25 mg	1 1	"
10		"	50 mg	"	"
11	"	"	50 mg	1 1	"
12	"		50 mg	1 1	"
13			50 mg	1 1	
14	"	"	50 mg	1 1	"
15	"		50 mg	"	"
16	"		50 mg	"	"
17			50 mg	1 1	가
18	"		50 mg	1 1	"

19			50 mg	"	
----	--	--	-------	---	--

가

(57)

1.

i) (follistatin)

ii) 가

2.

1 78 GASP2, FLRG, FRP, (agrin), (osteonectin), (hevin), IGFBP7, U198

3.

1

4.

3, IgG Fc

5.

4, IgG 가 IgG1 IgG4,

6.

5, IgG 가 IgG1

7.

4, IgG 가

8.

3, 가

9.

3,

10.

3, 가

11.

3, 가

12.

3, peg 가

13.

:

i) ;

ii) / ;

iii) .

**14.**

13 , FLRG, FRP, , , IGFBP7, U19878 GASP2

**15.**

**16.**

15 , .

**17.**

15 16 , FLRG, FRP, , , IGFBP7, U19878 GASP2

**18.**

-8 , GDF-8 , GDF

**19.**

GDF-8 ,

**20.**

GDF-8 ,

**21.**

, :

i) ,

ii) ,

iii) 가 .

**22.**

18 , 19 , 20 21 , FLRG, FRP, , ,  
 , IGFBP7, U19878 GASP2 .

**23.**

18 , 19 , 20 21 , .

**24.**

23 , IgG Fc .

**25.**

24 , IgG 가 IgG1 IgG4, .

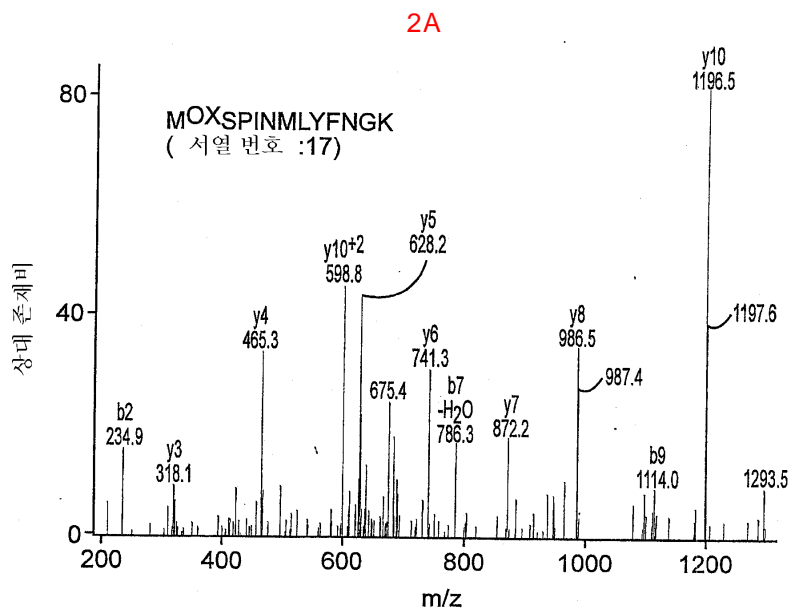
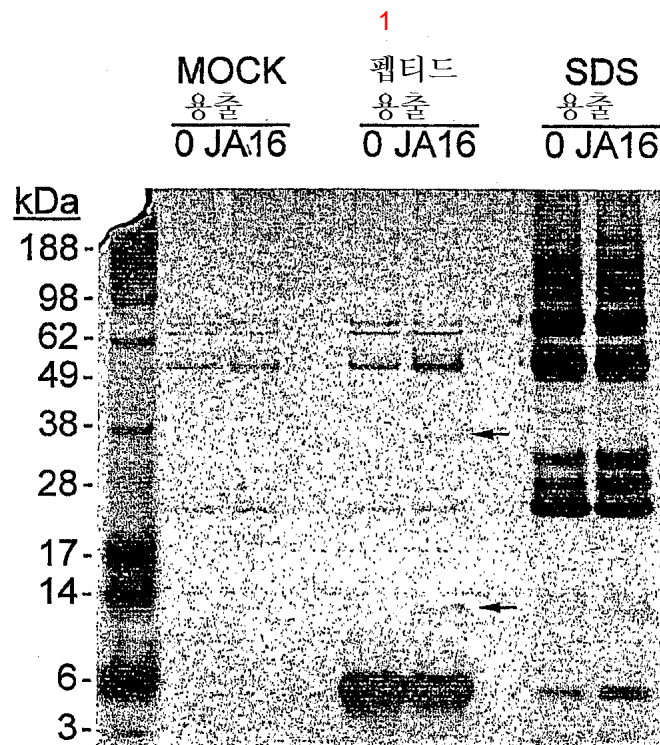
**26.**

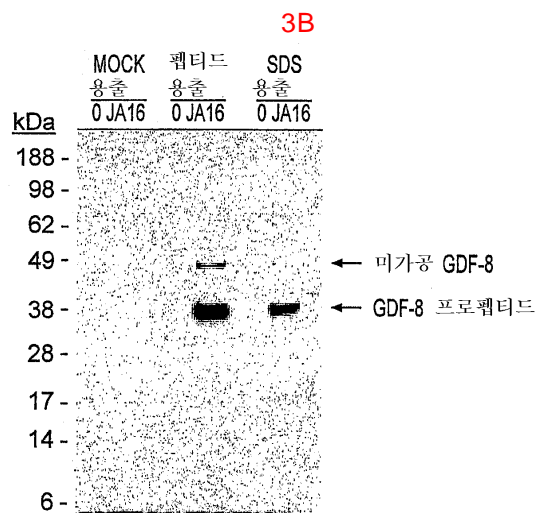
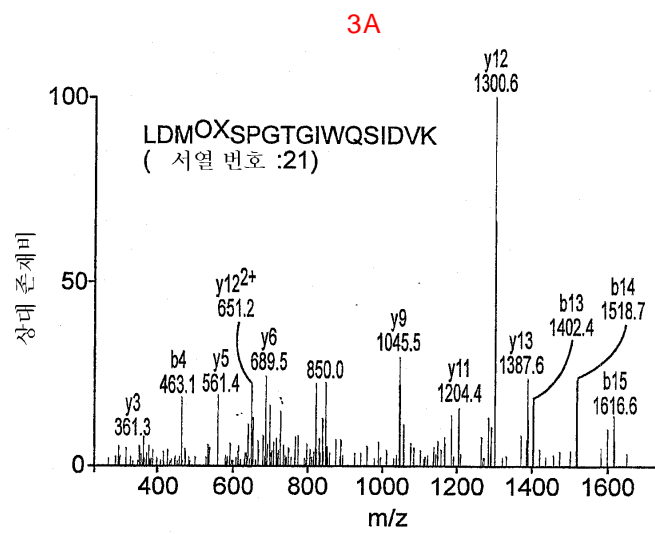
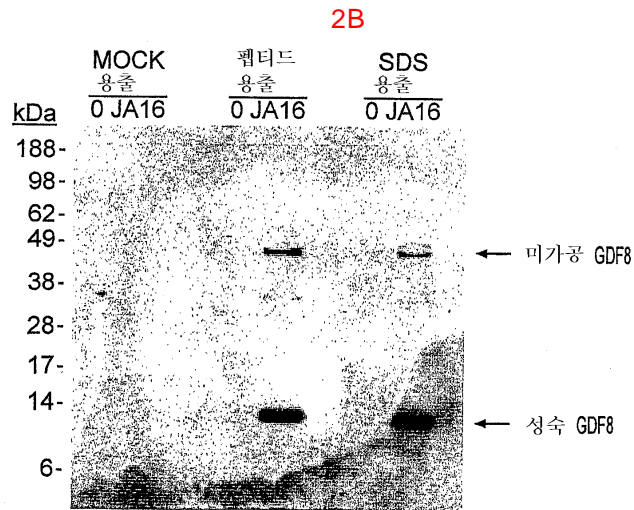
25 , IgG 가 IgG1 .

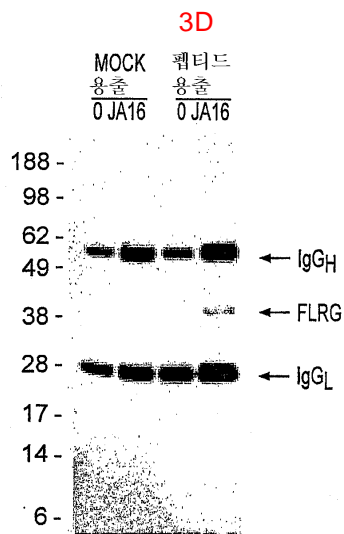
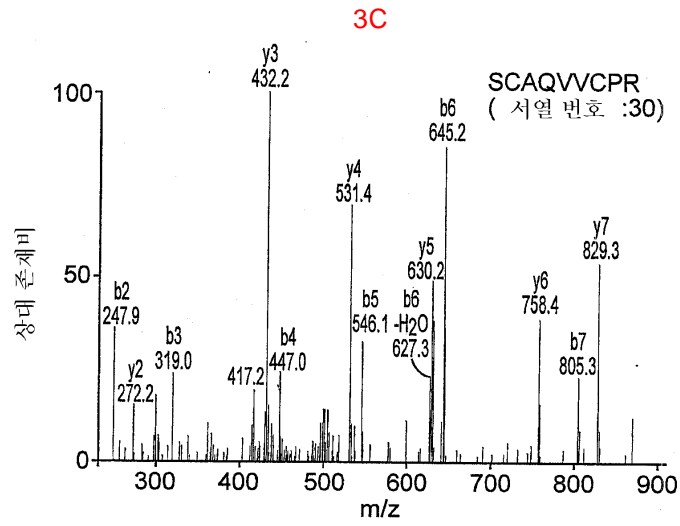
- 24 **27.** , IgG 가 .
- 23 **28.** , 가 .
- 23 **29.** , .
- 23 **30.** , 가 .
- 23 **31.** , 가 .
- 23 **32.** , peg 가 .
- 19 **33.** , 가 가 .
- 19 **34.** , 가 .
- 34 **35.** , 가 .
- 35 **36.** , X- , , (Fakuyama)- .
- 34 **37.** , 가 , 가 , , , (Eaton-Lambert) , , , .
- 34 **38.** , 가 .
- 19 **39.** , 가 .
- 39 **40.** , 가 2 , , .
- 19 **41.** , 가 .
- 19 **42.** , 가 .
- 19 **43.** , 1 , , .

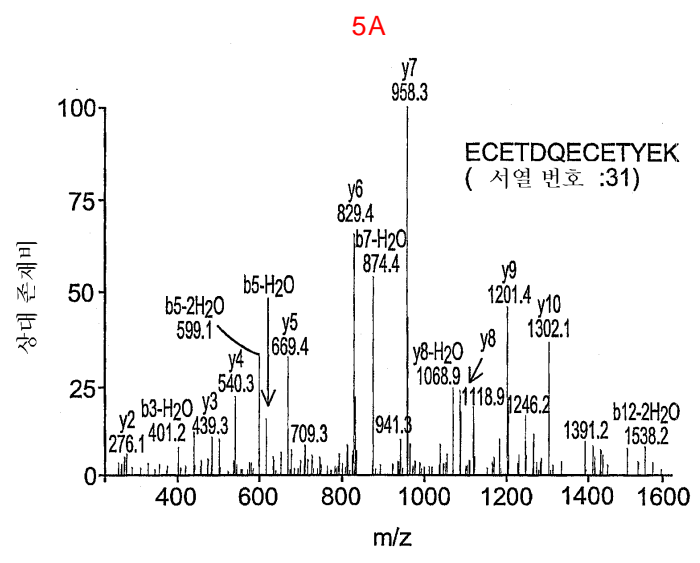
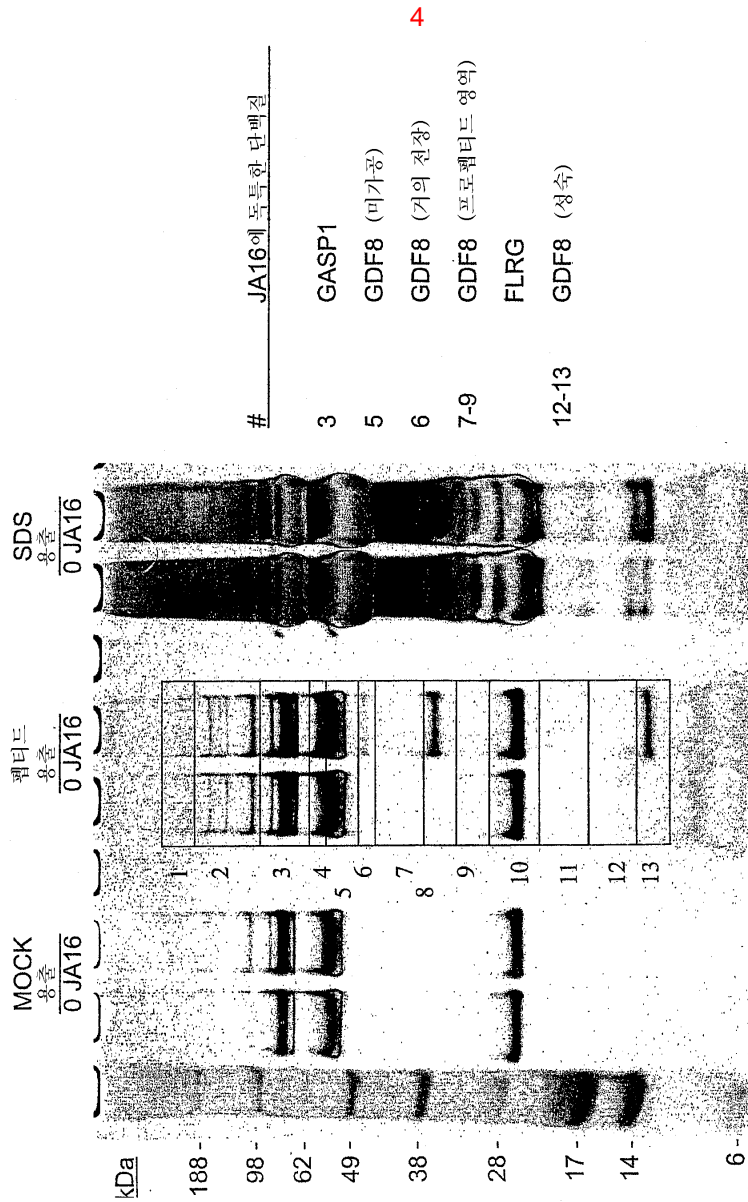


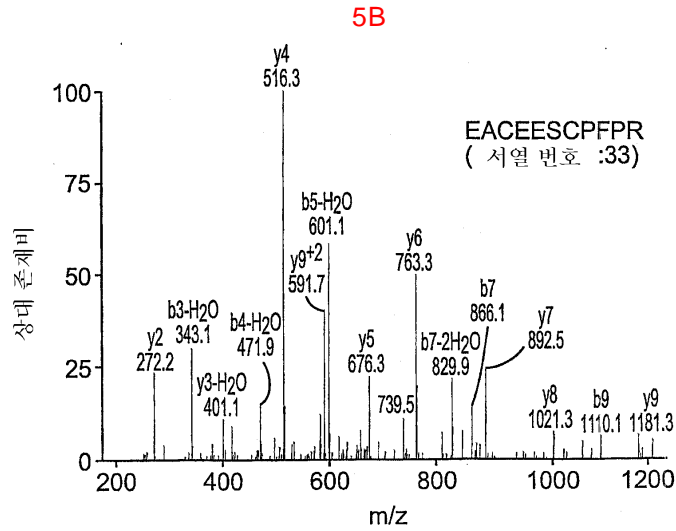
- 44. 19 , 5 mg 100 mg .
- 45. 19 , 15 mg 85 mg .
- 46. 19 , 3 mg 70 mg .
- 47. 19 , 40 mg 60 mg .











**6A**

예측되는 마우스 GASPI 뉴클레오티드 서열  
서열 번호 :1

```

1 atgtgtgccc cagggtatca tcggttctgg tttcactggg ggctgctggt gctgctgctc
61 ctcgaggctc cccttcgagg cctagcactg ccaccatcc gatactccca tgcgggcac
121 tgccccaacg acatgaaccc caacctctgg gtggatgcc agagcacctg caagcgagag
181 tgtgaaacag accaggaatg tgagacctat gagaaatgct gccccaatgt gtgtgggacc
241 aagagctgtg tggcagccc ctacatggat gtgaaagga agaagggccc tgtgggcatg
301 cccaaggagg ccacatgtga ccatttcacg tgctcgagc agggctctga gtgtgacatc
361 tgggacggcc agcccgtgtg taagtgaaa gatcgctgtg agaaggagcc cagcttcacc
421 tgtgcctctg atggccttac ctactacaac cgttgcttca tggacgccga agcctgtccc
481 aagggcatca cactgtctgt ggtcacctgt cgttatcact tcacctggcc taaccaccgc
541 cctccaccgc ctgagaccac ggtgcatccc accaccgcct ctccggagac tctcgggctg
601 gacatggcag ccccgccct gctcaaccac cctgtccatc agtcagtcac cgtgggtgag
661 actgtgagtt tcctctgtga cgtggtaggc cggcctcggc cagagctcac ttgggagaaa
721 cagctggagg accgagaaaa tgttgcacat aggcccaacc acgtgcgcgg taatgtggtg
781 gtcactaaca ttgccagct ggtcatctac aacgtccagc cccaggatgc tggcatatac
841 acctgtacag ctgaaatgt cgctggtgtc ctgagggctg acttcccgtt gtcggtggtc
901 aggggtggtc aggcagggc cacttcagag agcagttca atggcacagc tttccagca
961 acagagtgcc tgaagcccc agacagtgag gactgtggag aggagcagac acgctggcac
1021 ttcgacgccc aggctaaca ctgcctcact ttcaccttg gccactgcca ccacaatctc
1081 aaccactttg agacctacga ggcctgtatg ctggcttcta tgagtggcc attggccacc
1141 tgcagcctgc ctgccctgca agggccttgc aaagcttatg tcccacgctg ggcctacaac
1201 agccagacag gcctatgcca gtccttcgtc tatggcggct gtgagggcaa cggtaacaac
1261 ttgaaagcc gtgagccttg tgaggagtgc tgtcccttcc cgaggggtaa ccagcactgc
1321 cgggcctgca agccccgca aaaacttgtt accagcttct gtcggagtga ctttgtcatc
1381 ctgggcaggg tctctgagct gaccgaagag caagactcag gccgtgccct ggtgaccgtg
1441 gatgaggtct taaaagatga gaagatgggc ctcaagtttc tgggccggga gcctctggaa
1501 gtcaccctgc tcatgtaga ctggacctgt ccttgcacca acgtgacagt gggtagagaca
1561 ccaactcatca tcatggggga ggtcgacggc ggcattggca tgctgagacc cgatagcttt
1621 gtgggggcat cgagcacacg gcgggtcagg aagctccgtg aggtcatgta caagaaacc
1681 tgtgacgtcc tcaaggactt cctgggcttg caatga
    
```

## 6B

예측되는 마우스 GASP1 대안적 뉴클레오타이드 서열

서열 번호 :2

```

1 atgtgtgccc cagggatatca tcggttctg tttcactggg ggctgtctgtt
51 gctgtctgctc ctcgaggctc cccttcgagg cctagcactg ccacccatcc
101 gatactccca tgcgggcatc tgcccacaacg acatgaaccg caacctctgg
151 gtggatgccc agagcacctg caagcgagag tgtgaaacag accaggaatg
201 tgagacctat gagaaatgct gcccacatgt gtgtgggacc aagagctgtg
251 tggcagcccg ctacatggat gtgaaaggga agaagggggc tgtaggcatg
301 cccaaggagg ccacatgtga ccatttcacg tgcctgcagc agggctctga
351 gtgtgacatc tgggacggcc agcccgtgtg taagtgcaaa gatcgtctgtg
401 agaaggagcc cagcttcacc tbtgcctctg atggccttac ctactacaac
451 cgttgcttca tggacgcgga agcctgctcc aagggcatca cactgtctgt
501 ggtcacctgt cgttatcact tcacctggcc taacaccagc cctccaccgc
551 ctgagaccac ggtgcatccc accaccgcct ctccggagac tctcgggctg
601 gacatggcag cccagccctt gctcaaccac cctgtccatc agtcagtcac
651 cgtgggtgag actgtgagtt tcctctgtga cgtggtaggc cggcctcggc
701 cagagctcac ttgggagaaa cagctggagg accgagagaa tgttgtcatg
751 aggcccaacc acgtgctggtg taatgtggtg gtcactaaca ttgcccagct
801 ggtcatctac aacgtccagc cccaggatgc tggcatatac acctgtacag
851 ctcgaaatgt cgctggtgtc ctgagggctg acttcccgtt gtcggtggtc
901 aggggtggtc aggccagggc cacttcagag agcagtctca atggcacagc
951 ttttcagca acagagtgcc tgaagcccc agacagtgag gactgtggag
1001 aggagcagac acgctggcac ttcgacgccc aggctaaca ctgcctcact
1051 ttcacctttg gccactgcca ccacaatctc aaccactttg agacctacga
1101 ggcctgtatg ctggccttga tgagtgggcc attggccacc tgcagcctgc
1151 ctgccctgca agggccttgc aaagcttatg tcccacgctg ggcctacaac
1201 agccagacag gcctatgcca gtccttctgc tatggcggct gtgagggcaa
1251 cggtaacaac tttgaaagcc gtgaggcttg tgaggagtcg tgtcccttcc
1301 cgaggggtaa ccagcactgc cgggcctgca agccccggca aaaacttggt
1351 accagcttct gtcggagtga ctttgtcatc ctgggcaggg tctctgagct
1401 gaccgaggag caagactcgg gccgtgccct ggtgaccctg gatgaggtct
1451 taaaagatga gaagatggc ctcaagttc tgggcccggga gcctctggaa
1501 gtcaccctgc ttcattgtaga ctggacctgt ccttgcecca acgtgacagt
1551 gggtagagaca cactcatca tcatggggga ggtggacggc ggcagtgcca
1601 tgctgagacc cgatagcttt gtgggggcat cgagcacacg gcggtcagg
1651 aagctccgtg aggtcatgta caagaaaacc tgtgacgtcc tcaaggactt
1701 cctgggcttg caatga

```

## 6C

예측되는 마우스 GASP1 아미노산 서열

서열 번호 :3

```

1 MCAPGYHRFW FHWGLLLLLL LEAPLRGLAL PPIRYSHAGI CPNDMNPNLW VDAQSTCKRE
61 CETDQECETY EKCCPNVCGT KSCVAARYMD VKGKKGPMVM PKEATCDHFM CLOQSECDI
121 WDGQPVCKCK DRCEKEPSFT CASDGLTYYN RCFMDAACS KGITLSVVC RYHFTWPNTS
181 PPPPETTVHP TTASPETLGL DMAAPALLNH PVHQSVTVGE TVSFLCDVVG RPRPELTWEK
241 QLEDRENVVM RPNHVRGNV VTNIAQLVIY NVQPQDAGIY TCTARNVAGV LRADFPLSVV
301 RGGQARATSE SSLNGTAFPA TECLKPPDSE DCGEEQTRWH FDAQANNCLT FTFGHCHHNL
361 NHFETYEACM LACMSGPLAT CSLPALQGPC KAYVPRWAYN SQTGLCQSFV YGGCEGNGNN
421 FESREACEES CPFPRGNQHC RACKPRQKLV TSFCSRDFVI LGRVSELTEE QDSGRALVTV
481 DEVLKDEKMG LKFLGREPLE VTLHVDWTC PCPNVTVGET PLIIMGEVDG GMAMLRPDSF
541 VGASSTRVRV KLREVMYKKT CDVLKDFLGL Q

```

## 7A

예측되는 인간 GASP1 뉴클레오타드 서열

서열 번호 :4

1 atgaatccca acctctgggt ggacgcacag agcacctgca ggcgggagtg tgagacggac  
 61 caggagtgtg agatggacca ggtgagtggg atccagaagc cacagtgtga ggcagaccag  
 121 gtgaatgggg tccagaagcc gcaatgtgag atggaccaga agtgggagtg tgaggttgac  
 181 caggtgagtg gggccagaa gccggtgtgt gaggcggacc aggtgagtgg ggtccagaag  
 241 ccacagtgtg agatggacca ggtgagtggg atccagaagc tggagtgtga ggcggaccag  
 301 aagtgggagt atgagtgga ccaggtgagt ggggtccaga agccacagtg tgagatggac  
 361 caggtgagtg ggatccagaa gctggagtgt gaggcggacc aggagtgtga gacctatgag  
 421 aagtgtgtcc ccaacgtatg tgggaccaag agctgctgtg cggcccgtca catggacgtg  
 481 aaagggaga agggcccagt gggcatgccc aaggaggcca catgtgacca cttcatgtgt  
 541 ctgcagcagg gctctgagtg tgacatctgg gatggccagc ccgtgtgtaa gtgcaaagac  
 601 cgctgtgaga aggagcccag ctttacctgc gcctcgagc gcctcaccta ctataaccgc  
 661 tgctacatgg atgccgaggc ctgctccaaa ggcacacac tggccgttgt aacctgccgc  
 721 tatacttca cntggcccaa caccagcccc ccaccactg agaccacat gaccccacc  
 781 acagcctccc cagagacccc tgagctggac atggcggccc ctgctgtgct caacaacctt  
 841 gtgcaccagt cggtcacat gggtagaca gtgagcttcc tctgtgatgt ggtgggcccg  
 901 ccccgccctg agatcacctg ggagaagcag ttggaggatc gggagaatgt ggtcatgccc  
 961 cccaaccatg tgcgtggcaa cgtggtggtc accaacattg cccagctggt catctataac  
 1021 gccagctgac aggatgctgg gatctacacc tgcacggccc ggaacctggc tggggtcctg  
 1081 agggctgatt tcccgtgtc ggtggtcagg ggtcatcagg ctgcagccac ctcagagagc  
 1141 agccccaatg gcacggcttt cccggcggcc gactgctga agccccaga cagtgaggac  
 1201 tgtggcgaag agcagaccgc ctggcacttc gatgccagg ccaacaactg cctgacctt  
 1261 accttcggcc actgccaccg taacctcaac cactttgaga cctatgaggc ctgcatgctg  
 1321 gcctgcatga gcgggcccgt ggcgcgtgc agcctgcccg ccctgcaggg gcctgcaaaa  
 1381 gcctacgcgc ctgctggggc ttacaacagc cagacggccc agtgccagtc ctttgtctat  
 1441 ggtggtgctg agggcaatgg caacaacttt gagagccgtg aggcctgtga ggagtctgac  
 1501 cccttcccca gggggaacca gcgctgtcgg gcctgcaagc ctgcgcagaa gctcgttacc  
 1561 agcttctgtc gcagcgactt tgtcatctg gcccgagtct ctgagctgac cgaggagcct  
 1621 gactcggggc gcgcctggt gactgtggat gaggtcctaa aggatgagaa aatgggccc  
 1681 aagttcctgg gccaggagcc attggaggtc actctgcttc acgtggactg ggcagcccc  
 1741 tgcccacagc tgaccgtgag cgagatgccg ctcatcatca tgggggaggt ggacggcggc  
 1801 atggccatgc tgcgccccga tagctttgtg ggcgcacga gtgcccggc ggtcaggaag  
 1861 cttctgtagg tcatgcacaa gaagacctgt gacgtcctca aggagtttct tggcttgacc  
 1921 tga

## 7B

인간 GASP1 의 예측아미노산 서열

서열 번호 :5

1 MNPNLWVDAQ STCRRECETD QECEMDQVSG IQKPQCEADQ VNGVQKPQCE MDQKWECEVD  
 61 QVSGVQKPVK EADQVSGVQK PQCEMDQVSG IQKLECEADQ KWEYEVDQVS GVQKPQCEMD  
 121 QVSGIQKLEC EADQECETYE KCCPNVCGTK SCVAARYMDV KGKKGPVGMK KEAT**CDHFMC**  
 181 **LQOQSECDIW DGQPVCKCKD RCEKEPSFTC ASDGLTYTNR CYMDAEACSK GITLAVVTCR**  
 241 YHFTWNTSP PPPETTMHPT TASPETPELD MAAPALLNPN VHQSVMGET VSFLCDVVRG  
 301 PRPEITWEKQ LEDRENVVMR PNHVGRNVVV TNIAQLVIYN AQLQDAGIYT CTARNVAGVL  
 361 RADFPLSVVR GHQAAATSES SPNGTAFPAE ECLKPPDSED CGEEQTRWHF DAQANNCLTF  
 421 TFGHCHRNLN HFETYEACML ACMSGPLAAC SLPALQGPCK AYAPRWAYNS QTGCQCSFVY  
 481 GGCEGNGNNF ESREACEESC PFPRGNQRCR ACKPRQKLVV SFCRSDFVIL GRVSELTEEP  
 541 DSGRALVTVD EVLKDEKMGK KFLGQEPLEV TLLHVDWACP CPNVTVSEMP LIIMGEVDGG  
 601 MAMLRPDSFV GASSARRVRK LREVMHKKTC DVLKEFLGLH



## 7C

대안적 개시 부위를 이용한 인간 GASP1 의 예측 뉴클레오타이드 서열

서열 번호 :6

```

1 atgtgggccc caaggtgtcg cgggttctgg tctcgtctgg agcaggtggc agcgtgtctg
61 ctgctgtctg tactgctcgg ggtgcccccg cgaagcctgg cgctgcccgc catccgctat
121 tcccacgccg gcatctgccc caacgacatg aatcccaacc tctgggtgga cgcacagagc
181 acctgcaggc gggagtgtga gacggaccag gagtgtgaga cctatgagaa gtgctgcccc
241 aacgtatgtg ggaccaagag ctgctgtggc gcccgctaca tggacgtgaa agggaaagaag
301 ggcccagtgg gcatgcccga ggaggccaca tgtgaccact tcatgtgtct gcagcagggc
361 tctgagtgtg acatctggga tggccagccc gtgtgtaagt gcaaagaccg ctgtgagaag
421 gagcccagct ttacctgctc ctcggacggc ctcacctact ataaccgctg ctacatggat
481 gccgaggcct gctccaaagg catcacactg gccgttgtaa cctgccgcta tcacttcacc
541 tggcccaca cagcccccc accacctgag accaccatgc accccaccac agcctcccac
601 gagaccctg agctggacat ggcggcccct gcgctgtctc acaaccctgt gcaccagtgc
661 gtcaccatgg gtgagacagt gagtttctc tgtgatgtgg tgggcccggc ccggcctgag
721 atcacctggg agaagcagtt ggaggatcgg gagaatgtgg tcatgcccgc caaccatgtg
781 cgtggcaacg tggtggtcac caacatgcc cagctggcct tctataacgc ccagctgcag
841 gatgtggga tctacacctg caccggcccgg aacgtggctg gggcctgag ggtgatttc
901 ccgctgtcgg tggtcagggg tcatcaggct gcagccact cagagagcag cccaatggc
961 acggctttcc cggcggccga gtgcctgaag cccccagaca gtgaggactg tggcgaagag
1021 cagaccctg ggcacttcga tgcccaggcc aacaactgcc tgaccttcac cttcggccac
1081 tgccaccgta acctcaacca ctttgagacc tatgaggcct gcatgctggc ctgcatgagc
1141 gggccgctgg ccgctgcag cctgcccgcc ctgcaggggc cctgcaaagc ctacgcgcct
1201 cgctgggctt acaacagcca gacgggccag tgccagtcct ttgtctatgg tggctgcgag
1261 ggcaatggca acaacttga gagccgtgag gcctgtgagg agtcgtgcc cttccccagg
1321 ggaaccagc gctgtcggc ctgcaagcct cggcagaagc tegtaccag cttctgtcgc
1381 acgactttg tcatcctggg ccgagtctct gagctgaccg aggagcctga ctcgggccgc
1441 gccctggtga ctgtggatga ggtcctaaag gatgagaaa tgggctcaa gttcctgggc
1501 caggagccat tggaggtcac tctgcttcac gtggactggg catgcccctg cccaacgtg
1561 accgtgagcg agatgccgct catcatcatg ggggaggtgg acggcggcat ggcatgctg
1621 cccccgata gctttgtggg cgcacagagt gcccgccggg tcaggaagct tctgtgagtc
1681 atgcacaaga agacctgtga cgtcctcaag gagtttctt gcttgactg a

```

## 7D

대안적 개시 부위를 이용한 인간 GASP1 의 예측 아미노산 서열

서열 번호 :7

```

1 MWAPRCRRFW SRWEQVAALL LLLLLLGVPP RSLALPPIRY SHAGICPNDM NPNLWVDAQS
61 TCRRECETDQ ECETYKCCP NVCGTKSCVA ARYMDVKGKK GPVGMPEAT CDHFMCLOQG
121 SECDIWDGQP VCKCKDRCEK EPSFTCASDG LTYYNRCYMD AEACSKGITL AVVTCRYHFT
181 WPNTSPPPPE TTMHPTTASP ETPELDMAAP ALLNPNVHQS VTMGETVSFL CDVVGRPRPE
241 ITWEKQLEDR ENVVMRPNHV RGNVVVTNIA QLVYNAQLQ DAGIYTCTAR NVAGVLRADF
301 PLSVVRGHQA AATSESSPNG TAFPAAECLK PPSSEDCGEE QTRWHFDAQA NNCLTFTFGH
361 CHRNLNHFET YEACMLACMS GPLAACSLPA LQGPKAYAP RWAYNSQTGQ CQSFVYGGCE
421 GNGNPFESRE ACEESCPFPR GNQRCRACKP RQKLVTSFCR SDFVILGRVS ELTEEPDSGR
481 ALVTVDEVLK DEKMGLKFLG QEPLEVTLLH VDWACPCPNV TVSEMPLIIM GEVDGGMAML
541 RPSDFVGASS ARRVRKLEEV MHHKTCVLLK EFLGLH*

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## 8A

예측되는 마우스 GASP2 뉴클레오티드 서열

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## 8B

예측되는 마우스 GASP2 아미노산 서열

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421 CRACRLKSKL ALSLCRSDFA IVGRLTEVLE EPEAAGGIAR VALDDVLKDD KMGLKFLGTK
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541 KKACELLNRF QD

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## 9A

인간 GASP-2 의 예측 뉴클레오타이드 서열

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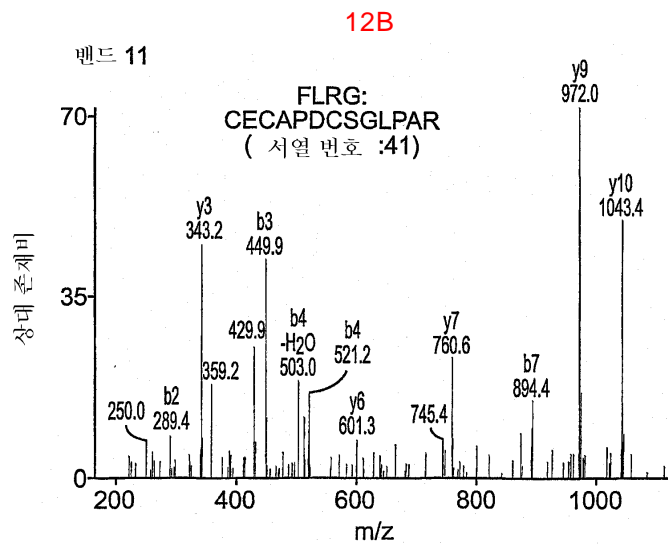
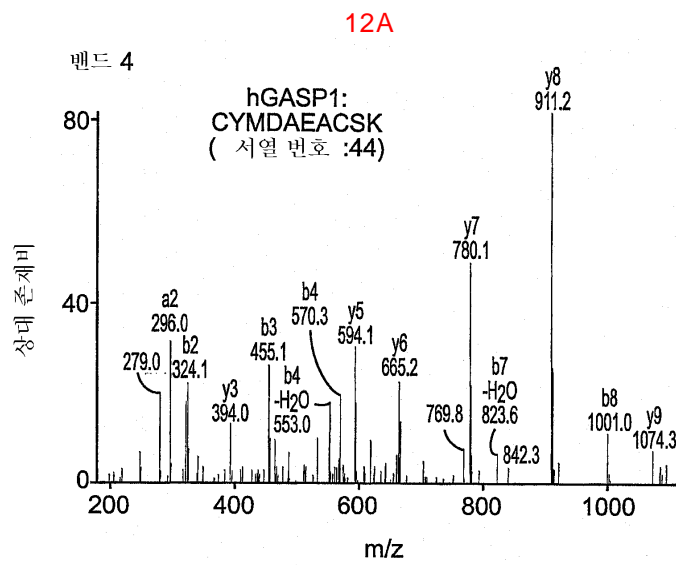
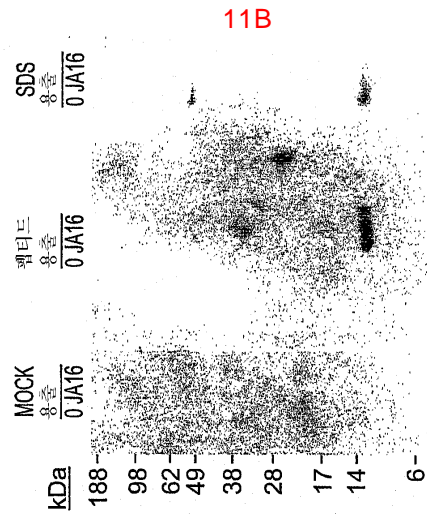
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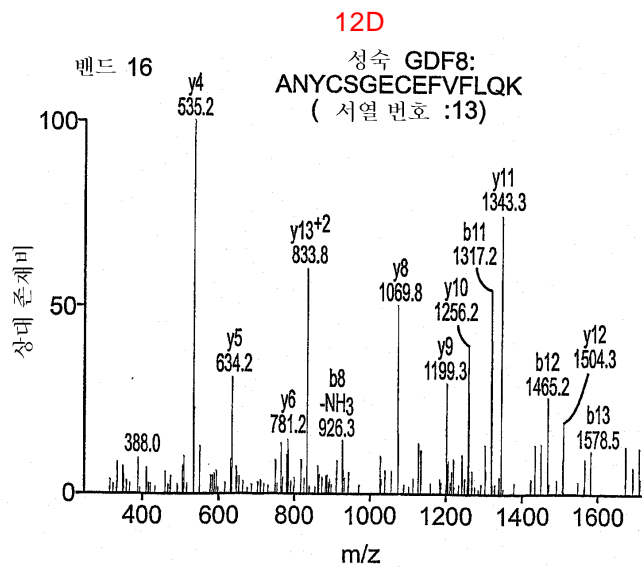
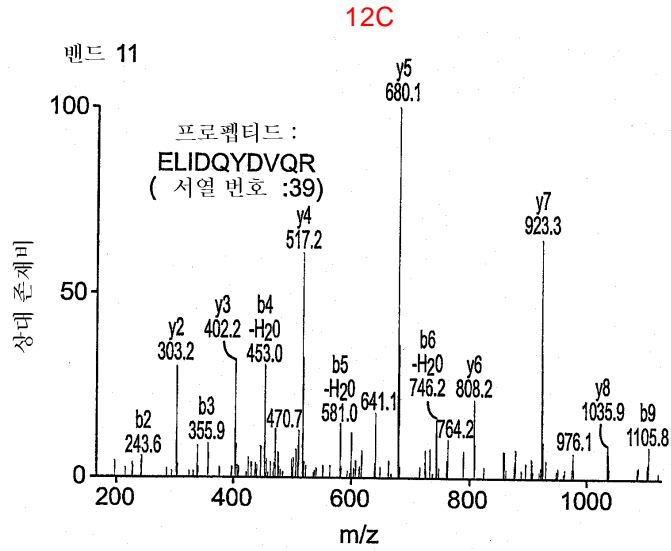
인간 GASP-2 의 예측 아미노산 서열

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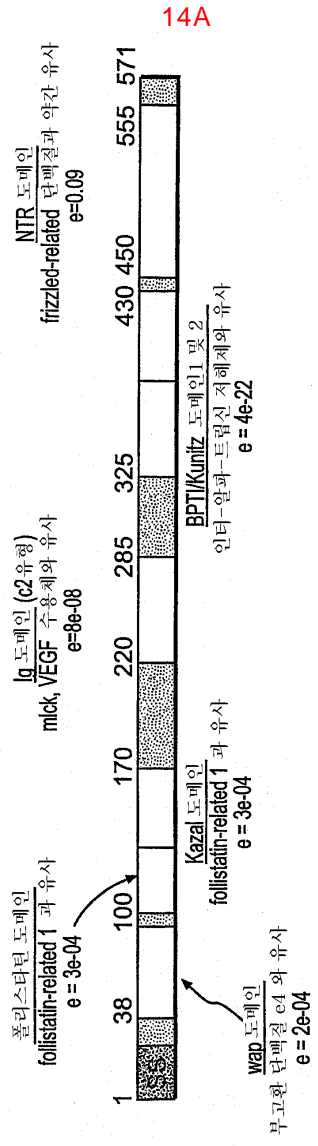


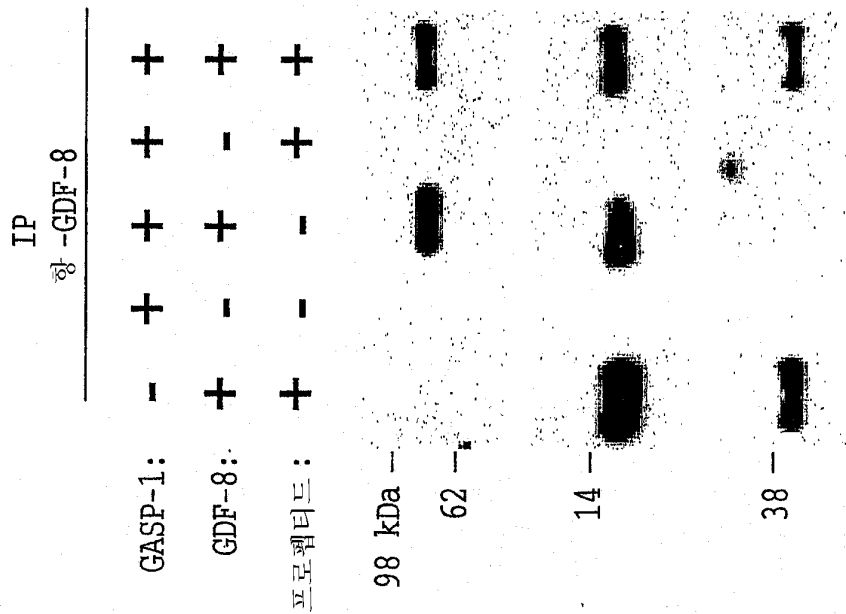


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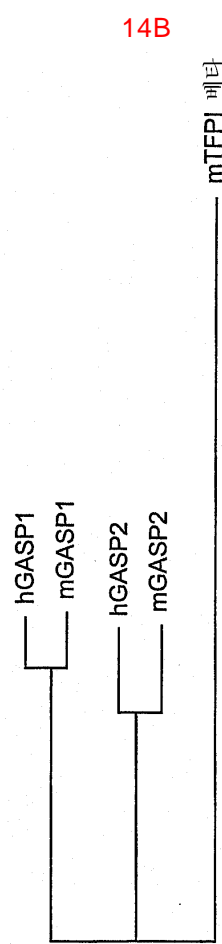
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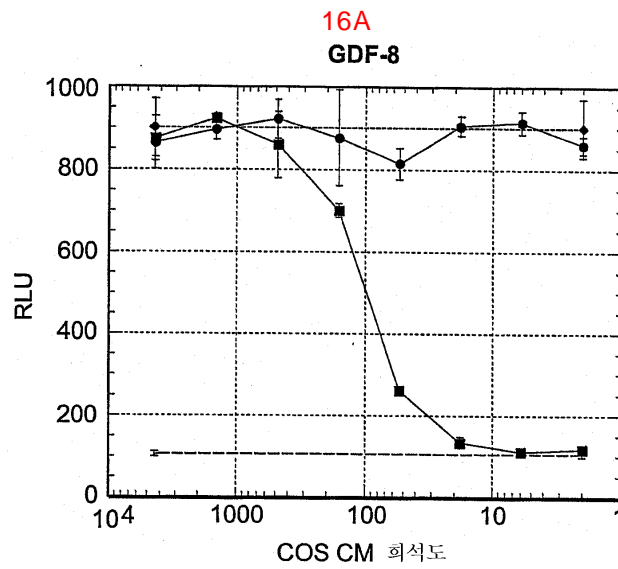
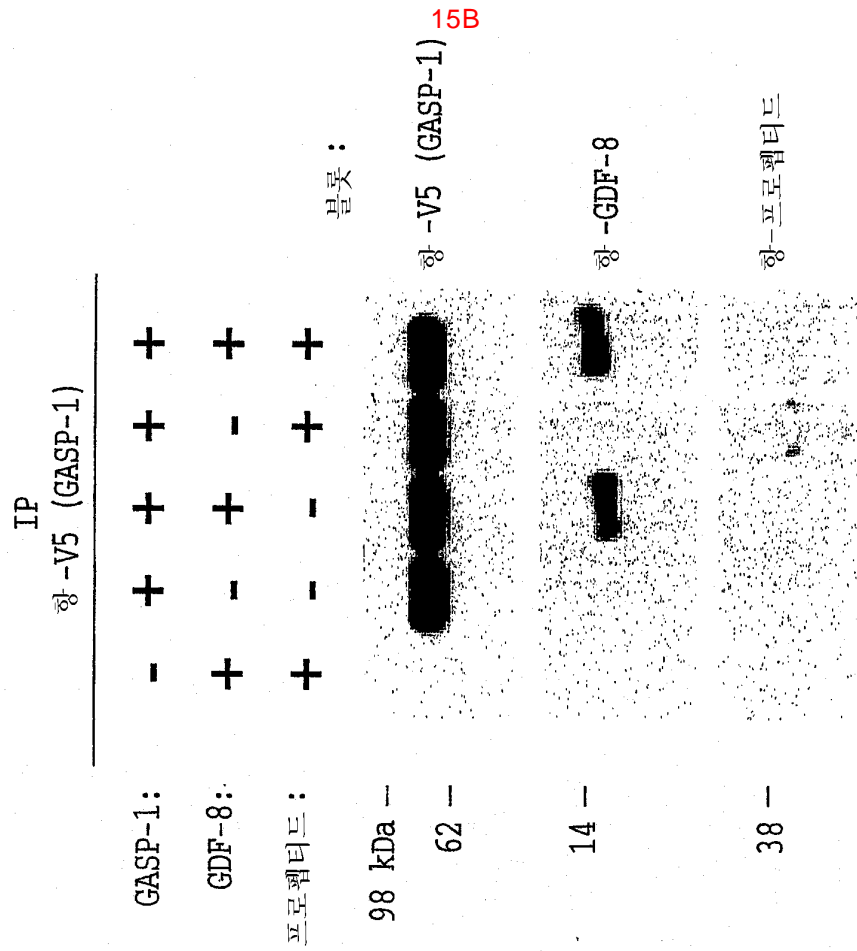


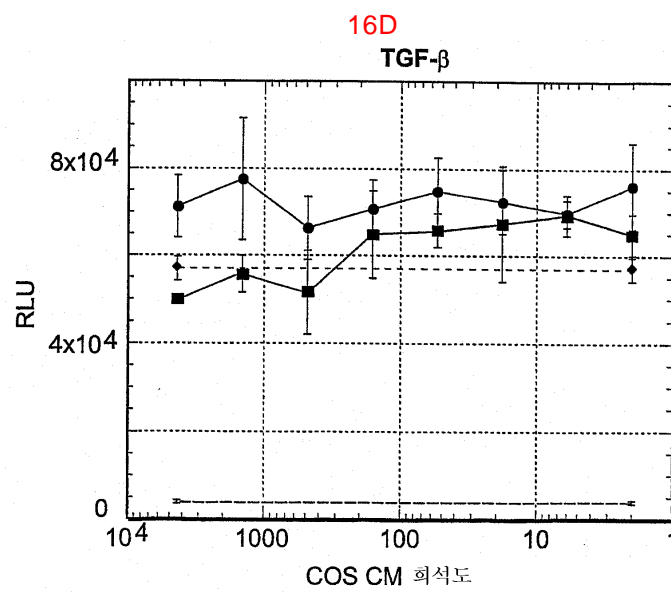
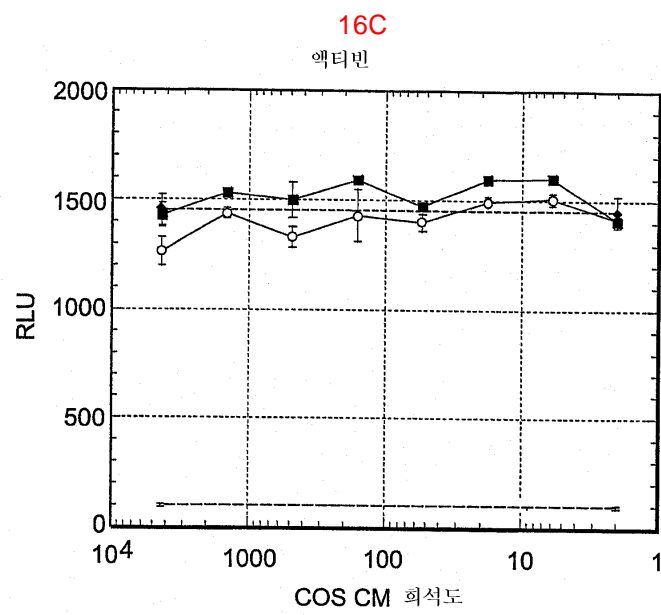
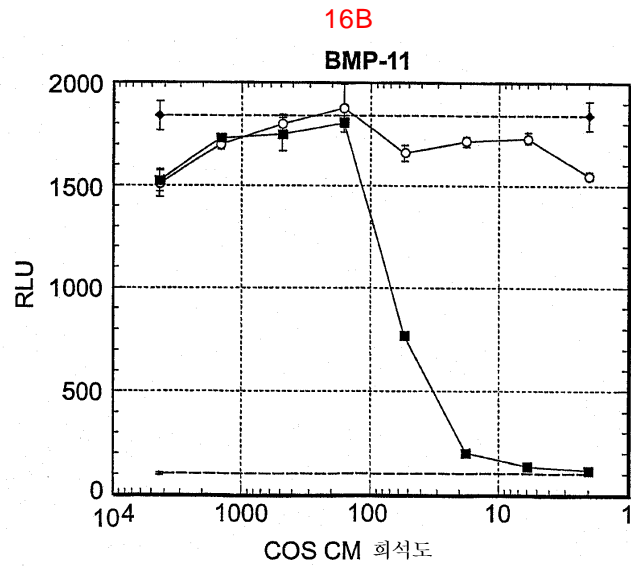
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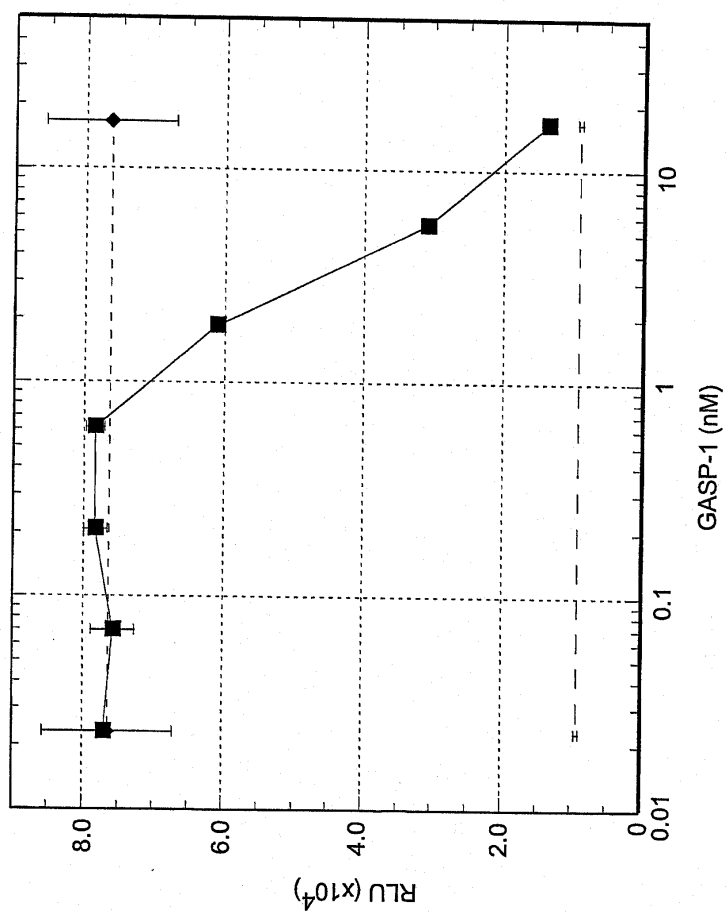
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gatgaggtct taaaagatga gaagatggc ctcaagtttc tgggccggga gcctctgaa 1500

gtcaccctgc ttcatgtaga ctggacctgt ccttgcccca acgtgacagt gggtagaca 1560

ccactcatca tcatggggga ggtggacggc ggcatggcca tgctgagacc cgatagcttt 1620

gtgggggcat cgagcacacg gcgggtcagg aagctccgtg aggtcatgta caagaaaacc 1680

tgtgacgtcc tcaaggactt cctgggcttg caatga 1716

<210> 3

<211> 571

<212> PRT

<213> Mus sp.

<400> 3

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20 25 30

Ile Arg Tyr Ser His Ala Gly Ile Cys Pro Asn Asp Met Asn Pro Asn

35 40 45

Leu Trp Val Asp Ala Gln Ser Thr Cys Lys Arg Glu Cys Glu Thr Asp

50 55 60

Gln Glu Cys Glu Thr Tyr Glu Lys Cys Cys Pro Asn Val Cys Gly Thr

65 70 75 80

Lys Ser Cys Val Ala Ala Arg Tyr Met Asp Val Lys Gly Lys Lys Gly

85 90 95

Pro Val Gly Met Pro Lys Glu Ala Thr Cys Asp His Phe Met Cys Leu

100 105 110

Gln Gln Gly Ser Glu Cys Asp Ile Trp Asp Gly Gln Pro Val Cys Lys

115 120 125

Cys Lys Asp Arg Cys Glu Lys Glu Pro Ser Phe Thr Cys Ala Ser Asp

130 135 140

Gly Leu Thr Tyr Tyr Asn Arg Cys Phe Met Asp Ala Glu Ala Cys Ser

145 150 155 160

Lys Gly Ile Thr Leu Ser Val Val Thr Cys Arg Tyr His Phe Thr Trp

165 170 175

Pro Asn Thr Ser Pro Pro Pro Pro Glu Thr Thr Val His Pro Thr Thr



180

185

190

Ala Ser Pro Glu Thr Leu Gly Leu Asp Met Ala Ala Pro Ala Leu Leu

195

200

205

Asn His Pro Val His Gln Ser Val Thr Val Gly Glu Thr Val Ser Phe

210

215

220

Leu Cys Asp Val Val Gly Arg Pro Arg Pro Glu Leu Thr Trp Glu Lys

225

230

235

240

Gln Leu Glu Asp Arg Glu Asn Val Val Met Arg Pro Asn His Val Arg

245

250

255

Gly Asn Val Val Val Thr Asn Ile Ala Gln Leu Val Ile Tyr Asn Val

260

265

270

Gln Pro Gln Asp Ala Gly Ile Tyr Thr Cys Thr Ala Arg Asn Val Ala

275

280

285

Gly Val Leu Arg Ala Asp Phe Pro Leu Ser Val Val Arg Gly Gly Gln

290

295

300

Ala Arg Ala Thr Ser Glu Ser Ser Leu Asn Gly Thr Ala Phe Pro Ala

305

310

315

320

Thr Glu Cys Leu Lys Pro Pro Asp Ser Glu Asp Cys Gly Glu Glu Gln

325

330

335

Thr Arg Trp His Phe Asp Ala Gln Ala Asn Asn Cys Leu Thr Phe Thr

340

345

350

Phe Gly His Cys His His Asn Leu Asn His Phe Glu Thr Tyr Glu Ala

355

360

365

Cys Met Leu Ala Cys Met Ser Gly Pro Leu Ala Thr Cys Ser Leu Pro  
 370 375 380

Ala Leu Gln Gly Pro Cys Lys Ala Tyr Val Pro Arg Trp Ala Tyr Asn  
 385 390 395 400

Ser Gln Thr Gly Leu Cys Gln Ser Phe Val Tyr Gly Gly Cys Glu Gly  
 405 410 415

Asn Gly Asn Asn Phe Glu Ser Arg Glu Ala Cys Glu Glu Ser Cys Pro  
 420 425 430

Phe Pro Arg Gly Asn Gln His Cys Arg Ala Cys Lys Pro Arg Gln Lys  
 435 440 445

Leu Val Thr Ser Phe Cys Arg Ser Asp Phe Val Ile Leu Gly Arg Val  
 450 455 460

Ser Glu Leu Thr Glu Glu Gln Asp Ser Gly Arg Ala Leu Val Thr Val  
 465 470 475 480

Asp Glu Val Leu Lys Asp Glu Lys Met Gly Leu Lys Phe Leu Gly Arg  
 485 490 495

Glu Pro Leu Glu Val Thr Leu Leu His Val Asp Trp Thr Cys Pro Cys  
 500 505 510

Pro Asn Val Thr Val Gly Glu Thr Pro Leu Ile Ile Met Gly Glu Val  
 515 520 525

Asp Gly Gly Met Ala Met Leu Arg Pro Asp Ser Phe Val Gly Ala Ser  
 530 535 540

Ser Thr Arg Arg Val Arg Lys Leu Arg Glu Val Met Tyr Lys Lys Thr

545 550 555 560

Cys Asp Val Leu Lys Asp Phe Leu Gly Leu Gln

565 570

<210> 4  
 <211> 1923  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> modified\_base  
 <222> (732)  
 <223> a, t, c or g

<400> 4

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gtgaatgggg tccagaagcc gcaatgtgag atggaccaga agtgggagtg tgaggttgac 180

caggtgagtg ggtccagaa gccggtgtgt gaggcggacc aggtgagtgg ggtccagaag 240

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aagtgggagt atgaggtgga ccaggtgagt ggggtccaga agccacagtg tgagatggac 360

caggtgagtg ggatccagaa gctggagtgt gaggcggacc aggagtgtga gacctatgag 420

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 tga 1923

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 <211> 640  
 <212> PRT  
 <213> Homo sapiens

<400> 5  
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 Cys Glu Thr Asp Gln Glu Cys Glu Met Asp Gln Val Ser Gly Ile Gln  
 20 25 30  
 Lys Pro Gln Cys Glu Ala Asp Gln Val Asn Gly Val Gln Lys Pro Gln  
 35 40 45  
 Cys Glu Met Asp Gln Lys Trp Glu Cys Glu Val Asp Gln Val Ser Gly

50

55

60

Val Gln Lys Pro Val Cys Glu Ala Asp Gln Val Ser Gly Val Gln Lys  
 65 70 75 80

Pro Gln Cys Glu Met Asp Gln Val Ser Gly Ile Gln Lys Leu Glu Cys  
 85 90 95

Glu Ala Asp Gln Lys Trp Glu Tyr Glu Val Asp Gln Val Ser Gly Val  
 100 105 110

Gln Lys Pro Gln Cys Glu Met Asp Gln Val Ser Gly Ile Gln Lys Leu  
 115 120 125

Glu Cys Glu Ala Asp Gln Glu Cys Glu Thr Tyr Glu Lys Cys Cys Pro  
 130 135 140

Asn Val Cys Gly Thr Lys Ser Cys Val Ala Ala Arg Tyr Met Asp Val  
 145 150 155 160

Lys Gly Lys Lys Gly Pro Val Gly Met Pro Lys Glu Ala Thr Cys Asp  
 165 170 175

His Phe Met Cys Leu Gln Gln Gly Ser Glu Cys Asp Ile Trp Asp Gly  
 180 185 190

Gln Pro Val Cys Lys Cys Lys Asp Arg Cys Glu Lys Glu Pro Ser Phe  
 195 200 205

Thr Cys Ala Ser Asp Gly Leu Thr Tyr Tyr Asn Arg Cys Tyr Met Asp  
 210 215 220

Ala Glu Ala Cys Ser Lys Gly Ile Thr Leu Ala Val Val Thr Cys Arg  
 225 230 235 240

Tyr His Phe Thr Trp Pro Asn Thr Ser Pro Pro Pro Pro Glu Thr Thr  
 245 250 255

Met His Pro Thr Thr Ala Ser Pro Glu Thr Pro Glu Leu Asp Met Ala  
 260 265 270

Ala Pro Ala Leu Leu Asn Asn Pro Val His Gln Ser Val Thr Met Gly  
 275 280 285

Glu Thr Val Ser Phe Leu Cys Asp Val Val Gly Arg Pro Arg Pro Glu  
 290 295 300

Ile Thr Trp Glu Lys Gln Leu Glu Asp Arg Glu Asn Val Val Met Arg  
 305 310 315 320

Pro Asn His Val Arg Gly Asn Val Val Val Thr Asn Ile Ala Gln Leu  
 325 330 335

Val Ile Tyr Asn Ala Gln Leu Gln Asp Ala Gly Ile Tyr Thr Cys Thr  
 340 345 350

Ala Arg Asn Val Ala Gly Val Leu Arg Ala Asp Phe Pro Leu Ser Val  
 355 360 365

Val Arg Gly His Gln Ala Ala Ala Thr Ser Glu Ser Ser Pro Asn Gly  
 370 375 380

Thr Ala Phe Pro Ala Ala Glu Cys Leu Lys Pro Pro Asp Ser Glu Asp  
 385 390 395 400

Cys Gly Glu Glu Gln Thr Arg Trp His Phe Asp Ala Gln Ala Asn Asn  
 405 410 415

Cys Leu Thr Phe Thr Phe Gly His Cys His Arg Asn Leu Asn His Phe

420 425 430

Glu Thr Tyr Glu Ala Cys Met Leu Ala Cys Met Ser Gly Pro Leu Ala

435 440 445

Ala Cys Ser Leu Pro Ala Leu Gln Gly Pro Cys Lys Ala Tyr Ala Pro

450 455 460

Arg Trp Ala Tyr Asn Ser Gln Thr Gly Gln Cys Gln Ser Phe Val Tyr

465 470 475 480

Gly Gly Cys Glu Gly Asn Gly Asn Asn Phe Glu Ser Arg Glu Ala Cys

485 490 495

Glu Glu Ser Cys Pro Phe Pro Arg Gly Asn Gln Arg Cys Arg Ala Cys

500 505 510

Lys Pro Arg Gln Lys Leu Val Thr Ser Phe Cys Arg Ser Asp Phe Val

515 520 525

Ile Leu Gly Arg Val Ser Glu Leu Thr Glu Glu Pro Asp Ser Gly Arg

530 535 540

Ala Leu Val Thr Val Asp Glu Val Leu Lys Asp Glu Lys Met Gly Leu

545 550 555 560

Lys Phe Leu Gly Gln Glu Pro Leu Glu Val Thr Leu Leu His Val Asp

565 570 575

Trp Ala Cys Pro Cys Pro Asn Val Thr Val Ser Glu Met Pro Leu Ile

580 585 590

Ile Met Gly Glu Val Asp Gly Gly Met Ala Met Leu Arg Pro Asp Ser



595

600

605

Phe Val Gly Ala Ser Ser Ala Arg Arg Val Arg Lys Leu Arg Glu Val

610

615

620

Met His Lys Lys Thr Cys Asp Val Leu Lys Glu Phe Leu Gly Leu His

625

630

635

640

&lt;210&gt; 6

&lt;211&gt; 1731

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 6

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ctgctgctgc tactgctcgg ggtgccccg cgaagcctgg cgctgccgcc catccgctat 120

tcccacgccg gcatctgccc caacgacatg aatcccaacc tctgggtgga cgcacagagc 180

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aacgtatgtg ggaccaagag ctgctgtggc gcccgctaca tggacgtgaa agggaagaag 300

ggcccagtgg gcatgcccga ggaggccaca tgtgaccact tcatgtgtct gcagcagggc 360

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gagcccagct ttacctgctc ctcggacggc ctcacctact ataaccgctg ctacatggat 480

gccgaggcct gctccaaagg catcacactg gccgttgtaa cctgccgcta tcacttcacc 540

tggccaaca ccagcccccc accacctgag accacatgc accccaccac agcctcccca 600

gagaccctg agctggacat ggcggcccct gcgctgctca acaaccctgt gcaccagtgc	660
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accgtgagcg agatgccgct catcatcatg ggggaggtgg acggcggcat ggccatgctg	1620

cgccccgata gctttgtggg cgcatcgagt gcccgccggg tcaggaagct tcgtgaggtc 1680

atgcacaaga agacctgtga cgtcctcaag gagtttcttg gcttgactg a 1731

<210> 7

<211> 576

<212> PRT

<213> Homo sapiens

<400> 7

Met Trp Ala Pro Arg Cys Arg Arg Phe Trp Ser Arg Trp Glu Gln Val

1 5 10 15

Ala Ala Leu Leu Leu Leu Leu Leu Leu Leu Gly Val Pro Pro Arg Ser

20 25 30

Leu Ala Leu Pro Pro Ile Arg Tyr Ser His Ala Gly Ile Cys Pro Asn

35 40 45

Asp Met Asn Pro Asn Leu Trp Val Asp Ala Gln Ser Thr Cys Arg Arg

50 55 60

Glu Cys Glu Thr Asp Gln Glu Cys Glu Thr Tyr Glu Lys Cys Cys Pro

65 70 75 80

Asn Val Cys Gly Thr Lys Ser Cys Val Ala Ala Arg Tyr Met Asp Val

85 90 95

Lys Gly Lys Lys Gly Pro Val Gly Met Pro Lys Glu Ala Thr Cys Asp

100 105 110

His Phe Met Cys Leu Gln Gln Gly Ser Glu Cys Asp Ile Trp Asp Gly

115

120

125

Gln Pro Val Cys Lys Cys Lys Asp Arg Cys Glu Lys Glu Pro Ser Phe

130

135

140

Thr Cys Ala Ser Asp Gly Leu Thr Tyr Tyr Asn Arg Cys Tyr Met Asp

145

150

155

160

Ala Glu Ala Cys Ser Lys Gly Ile Thr Leu Ala Val Val Thr Cys Arg

165

170

175

Tyr His Phe Thr Trp Pro Asn Thr Ser Pro Pro Pro Pro Glu Thr Thr

180

185

190

Met His Pro Thr Thr Ala Ser Pro Glu Thr Pro Glu Leu Asp Met Ala

195

200

205

Ala Pro Ala Leu Leu Asn Asn Pro Val His Gln Ser Val Thr Met Gly

210

215

220

Glu Thr Val Ser Phe Leu Cys Asp Val Val Gly Arg Pro Arg Pro Glu

225

230

235

240

Ile Thr Trp Glu Lys Gln Leu Glu Asp Arg Glu Asn Val Val Met Arg

245

250

255

Pro Asn His Val Arg Gly Asn Val Val Val Thr Asn Ile Ala Gln Leu

260

265

270

Val Ile Tyr Asn Ala Gln Leu Gln Asp Ala Gly Ile Tyr Thr Cys Thr

275

280

285

Ala Arg Asn Val Ala Gly Val Leu Arg Ala Asp Phe Pro Leu Ser Val

290

295

300

Val Arg Gly His Gln Ala Ala Ala Thr Ser Glu Ser Ser Pro Asn Gly  
 305 310 315 320

Thr Ala Phe Pro Ala Ala Glu Cys Leu Lys Pro Pro Asp Ser Glu Asp  
 325 330 335

Cys Gly Glu Glu Gln Thr Arg Trp His Phe Asp Ala Gln Ala Asn Asn  
 340 345 350

Cys Leu Thr Phe Thr Phe Gly His Cys His Arg Asn Leu Asn His Phe  
 355 360 365

Glu Thr Tyr Glu Ala Cys Met Leu Ala Cys Met Ser Gly Pro Leu Ala  
 370 375 380

Ala Cys Ser Leu Pro Ala Leu Gln Gly Pro Cys Lys Ala Tyr Ala Pro  
 385 390 395 400

Arg Trp Ala Tyr Asn Ser Gln Thr Gly Gln Cys Gln Ser Phe Val Tyr  
 405 410 415

Gly Gly Cys Glu Gly Asn Gly Asn Asn Phe Glu Ser Arg Glu Ala Cys  
 420 425 430

Glu Glu Ser Cys Pro Phe Pro Arg Gly Asn Gln Arg Cys Arg Ala Cys  
 435 440 445

Lys Pro Arg Gln Lys Leu Val Thr Ser Phe Cys Arg Ser Asp Phe Val  
 450 455 460

Ile Leu Gly Arg Val Ser Glu Leu Thr Glu Glu Pro Asp Ser Gly Arg  
 465 470 475 480

Ala Leu Val Thr Val Asp Glu Val Leu Lys Asp Glu Lys Met Gly Leu

485 490 495

Lys Phe Leu Gly Gln Glu Pro Leu Glu Val Thr Leu Leu His Val Asp

500 505 510

Trp Ala Cys Pro Cys Pro Asn Val Thr Val Ser Glu Met Pro Leu Ile

515 520 525

Ile Met Gly Glu Val Asp Gly Gly Met Ala Met Leu Arg Pro Asp Ser

530 535 540

Phe Val Gly Ala Ser Ser Ala Arg Arg Val Arg Lys Leu Arg Glu Val

545 550 555 560

Met His Lys Lys Thr Cys Asp Val Leu Lys Glu Phe Leu Gly Leu His

565 570 575

<210> 8

<211> 1659

<212> DNA

<213> Mus sp.

<400> 8

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cgtagccgct gtgaaaaaga acccagcttc acatgtgctt ctgatggcct tacctattac	420
aaccgctgct acatggacgc agaagcctgc ctgcggggtc tccacctgca cgttgtacct	480
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 aagaaggctt gtgaactgct caaccgcttc caagactag 1659

<210> 9  
 <211> 552  
 <212> PRT  
 <213> Mus sp.

<400> 9

Met Pro Ala Pro Gln Pro Phe Leu Pro Leu Leu Phe Val Phe Val Leu  
 1 5 10 15

Ile His Leu Thr Ser Glu Thr Asn Leu Leu Pro Asp Pro Gly Ser His  
 20 25 30

Pro Gly Met Cys Pro Asn Glu Leu Ser Pro His Leu Trp Val Asp Ala  
 35 40 45

Gln Ser Thr Cys Glu Arg Glu Cys Thr Gly Asp Gln Asp Cys Ala Ala  
 50 55 60



Ser Glu Lys Cys Cys Thr Asn Val Cys Gly Leu Gln Ser Cys Val Ala  
 65 70 75 80

Ala Arg Phe Pro Ser Gly Gly Pro Ala Val Pro Glu Thr Ala Ala Ser  
 85 90 95

Cys Glu Gly Phe Gln Cys Pro Gln Gln Gly Ser Asp Cys Asp Ile Trp  
 100 105 110

Asp Gly Gln Pro Val Cys Arg Cys Arg Asp Arg Cys Glu Lys Glu Pro  
 115 120 125

Ser Phe Thr Cys Ala Ser Asp Gly Leu Thr Tyr Tyr Asn Arg Cys Tyr  
 130 135 140

Met Asp Ala Glu Ala Cys Leu Arg Gly Leu His Leu His Val Val Pro  
 145 150 155 160

Cys Lys His Ile Leu Ser Trp Pro Pro Ser Ser Pro Gly Pro Pro Glu  
 165 170 175

Thr Thr Ala Arg Pro Thr Pro Gly Ala Ala Pro Met Pro Pro Ala Leu  
 180 185 190

Tyr Asn Ser Pro Ser Pro Gln Ala Val His Val Gly Gly Thr Ala Ser  
 195 200 205

Leu His Cys Asp Val Ser Gly Arg Pro Pro Pro Ala Val Thr Trp Glu  
 210 215 220

Lys Gln Ser His Gln Arg Glu Asn Leu Ile Met Arg Pro Asp Gln Met  
 225 230 235 240

Tyr Gly Asn Val Val Val Thr Ser Ile Gly Gln Leu Val Leu Tyr Asn

245

250

255

Ala Gln Leu Glu Asp Ala Gly Leu Tyr Thr Cys Thr Ala Arg Asn Ala

260

265

270

Ala Gly Leu Leu Arg Ala Asp Phe Pro Leu Ser Val Leu Gln Arg Ala

275

280

285

Thr Thr Gln Asp Arg Asp Pro Gly Ile Pro Ala Leu Ala Glu Cys Gln

290

295

300

Ala Asp Thr Gln Ala Cys Val Gly Pro Pro Thr Pro His His Val Leu

305

310

315

320

Trp Arg Phe Asp Pro Gln Arg Gly Ser Cys Met Thr Phe Pro Ala Leu

325

330

335

Arg Cys Asp Gly Ala Ala Arg Gly Phe Glu Thr Tyr Glu Ala Cys Gln

340

345

350

Gln Ala Cys Val Arg Gly Pro Gly Asp Val Cys Ala Leu Pro Ala Val

355

360

365

Gln Gly Pro Cys Gln Gly Trp Glu Pro Arg Trp Ala Tyr Ser Pro Leu

370

375

380

Leu Gln Gln Cys His Pro Phe Val Tyr Ser Gly Cys Glu Gly Asn Ser

385

390

395

400

Asn Asn Phe Glu Thr Arg Glu Ser Cys Glu Asp Ala Cys Pro Val Pro

405

410

415

Arg Thr Pro Pro Cys Arg Ala Cys Arg Leu Lys Ser Lys Leu Ala Leu

420

425

430

Ser Leu Cys Arg Ser Asp Phe Ala Ile Val Gly Arg Leu Thr Glu Val  
 435 440 445

Leu Glu Glu Pro Glu Ala Ala Gly Gly Ile Ala Arg Val Ala Leu Asp  
 450 455 460

Asp Val Leu Lys Asp Asp Lys Met Gly Leu Lys Phe Leu Gly Thr Lys  
 465 470 475 480

Tyr Leu Glu Val Thr Leu Ser Gly Met Asp Trp Ala Cys Pro Cys Pro  
 485 490 495

Asn Val Thr Ala Val Asp Gly Pro Leu Val Ile Met Gly Glu Val Arg  
 500 505 510

Glu Gly Val Ala Val Leu Asp Ala Asn Ser Tyr Val Arg Ala Ala Ser  
 515 520 525

Glu Lys Arg Val Lys Lys Ile Val Glu Leu Leu Glu Lys Lys Ala Cys  
 530 535 540

Glu Leu Leu Asn Arg Phe Gln Asp  
 545 550

<210> 10

<211> 1695

<212> DNA

<213> Homo sapiens

<400> 10

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60

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ctgtgggtgg acgcccagag cacctgtgag cgcgagtgtg gcagggacca ggactgtgcg	180
gctgctgaga agtgctgcat caacgtgtgt ggactgcaca gctgcgtggc agcacgcttc	240
cccggcagcc cagctgcgcc gacgacagcg gcctcctgcg agggctttgt gtgcccacag	300
cagggctcgg actgcgacat ctgggacggg cagcccgtgt gccgctgccg cgaccgctgt	360
gagaaggagc ccagcttcac ctgcccctcg gacggcctca cctactaaa ccgctgctat	420
atggacgccg aggcctgcct gcggggcctg cacctccaca tcgtgccctg caagcacgtg	480
ctcagctggc cgcccagcag cccggggccg ccggagacca ctgcccgcc cacacctggg	540
gccgcgcccg tgctcctgc cctgtacagc agcccctccc cacaggcggg gcaggttggg	600
ggtacggcca gcctccactg cgacgtcagc ggccgcccgc cgctgctgt gacctgggag	660
aagcagagtc accagcgaga gaacctgatc atgcgccctg atcagatgta tggcaacgtg	720
gtggtcacca gcatcgggca gctggtgctc tacaacgcgc ggcccgaaga cgccggcctg	780
tacacctgca ccgcgcgcaa cgctgctggg ctgctgcggg ctgacttccc actctctgtg	840
gtccagcgag agccggccag ggacgcagcc cccagcatcc cagccccggc cgagtgcctg	900
ccggatgtgc aggcctgcac gggccccact tccccacacc ttgtcctctg gcactacgac	960
ccgcagcggg gcggctgcat gaccttcccg gcccgctggct gtgatggggc ggcccgcggc	1020
tttgagacct acgaggcatg ccagcaggcc tgtgcccgcg gcccggcga cgcctgcgtg	1080

ctgcctgccg tgcagggccc ctgccggggc tgggagccgc gctgggccta cagcccgtg 1140  
 ctgcagcagt gccatccctt cgtgtacggt ggctgcgagg gcaacggcaa caacttcac 1200  
 agccgcgaga gctgcgagga tgccctgcccc gtgccgcgca caccgccctg ccgcgccctgc 1260  
 cgccctccgga gcaagctggc gctgagcctg tgccgcagcg acttcgcat cgtggggcgg 1320  
 ctcacggagg tgctggagga gcccgaggcc gccggcggca tcgcccgcgt ggcgctcgag 1380  
 gacgtgctca aggatgacaa gatgggcctc aagtctctgg gcaccaagta cctggaggtg 1440  
 acgtgagtg gcatggactg ggccctgcccc tgccccaaca tgacggcggg cgacgggccg 1500  
 ctggtcatca tgggtgaggt gcgcatggc gtggccgtgc tggacgccgg cagctacgtc 1560  
 cgcgccgcca gcgagaagcg cgtcaagaag atcttggagc tgctggagaa gcaggcctgc 1620  
 gagctgctca accgcttcca ggactagccc ccgcaggggc ctgcgccacc ccgtcctggt 1680  
 gaataaacgc actcc 1695

<210> 11  
 <211> 548  
 <212> PRT  
 <213> Homo sapiens

<400> 11  
 Met Pro Ala Leu Arg Pro Leu Leu Pro Leu Leu Leu Leu Arg Leu  
 1 5 10 15

Thr Ser Gly Ala Gly Leu Leu Pro Gly Leu Gly Ser His Pro Gly Val  
 20 25 30

Cys Pro Asn Gln Leu Ser Pro Asn Leu Trp Val Asp Ala Gln Ser Thr  
 35 40 45

Cys Glu Arg Glu Cys Ser Arg Asp Gln Asp Cys Ala Ala Ala Glu Lys  
 50 55 60

Cys Cys Ile Asn Val Cys Gly Leu His Ser Cys Val Ala Ala Arg Phe  
 65 70 75 80

Pro Gly Ser Pro Ala Ala Pro Thr Thr Ala Ala Ser Cys Glu Gly Phe  
 85 90 95

Val Cys Pro Gln Gln Gly Ser Asp Cys Asp Ile Trp Asp Gly Gln Pro  
 100 105 110

Val Cys Arg Cys Arg Asp Arg Cys Glu Lys Glu Pro Ser Phe Thr Cys  
 115 120 125

Ala Ser Asp Gly Leu Thr Tyr Tyr Asn Arg Cys Tyr Met Asp Ala Glu  
 130 135 140

Ala Cys Leu Arg Gly Leu His Leu His Ile Val Pro Cys Lys His Val  
 145 150 155 160

Leu Ser Trp Pro Pro Ser Ser Pro Gly Pro Pro Glu Thr Thr Ala Arg  
 165 170 175

Pro Thr Pro Gly Ala Ala Pro Val Pro Pro Ala Leu Tyr Ser Ser Pro  
 180 185 190

Ser Pro Gln Ala Val Gln Val Gly Gly Thr Ala Ser Leu His Cys Asp  
 195 200 205

Val Ser Gly Arg Pro Pro Pro Ala Val Thr Trp Glu Lys Gln Ser His

210 215 220

Gln Arg Glu Asn Leu Ile Met Arg Pro Asp Gln Met Tyr Gly Asn Val

225 230 235 240

Val Val Thr Ser Ile Gly Gln Leu Val Leu Tyr Asn Ala Arg Pro Glu

245 250 255

Asp Ala Gly Leu Tyr Thr Cys Thr Ala Arg Asn Ala Ala Gly Leu Leu

260 265 270

Arg Ala Asp Phe Pro Leu Ser Val Val Gln Arg Glu Pro Ala Arg Asp

275 280 285

Ala Ala Pro Ser Ile Pro Ala Pro Ala Glu Cys Leu Pro Asp Val Gln

290 295 300

Ala Cys Thr Gly Pro Thr Ser Pro His Leu Val Leu Trp His Tyr Asp

305 310 315 320

Pro Gln Arg Gly Gly Cys Met Thr Phe Pro Ala Arg Gly Cys Asp Gly

325 330 335

Ala Ala Arg Gly Phe Glu Thr Tyr Glu Ala Cys Gln Gln Ala Cys Ala

340 345 350

Arg Gly Pro Gly Asp Ala Cys Val Leu Pro Ala Val Gln Gly Pro Cys

355 360 365

Arg Gly Trp Glu Pro Arg Trp Ala Tyr Ser Pro Leu Leu Gln Gln Cys

370 375 380

His Pro Phe Val Tyr Gly Gly Cys Glu Gly Asn Gly Asn Asn Phe His

385                      390                      395                      400

Ser Arg Glu Ser Cys Glu Asp Ala Cys Pro Val Pro Arg Thr Pro Pro

405                      410                      415

Cys Arg Ala Cys Arg Leu Arg Ser Lys Leu Ala Leu Ser Leu Cys Arg

420                      425                      430

Ser Asp Phe Ala Ile Val Gly Arg Leu Thr Glu Val Leu Glu Glu Pro

435                      440                      445

Glu Ala Ala Gly Gly Ile Ala Arg Val Ala Leu Glu Asp Val Leu Lys

450                      455                      460

Asp Asp Lys Met Gly Leu Lys Phe Leu Gly Thr Lys Tyr Leu Glu Val

465                      470                      475                      480

Thr Leu Ser Gly Met Asp Trp Ala Cys Pro Cys Pro Asn Met Thr Ala

485                      490                      495

Gly Asp Gly Pro Leu Val Ile Met Gly Glu Val Arg Asp Gly Val Ala

500                      505                      510

Val Leu Asp Ala Gly Ser Tyr Val Arg Ala Ala Ser Glu Lys Arg Val

515                      520                      525

Lys Lys Ile Leu Glu Leu Leu Glu Lys Gln Ala Cys Glu Leu Leu Asn

530                      535                      540

Arg Phe Gln Asp

545

<210> 12



<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Illustrative competing peptide

<400> 12

Asp Phe Gly Leu Asp Ser Asp Glu His Ser Thr Glu Ser Arg Ser Ser

1 5 10 15

Arg Tyr Pro Leu Thr Val Asp Phe Glu Ala Phe Gly Trp Asp

20 25 30

<210> 13

<211> 15

<212> PRT

<213> Mus sp.

<400> 13

Ala Asn Tyr Cys Ser Gly Glu Cys Glu Phe Val Phe Leu Gln Lys

1 5 10 15

<210> 14

<211> 12

<212> PRT

<213> Mus sp.

<400> 14

Met Ser Pro Ile Asn Met Leu Tyr Phe Asn Gly Lys

1 5 10

<210> 15

<211> 14

<212> PRT

<213> Mus sp.

<400> 15

Asp Phe Gly Leu Asp Cys Asp Glu His Ser Thr Glu Ser Arg

1 5 10

<210> 16

<211> 15

<212> PRT

<213> Mus sp.

<400> 16

Ala Asn Tyr Cys Ser Gly Glu Cys Glu Phe Val Phe Leu Gln Lys

1 5 10 15

<210> 17

<211> 12

<212> PRT

<213> Mus sp.

<400> 17

Met Ser Pro Ile Asn Met Leu Tyr Phe Asn Gly Lys

1 5 10

<210> 18

<211> 19

<212> PRT

<213> Mus sp.

<400> 18

Tyr Pro Leu Thr Val Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile Ile

1 5 10 15

Ala Pro Lys

<210> 19

<211> 12

<212> PRT

<213> Mus sp.

<400> 19

Met Ser Pro Ile Asn Met Leu Tyr Phe Asn Gly Lys

1 5 10

<210> 20

<211> 11

<212> PRT

<213> Mus sp.

<400> 20

Gly Ser Ala Gly Pro Cys Cys Thr Pro Thr Lys

1 5 10

<210> 21

<211> 16

<212> PRT

<213> Mus sp.

<400> 21

Leu Asp Met Ser Pro Gly Thr Gly Ile Trp Gln Ser Ile Asp Val Lys

1 5 10 15

<210> 22

<211> 28

<212> PRT

<213> Mus sp.

<400> 22

Ala Leu Asp Glu Asn Gly His Asp Leu Ala Val Thr Phe Pro Gly Pro

1 5 10 15

Gly Glu Asp Gly Leu Asn Pro Phe Leu Glu Val Lys

20 25

<210> 23

<211> 16

<212> PRT

<213> Mus sp.

<400> 23

Leu Asp Met Ser Pro Gly Thr Gly Ile Trp Gln Ser Ile Asp Val Lys

1 5 10 15

<210> 24  
 <211> 10  
 <212> PRT  
 <213> Mus sp.

<400> 24  
 Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg  
 1 5 10

<210> 25  
 <211> 11  
 <212> PRT  
 <213> Mus sp.

<400> 25  
 Thr Pro Thr Thr Val Phe Val Gln Ile Leu Arg  
 1 5 10

<210> 26  
 <211> 11  
 <212> PRT  
 <213> Mus sp.

<400> 26  
 Ala Gln Leu Trp Ile Tyr Leu Arg Pro Val Lys  
 1 5 10

<210> 27  
 <211> 10  
 <212> PRT

<213> Mus sp.

<400> 27

Glu Gly Leu Cys Asn Ala Cys Ala Trp Arg

1 5 10

<210> 28

<211> 18

<212> PRT

<213> Mus sp.

<400> 28

Pro Gln Ser Cys Leu Val Asp Gln Thr Gly Ser Ala His Cys Val Val

1 5 10 15

Cys Arg

<210> 29

<211> 12

<212> PRT

<213> Mus sp.

<400> 29

Asp Ser Cys Asp Gly Val Glu Cys Gly Pro Gly Lys

1 5 10

<210> 30

<211> 9

<212> PRT

<213> Mus sp.

&lt;400&gt; 30

Ser Cys Ala Gln Val Val Cys Pro Arg

1 5

&lt;210&gt; 31

&lt;211&gt; 13

&lt;212&gt; PRT

&lt;213&gt; Mus sp.

&lt;400&gt; 31

Glu Cys Glu Thr Asp Gln Glu Cys Glu Thr Tyr Glu Lys

1 5 10

&lt;210&gt; 32

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Mus sp.

&lt;400&gt; 32

Ala Asp Phe Pro Leu Ser Val Val Arg

1 5

&lt;210&gt; 33

&lt;211&gt; 11

&lt;212&gt; PRT

&lt;213&gt; Mus sp.

&lt;400&gt; 33

Glu Ala Cys Glu Glu Ser Cys Pro Phe Pro Arg

1 5 10

<210> 34

<211> 8

<212> PRT

<213> Mus sp.

<400> 34

Ser Asp Phe Val Ile Leu Gly Arg

1 5

<210> 35

<211> 12

<212> PRT

<213> Mus sp.

<400> 35

Val Ser Glu Leu Thr Glu Glu Gln Asp Ser Gly Arg

1 5 10

<210> 36

<211> 15

<212> PRT

<213> Homo sapiens

<400> 36

Ala Asn Tyr Cys Ser Gly Glu Cys Glu Phe Val Phe Leu Gln Lys

1 5 10 15

<210> 37

<211> 14



<212> PRT

<213> Homo sapiens

<400> 37

Asp Phe Gly Leu Asp Cys Asp Glu His Ser Thr Glu Ser Arg

1 5 10

<210> 38

<211> 28

<212> PRT

<213> Homo sapiens

<400> 38

Ala Leu Asp Glu Asn Gly His Asp Leu Ala Val Thr Phe Pro Gly Pro

1 5 10 15

Gly Glu Asp Gly Leu Asn Pro Phe Leu Glu Val Lys

20 25

<210> 39

<211> 10

<212> PRT

<213> Homo sapiens

<400> 39

Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg

1 5 10

<210> 40

<211> 18

<212> PRT

<213> Homo sapiens

<400> 40

Pro Gln Ser Cys Val Val Asp Gln Thr Gly Ser Ala His Cys Val Val

1 5 10 15

Cys Arg

<210> 41

<211> 13

<212> PRT

<213> Homo sapiens

<400> 41

Cys Glu Cys Ala Pro Asp Cys Ser Gly Leu Pro Ala Arg

1 5 10

<210> 42

<211> 12

<212> PRT

<213> Homo sapiens

<400> 42

Leu Gln Val Cys Gly Ser Asp Gly Ala Thr Tyr Arg

1 5 10

<210> 43

<211> 12

<212> PRT

<213> Homo sapiens

<400> 43

Val Ser Glu Leu Thr Glu Glu Pro Asp Ser Gly Arg

1 5 10

<210> 44

<211> 10

<212> PRT

<213> Homo sapiens

<400> 44

Cys Tyr Met Asp Ala Glu Ala Cys Ser Lys

1 5 10

<210> 45

<211> 10

<212> PRT

<213> Homo sapiens

<400> 45

Gly Ile Thr Leu Ala Val Val Thr Cys Arg

1 5 10

<210> 46

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

&lt;400&gt; 46

ttggccactg ccaccacaat ctcaaccact t

31

&lt;210&gt; 47

&lt;211&gt; 26

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Description of Artificial Sequence: Primer

&lt;400&gt; 47

tctcagcatg gccatgccgc cgtcga

26

&lt;210&gt; 48

&lt;211&gt; 1716

&lt;212&gt; DNA

&lt;213&gt; Mus sp.

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1)..(1713)

&lt;400&gt; 48

atg tgt gcc cca ggg tat cat cgg ttc tgg ttt cac tgg ggg ctg ctg

48

Met Cys Ala Pro Gly Tyr His Arg Phe Trp Phe His Trp Gly Leu Leu

1

5

10

15

ttg ctg ctg ctc ctc gag gct ccc ctt cga ggc cta gca ctg cca ccc

96

Leu Leu Leu Leu Leu Glu Ala Pro Leu Arg Gly Leu Ala Leu Pro Pro

20	25	30	
atc cga tac tcc cat gcg ggc atc tgc ccc aac gac atg aac ccc aac			144
Ile Arg Tyr Ser His Ala Gly Ile Cys Pro Asn Asp Met Asn Pro Asn			
35	40	45	
ctc tgg gtg gat gcc cag agc acc tgc aag cga gag tgt gaa aca gac			192
Leu Trp Val Asp Ala Gln Ser Thr Cys Lys Arg Glu Cys Glu Thr Asp			
50	55	60	
cag gaa tgt gag acc tat gag aaa tgc tgc ccc aat gtg tgt ggg acc			240
Gln Glu Cys Glu Thr Tyr Glu Lys Cys Cys Pro Asn Val Cys Gly Thr			
65	70	75	80
aag agc tgt gtg gca gcc cgc tac atg gat gtg aaa ggg aag aag ggg			288
Lys Ser Cys Val Ala Ala Arg Tyr Met Asp Val Lys Gly Lys Lys Gly			
85	90	95	
cct gta ggc atg ccc aag gag gcc aca tgt gac cat ttc atg tgc ctg			336
Pro Val Gly Met Pro Lys Glu Ala Thr Cys Asp His Phe Met Cys Leu			
100	105	110	
cag cag ggc tct gag tgt gac atc tgg gac ggc cag ccc gtg tgt aag			384
Gln Gln Gly Ser Glu Cys Asp Ile Trp Asp Gly Gln Pro Val Cys Lys			
115	120	125	
tgc aaa gat cgc tgt gag aag gag ccc agc ttc acc tgt gcc tct gat			432
Cys Lys Asp Arg Cys Glu Lys Glu Pro Ser Phe Thr Cys Ala Ser Asp			
130	135	140	
ggc ctt acc tac tac aac cgt tgc ttc atg gac gcc gaa gcc tgc tcc			480
Gly Leu Thr Tyr Tyr Asn Arg Cys Phe Met Asp Ala Glu Ala Cys Ser			
145	150	155	160

aag ggc atc aca ctg tct gtg gtc acc tgt cgt tat cac ttc acc tgg	528
Lys Gly Ile Thr Leu Ser Val Val Thr Cys Arg Tyr His Phe Thr Trp	
165 170 175	
cct aac acc agc cct cca ccg cct gag acc acg gtg cat ccc acc acc	576
Pro Asn Thr Ser Pro Pro Pro Pro Glu Thr Thr Val His Pro Thr Thr	
180 185 190	
gcc tct ccg gag act ctc ggg ctg gac atg gca gcc cca gcc ctg ctc	624
Ala Ser Pro Glu Thr Leu Gly Leu Asp Met Ala Ala Pro Ala Leu Leu	
195 200 205	
aac cac cct gtc cat cag tca gtc acc gtg ggt gag act gtg agt ttc	672
Asn His Pro Val His Gln Ser Val Thr Val Gly Glu Thr Val Ser Phe	
210 215 220	
ctc tgt gac gtg gta ggc cgg cct cgg cca gag ctc act tgg gag aaa	720
Leu Cys Asp Val Val Gly Arg Pro Arg Pro Glu Leu Thr Trp Glu Lys	
225 230 235 240	
cag ctg gag gac cga gag aat gtt gtc atg agg ccc aac cac gtg cgt	768
Gln Leu Glu Asp Arg Glu Asn Val Val Met Arg Pro Asn His Val Arg	
245 250 255	
ggt aat gtg gtg gtc act aac att gcc cag ctg gtc atc tac aac gtc	816
Gly Asn Val Val Val Thr Asn Ile Ala Gln Leu Val Ile Tyr Asn Val	
260 265 270	
cag ccc cag gat gct ggc ata tac acc tgt aca gct cga aat gtc gct	864
Gln Pro Gln Asp Ala Gly Ile Tyr Thr Cys Thr Ala Arg Asn Val Ala	
275 280 285	
ggt gtc ctg agg gct gac ttc ccg ttg tcg gtg gtc agg ggt ggt cag	912
Gly Val Leu Arg Ala Asp Phe Pro Leu Ser Val Val Arg Gly Gly Gln	

290	295	300	
gcc agg gcc act tca gag agc agt ctc aat ggc aca gct ttt cca gca			960
Ala Arg Ala Thr Ser Glu Ser Ser Leu Asn Gly Thr Ala Phe Pro Ala			
305	310	315	320
aca gag tgc ctg aag ccc cca gac agt gag gac tgt gga gag gag cag			1008
Thr Glu Cys Leu Lys Pro Pro Asp Ser Glu Asp Cys Gly Glu Glu Gln			
	325	330	335
aca cgc tgg cac ttc gac gcc cag gct aac aac tgc ctc act ttc acc			1056
Thr Arg Trp His Phe Asp Ala Gln Ala Asn Asn Cys Leu Thr Phe Thr			
	340	345	350
ttt ggc cac tgc cac cac aat ctc aac cac ttt gag acc tac gag gcc			1104
Phe Gly His Cys His His Asn Leu Asn His Phe Glu Thr Tyr Glu Ala			
	355	360	365
tgt atg ctg gct tgt atg agt ggg cca ttg gcc acc tgc agc ctg cct			1152
Cys Met Leu Ala Cys Met Ser Gly Pro Leu Ala Thr Cys Ser Leu Pro			
370	375	380	
gcc ctg caa ggg cct tgc aaa gct tat gtc cca cgc tgg gcc tac aac			1200
Ala Leu Gln Gly Pro Cys Lys Ala Tyr Val Pro Arg Trp Ala Tyr Asn			
385	390	395	400
agc cag aca ggc cta tgc cag tcc ttc gtc tat ggc ggc tgt gag ggc			1248
Ser Gln Thr Gly Leu Cys Gln Ser Phe Val Tyr Gly Gly Cys Glu Gly			
	405	410	415
aac ggt aac aac ttt gaa agc cgt gag gct tgt gag gag tcg tgt ccc			1296
Asn Gly Asn Asn Phe Glu Ser Arg Glu Ala Cys Glu Glu Ser Cys Pro			
	420	425	430

ttc ccg agg ggt aac cag cac tgc cgg gcc tgc aag ccc cgg caa aaa	1344
Phe Pro Arg Gly Asn Gln His Cys Arg Ala Cys Lys Pro Arg Gln Lys	
435 440 445	
ctt gtt acc agc ttc tgt cgg agt gac ttt gtc atc ctg ggc agg gtc	1392
Leu Val Thr Ser Phe Cys Arg Ser Asp Phe Val Ile Leu Gly Arg Val	
450 455 460	
tct gag ctg acc gag gag caa gac tcg ggc cgt gcc ctg gtg acc gtg	1440
Ser Glu Leu Thr Glu Glu Gln Asp Ser Gly Arg Ala Leu Val Thr Val	
465 470 475 480	
gat gag gtc tta aaa gat gag aag atg ggc ctc aag ttt ctg ggc cgg	1488
Asp Glu Val Leu Lys Asp Glu Lys Met Gly Leu Lys Phe Leu Gly Arg	
485 490 495	
gag cct ctg gaa gtc acc ctg ctt cat gta gac tgg acc tgt cct tgc	1536
Glu Pro Leu Glu Val Thr Leu Leu His Val Asp Trp Thr Cys Pro Cys	
500 505 510	
ccc aac gtg aca gtg ggt gag aca cca ctc atc atc atg ggg gag gtg	1584
Pro Asn Val Thr Val Gly Glu Thr Pro Leu Ile Ile Met Gly Glu Val	
515 520 525	
gac ggc ggc atg gcc atg ctg aga ccc gat agc ttt gtg ggg gca tcg	1632
Asp Gly Gly Met Ala Met Leu Arg Pro Asp Ser Phe Val Gly Ala Ser	
530 535 540	
agc aca cgg cgg gtc agg aag ctc cgt gag gtc atg tac aag aaa acc	1680
Ser Thr Arg Arg Val Arg Lys Leu Arg Glu Val Met Tyr Lys Lys Thr	
545 550 555 560	
tgt gac gtc ctc aag gac ttc ctg ggc ttg caa tga	1716
Cys Asp Val Leu Lys Asp Phe Leu Gly Leu Gln	



565

570

&lt;210&gt; 49

&lt;211&gt; 571

&lt;212&gt; PRT

&lt;213&gt; Mus sp.

&lt;400&gt; 49

Met Cys Ala Pro Gly Tyr His Arg Phe Trp Phe His Trp Gly Leu Leu

1 5 10 15

Leu Leu Leu Leu Leu Glu Ala Pro Leu Arg Gly Leu Ala Leu Pro Pro

20 25 30

Ile Arg Tyr Ser His Ala Gly Ile Cys Pro Asn Asp Met Asn Pro Asn

35 40 45

Leu Trp Val Asp Ala Gln Ser Thr Cys Lys Arg Glu Cys Glu Thr Asp

50 55 60

Gln Glu Cys Glu Thr Tyr Glu Lys Cys Cys Pro Asn Val Cys Gly Thr

65 70 75 80

Lys Ser Cys Val Ala Ala Arg Tyr Met Asp Val Lys Gly Lys Lys Gly

85 90 95

Pro Val Gly Met Pro Lys Glu Ala Thr Cys Asp His Phe Met Cys Leu

100 105 110

Gln Gln Gly Ser Glu Cys Asp Ile Trp Asp Gly Gln Pro Val Cys Lys

115 120 125

Cys Lys Asp Arg Cys Glu Lys Glu Pro Ser Phe Thr Cys Ala Ser Asp

130                      135                      140  
 Gly Leu Thr Tyr Tyr Asn Arg Cys Phe Met Asp Ala Glu Ala Cys Ser  
 145                      150                      155                      160  
  
 Lys Gly Ile Thr Leu Ser Val Val Thr Cys Arg Tyr His Phe Thr Trp  
                          165                      170                      175  
  
 Pro Asn Thr Ser Pro Pro Pro Pro Glu Thr Thr Val His Pro Thr Thr  
                          180                      185                      190  
  
 Ala Ser Pro Glu Thr Leu Gly Leu Asp Met Ala Ala Pro Ala Leu Leu  
                          195                      200                      205  
  
 Asn His Pro Val His Gln Ser Val Thr Val Gly Glu Thr Val Ser Phe  
                          210                      215                      220  
  
 Leu Cys Asp Val Val Gly Arg Pro Arg Pro Glu Leu Thr Trp Glu Lys  
 225                      230                      235                      240  
  
 Gln Leu Glu Asp Arg Glu Asn Val Val Met Arg Pro Asn His Val Arg  
                          245                      250                      255  
  
 Gly Asn Val Val Val Thr Asn Ile Ala Gln Leu Val Ile Tyr Asn Val  
                          260                      265                      270  
  
 Gln Pro Gln Asp Ala Gly Ile Tyr Thr Cys Thr Ala Arg Asn Val Ala  
                          275                      280                      285  
  
 Gly Val Leu Arg Ala Asp Phe Pro Leu Ser Val Val Arg Gly Gly Gln  
                          290                      295                      300  
  
 Ala Arg Ala Thr Ser Glu Ser Ser Leu Asn Gly Thr Ala Phe Pro Ala  
 305                      310                      315                      320

Thr Glu Cys Leu Lys Pro Pro Asp Ser Glu Asp Cys Gly Glu Glu Gln  
 325 330 335

Thr Arg Trp His Phe Asp Ala Gln Ala Asn Asn Cys Leu Thr Phe Thr  
 340 345 350

Phe Gly His Cys His His Asn Leu Asn His Phe Glu Thr Tyr Glu Ala  
 355 360 365

Cys Met Leu Ala Cys Met Ser Gly Pro Leu Ala Thr Cys Ser Leu Pro  
 370 375 380

Ala Leu Gln Gly Pro Cys Lys Ala Tyr Val Pro Arg Trp Ala Tyr Asn  
 385 390 395 400

Ser Gln Thr Gly Leu Cys Gln Ser Phe Val Tyr Gly Gly Cys Glu Gly  
 405 410 415

Asn Gly Asn Asn Phe Glu Ser Arg Glu Ala Cys Glu Glu Ser Cys Pro  
 420 425 430

Phe Pro Arg Gly Asn Gln His Cys Arg Ala Cys Lys Pro Arg Gln Lys  
 435 440 445

Leu Val Thr Ser Phe Cys Arg Ser Asp Phe Val Ile Leu Gly Arg Val  
 450 455 460

Ser Glu Leu Thr Glu Glu Gln Asp Ser Gly Arg Ala Leu Val Thr Val  
 465 470 475 480

Asp Glu Val Leu Lys Asp Glu Lys Met Gly Leu Lys Phe Leu Gly Arg  
 485 490 495

Glu Pro Leu Glu Val Thr Leu Leu His Val Asp Trp Thr Cys Pro Cys  
 500 505 510

Pro Asn Val Thr Val Gly Glu Thr Pro Leu Ile Ile Met Gly Glu Val  
 515 520 525

Asp Gly Gly Met Ala Met Leu Arg Pro Asp Ser Phe Val Gly Ala Ser  
 530 535 540

Ser Thr Arg Arg Val Arg Lys Leu Arg Glu Val Met Tyr Lys Lys Thr  
 545 550 555 560

Cys Asp Val Leu Lys Asp Phe Leu Gly Leu Gln  
 565 570

<210> 50

<211> 34

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 50

caccatgtgt gccccagggt atcatcggtt ctgg

34

<210> 51

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 51

ttgcaagccc aggaagtcct tgaggac

27

<210> 52

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Illustrative N-terminal  
peptide sequence

<400> 52

Leu Pro Pro Ile Arg Tyr Ser His Ala Gly Ile

1 5 10

<210> 53

<211> 48

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 53

cagacagaca gacagacaga cagacagaca gacagacaga cagacaga

48