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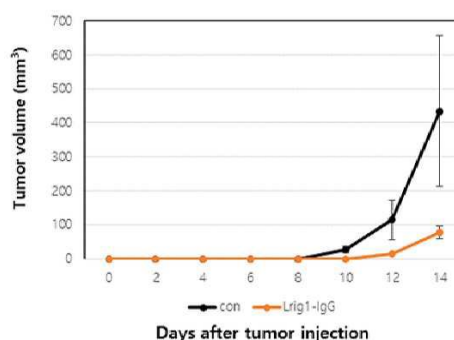
(54) 발명의 명칭 신규한 융합 단백질 및 이를 포함하는 암의 예방 또는 치료용 약학적 조성물

(57) 요약

본 발명은 Lrig-1(leucine-rich and immunoglobulin-like domains 1) 단백질의 세포 외 도메인(extracellular domain) 및 면역글로불린(immunoglobulin) Fc 영역을 포함하는 융합 단백질에 관한 것이다.

본 발명에서 제공하는 융합 단백질은 이펙터 T 세포(effector T cell)에 존재하는 Lrig-1 단백질에 대한 리간드와 상호 작용하여, Lrig-1 단백질을 표면에 포함하고 있는 조절 T 세포(regulatory T cell, Treg cell)와 이펙터 T 세포간의 상호 작용을 저해함에 따라 조절 T 세포의 활성을 억제하고 이펙터 T 세포의 활성은 유지 혹은 상승시켜 암 세포 중에서도 특히 고형암 세포의 성장을 효과적으로 억제할 수 있다.

대표도 - 도14



	Lrig1-IgG
B16F10	---

✓ control 대비 암크기 감소 표시 (0~30 %: ---, 31~70 %: --, 71~100 %: -)
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명세서

청구범위

청구항 1

Lrig-1(leucine-rich and immunoglobulin-like domains 1) 단백질의 세포 외 도메인(extracellular domain) 및 면역글로불린(immunoglobulin) Fc 영역을 포함하고,

상기 Lrig-1 단백질의 세포 외 도메인은 서열번호 1 또는 3으로 표시되는, 융합 단백질.

청구항 2

삭제

청구항 3

제1항에 있어서,

상기 면역글로불린 Fc 영역은 CH1, CH2, CH3 및 CH4 도메인으로 이루어진 그룹으로부터 선택된 1개 내지 4개 도메인을 포함하는, 융합 단백질.

청구항 4

제1항에 있어서,

상기 면역글로불린 Fc 영역은 IgG, IgA, IgD, IgE 또는 IgM 유래 Fc 영역, 중쇄 불변영역 2(CH2), 중쇄 불변영역 3(CH3), 힌지(hinge), 이의 단편, 이들의 조합(combination), 또는 이들의 조합을 포함하는 하이브리드 Fc(hybrid Fc)인, 융합 단백질.

청구항 5

제1항에 있어서,

상기 면역글로불린 Fc 영역은 IgG, IgA, IgD, IgE 또는 IgM 유래의 CH2 및 CH3 도메인을 포함하는, 융합 단백질

청구항 6

제1항에 있어서,

상기 면역글로불린 Fc 영역은 IgG1, IgG2, IgG3 또는 IgG4 유래의 CH2 및 CH3 도메인을 포함하는, 융합 단백질.

청구항 7

제1항에 있어서,

상기 면역글로불린 Fc 영역은 힌지(hinge) 영역을 포함하는, 융합 단백질.

청구항 8

제7항에 있어서,

상기 면역글로불린 Fc 영역은 IgG, IgA, IgM, IgD, IgE, 또는 아바타셉트(Abatcept) 유래의 힌지 영역을 포함하는, 융합 단백질.

청구항 9

제7항에 있어서,

상기 힌지(hinge) 영역은 IgG1, IgG2, IgG3, IgG4, IgD 또는 아바타셉트(Abatcept) 유래의 힌지 영역을 포함하는, 융합 단백질.

청구항 10

제1항에 있어서,

상기 면역글로불린 Fc 영역은 서열번호 5 또는 6으로 표시되는 CH2 및 CH3을 포함하는, 융합 단백질.

청구항 11

제1항에 있어서,

상기 면역글로불린 Fc 영역은 서열번호 7 내지 10 중 어느 하나로 표시되는 힌지 영역을 포함하는, 융합 단백질.

청구항 12

제1항에 있어서,

상기 Lrig-1 단백질의 세포 외 도메인은 상기 면역글로불린 Fc 영역의 N-말단 또는 C-말단에 직접 연결되는, 융합 단백질.

청구항 13

제1항에 있어서,

상기 Lrig-1 단백질의 세포 외 도메인은 링커를 통하여 상기 면역글로불린 Fc 영역의 N-말단 또는 C-말단에 연결되는, 융합 단백질.

청구항 14

제13항에 있어서,

상기 링커는 서열번호 11로 표시되는 펩타이드 링커; 및 서열번호 12로 표시되는 펩타이드 링커; 중 적어도 하나인, 융합 단백질.

청구항 15

제1항, 제3항 내지 제14항 중 어느 한 항의 융합 단백질을 코딩하는 핵산 분자.

청구항 16

제15항의 핵산 분자가 삽입된 발현 벡터.

청구항 17

제16항의 발현 벡터가 형질 감염된 숙주 세포주.

청구항 18

제1항, 제3항 내지 제14항 중 어느 한 항의 융합 단백질을 유효 성분으로 포함하는 암의 예방 또는 치료용 약학 조성물.

청구항 19

제18항에 있어서,

상기 암은 고형암인, 약학 조성물.

청구항 20

제18항에 있어서,

상기 암은 위암, 간암, 교세포종, 난소암, 대장암, 두경부암, 방광암, 신장세포암, 유방암, 전이암, 전립선암, 췌장암, 흑색종 또는 폐암인, 약학 조성물.

발명의 설명

기술 분야

[0001] 본 발명은 Lrig-1(leucine-rich and immunoglobulin-like domains 1) 단백질의 세포 외 도메인(extracellular domain)과 면역글로불린(immunoglobulin) Fc 영역을 포함하는 신규한 융합 단백질과, 이의 용도에 관한 것이다.

배경 기술

[0002] 면역글로불린(immunoglobulin)은 4개의 폴리펩타이드 쇄, 즉 쇄간 디설피드 결합을 통해 회합된 2개의 중쇄 및 2개의 경쇄를 포함한다. 각각의 경쇄는 2개의 도메인, 즉 가변 경쇄 도메인 (VL) 및 불변 경쇄 도메인 (CL)을 갖고, 각각의 중쇄는 2개의 영역, 즉 가변 중쇄 영역 (VH) 및 불변 중쇄 영역 (CH)을 갖는다. 불변 중쇄 영역 (CH)은 숫자에 의해 지정된 불변 중쇄 영역 (예를 들어, CH1, CH2, CH3 등)으로 이루어진다 (예를 들어, US 6,086,875 (블룸버그 알. 에스.(Blumberg R. S.) 등), US 5,624,821 (윈터 (Winter G. P.) 등) 및 US 5,116,964 (카폰 디. 제이.(Capon D. J.) 및 라스키 엘. 에이.(Lasky L. A.)) 참조). 면역글로불린은 그의 생물학적 특성, 유기체 내의 위치 및 상이한 항원을 처리하는 능력에 기초하여 상이한 이소형(즉, IgG, IgM, IgA, IgD 및 IgE)으로 분류된다. 이뮤노글로불린 이소형에 따라, 불변 중쇄 영역 (CH)은 3개 또는 4개의 CH 도메인을 가질 수 있다. 또한, 일부 이소형 (IgA, IgD 및 IgG)에서, 중쇄는 분자에 유연성을 부가하는 힌지 영역을 포함한다 (Janeway et al. 2001, Immunobiology, Garland Publishing, N.Y., N.Y.).

[0003] 인간에는 4개의 IgG 하위클래스 (IgG1, 2, 3, 4)가 있고, 이들은 혈청에 풍부한 순서에 따라 명명된다 (IgG1이 가장 풍부하다). IgG 이소형은 2개의 경쇄 및 2개의 중쇄로 이루어지고, 각각의 중쇄는 3개의 불변 중쇄 도메인 (CH1, CH2, CH3)을 포함한다. IgG의 2개의 중쇄는 서로에 대해 및 경쇄에 각각 디설피드 결합 (-S-S-)에 의해 연결되어 있다. IgG의 항원 결합 부위는 가변 경쇄 (VL) 및 가변 중쇄 (VH) 도메인뿐만 아니라 불변 경쇄 (CL) 및 불변 중쇄 (CH1) 도메인을 포함하는 단편 항원 결합 영역 (Fab 영역)에 위치한다. IgG의 단편 결정화가능 영역 (Fc 영역)은 신생아 Fc 수용체 (FcRn)를 포함하는 특정 세포의 표면에서 발견되는 Fc 수용체에 결합하는 CH2 및 CH3 도메인을 함유하는 중쇄의 일부이다. IgG의 중쇄는 또한 Fab 영역을 Fc 영역으로부터 분리하고 2개의 중쇄를 디설피드 결합을 통해 함께 연결할 때 참여하는, CH1과 CH2 사이의 힌지 영역 (힌지)을 갖는다. 힌지 영역의 구조는 4개의 IgG 하위클래스 각각의 특유한 생물학적 특성에 기여한다.

[0004] IgG는 쉽게 조직을 관류할 수 있도록 허용하는 크기가 작은 단량체로 분비된다. 이것은 자궁 내의 태아를 보호하기 위해 인간 태반을 통과하는 것을 촉진하는 수용체 (신생아 Fc 수용체 (FcRn))를 갖는 유일한 이소형이다. 태반을 통해 흡수된 IgG는 그 자체 면역계가 발달하기 전에 체액성 면역을 신생아에게 제공한다.

[0005] IgG 신생아 Fc 수용체 (FcRn) 결합 부위는 항체의 Fc 영역에 위치한다. FcRn은 일반적으로 인간의 태반 및 상피 세포에서 발현되고, IgG의 분해를 막는 세포내이입 샤펠지 경로에 참여한다. 이 샤펠지 경로는 산성 pH에서 FcRn에 대한 IgG의 높은 pH 의존성 결합 친화도에 의해 매개된다. 산성 pH에서 FcRn에 대한 IgG의 높은 친화도는 산성 엔도솜 내로의 흡수 후에 내재화된 IgG의 FcRn에 대한 결합을 유발하는 것으로 생각된다 ([Goeb1 NA, et al., 2008]; [Junghans RP, et al., 1996]). 대부분의 가용성 단백질은 내재화 후에 리소솜으로 향하지만, 내재화된 FcRn-결합 IgG는 형질 막으로 되돌아가고, 기본 분해 경로로부터 효과적으로 구출된다. 세포의 공간의 중성 pH에 노출시, IgG는 FcRn으로부터 해리되어 순환계로 되돌아갈 수 있다. 따라서, 항체의 연장된 혈청 반감기 특성은 Fc 단편에서 유지된다.

[0006] 상기 샤펠지 경로는 비변형된 단백질 약물에 비해 혈액 순환에서 반감기가 연장된 차세대 단백질 약물의 개발을 위한 하나의 메커니즘을 제공한다. 특히, 비변형된 단백질 약물은 순환 반감기가 짧고, 따라서 필요한 장기간의 치료 기간에 걸쳐 빈번한 투여가 필요하다. PEG화 융합 단백질 기술 (미국 식품의약국 (Food and Drug Administration), [Osborn BL, et al., 2002])을 포함한 많은 방법에 의해 단백질 약물의 반감기를 연장하기 위한 광범위한 노력이 이루어졌지만, 이러한 노력의 결과는 이상적이지 않았다.

발명의 내용

해결하려는 과제

[0007] 본 발명의 일 목적은 Lrig-1(leucine-rich and immunoglobulin-like domains 1) 단백질의 세포 외 도메인 (extracellular domain)과 면역글로불린(immunoglobulin) Fc 영역을 포함하는 신규한 융합 단백질을 제공하는

것이다.

- [0008] 본 발명의 다른 목적은 본 발명에 따른 상기 융합 단백질을 코딩하는 핵산 분자에 관한 것이다.
- [0009] 본 발명의 또 다른 목적은 본 발명에 따른 상기 핵산 분자가 삽입된 발현 벡터를 제공하는 것이다.
- [0010] 본 발명의 또 다른 목적은 본 발명에 따른 상기 발현 벡터가 형질 감염된 숙주 세포주를 제공하는 것이다.
- [0011] 본 발명의 또 다른 목적은 본 발명에 따른 융합 단백질을 포함하는 암의 예방 또는 치료용 약학 조성물을 제공하는 것이다.
- [0012] 그러나 본 발명이 이루고자 하는 기술적 과제는 이상에서 언급한 과제에 제한되지 않으며, 언급되지 않은 또 다른 과제들은 아래의 기재로부터 당업계에서 통상의 지식을 가진 자에게 명확하게 이해될 수 있을 것이다.

과제의 해결 수단

- [0013] 본 발명의 일 구현 예에 따르면, Lrig-1(leucine-rich and immunoglobulin-like domains 1) 단백질의 세포 외 도메인(extracellular domain) 및 면역글로불린(immunoglobulin) Fc 영역을 포함하는 융합 단백질에 관한 것이다.
- [0014] 본 발명에서, 상기 "Lrig-1 단백질"은 조절 T 세포의 표면에 존재하는 1091개의 아미노산으로 이루어진 막관통 단백질로서, 세포 외 혹은 루멘 쪽의 루신 반복 서열(leucine-rich repeat(LRR))과 세계의 면역체 유사 도메인(immunoglobulin-like domains), 세포막 관통 서열 및 세포질 꼬리부분으로 구성되어 있다. LRIG 유전자 패밀리는 LRIG1, LRIG2와 LRIG3이 존재하며, 이들간의 아미노산들은 매우 보존적으로 구성되어 있다.
- [0015] 본 발명의 일 예시에서 상기 Lrig-1 단백질의 세포 외 도메인은 인간, 원숭이 등의 영장류, 마우스, 래트 등의 설치류, 등을 포함하는 포유류로부터 유래된 Lrig-1 단백질의 세포 외 도메인일 수 있다.
- [0016] 본 발명의 일 예시에서 상기 Lrig-1 단백질의 세포 외 도메인은 인간 유래 Lrig-1 단백질의 35번째 내지 794번째 아미노산 서열에 해당하는 서열번호 1로 표시될 수 있고, 이는 서열번호 2로 표시되는 핵산 서열에 의해 코딩될 수 있으나, 이에 제한되는 것은 아니다(표 1 참조).

표 1

서열목록	서열정보
서열번호 1	AGPRAPCAAACCTCAGDSLDCGGRGLAALPGDLPSWTRSLNLSYNKLSEIDPAGFEDLPNLQEVYLNNNELTA VPSLGAASSHVVSFLQHNKIRSVEGSQLKAYLSLEVLDLSLNNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVCLKQRNNISKL TDGAFWGLSKMHVLHLEYNLSLEVNSGSLYGLTALHQLHLNNNSIARIHRKGWSFCQKLHELVLFSNNLTR DEESLAELSSLSVRLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDLSKLTFLGNGKI KSVAKRAFSGLEGLEHLNLGGNAIRSVQFADFVKMKNLKEHLISSDSFLCDCQLKWLPPWLI GRMLQAFVTA TCAHPESLKGQSIFSVPPESFVCDLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKDNEVLT NADMFNFVHVAQDGEVMEYTTILHLRQVTFGHEGRYQCVITNHFGSTYSHKARLTVNVLPSTFKTPHDTIT RTTTVARLECAATGHPNPQIAWQKDGDTDFPAARERRMHVMPDDVFFITDVKIDDAGVYSCTAQNAGSIS ANATLTVLETPSLVVPLEDVSVGETVALQCKATGNPPPRITWFKGDRPLSLTERHHLTPDNQLLVQNVV AEDAGRYTCMSNTLGTERRAHSQSVLPAAGCRKDGTTVGIF

서열번호 2	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCTTGGACCCGGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCGCCGGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggagctgcttcatcacatgtcgtctctctcttctgcagcacacaagattcgagcgtg gaggggagccagctgaaggcctaccttcccttagaagtgttagatctgagttgaacaacatcacggaagt cggaacacctgctttccacacggaccgctataaaggagctcaacctggcaggcaatcgattggcaccctg gagttgggagcatttgatggctgtcacggctcgctgctaactcttcgacctgagcaaaaacaggatcacccag cttctgtgaagagcatccaagctaccaggctgacacaactggacctcaatcggaacaggattcggtgata gagggcctcaccttcaggggctcaacagcttgagggtgctgaagcttcagcgaacaacatcagcaactg acagatggggccttctggggactgtccaagatgcatgtgctgcacctggagtacaacagcctggtagaagt aacagcgctcgctctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgatt caccgcaagggtggagcttctgccagaagctgcatgagttggtcctgtccttcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcctgcgtctcagccacaattccatcagccacatt gcggagggtgccttcaaggggactcaggagcctgcgagctctggatctggaccataacagagatttcgggcaca atagaggacacgagcgccgcttctcagggtcgacagcctcagcaagctgactctgttggaaacaagatc aagtctgtggctaaagagagcatctcggggctggaaggcctggagcacctgaaccttggagggaatgcgatc agatctgtccagtttgatgcctttgtgaagatgaagaatcttaaagagctccatcagcagcgacagcttc ctgtgtgactgccagctgaagtggctgccccctggctaatggcaggatgctgcaggccttctgtgacagcc acctgtgcccaccagaatcactgaagggtcagagcatttctctgtgccaccagagagtttctgtgctgcat gacttctgaagccacagatcatcacccagccagaaaccaccatggctatggagggaaggacatccggttt acatgctcagcagccagcagcagcagctccccatgacctttgctggaagaaagacaatgaagtcctgacc aatgcagacatggagaactttgtccagctccacgcgcaggacggggaagtgatggagtacaccaccatcctg cacctccgtcaggtcactttcgggcacgaggccgctaccaatgtgtcatcaccaaccactttggctccacc tattcacataaggccaggctcacctgaatgtgttgccatcattcaccaaaacgccccacgacataaacatc cggaccaccacgtggcccgctcgaatgtgtgccacaggtcaccaaaacacctcagattgcctggcagaag gatggaggcacgatttccccgctgcccgtgagcgcagcagcatgcatgtcatgccggatgacgacgtgttttc atcactgatgtgaaaatagatgacgcagggtttacagctgtactgctcagaactcagccggttctatttca gctaatgccaccctgactgtcctagagaccccatccttgggtggctccccttggagaccgtgtggtatctgtg ggagaaacagtgccctccaatgcaagccacggggaacctccgccccgcatcacctggttcaagggggac cgccccgtgagcctcactgagcggcaccacctgacccctgacaaccagctcctggtggttcagaacgtggtg gcagaggatgcgggcccagatacctgtgagatgtccaacacctgggcacggagcgagctcacagccagctg agcgtcctgcccgcagcaggtgcaggaaggatgggaccacggtaggcatcttc

[0019] 본 발명의 다른 예시에서 상기 Lrig-1 단백질의 세포 외 도메인은 마우스 유래 Lrig-1 단백질의 35번째 내지 794번째 아미노산 서열에 해당하는 서열번호 3으로 표시될 수 있고, 이는 서열번호 4로 표시되는 핵산 서열에 의해 코딩될 수 있으나, 이에 제한되는 것은 아니다(표 2 참조).

표 2

서열목록	서열정보					
서열번호 3	AQAGPRAPCA	AACTCAGDSL	DCSGRGLATL	PRDLPSWTRS	LNL SYNRLSE	IDSAAFEDLT
	NLQEVYLSN	ELTAIPSLGA	ASIGVVSFL	QHNKILSVDG	SQLKSYLSLE	VLDLSSNNIT
	EIRSSCFPNG	LRIRELNLAS	NRISILESGA	FDGLSRSLLT	LRLSKNRITQ	LPVKAFKLPR
	LTQLDLNRNR	IRLIEGLTFQ	GLDSLEVLRL	QRNNISRLTD	GAFWGLSKMH	VLHLEYNSLV
	EVNSGSLYGL	TALHQLHLSN	NSISRIQRDG	WSFCQKLHEL	ILSFNNLTRL	DEESLAEISS
	LSILRLSHNA	ISHIAEGAFK	GLKSLRVLDL	DHNEISGTIE	DTSGAFTGLD	NLSKLTFLGN
	KIKSVAKRAF	SGLESLEHLN	LGENAIRSVQ	FDAFAKMKNL	KELYISSESF	LCDCQLKWLP
	PWLMGRMLQA	FVTATCAHPE	SLKGQSIFSV	LPDSFVCDDF	PKPQIITQPE	TTMAVVGKDI
	RFTCSAASSS	SSPMTFAWK	DNEVLNADM	ENFAHVRAQD	GEVMEYTTIL	HLRHVTFGHE
	GRYQCIITNH	FGSTYSHKAR	LTVNVLPST	KIPHDIAIRT	GTTARLECAA	TGHPNPQIAW
	QKDGGTDFPA	ARERRMHVMP	DDDVFFITDV	KIDDMGVYSC	TAQNSAGSVS	ANATLTVLET
	PSLAVPLEDR	VVTVGETVAF	QCKATGSPTP	RITWLKGGRP	LSLTERHHFT	PGNQLLVQVN
	VMIDDAGRYT	CEMSNPLGTE	RAHSQLSILP	TPGCRKDGTT		

서열번호 4	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTTGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTTATCGGCGTGGTGAAGCCTGTCTCTGCAGCACAACAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTCTTAATGGCTGCGGATCAGAGAGCTGAACCTGGCCTTAATCGGATCAGC ATCCTGGAGTCCGGCGCTTCGATGGCTGAGCAGATCCCTGCTGACACTGCGCCTGTCCAAAGACCGGATC ACCGAGCTGCCGCTGAAGGCCTTTAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACAATAGCCTGGTG GAGGTGAATCTGGCAGCCTGTATGGCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCTGTCTTTAACAATCTGACC AGGTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTGTCCATCCTGCGCCTGTCTACAATGCCATCAGC CACATCGCCGAGGGCGCTTTAAGGGCTGAAGAGCCTGAGGGTGGTGGATCTGGACCAACAAGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCTTACAGGCCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCTTCTCTGGCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTGGCCAGATGAAGAATCTGAAGGAGCTGTACATCAGCTCCGAG AGCTTCTGTGCGACTGTCAGCTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGCAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCGTGTGCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCACCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCGCTTAGCTCTCTAGCCCCATGACCTTCGCTGGAGAGATACAGAGGTG CTGGCCAATGCCGACATGGAGAATTCGCCACGTGAGAGCCAGGATGGCGAAGTGTGAGGATATACCACA ATCCTGCACCTGCGGCACGTGACCTTGGCCACGAGGGCAGATACCAGTGCATCATCACAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGCAGCAACCGGACACCCAAACCCCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGGAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGGCGTGTACTCTGCACCGCAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGAAGGCCACCGGCTCTCCAACACCAAGGATCACCTGGCTGAAG GGCGGCAGGCCCTGAGCCTGACAGAGGCCACCACTTACCCCTGGCAATCAGTGTGTTGGTGCAGAAC GTGATGATCGATGACCGCGCAGGTATACATGCGAGATGAGCAATCTCTGGGCACCGAGAGGGCACACTCC CAGCTGTCTATCTGCCTACCCAGGCTGCGGAAGGATGGCACCACA

- [0022] 본 발명에서, "면역글로불린 Fc 영역"은, 면역글로불린의 중쇄와 경쇄 가변영역을 제외한, 중쇄 불변영역 2(CH2) 및/또는 중쇄 불변영역 3(CH3) 부분을 포함하는 부위를 의미한다. 상기 면역글로불린 Fc 영역은 본 발명의 단백질 결합체의 모이어티를 이루는 일 구성일 수 있다.
- [0023] 본 발명에서 상기 면역글로불린 Fc 영역은 중쇄 불변영역에 힌지(hinge) 부분을 포함함으로써 최종 제조될 융합 단백질의 구조적 유연성(flexibility)에 영향을 줄 수 있고, 융합 단백질의 생산성 및 안정성을 보다 높일 수 있으나, 이에 제한되는 것은 아니다.
- [0024] 또한 본 발명의 면역글로불린 Fc 영역은 천연형과 실질적으로 동등하거나 향상된 효과를 갖는 한, 면역 글로불린의 중쇄와 경쇄 가변영역만을 제외하고, 일부 또는 전체 중쇄 불변영역 1(CH1) 및/또는 경쇄 불변영역 1(CL1)을 포함하는 확장된 Fc영역일 수 있다. 또한, CH2 및/또는 CH3에 해당하는 상당히 긴 일부 아미노산 서열이 제거된 영역일 수도 있다.
- [0025] 예컨대, 본 발명의 면역글로불린 Fc 영역은 1) CH1 도메인, CH2 도메인, CH3 도메인 및 CH4 도메인, 2) CH1 도메인 및 CH2 도메인, 3) CH1 도메인 및 CH3 도메인, 4) CH2 도메인 및 CH3 도메인, 5) CH1 도메인, CH2 도메인, CH3 도메인 및 CH4 도메인 중 1개 또는 2개의 이상의 도메인과 면역글로불린 힌지 영역(또는 힌지 영역의 일부)와의 조합, 6) 중쇄 불변 영역 각 도메인과 경쇄 불변영역의 이량체일 수 있다. 그러나, 이에 제한되는 것은 아니다.
- [0026] 또한, 본 발명의 면역글로불린 Fc 영역은 천연형 아미노산 서열뿐만 아니라 이의 서열 유도체를 포함한다. 아미노산 서열 유도체란 천연 아미노산 서열 중의 하나 이상의 아미노산 잔기가 결실, 삽입, 비보전적 또는 보전적 치환 또는 이들의 조합에 의하여 상이한 서열을 가지는 것을 의미한다.
- [0027] 예를 들면, IgG Fc의 경우 결합에 중요하다고 알려진 214 내지 238, 297 내지 299, 318 내지 322 또는 327 내지 331번째 아미노산 잔기들이 변형을 위해 적당한 부위로서 이용될 수 있다.
- [0028] 또한, 이항화 결합을 형성할 수 있는 부위가 제거되거나, 천연형 Fc에서 N-말단의 몇몇 아미노산이 제거되거나 또는 천연형 Fc의 N-말단에 메티오닌 잔기가 부가될 수도 있는 등 다양한 종류의 유도체가 가능하다. 또한, 이펙터 기능을 없애기 위해 보체결합부위, 예로 C1q 결합부위가 제거될 수도 있고, ADCC (antibody dependent

cell mediated cytotoxicity) 부위가 제거될 수도 있다. 이러한 면역글로불린 Fc 영역의 서열 유도체를 제조하는 기술은 국제특허공개 제WO 97/34631호, 국제특허공개 제96/32478호 등에 개시되어 있다.

[0029] 분자의 활성을 전체적으로 변경시키지 않는 단백질 및 펩타이드에서의 아미노산 교환은 당해 분야에 공지되어 있다(H.Neurath, R.L.Hill, The Proteins, Academic Press, New York, 1979). 가장 통상적으로 일어나는 교환은 아미노산 잔기 Ala/Ser, Val/Ile, Asp/Glu, Thr/Ser, Ala/Gly, Ala/Thr, Ser/Asn, Ala/Val, Ser/Gly, Thy/Phe, Ala/Pro, Lys/Arg, Asp/Asn, Leu/Ile, Leu/Val, Ala/Glu, Asp/Gly 간의 교환이다. 경우에 따라서는 인산화(phosphorylation), 황화(sulfation), 아크릴화(acrylation), 당화(glycosylation), 메틸화(methylation), 파네실화(farnesylation), 아세틸화(acetylation) 및 아미드화(amidation) 등으로 수식(modification)될 수도 있다.

[0030] 상기 기술한 Fc 유도체는 본 발명의 Fc 영역과 동등한 생물학적 활성을 나타내며 Fc 영역의 열, pH 등에 대한 구조적 안정성을 증대시킨 것일 수 있다.

[0031] 또한, 이러한 Fc 영역은 인간, 소, 염소, 돼지, 마우스, 래빗, 햄스터, 랫트 또는 기니아 피그 등의 동물의 생체 내에서 분리한 천연형으로부터 얻어질 수도 있고, 형질 전환된 동물세포 또는 미생물로부터 얻어진 재조합형 또는 이의 유도체일 수 있다. 여기서, 천연형으로부터 획득하는 방법은 전체 면역글로불린을 인간 또는 동물의 생체로부터 분리한 후, 단백질 분해효소를 처리하여 획득하는 방법일 수 있다. 파파인으로 처리할 경우에는 Fab 및 Fc로 절단되고, 펩신으로 처리할 경우에는 pF'c 및 F(ab)2로 절단된다. 크기 배제 크로마토그래피(size-exclusion chromatography) 등을 이용하여 Fc 또는 pF'c를 분리할 수 있다. 더 구체적인 실시 형태에서는 인간 또는 마우스 유래의 Fc 영역을 미생물로부터 수득한 재조합형 면역글로불린 Fc 영역이다.

[0032] 또한, 면역글로불린 Fc 영역은 천연형 당쇄, 천연형에 비해 증가된 당쇄, 천연형에 비해 감소한 당쇄 또는 당쇄가 제거된 형태일 수 있다. 이러한 면역글로불린 Fc 당쇄의 증감 또는 제거에는 화학적 방법, 효소학적 방법 및 미생물을 이용한 유전 공학적 방법과 같은 통상적인 방법이 이용될 수 있다. 여기서, Fc에서 당쇄가 제거된 면역글로불린 Fc 영역은 보체(c1q)와의 결합력이 현저히 저하되고, 항체-의존성 세포독성 또는 보체-의존성 세포독성이 감소 또는 제거되므로, 생체 내에서 불필요한 면역 반응을 유발하지 않는다. 이런 점에서 약물의 캐리어로서의 본래의 목적에 보다 부합하는 형태는 당쇄가 제거되거나 비당쇄화된 면역글로불린 Fc 영역이라 할 것이다.

[0033] 본 발명에서 "당쇄의 제거(Deglycosylation)"는 효소로 당을 제거한 Fc 영역을 말하며, 비당쇄화(Aglycosylation)는 원핵동물, 더 구체적인 실시 형태에서는 대장균에서 생산하여 당쇄화되지 않은 Fc 영역을 의미한다.

[0034] 한편, 면역글로불린 Fc 영역은 인간 또는 소, 염소, 돼지, 마우스, 래빗, 햄스터, 랫트, 기니아 피그 등의 동물 유래일 수 있으며, 바람직한 일 예시로 인간 또는 마우스 유래일 수 있다.

[0035] 또한, 본 발명의 면역글로불린 Fc 영역은 IgG, IgA, IgD, IgE, IgM 유래 Fc 영역, 중쇄 불변영역 2(CH2), 중쇄 불변영역 3(CH3), 힌지(hinge), 이의 단편, 또는 이들의 조합(combination), 또는 이들의 조합을 포함하는 하이브리드 Fc(hybrid Fc)일 수 있다.

[0036] 한편, 본 발명에서 "조합(combination)"이란 이량체 또는 다량체를 형성할 때, 동일 기원 단쇄 면역글로불린 Fc 영역, 중쇄 불변영역 2(CH2) 또는 중쇄 불변영역 3(CH3)을 코딩하는 폴리펩타이드가 상이한 기원의 단쇄 폴리펩타이드와 결합을 형성하는 것을 의미한다. 즉, IgG, IgA, IgM, IgD 또는 IgE 유래의 Fc 영역, 중쇄 불변영역 2(CH2) 또는 중쇄 불변영역 3(CH3)으로부터 선택된 2개 이상의 단편으로부터 이량체 또는 다량체의 제조가 가능하다.

[0037] 본 발명에서 상기 "하이브리드 Fc"는 인간 IgG 서브클래스의 조합 또는 인간 IgD 및 IgG의 조합으로부터 유도될 수 있다. 하나의 실시예에서, 상기 하이브리드 Fc는 예를 들어, IgD 힌지 영역 및 CH2 N-말단 영역 + IgG4 CH2 및 CH3 영역을 포함할 수 있으며, 예를 들어, 한국등록특허 제0897938호에 개시된 하이브리드 Fc 형태를 동일하게 차용하여 사용할 수 있고, 본 명세서에 참조로서 도입된다. 본 발명에서 상기 하이브리드 Fc는 생물학적 활성 분자, 폴리펩타이드 등에 결합하는 경우, 생물학적 활성 분자의 혈청 반감기를 증가시킬 뿐만 아니라 Fc-폴리펩타이드 융합 단백질을 코딩하는 뉴클레오타이드가 발현될 때 폴리펩타이드의 발현 수준을 높이는 효과가 있다.

[0038] 본 발명의 일 예시로 상기 면역글로불린 Fc 영역은 IgG, IgA, IgM, IgD 또는 IgE 유래의 Fc 영역이거나, 혹은 상기 IgG, IgA, IgM, IgD 또는 IgE 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함할 수

있으나, 이에 제한되는 것은 아니다.

[0039] 본 발명의 일 예시로 상기 면역글로불린 Fc 영역은 인간 혈액에 가장 풍부한 IgG 또는 IgM 유래 Fc 영역이거나, 혹은 상기 IgG 또는 IgM 유래 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함할 수 있고, 다른 예시로 리간드 결합 단백질의 반감기를 향상시키는 것으로 공지된 IgG 유래 Fc 영역이거나, 혹은 상기 IgG 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함할 수 있고, 또 다른 예시로 IgG1, IgG2, IgG3 또는 IgG4 유래 Fc 영역이거나, 혹은 상기 IgG1, IgG2, IgG3 또는 IgG4 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함할 수 있으며, 또 다른 예시로 IgG1 또는 IgG2 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함할 수 있다.

[0040] 본 발명에서 바람직한 예시로서 상기 면역글로불린 Fc 영역은 서열번호 5로 표시되는 인간 IgG1 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함하거나, 서열번호 6으로 표시되는 마우스 IgG2 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함할 수 있으나, 이에 제한되는 것은 아니다(하기 표 3 참조).

표 3

서열목록	서열정보
서열번호 5	LFPPKPKDLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSPGK
서열번호 6	IFPPKIKDVLMISSLPIVTCVVVDVSEDDPDVQISWFWNNVEVHTAQTQTHREDYNSLTVVVSALPIQHQQDWMMSGKEFKCKVNNKDLPAPIERTISKPKGSRAPQVYVLPPEEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHEGLHNHHTTKSFSRTPGK

[0043] 본 발명의 일 예시로, 상기 면역글로불린 Fc 영역은 IgG, IgA, IgM, IgD, IgE, 또는 아바타셉트(Abatacept) 유래의 힌지 영역을 포함할 수 있고, 또 다른 예시로 IgG, IgD 또는 아바타셉트(Abatacept) 유래의 힌지 영역을 포함할 수 있으며, 혹은 IgG1, IgG2, IgG3, IgG4, IgD 또는 아바타셉트(Abatacept) 유래의 힌지 영역을 포함할 수 있으나, 이에 제한되는 것은 아니다.

[0044] 본 발명에서 바람직한 예시로서 상기 면역글로불린 Fc 영역은 서열번호 7로 표시되는 인간 IgG1 유래의 힌지 영역; 서열번호 8로 표시되는 마우스 IgG2 유래의 힌지 영역; 서열번호 9로 표시되는 인간 IgD 유래의 힌지 영역; 및 서열번호 10으로 표시되는 아바타셉트(Abatacept)의 힌지 영역;으로 이루어진 군에서 선택된 1종 이상을 포함함으로써(하기 표 4 참조) 최종 제조될 융합 단백질의 구조적 유연성(flexibility)을 높이고, 융합 단백질의 생산성 및 안정성을 현저히 향상시킬 수 있으나, 이에 제한되는 것은 아니다.

표 4

서열목록	서열정보
서열번호 7	EPKSSDKTHTSPPCPAPELLGGPSVF
서열번호 8	EPRGPTIKPCPPCKCPAPNLLGGPSVF
서열번호 9	RNTGRGGEKKKEKEKEEQEERETKTPECPSHTQPLGVF
서열번호 10	EPKSSDKTHTSPSPAPELLGGSSVF

[0047] 본 발명에서 상기 Lrig-1 단백질의 세포 외 도메인과 Fc 영역이 링커를 통해 연결되는 경우, 상기 링커는 Fc 단편의 N-말단, C-말단 또는 유리기 (free radical)에 연결될 수 있고, Lrig-1 단백질의 세포 외 도메인의 N-말단, C-말단 또는 유리기에 연결될 수 있다. 링커가 펩타이드 링커인 경우, 연결은 임의의 부위에서 일어날 수 있다. 예를 들면, 상기 링커는 상기 Lrig-1 단백질의 세포 외 도메인의 C-말단 및 상기 면역글로불린의 Fc 영역의 N-말단에 연결될 수 있고, 혹은 상기 면역글로불린의 Fc 영역의 C-말단 및 상기 Lrig-1 단백질의 세포 외 도메인의 N-말단에 연결될 수 있다.

[0048] 본 발명에서 상기 "링커(linker)"는 융합 단백질 내 Lrig-1 단백질의 세포 외 도메인과 면역글로불린 Fc 영역 사이의 간섭 효과를 줄여 타겟 세포에서 상기 Lrig-1 단백질의 세포 외 도메인의 목적하는 활성을 높일 수 있다. 또한, 본 발명에서 상기 링커는 목적하는 질환의 조직 또는 세포 내에서 과발현되는 효소에 의해 절단될 수 있는 서열을 포함할 수 있다. 상기과 같이 과발현되는 효소에 의해 절단될 수 있는 경우에는 Fc 부분으로 인하여 폴리펩타이드의 활성이 저하되는 것을 효과적으로 방지할 수 있다.

[0049] 본 발명의 일 예시로서 상기 링커는 1 내지 100개의 아미노산을 갖는 것이 바람직하나, 이에 제한되지는 않으며, Lrig-1 단백질의 세포 외 도메인과 면역글로불린 Fc 영역을 분리시킬 수 있는 어떠한 펩타이드라도 가능하다. 상기 링커를 구성하는 아미노산 서열에는 특별한 제한은 없으나, 글라이신(G) 및 세린(S)을 포함하거나, 이들을 반복적으로 또는 무작위적 패턴으로 포함하는 것이 바람직하다. 그러한 예로서, 상기 링커는 서열번호 11로 표시되는 펩타이드 링커; 및 서열번호 12로 표시되는 펩타이드 링커; 중 적어도 하나를 포함할 수 있고, 혹은 (GGGS)_N(N은 1 이상의 정수, 바람직하게는 1 내지 20의 정수임)의 아미노산 서열을 포함함으로써(하기 표 5 참조), 세포 내 활성 물질의 안정성을 높이고, 생산성을 보다 향상시킬 수 있다.

표 5

서열목록	서열정보
서열번호 11	GS
서열번호 12	GGG

[0052] 또한, 본 발명에서 상기 링커의 일 예시로, 혈액 내에 가장 많이 존재하는 인간 알부민의 282번 내지 314번째 부분에 위치한 33개의 아미노산으로 이루어진 펩타이드 링커, 보다 바람직하게는 292번 내지 304번째 부분에 위치한 13개의 아미노산으로 이루어진 펩타이드 링커일 수 있으며, 이러한 부분은 3차원적인 구조상 대부분 외부에 노출된 부분으로서 체내에서 면역반응을 유도할 가능성이 최소화된 부분이다. 단, 이에 제한되는 것은 아니다.

[0053] 또한, 본 발명에서 상기 링커 및 Fc 영역이 별개로 발현된 후에 서로 결합될 때, 링커는 당업계에 알려진 가교제일 수 있다. 상기 가교제는, 예를 들어, 1,1-비스(디아조아세틸)-2-페닐에탄 (1,1-bis(diazoacetyl)-2-phenylethane), 글루타르알데하이드 (glutaraldehyde), 4-아지도살리실릭산 (4-azidosalicylic acid)과 같은 N-하이드로옥시석신이미드 에스테르 (N-hydroxysuccinimide ester), 3,3'-디사이오비스(석신이미딜프로피오네이트) (3,3'-dithiobis(succinimidylpropionate))와 같은 디석신이미딜에스테르 (disuccinimidyl esters)를 포함하는 이미도에스테르 (imidoesters), 및 비스-N-말레이미도-1,8-옥테인과 같은 이중 기능적 말레이미드 (bifunctional maleimides)일 수 있으나, 이에 제한되는 것은 아니다.

[0054] 본 발명에서 제공하는 융합 단백질의 일 예시는 상기 서열번호 1로 표시되는 Lrig-1 단백질의 세포 외 도메인; 서열번호 7 내지 10 중 어느 하나로 표시되는 힌지 영역; 서열번호 5로 표시되는 인간 IgG1 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함하는 융합 단백질일 수 있다(하기 표 6 참조). 하기 표 6의 서열번호 13 내지 16으로 표시되는 융합 단백질은 하기 표 7의 서열번호 17 내지 20으로 표시되는 핵산 서열에 의해 코딩될 수 있다(하기 표 7 참조)

표 6

서열목록	서열정보
서열번호 13	AGPRAPCAAACCTCAGDSLDCGGRGLAALPGDLPSTWTRSLNLSYNKLSEIDPAGFEDLPNLQEVYLNNNELTA VPSLGAASSHVVSFLQHNKIRSVESGSQLKAYLSLEVLDLSLNNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVLKLQRNNISKL TDGAFWGLSKMHVLHLEYNSLEVNSGSLYGLTALHQLHLNNISARIHRKGWSFCQKLHELVLSENNLTRL DEESLAELSSLSVLRSLSHNSISHIAEGAFKGLRSLRVLDLHNEISGTIEDTSGAFSGLDLSKLTFLGKNI KSVAKRAFSGLEGLHLNLGGNAIRSVQFADFVKMKNLKELHISSDSFLCDCQLKWLPWWLIGRMLQAFVTA TCAHPESLKGQSIFSVPPESFVCDLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKDNEVLT NADMFNFVHVAQDGEVMEYTTILHLRQVTFGHEGRYQCVITNHFGSTYSHKARLTNVNLPSTFTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGDTDFPAARERRMHVMPDDVFFITDVKIDDAGVYSCTAQSAGSIS ANATLTVLETPSLVPLEDRVSVGETVALQCKATGNPPPRITWFKGDRPLSLTERHHLTPDNQLLVVQNVV AEDAGRYTCEMSNTLGTERRAHSQSVLPAAAGCRKDGTTVGIF EPKSSDKTHTSPPCPAPELLGGPSVF LFPPKPKDTLMSRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMEALHNHYTQKSLSLSPGK

서열번호 14	AGPRAPCAAACTCAGDSLDCGGRGLAALPGDLPWTRSLNLSYNKLSEIDPAGFEDLPNLQEVYLNNNELTA VPSLGAASSHVSLFLQHNRIRSVEGSQLKAYLSLEVLDLNLNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVCLKQRNNISKL TDGAFWGLSKMHVLHLEYNLSLEVNSGSLYGLTALHQLHLNNIARIHRKGWSFCQKLHELVLSENNLTRL DEESLAELSSLVLRLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDLSKLTFLGKNI KSAKRAFSGLEGLEHLNLGGNAIRSVQFADFVKMKNLKELHISSDSFLCDCQKWLPPWLGRLQAFVTA TCAHPESLKGQSIFSVPPESFVCDDFLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKDNEVLT NADMFNFVHVAQDGEVMEYTTILHLRQVTFGHEGRYQCVITNHFGSTYSHKARLTNNVLPSTFTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDVFFITDVKIDDAGVYCTAQNAGSIS ANATLTVLETPSLVPLEDRVVSGETVALQCKATGNPPRITWFKGDRPLSLTERHHLTPDNQLLVQNVV AEDAGRYTCEMSNTLGTERRAHSQSVLPAAGCRKDGTTVGIF EPRGPTIKPCPPCKCPAPNLLGGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK
서열번호 15	AGPRAPCAAACTCAGDSLDCGGRGLAALPGDLPWTRSLNLSYNKLSEIDPAGFEDLPNLQEVYLNNNELTA VPSLGAASSHVSLFLQHNRIRSVEGSQLKAYLSLEVLDLNLNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVCLKQRNNISKL TDGAFWGLSKMHVLHLEYNLSLEVNSGSLYGLTALHQLHLNNIARIHRKGWSFCQKLHELVLSENNLTRL DEESLAELSSLVLRLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDLSKLTFLGKNI KSAKRAFSGLEGLEHLNLGGNAIRSVQFADFVKMKNLKELHISSDSFLCDCQKWLPPWLGRLQAFVTA TCAHPESLKGQSIFSVPPESFVCDDFLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKDNEVLT NADMFNFVHVAQDGEVMEYTTILHLRQVTFGHEGRYQCVITNHFGSTYSHKARLTNNVLPSTFTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDVFFITDVKIDDAGVYCTAQNAGSIS ANATLTVLETPSLVPLEDRVVSGETVALQCKATGNPPRITWFKGDRPLSLTERHHLTPDNQLLVQNVV AEDAGRYTCEMSNTLGTERRAHSQSVLPAAGCRKDGTTVGIF RNTGRGGEKKKEKEKEEQEERETKTPECSHTQPLGVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK
서열번호 16	AGPRAPCAAACTCAGDSLDCGGRGLAALPGDLPWTRSLNLSYNKLSEIDPAGFEDLPNLQEVYLNNNELTA VPSLGAASSHVSLFLQHNRIRSVEGSQLKAYLSLEVLDLNLNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVCLKQRNNISKL TDGAFWGLSKMHVLHLEYNLSLEVNSGSLYGLTALHQLHLNNIARIHRKGWSFCQKLHELVLSENNLTRL DEESLAELSSLVLRLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDLSKLTFLGKNI KSAKRAFSGLEGLEHLNLGGNAIRSVQFADFVKMKNLKELHISSDSFLCDCQKWLPPWLGRLQAFVTA TCAHPESLKGQSIFSVPPESFVCDDFLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKDNEVLT NADMFNFVHVAQDGEVMEYTTILHLRQVTFGHEGRYQCVITNHFGSTYSHKARLTNNVLPSTFTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDVFFITDVKIDDAGVYCTAQNAGSIS ANATLTVLETPSLVPLEDRVVSGETVALQCKATGNPPRITWFKGDRPLSLTERHHLTPDNQLLVQNVV AEDAGRYTCEMSNTLGTERRAHSQSVLPAAGCRKDGTTVGIF EPKSSDKTHTSPSPAPELLGGSSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK

표 7

[0057]

서열목록	서열정보
서열번호 17	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCCTGGACCCGGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggcgctgcttcatcacatgtcgtctctctcttctgcagcacaacaagattcgcagcgtg gaggggagccagctgaaggcctaccttcccttagaagtgttagatctgagtttgaacaacatcacggaagtgc cggaacacctgcttccacacggaccgctataaaggagctcaacctggcaggcaatcggtatggcacctg gagttgggagcatttgatggctgtcacggctcgtgctaactctcgctgagcaaaaacaggatcaccag cttccctgtaagagcattcaagctaccaggctgacacaactggacctcaatcggaacaggatcggctgata gagggcctcaccttccaggggctcaacagcttggaggtgctgaagcttcagcgaacaacatcagcaactg acagatggggccttctggggactgtccaagatgcatgtctgcacctggagtacaacagcctggtagaagtgc aacagcggctcgtctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgcat caccgcaagggtggagcttctgccagaagctgcatgagttggtcctgtccttcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcgtcgtcagccacaattccatcagccacatt gaggaggggtgcttcaagggaactcaggagcctgcagtgcttggtatctggaccataacgagatttcgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgttggaaacaagatc aagctctgtggctaagagagcattctcggggctggaaggcctggagcactgaaccttggagggaatgcgac agatctgtccagtttgatgcctttgtgaagatgaagaatcttaagagctccatcagcagcgacagcttc ctgtgtgactgccagctgaagtggtgccccgtggctaatggcaggatgctgcaggcctttgtgacagcc acctgtgccaccaggaatcactgaagggtcagagcatttctctgtgccaccagagagtttctgtgagat gacttctgaagccacagatcatcaccagccagaaaccacatggctatggtgggcaaggacatccggttt acatgctcagcagccagcagcagcagctccccatgacctttgcctggaagaagacaatgaagtcctgacc aatgcagacatggagaactttgtccacgtccacgcgaggaagggaagtgatggagtacaccacctcctg cacctcgtcaggtcacttccggcagcagggcgctaccaatgtgcatcaccaaccactttggctccacc tattcacataaaggccaggtcacctgaatgtgttgccatcattcaccaaaacgccccacgacataaacatc cggaccaccaccgtggcccgctcgaatgtgtgccacaggtcaccaaacctcagattgcctggcagaag gatggaggcacggatttccccgtgccctgagcagcagcatgcatgtcatgccggatgacgacgtgttttc atcactgatgtgaaatagatgacgcagggtttacagctgactgctcagaactcagccggttctatttca gctaatgccacctgactgtctagagaccctccttgggtggtcccttgggaagaccgtgtggtatctgtg ggagaaacagtggcctccaatgcaaagccacggggaaccctcgccccgcatcacctggttcaagggggac cgcccgctgagcctcactgagcggcaccacctgacccctgacaaccagctcctgggtggttcagaacgtgggtg gcagaggatgcgggccgatatacctgtgagatgtccaacacctgggcacggagcgagctcacagccagctg agcgtcctgcccgcagcaggtgcaggaaggatgggaccaggtaggcatctc GAGCCAAAGTCCTCTGATAAGACACACACCTCTCCACCATGCCAGCACCAGAGCTGCTGGGAGGACCAAGC GTGTTCTC CTGTTTCCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGAC GTGAGCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTACCTATAGGGTGGTGAGCGTGCTGACAGTGCTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGAGTGAGGTGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTACGTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 18	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCCTGGACCCGGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggctgcttcatcacatgtcgtctctctcttctcagcacaacaagattcgcagcgtg gaggggagccagctgaaggcctaccttcccttagaagtgttagatctgagtttgaacaacatcacggaagtg cggaacacctgcttccacacggaccgctataaaggagctcaacctggcaggcaatcggaattggcaccctg gagttgggagcatttgatggctgtcacggctcgtgctaactcttcgctgagcaaaaacaggatcaccag cttctgtgaagagcattcaagctaccaggtgacacaactggacctcaatcggaacaggatctggctgata gagggcctcaccttccaggggctcaacagcttggaggtgctgaagcttcagcgaaacaacatcagcaactg acagatggggccttctggggactgtccaagatgcatgtgctgcacctggagtacaacagcctggtagaagtg aacagcggctcgtctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgctt caccgaagggtggagcttctgccagaagctgcatgagttggtcctgtcctcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcctgctctcagccacaattccatcagccacct gaggagggtgccttcaaggagctcaggagcctgcgagcttggtatggaccataacagagatttcgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgtttggaaacaagatc aagctctgtggctaagagagcattctcggggctggaaggcctggagcacctgaaccttggagggaatgcgac agatctgtccagtttgatgcctttgtgaagatgaagaatctaaagagctccatcagcagcgacagcttc ctgtgtgactgccagctgaagtggtgccccgtggctaatggcaggatgctgcagccttctgtgacagcc acctgtgcccaccagaatcactgaagggtcagagcatttctctgtgccaccagagagtttctgtgcat gacttctgaagccacagatcatcaccagccagaaccaccatggctatggtgggcaaggacatccggtt acatgctcagcagccagcagcagcagctccccatgaccttgcctggaagaaagacaatgaagtcctgacc aatgcagacatggagaacttctccacgtccacgcgcaggacggggaagtgatggagtacaccaccatcctg cacctccgtcaggtcacttccgggcacgagggcctaccaatgtgtcatcaccaaccacttggctccacc tattacataaaggccagctcaccgtgaatgtgttgccatcattcaccaaaacgccccacgacataaccatc cggaccaccaccgtggcccgctcgaatgtgctgccacaggtcaccaaacctcagattgcctggcagaag gatggaggcacggatttccccgctgcccgtagcgacgcatgcatgtcatgccggatgacgacgtgttttc atcactgatgtgaaaatagatgacgcagggtttacagctgtactgctcagaactcagccggttctatttca gctaattgccaccctgactgtcctagagaccccatccttgggtggtcccttgggaagaccgttggtatctgtg ggagaaacagtggcctccaatgcaaagccacggggaacctcgcgcccgcatcacctggttcaagggggac cgcccgctgagcctcactgagcggcaccacctgaccttgacaaccagctcctggtggttcagaacgtggtg gcagaggatgcgggcccgatatacctgtgagatgtccaacacctgggcacggagcagctcacagccagctg agcgtcctgcccgcagcaggctgcaggaaggatgggaccacggtaggcatcttc Gagcctcggggcctaccatcaagccctgcccccttgcaagtgcctgccctaatctgctgggcggacc tccgtgttc CTGTTTCCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGGAC GTGAGCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTACCTATAGGGTGGTGAGCGTGCTGACAGTGCTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTAGCTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 19	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCCTGGACCCGGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggcgtgcttcatcacatgtcgtctctctcttctcagcacacaagaattcgcagcgtg gaggggagccagctgaaggcctaccttcccttagaagtgttagatctgagtttgaacaacatcacggaagtg cggaacacctgcttccacacggaccgcctataaaggagctcaacctggcaggcaatcggaattggcaccctg gagttgggagcatttgatggctgtcacggctcgtgctaactcttcgctgagcaaaaacaggatcaccag cttctgtgaagagcattcaagctaccaggtgacacaactggacctcaatcggaacaggatctggctgata gagggcctcaccttccaggggctcaacagcttggaggtgctgaagcttcagcgaaacaacatcagcaactg acagatggggccttctggggactgtccaagatgcatgtgctgcacctggagtacaacagcctggtagaagtg aacagcggctcgtctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgctt caccgcaagggtggagcttctgccagaagctgcatgagttggtcctgtcctcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcctgctctcagccacaattccatcagccacct gaggagggtgccttcaaggagctcaggagcctgcgagcttggtatcggaacataacagagatttcgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgtttggaaacaagatc aagctctgtggctaagagagcattctcggggctggaaggcctggagcacctgaaccttggagggaatgcgatc agatctgtccagtttgatgcctttgtgaagatgaagaatctaaagagctccatcagcagcgacagcttc ctgtgtgactgccagctgaagtggtgccccgtggctaatggcaggatgctgcagccttctgtgacagcc acctgtgcccaccagaatcactgaagggtcagagcatttctctgtgccaccagagagtttctgtgcat gacttctgaagccacagatcatcaccagccagaaccaccatggctatggtgggaaggacatccggtt acatgctcagcagccagcagcagcagctccccatgaccttgcctggaagaaagacaatgaagtcctgacc aatgcagacatggagaacttctccacgtccacgcgcaggacggggaagtgatggagtacaccaccatcctg cacctccgtcaggtcacttccgggcacgagggcctaccaatgtgtcatcaccaaccacttggctccacc tattacataaaggccaggtcaccgtgaatgtgttgccatcattcaccaaaacgccccacagacataaccatc cggaccaccaccgtggcccgctcgaatgtgctgccacaggtcaccaaacctcagattgcctggcagaag gatggaggcacggatttccccgtgcccgtgagcgacgcatgcatgtcatgccggatgacgacgtgttttc atcactgatgtgaaaatagatgacgcagggtttacagctgtactgctcagaactcagccggttctatttca gctaattgccaccctgactgtcctagagaccccatccttgggtggtcccttgggaagaccgttggtatctgtg ggagaaacagtggcctccaatgcaaagccacggggaacctccgccccgcatcacctggttcaagggggac cgcccgtgagcctcactgagcggcaccacctgaccttgacaaccagctcctggtggttcagaacgtggtg gcagaggatgcgggccgatatacctgtgagatgtccaacacctgggcacggagcagctcacagccagctg agcgtcctgcccgcagcaggctgcaggaaggatgggaccacggtaggcatcttc cgcaacaccggccgcgcgaggagaagaaggagaaggagaaggaggagcaggaggagcgcgagacc aagacccccgagtgccccagccacaccagccccgggcgtgttc CTGTTTCCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGGAC GTGAGCCACGAGGACCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCCAGAGAGGAGCAGTACAACCTTACCTATAGGGTGGTGAGCGTGCTGACAGTGCTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTAGCTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 20	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCCTGGACCCGGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggcgtgcttcatcacatgtcgtctctctcttctcagcacacaagaatcgcagcgtg gaggggagccagctgaaggcctaccttcccttagaagtgttagatctgagtttgaacaacatcacggaagt cggaacacctgcttccacacggaccgcctataaaggagctcaacctggcaggcaatcggatggcaccctg gagttgggagcatttgatggctgtcacggctgctgctaactcttcgctgagcaaaaaacaggatcaccag cttctgtgaagagcattcaagctaccaggtgacacaactggacctcaatcggaacaggatcggctgata gagggcctcacctccaggggctcaacagcttggaggtgctgaagcttcagcgaacaacatcagcaactg acagatggggccttctggggactgtccaagatgcatgtgctgcacctggagtacaacagcctggtagaagt aacagcggctcgctctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgctt caccgaagggtggagcttctgccagaagctgcatgagtggctcctgcttcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgtcctgctctcagccacaattccatcagccacct gaggagggtgccttcaaggagctcaggagcctgcgagcttggatctggagataacagagatttcgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgttggaaacaagatc aagtctgtggctaagagagcattctcggggctggaaggcctggagcacctgaaccttggagggaatgcgatc agatctgtccagtttgatgccttctgaagatgaagaatctaaagagctccatcagcagcgacagcttc ctgtgtgactgccagctgaagtggctgccccctggctaatggcaggatgctgcagccttctgtgacagcc acctgtgcccaccagaatcactgaagggtcagagcatttctctgtgccaccagagagttctgtgctgat gacttctgaagccacagatcatcaccagccagaaccaccatggctatggtgggaaggacatccggtt acatgctcagcagccagcagcagcagctccccatgaccttgcctggaagaagaacaatgaagtccctgacc aatgcagacatggagaacttctccacgtccacgcgcaggacggggaagtgatggagtacaccaccatcctg cacctccgtcaggtcacttccgggcacgaggccgctaccaatgtgtcatcaccaaccacttggctccacc tattacataaaggccagctcaccgtgaatgtgttgccatcattcaccaaaacgccccacagataaccatc cggaccaccaccgtggcccgctcgaatgtgctgccacaggtcaccaaacctcagattgcctggcagaag gatggaggcacggatttccccctgcccgtgagcgacgcatgcatgtcatgccggatgacgacgtgttttc atcactgatgtgaaaatagatgacgcagggtttacagctgtactgctcagaactcagccggttctatttca gctaagccaccctgactgtcctagagaccctccttgggtggctcccttgggaagacagctgtggtatctgtg ggagaaacagtggccctccaatgcaaagccacggggaacctccgccccgcatcacctggttcaagggggac cgcccgctgagcctcactgagcggcaccacctgaccttgacaaccagctcctggtggttcagaacgtggtg gcagaggatgcgggccgatatacctgtgagatgtccaacacctgggcacggagcagctcacagccagctg agcgtcctgcccgcagcaggctgcaggaaggatgggaccacggtaggcatcttc gaaccgaaatcttctgacaaaaccacacctctccgctcctcggtcgggaactgctgggtggttcttct gttttc CTGTTTCCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGGAC GTGAGCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCCAGAGAGGAGCAGTACAACCTTACCTATAGGGTGGTGAGCGTGCTGACAGTGCTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTAGCTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

[0059] 본 발명에서 제공하는 융합 단백질의 일 예시는 상기 서열번호 3로 표시되는 Lrig-1 단백질의 세포 외 도메인; 서열번호 7 내지 10 중 어느 하나로 표시되는 힌지 영역; 서열번호 5로 표시되는 인간 IgG1 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함하는 융합 단백질일 수 있다(하기 표 8 참조). 하기 표 8의 서열번호 21 내지 24로 표시되는 융합 단백질은 각각 하기 표 9의 서열번호 25 내지 28으로 표시되는 핵산 서열에 의해 코딩될 수 있다(하기 표 9 참조)

표 8

[0060]

서열목록	서열정보
서열번호 21	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSLFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RLEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVHLLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLESLEHLNLGENA IRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQSAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT EPKSSDKTHT SPPCAPELL GGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
서열번호 22	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSLFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RLEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVHLLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLESLEHLNLGENA IRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQSAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT EPRGPTIKPCPPCKCAPNLLGGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
서열번호 23	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSLFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RLEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVHLLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLESLEHLNLGENA IRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQSAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT RNTGRGGEKKKEKEKEEEREKTKTPECPSHTQPLGVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
서열번호 24	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSLFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RLEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVHLLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLESLEHLNLGENA IRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQSAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT EPKSSDKTHTSPSPAPELLGGSSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK

표 9

[0062]

서열목록	서열정보
서열번호 25	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGCCGGGG CCTGGCCACACTGCCCAGGGACCTGCCTTCCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTGTCCGAGATCG ATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTATCTGAACAGCAATGAGCTGACCGCAATCCCCTCC CTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTCTGCAGCACAACAAGATCCTGAGCGTGAGTGCCAGCT GAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACCGAGATCAGATCTAGCTGTTTTCTA ATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGCATCTGGAGTCCGGCGCCTTCGATGGCCTG AGCAGATCCCTGCTGACACTGCGCCTGTCCAAGAACCAGATCACCCAGCTGCCGTGAAGGCTTTAAGCTGCCTAG GCTGACACAGCTGGACCTGAACCGGAATAGAATCAGGCTGATCGAGGGCTGACCTCCAGGGCTGGATAGCCTGG AGGTGCTGCGCTGCAGCGGAACAATATCTCCGCTGACAGACGGAGCATTTTGGGGCTGTCTAAGATGCACGTG CTGCACCTGGAGTACAATAGCCTGGTGGAGGTGAATCTGGCAGCCTGTATGGCCTGACCGCCTGCACAGCTGCA CCTGTCCAACAATAGCATCAGCAGAATCCAGAGGATGGCTGGTCTCTGCCAGAGCTGCACAGCTGATCCTGT CTTTTAAATCTGACAGGCTGGACGAGGAGAGCTGGCAGAGCTGTCTCTCTGTCCATCCTGCGCCTGTCTCAC AATGCCATCAGCCACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCTGAGGGTGTGGATCTGGACCACAACGA GATCTCTGGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCTGGACAATCTGTCCAAGCTGACCTGTTTGGCA ACAAGATCAAGTCTGTGGCCAAGCGGGCCTTCTCTGGCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAATGCC ATCAGATCCGTGCAGTTCGATGCCTTTGCCAAGATGAAGAATCTGAAGGAGCTGTACATCAGCTCCGAGAGCTTCT GTGCGACTGTGAGTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGCAGGCTTTGTGACCGCCACATGCG CCCACCCAGAGAGCTGAAGGGCAGAGCATCTTCCGTGCTGCCGATAGCTTCGTGTGCGACGATTTTCCCTAAG CCACAGATCATCACCCAGCCAGAGACAACAATGGCGTGGTGGGCAAGGACATCCGGTTTACATGTTCCGCGCCTC TAGCTCCTTAGCCCCATGACCTTCGCTGGAAGAAGGATAACGAGGTGCTGGCCAATGCCGACATGGAGAATTCG CCCACGTGAGAGCCAGGATGGCGAAGTGATGGAGTATACCACAATCCTGCACCTGCGGCACGTGACCTTTGGCCAC GAGGGCAGATACCAGTGATCATCACAAATCACTTCGGCTCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGT GCTGCCTAGCTTTACCAAGATCCACACGACATCGCCATCAGAACAGGACCCACAGCAAGGCTGGAGTGTGCAGCAA CCGGACACCCAAACCTCAGATCGCATGGCAGAAGGATGGAGGCACAGACTTCCTGTCAGCCCGGAGAGGAGAATG CACGTGATGCCAGACGATGACGTGTTCTTTATCAGATGTGAAGATCGATGACATGGGCGTGTACTCCTGCACCGC ACAGAACAGCGCCGCGCAGCGTGTCCGCCAACGCCACCTGACCGTGCTGGAGACACCATCCTGGCCGTGCCCTGG AGGACAGGGTGGTGACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGCTCTCCAACACCAAGGATCACC TGGCTGAAGGGCGGCAGGCCCTGAGCCTGACAGAGCGCCACCACTTCACCCCTGGCAATCAGCTGCTGGTGGTGCA GAACGTGATGATCGATGACGCCGCGCAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCCC AGCTGTCTATCCTGCCTACCCAGGCTGCCGAAGGATGGCACCACA GAGCCAAAGTCCTCTGATAAGACACACACCTCTCCACCATGCCAGCACCAGAGCTGCTGGGAGGACCAAGCGTGT C CTGTTTCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGACGTGAG CCACGAGGACCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGAGGTGCACAATGCCAAGACCAAGCCAGAG AGGAGCAGTACAATCTACCTATAGGGTGGTGAGCGTGCTGACAGTGTGACACAGGACTGGCTGAACGGCAAGGAG TATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCCAAGGCCAAGGGCCAGCCAAG AGAGCCCAGGTGTACACCTGCCCCCTAGCAGGGATGAGCTGACAAAGAACCAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGCCAGCCTGAGAATAACTACAAGACAACCCCA CCCGTGTGGATTCTGACGGCAGCTTCTTTCTGATTCTAAGCTGACCGTGGACAAGAGCAGGTGACGAGGGCAA CGTGTTCAGCTGCTCCGTGATGCACGAAGCACTGCACAATCACTACCCAGAAATCACTGTCACTGAGCCCTGGCA AA

서열번호 26	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGCCGGGG CCTGGCCACACTGCCCAGGGACCTGCCTTCCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTGTCCGAGATCG ATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTGACCGCAATCCCTCC CTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTTGACGACAACAAGATCCTGAGCGTGGATGGCTCCAGCT GAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACCGAGATCAGATCTAGCTGTTTTCTA ATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGCATCCTGGAGTCCGGCGCCTTCGATGGCCTG AGCAGATCCCTGCTGACACTGCGCCTGTCCAAGAACCAGGATCACCCAGCTGCCGCTGAAGGCCTTTAAGCTGCCCTAG GCTGACACAGCTGGACCTGAACCGAATAGAATCAGGCTGATCGAGGGCCTGACCTTCCAGGGCCTGGATAGCCTGG AGGTGCTGCGCTGCAGCGGAACAATATCTCCGCTGACAGACGAGCATTGTTGGGCTGTCTAAGATGCACGTG CTGCACCTGGAGTACAATAGCCTGGTGGAGGTGAACCTCTGGCAGCCTGTATGGCCTGACCGCCTGCACCAGCTGCA CCTGTCCAACAATAGCATCAGCAGAATCCAGAGGGATGGTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGT CTTTTAACAATCTGACCAGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCTGCGCCTGTCTCAC AATGCCATCAGCCACATCGCCGAGGGCGCCTTTAAGGGCCTGAAGAGCCTGAGGGTGTGGATCTGGACCACAACGA GATCTCTGGCACCATCGAGGATACAAGCGCGCCTTCACAGGCTGGAACAATCTGTCCAAGCTGACCTGTTGGCA ACAAGATCAAGTCTGTGGCAAGCGGCCTTCTCTGGCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAATGCC ATCAGATCCGTGCAGTTCGATGCCTTTGCCAAGATGAAGAATCTGAAGGAGCTGTACATCAGCTCCGAGAGCTTCT GTGCGACTGTCAGTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGAGGGCTTTGTGACCGCCACATGCG CCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCGATAGCTTCGTGTGCGACGATTTTCTTAAG CCACAGATCATCACCCAGCCAGAGACAACAATGGCGTGGTGGCAAGGACATCCGGTTTACATGTTCCGCCGCTC TAGCTCCTCTAGCCCCATGACCTTCGCTGGAAGAAGGATAACGAGGTGCTGGCCAATGCCGACATGGAGAATTCG CCCACGTGAGAGCCAGGATGGCGAAGTGTAGGAGTATACCCACAATCCTGCACCTGGGCAAGTGAACCTTTGGCCAC GAGGGCAGATACCAGTGCATCATCACAATCACTTCGGCTCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGT GCTGCCTAGCTTTACCAAGATCCACACGACATCGCCATCAGAACAGGACCCACAGCAAGGCTGGAGTGTGACAGAA CCGGACACCCAAACCTCAGATCGCATGGCAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATG CACGTGATGCCAGACGATGACGTGTTCTTTATCAGATGTGAAGATCGATGACATGGGCGTGTACTCTGCACCCG ACAGAACAGCGCCGCGCAGCGTGTCCGCCAACGCCACCCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGG AGGACAGGGTGGTGACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGCCACCGCTCTCCAACCAAGGATCACC TGGCTGAAGGGCGCAGGCCCTGAGCCTGACAGAGCGCCACCCTTACCCCTGGCAATCAGTGTCTGGTGGTGCA GAACGTGATGATCGATGACGCCGCGAGGTATACATGCGAGATGAGCAATCCTCTGGGACCCGAGAGGGCACACTCC AGCTGTCTATCCTGCCTACCCAGGCTGCCGAAGGATGGCACCACA Gagcctcggggcctaccatcaagcctgcccccttgaagtgcctgccccctaatctgctggcgccaccctccgt gttc CTGTTTCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGGACGTGAG CCACGAGGACCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGCAAGCCAGAG AGGAGCAGTACAACCTCTACCTATAGGGTGGTGAGCGTGTGACAGTGTGACACAGGACTGGCTGAACGCAAGGAG TATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCCAAGGCCAAGGGCCAGCCAAG AGAGCCCCAGGTGTACCCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAACCAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGCCAGCCTGAGAATAACTACAAGACAACCCCA CCCGTGTGATTCTGACGGCAGCTTCTTTCTGTATTCTAAGCTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAA CGTGTTAGCTGCTCCGTGATGCACGAAGCACTGCACAATCACTACCCAGAAATCACTGTCACTGAGCCCTGGCA AA

서열번호 27	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGCCGGGG CCTGGCCACACTGCCCAGGGACCTGCCCTTCCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTGTCCGAGATCG ATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTGACCGCAATCCCTCC CTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTTGACGACAACAAGATCCTGAGCGTGGATGGCTCCAGCT GAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACCGAGATCAGATCTAGCTGTTTTCTA ATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGCATCCTGGAGTCCGGCGCCTTCGATGGCCTG AGCAGATCCCTGCTGACACTGCCCTGTCCAAGAACCAGGATCACCCAGCTGCCGCTGAAGGCCTTTAAGCTGCCCTAG GCTGACACAGCTGGACCTGAACCGAATAGAATCAGGCTGATCGAGGGCCTGACCTTCCAGGGCCTGGATAGCCTGG AGGTGCTGCGCTGCAGCGGAACAATATCTCCGCTGACAGACGAGCATTGTTGGGCTGTCTAAGATGCACGTG CTGCACCTGGAGTACAATAGCCTGGTGGAGGTGAACCTTGCGAGCCTGTATGGCCTGACCGCCTGCACCGAGCTGCA CCTGTCCAACAATAGCATCAGCAGAATCCAGAGGGATGGTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGT CTTTTAACAATCTGACAGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCTGCGCCTGTCTCAC AATGCCATCAGCCACATCGCCGAGGGCGCCTTTAAGGGCCTGAAGAGCCTGAGGGTGTGGATCTGGACCACAACGA GATCTCTGGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCTGGACAATCTGTCCAAGCTGACCTGTTGGCA ACAAGATCAAGTCTGTGGCAAGCGGCTTCTCTGGCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAATGCC ATCAGATCCGTGCAGTTCGATGCCTTTGCCAAGATGAAGAATCTGAAGGAGCTGTACATCAGCTCCGAGAGCTTCT GTGCGACTGTGAGTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGAGGCTTTGTGACCGCCACATGCG CCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCGATAGCTTCGTGTGCGACGATTTTCTTAAG CCACAGATCATCACCCAGCCAGAGACAACAATGGCCGTGGTGGCAAGGACATCCGGTTTACATGTTCCGCCGCTC TAGCTCCTCTAGCCCCATGACCTTCGCTGGAAGAAGGATAACGAGGTGCTGGCCAATGCCGACATGGAGAATTCG CCCACGTGAGAGCCAGGATGGCGAAGTGTGAGGTATACCCACAATCTGACCTGGGCGACGTGACCTTTGGCCAC GAGGGCAGATACAGTGCATCATCACAATCACTTCGGCTCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGT GCTGCCTAGCTTTACCAAGATCCACACGACATCGCCATCAGAACAGGCACCACAGAAGGCTGGAGTGTGACAGAA CCGGACACCCAAACCTCAGATCGCATGGCAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGGAGAGGAGAATG CACGTGATGCCAGACGATGACGTGTTCTTTATCAGATGTGAAGATCGATGACATGGGCGTGTACTCTGCACCCG ACAGAACAGCGCCGCGAGCGTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGG AGGACAGGGTGGTGACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGCCACCGCTCTCCAACCAAGGATCACC TGGCTGAAGGGCGGAGGCCCTGAGCCTGACAGAGCGCCACCACTTCAACCTGGCAATCAGTGTGTTGGTGCA GAACGTGATGATCGATGACGCCGCGAGGTATACATGCGAGATGAGCAATCCTCTGGGACCCGAGAGGGCACACTCC AGCTGTCTATCTGCCTACCCAGGCTGCCGAAGGATGGCACCACA cgcaacaccggccgcgcgaggagaagaagaaggagaaggagaaggaggagcaggaggagcgcgagaccaagac ccccgagtgcacccagccacaccagccctggcggtgttc CTGTTTCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGGACGTGAG CCACGAGGACCCGAGGTGAAGTTCACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACCAAGCCAGAG AGGAGCAGTACAACCTCTACCTATAGGGTGGTGAGCGTGTGACAGTGTGCACAGGACTGGCTGAACGCAAGGAG TATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCCAAGGCCAAGGGCCAGCCAAG AGAGCCCAGGTGTACCCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAACCAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGCCAGCCTGAGAATAACTACAAGACAACCCCA CCCGTGTGATTCTGACGGCAGCTTCTTCTGTATTCTAAGCTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAA CGTGTTCAGCTGCTCCGTGATGCACGAAGCACTGCACAATCACTACCCAGAAATCACTGTCACTGAGCCCTGGCA AA

서열번호 28	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGCCGGGG CCTGGCCACACTGCCAGGGACCTGCCTTCCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTGTCCGAGATCG ATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTGACCGCAATCCCTCC CTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAACACAAGATCCTGAGCGTGGATGGCTCCAGCT GAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACCGAGATCAGATCTAGCTGTTTTCTA ATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGCATCCTGGAGTCCGGCGCCTTCGATGGCCTG AGCAGATCCCTGCTGACACTGCCCTGTCCAAGAACCAGGATCACCCAGCTGCCGCTGAAGGCCTTTAAGCTGCCCTAG GCTGACACAGCTGGACCTGAACCGGAATAGAATCAGGCTGATCGAGGGCCTGACCTTCCAGGGCCTGGATAGCCTGG AGGTGCTGCGCTGCAGCGGAACAATATCTCCGCTGACAGACGGAGCATTTTGGGGCCTGTCTAAGATGCACGTG CTGCACCTGGAGTACAATAGCCTGGTGGAGGTGAATCTGGCAGCCTGTATGGCCTGACCGCCTGCACAGCTGCA CCTGTCCAACAATAGCATCAGCAGAATCCAGAGGGATGGTGGTCTTCTGCCAGAAGTGCACGAGCTGATCCTGT CTTTTAACAATCTGACAGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCTGCGCCTGTCTCAC AATGCCATCAGCCACATCGCCGAGGGCGCCTTTAAGGGCCTGAAGAGCCTGAGGGTGTGGATCTGGACCACAACGA GATCTCTGGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCTGGACAATCTGTCCAAGCTGACCTGTTTGGCA ACAAGATCAAGTCTGTGGCAAGCGGCCTTCTCTGGCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAATGCC ATCAGATCCGTGCAGTTCGATGCCTTTGCCAAGATGAAGAATCTGAAGGAGCTGTACATCAGCTCCGAGAGCTTCT GTGCGACTGTCAGTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGCAGGCTTTGTGACCGCCACATGCG CCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCGATAGCTTCGTGTGCACGATTTTCTTAAG CCACAGATCATCACCCAGCCAGAGACAACAATGGCCGTGGTGGCAAGGACATCCGGTTTACATGTTCCGCCGCTC TAGTCTCTTAGCCCCATGACCTTCGCTGGAAGAAGGATAACGAGGTGCTGGCCAATGCCGACATGGAGAATTCG CCCACGTGAGAGCCAGGATGGCGAAGTGTGAGTATACCCACAATCTGCACCTGGGCACTGACCTTTGGCCAC GAGGGCAGATACCAGTGCATCATCACAATCACTTCGGCTCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGT GCTGCCTAGCTTTACCAAGATCCACACGACATCGCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGCAGCAA CCGGACACCCAAACCTCAGATCGCATGGCAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGGAGAGGAGAATG CACGTGATGCCAGACGATGACGTGTTCTTTATCAGATGTGAAGATCGATGACATGGGCGTGTACTCTGCACCCG ACAGAACAGCGCCGCGAGCGTGTCCGCCAACGCCACCCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGG AGGACAGGGTGGTGACCGTGGGCGAGACAGTGGCCTTTCAGTGTGAAGGCCACCGGCTCTCCAACCAAGGATCACC TGGCTGAAGGGCGGCAGGCCCTGAGCCTGACAGAGCGCCACCACTTACCCCTGGCAATCAGTGTCTGGTGGTGA GAACGTGATGATCGATGACGCCGCGAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCCC AGCTGTCTATCTGCCTACCCAGGCTGCCGAAGGATGGCACCACA gaaccgaaatctctgacaaaaccacacctctcgccgtctcggtccggaactgctgggtggttctctgtttt c CTGTTTCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGGACGTGAG CCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACCAAGCCCAGAG AGGAGCAGTACAACCTCTACCTATAGGGTGGTGGAGCGTGTGACAGTGTGACACAGGACTGGCTGAACGCAAGGAG TATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCCAAGGCCAAGGGCCAGCCAAG AGAGCCCCAGGTGTACCCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAACCAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGAGTCTAATGGCCAGCCTGAGAATAACTACAAGACAACCCCA CCCGTGTGATTCTGACGGCAGCTTCTTTCTGTATTCTAAGCTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAA CGTGTTACAGTGTCCGTGATGCACGAAGCACTGCACAATCACTACCCAGAAATCACTGTCACTGAGCCCTGGCA AA

[0064] 본 발명에서 제공하는 융합 단백질의 다른 일 예시는 상기 서열번호 3으로 표시되는 Lrig-1 단백질의 세포 외 도메인; 서열번호 7 내지 10 중 어느 하나로 표시되는 힌지 영역; 서열번호 6으로 표시되는 마우스 IgG2 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함하는 융합 단백질일 수 있다(하기 표 10 참조). 하기 표 10의 서열번호 29 내지 32로 표시되는 융합 단백질은 각각 하기 표 11의 서열번호 33 내지 36으로 표시되는 핵 산 서열에 의해 코딩될 수 있다(하기 표 11 참조).

표 10

[0066]

서열목록	서열정보
서열번호 29	AQAGPRAPCAAACCTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSLFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RL IEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELESSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNLSKLTFLGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSTFKIPHDIA AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQSAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT EPKSSDKTHTSPPCAPELLGGPSVF IFPPKIKDVLMSLSPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQQTTHREDYNSTLRVVSALPIQHQDW MSGKEFKCKVNNKDLPAIERTISKPKGVRAPQVYVLPPEEEMTKKQVLTTCMVTDMPEDIYVEWTNNG KTELNYKNTEPVLDSGSYFMYSKLRVEKKNWVERNSYSCSVHEGLHNHHTTKSFRTPGK
서열번호 30	AQAGPRAPCAAACCTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSLFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RL IEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELESSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNLSKLTFLGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSTFKIPHDIA AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQSAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT EPRGPTIKPCPPCKCAPNLLGGPSVF IFPPKIKDVLMSLSPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQQTTHREDYNSTLRVVSALPIQHQDW MSGKEFKCKVNNKDLPAIERTISKPKGVRAPQVYVLPPEEEMTKKQVLTTCMVTDMPEDIYVEWTNNG KTELNYKNTEPVLDSGSYFMYSKLRVEKKNWVERNSYSCSVHEGLHNHHTTKSFRTPGK
서열번호 31	AQAGPRAPCAAACCTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSLFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RL IEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELESSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNLSKLTFLGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSTFKIPHDIA AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQSAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT RNTGRGGEKKKEKEKEEEREKTKTPECSHTQPLGVF IFPPKIKDVLMSLSPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQQTTHREDYNSTLRVVSALPIQHQDW MSGKEFKCKVNNKDLPAIERTISKPKGVRAPQVYVLPPEEEMTKKQVLTTCMVTDMPEDIYVEWTNNG KTELNYKNTEPVLDSGSYFMYSKLRVEKKNWVERNSYSCSVHEGLHNHHTTKSFRTPGK
서열번호 32	AQAGPRAPCAAACCTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSLFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RL IEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELESSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNLSKLTFLGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSTFKIPHDIA AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQSAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT EPKSSDKTHTSPPSPAPELLGGSSVF IFPPKIKDVLMSLSPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQQTTHREDYNSTLRVVSALPIQHQDW MSGKEFKCKVNNKDLPAIERTISKPKGVRAPQVYVLPPEEEMTKKQVLTTCMVTDMPEDIYVEWTNNG KTELNYKNTEPVLDSGSYFMYSKLRVEKKNWVERNSYSCSVHEGLHNHHTTKSFRTPGK

표 11

[0068]

서열목록	서열정보
서열번호 33	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCCAGGGACCTGCCTTCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCCTGCAGCACAACAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCCTGCCGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGGCGCCTTCGATGGCCTGAGCAGATCCCTGCTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCGTGAAGGCCTTTAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACAATAGCCTGGTG GAGGTGAATCTTGACAGCTGTATGGCTGACCGCCTGCACAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCTGTCTTTTAAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCCTGCGCCTGTCTACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGACCACAACGAGATCTCT GGCACCATCGAGGATACAGCGCGCCTTACAGGCTGGACAATCTTCCAGCTGATGGATGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCCTTCTTGCCCTGGAGAGCCTGGAGACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTTGCCAAGATGAAGAATCTGAAGGAGCTGTACATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGCAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCTGAAGGCCAGAGCATCTTCTCGTGCTGCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATACCCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTCTAGCCCCATGACCTTCGCCTGGAAGAAGGATAACGAGGTG CTGGCCAATGCGCATGGAGAATTCGCCCACGTGAGAGCCAGGATGGCGAAGTGTGGATGATACACACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACAGTGCATCATCAAAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGCAGCAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCCACAGAACAGCGCCGGCAGC GTGTCCGCCAACGCCACCCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACACCAAGGATCACCTGGCTGAAG GGCGGCAGGCCCCTGAGCCTGACAGAGCGCCACCCTTCAACCCCTGGCAATCAGTGTCTGGTGGTGCAGAAC GTGATGATCGATGACGCCGGCAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCC CAGCTGTCTATCTGCCTACCCAGGCTGCCGAAGGATGGCACCACA GAGCCAAAGTCTCTGATAAGACACACCTCTCCACCATGCCAGCACCAGAGCTGCTGGGAGGACCAAGC GTGTTT atcttcccacccaagatcaaggacgtgctgatgatctccctgtcccccatcgtgacctgcgtggtggtggac gtgtccgaggacgaccccgacgtgcagatcagttggttcgtgaacaacgtggaagtgcacaccgcccagacc cagaccacagagaggactacaactccacctgcgggtggtgtccgacctgcccacagaccaggactgg atgtccggcaagaattcaagtgcgaagtgaacaacaaggacctgcctgccccatcgagcggaccatctcc aagcccaagggtccgtgcgggctccccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgccgaggacatctacgtggaatggaccaacaatggc aagaccgagctgaactacaagaacaccgagcctgtgctggactccgacggctcctacttcatgtactccaag ctgcgggtggaaaagaagaactgggtcgagcggaactcctactcctgctccgtggtgcacgaggcctgcac aaccaccacaccaccaagtccttctccggacccccggcaaa

서열번호 34	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTTGACCAGATCTCTGAACCTGAGTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTCTTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCCTGAGCAGATCCCTGTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCGTGAAGGCCTTAAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCCTGACCTTCCAGGGCCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAATCTGGCAGCCTGTATGGCCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCCTGCGCCTGTCTCACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAAGCAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCCTTCTTGCCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCCTTGCCAAGATGAAGAATCTGAAGGAGCTGATACAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGCAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCCCCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTTAGCCCCATGACCTTGGCCTGGAAGAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCACGTGAGAGCCAGGATGGCGAAGTGTGGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGCAGCAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCTGAGCCTGACAGAGCGCCACCCTTACCCTGGCAATCAGCTGCTGGTGGTGAGAAC GTGATGATCGATGACGCGGCAGGTATACATGCGAGATGAGCAATCCTCTGGGACCGAGAGGGCACACTCC CAGCTGTCTATCCTGCCTACCCAGGCTGCCGGAAGGATGGACCACA Gagcctcggggcctaccatcaagcctgcccccttgcaagtgcctgcccctaatctgctgggcggaacct tccgtgttc atcttcccacccaagatcaaggacgtgctgatgatctccctgtcccccatcgtgacctgcgtggtggag gtgtccgaggaagaccccgacgtgcagatcagttggttcgtgaacaacgtggaagtgcacaccgcccagacc cagaccacagagaggactacaactccacctgcggtggtgtccgcccctgcccacagaccaggactgg atgtccggcaagaattcaagtgaagtgacaacaaggacctgcctgccccatcgagcggacctctcc aagcccaagggtccgtgcggtgctccccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgcccaggagacatctacgtggaatggaccaacaatggc aagaccgagctgaactacaagaacaccgagcctgtgctggactccgacggctcctacttcatgtactccaag ctgcggttggaagaagaactgggtcgagcggaactcctactcctgctccgtggtgcacgagggcctgcac aaccaccacaccaccaagtcttctccggacccccggcaaa

서열번호 35	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTTGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTCTTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGGCGCCTTCGATGGCCTGAGCAGATCCCTGTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCGTGAAGGCCTTTAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCCTGACCTTCCAGGGCCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAATCTTGGCAGCCTGTATGGCCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCCTGCGCCTGTCTCACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCCTGAAGAGCCTGAGGGTGTGGATCTGGAAGCAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCCTTCTTGCCCTGGAGAGCCTGGAGACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTTCGAAGATGAAGAATCTGAAGGAGCTGATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGTATGGGAAGGATGCTGCAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCCCCAGCAGAGACAACATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTCTAGCCCCATGACCTTGCCTGGAAGCAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCACGTGAGAGCCAGGATGGCGAAGTGTGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCTGAGCCTGACAGAGCGCCACCCTTACCCTGGCAATCAGCTGCTGGTGGTGCAGAAC GTGATGATCGATGACGCGGCAGGTATACATGCGAGATGAGCAATCCTCTGGGACCGAGAGGGCACACTCC CAGCTGTCTATCCTGCCTACCCAGGCTGCCGGAAGGATGGACCACA cgcaacaccggccgcgcgaggagaagaagaaggagaaggagaaggaggagcaggaggagcgcgagacc aagacccccgagtccccagccacaccagccccctggcggtgttc atcttcccaccaagatcaaggacgtgctgatgatctccctgtcccccatcgtgacctgcgtggtgggac gtgtccgaggacgacccccgacgtgcagatcagttggttcgtgaacaacgtggaagtgcacaccgcccagacc cagacccacagagaggactacaactccacctgcgggtggtgtccgacctgccccatccagaccaggactgg atgtccggcaaagaattcaagtgaagtgacaacaaggacctgcctgccccatcgagcggacctctcc aagcccaagggtccgtgcgggctccccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgcccaggacatctacgtggaatggaccaacaatggc aagaccgagctgaactacaagaacaccgagcctgtgctggactccgacggctcctacttcatgtactccaag ctgcgggtggaaaagaagaactgggtcgagcggaactcctactcctgctccgtggtgcacgaggcctgcac aaccaccacaccaccaagtcttctcccggacccccggcaaa

서열번호 36	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCCAGGGACCTGCCTTCTTGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTCTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGGCGCCTTCGATGGCTGAGCAGATCCCTGTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCCGTGAAGGCTTTAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACAATAGCCTGGTG GAGGTGAATCTGGCAGCCTGTATGGCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCTGGCAGAGCTGTCTCTCTGTCCATCCTGCGCCTGTCTACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAGCCACAAGCAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCTTCTTGCCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTGCCAAGATGAAGAATCTGAAGGAGCTGATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGCAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCCCCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTTAGCCCCATGACCTTGCCTGGAAGAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCACGTGAGAGCCAGGATGGCGAAGTGTGGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAACTACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCCGACAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCTGACCGTGTGAGAGACCCATCCCTGGCCGTGCCCTGGAGGACAGGTTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCTGAGCCTGACAGAGCGCCACCTTCAACCCCTGGCAATCAGCTGCTGGTGGTGCAGAAC GTGATGATCGATGACGCGGCAGGTATACATGCGAGATGAGCAATCCTCTGGGACCGAGAGGGCACACTCC CAGCTGTCTATCTGCCTACCCAGGCTGCCGAAGGATGGCACCACA gaaccgaaatcttctgacaaaacccacacctctcgcgctctcgggtcgggaactgctgggtggttcttct gttttc atcttcccacccaagatcaaggacgtgctgatgatctccctgtcccccatcgtgacctgcgtggtgggac gtgtccgaggacgaccccgacgtgcagatcagttggttcgtgaacaacgtggaagtgcacaccgcccagacc cagaccacagagaggactacaactccacctgcggtggtgtcgccctgccatccagcaccaggactgg atgtccggcaaagaattcaagtgcgaagtgaacaacaaggacctgcctgcccccatcgagcgaccatctcc aagcccaagggtccgtgcggtgctcccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgcccaggacatctacgtggaatggaccaacaatggc aagaccgagctgaactacaagaacaccgagcctgtgctggactccgacggtcctacttcatgtactccaag ctgcggtggaaaagaagaactgggtcgagcggaactctactcctgctcgtggtgcacgaggcgctgcac aaccaccacaccaccaagtcttctccggaccccgcaaa

[0070] 본 발명에서 제공하는 융합 단백질의 또 다른 일 예시는 상기 서열번호 1로 표시되는 Lrig-1 단백질의 세포 외 도메인; 서열번호 11로 표시되는 링커; 서열번호 7 내지 10 중 어느 하나로 표시되는 힌지 영역; 서열번호 5로 표시되는 인간 IgG1 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함하는 융합 단백질일 수 있다 (하기 표 12 참조). 하기 표 12의 서열번호 37 내지 40으로 표시되는 융합 단백질은 각각 하기 표 13의 서열번호 41 내지 44로 표시되는 핵산 서열에 의해 코딩될 수 있다(하기 표 13 참조).

표 12

[0072]

서열목록	서열정보
서열번호 37	AGPRAPCAAACACAGDSLDCGGRGLAALPGDLPSWTRSLNLSYNKLSIDPAGFEDLPNLQEVYLNNNELTA VPSLGAASSHVSLFLQHNKIRSVEGSQLKAYLSLEVLDLSLNNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVLKLQRNNISKL TDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSIARIHRKGWSFCQKLHELVL SFNNLTRL DEESLAELSSLVLRSLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDLSKLTFLGKNI KSAKRAFSGLEGLEHLNLGGNAIRSVQFADFVKMKNLKELHISSDSFLCDCQKWLPPWLI GRMLQAFVTA TCAHPESLKGQSFVSPPEFVCDLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKKDNEVLT NADMENFVHVHAQDGEVMEYTTILHLRQVTFGHEGGRYQCVITNHFGSTYSHKARLTNNVLPSTFTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGDTDFPAARERRMHVMPDDDVFFITDVKIDDAGVYSCTAQNAGSIS ANATLTVLETPSLVPLEDRVSVGETVALQCKATGNPPPRI TWFKGDRPLSLTERHHLTPDNQLLVVQNVV AEDAGRYTCEMSNTLGTERAHSQSVLPAAGCRKDGTTVGIF GS EPKSSDKTHT SPPCPAPELL GGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKLSLSLSPGK
서열번호 38	AGPRAPCAAACACAGDSLDCGGRGLAALPGDLPSWTRSLNLSYNKLSIDPAGFEDLPNLQEVYLNNNELTA VPSLGAASSHVSLFLQHNKIRSVEGSQLKAYLSLEVLDLSLNNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVLKLQRNNISKL TDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSIARIHRKGWSFCQKLHELVL SFNNLTRL DEESLAELSSLVLRSLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDLSKLTFLGKNI KSAKRAFSGLEGLEHLNLGGNAIRSVQFADFVKMKNLKELHISSDSFLCDCQKWLPPWLI GRMLQAFVTA TCAHPESLKGQSFVSPPEFVCDLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKKDNEVLT NADMENFVHVHAQDGEVMEYTTILHLRQVTFGHEGGRYQCVITNHFGSTYSHKARLTNNVLPSTFTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGDTDFPAARERRMHVMPDDDVFFITDVKIDDAGVYSCTAQNAGSIS ANATLTVLETPSLVPLEDRVSVGETVALQCKATGNPPPRI TWFKGDRPLSLTERHHLTPDNQLLVVQNVV AEDAGRYTCEMSNTLGTERAHSQSVLPAAGCRKDGTTVGIF GS EPRGPTIKPCPPCKCPAPNLLGGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKLSLSLSPGK
서열번호 39	AGPRAPCAAACACAGDSLDCGGRGLAALPGDLPSWTRSLNLSYNKLSIDPAGFEDLPNLQEVYLNNNELTA VPSLGAASSHVSLFLQHNKIRSVEGSQLKAYLSLEVLDLSLNNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVLKLQRNNISKL TDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSIARIHRKGWSFCQKLHELVL SFNNLTRL DEESLAELSSLVLRSLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDLSKLTFLGKNI KSAKRAFSGLEGLEHLNLGGNAIRSVQFADFVKMKNLKELHISSDSFLCDCQKWLPPWLI GRMLQAFVTA TCAHPESLKGQSFVSPPEFVCDLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKKDNEVLT NADMENFVHVHAQDGEVMEYTTILHLRQVTFGHEGGRYQCVITNHFGSTYSHKARLTNNVLPSTFTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGDTDFPAARERRMHVMPDDDVFFITDVKIDDAGVYSCTAQNAGSIS ANATLTVLETPSLVPLEDRVSVGETVALQCKATGNPPPRI TWFKGDRPLSLTERHHLTPDNQLLVVQNVV AEDAGRYTCEMSNTLGTERAHSQSVLPAAGCRKDGTTVGIF GS RNTGRGGEKKKEKEKEEQEERETKTPECSHTQPLGVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKLSLSLSPGK

서열번호 40	AGPRAPCAAACCTCAGDSLDCGGRGLAALPGDLPSWTRSLNLSYNKLSEIDPAGFEDLPNLQEVYLNNNELTA VPSLGAASSHVSLFLQHNKIRSVESGSQLKAYLSLEVLDLSLNNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVLKLRNNISKL TDGAFWGLSKMHVLHLEYNLSLEVNSGSLYGLTALHQLHLSNNSIARIHRKGSWFCQKLHELVLFSNNLTRL DEESLAELESSLVLRLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDLSKLTFLGNKI KSAKRAFSGLEGLHLNLGGNAIRSVQFADFVKMKNLKEHLISSDSFLCDCQLKWLPPWLI GRMLQAFVTA TCAHPESLKGQSIFSVPPESFVCDLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKKDNEVLT NADMENFVHVHAQDGEVMEYTTILHLRQVTFGHEGRYQCVITNHFGSTYSHKARLTVNVLPSFTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGDTFPAARERRMHVMPDDVFFITDVKIDDAGVYSCTAQNAGSIS ANATLTVLETPSLVPLEDRVVSGETVALQCKATGNPPPRITWFKGDRPLSLTERHHLTPDNQLLVQNVV AEDAGRYTCEMSNTLGTERRAHSLSLPAAGCRKDGTTVGIF GS EPKSSDKTHTSPPSPAPELLGGSSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNYHTQKSLSLSPGK

표 13

[0074]

서열목록	서열정보
서열번호 41	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCTCCTGCTGCGATCTGCCATCTGGACCCGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCCGCG GTACCAcctcctgggcgctgcttcacacatgtcgtctctctcttctcgcagcacaacaagatcgcagcgtg gaggggagccagctgaaggcctaccttctcttagaagtgttagatctgagtttgaacaacatcacggaagtgc cggaacacctgcttccacacgagaccgctataaaggagctcaacctggcaggcaatcggtatggcacctctg gagttgggagcatttgatggtctgtcacggtcgtgctaactcttcgctgagcaaaaacaggatcacccag cttctctgaagagcattcaagctaccaggctgacacaactggacctcaatcggaacaggatctggctgata gagggcctcacctccaggggctcaacagcttggaggtgctgaagcttcagcgaaacaacatcagcaaacctg acagatggggccttctggggactgtccaagatgcatgtgctgcacctggagtacaacagcctggtagaagtgc aacagcggctcgtctacggcctcagggcctgcatcagctccacctcagcaacaattccatcgctcgcatc caccgcaagggtggagcttctgccagaagctgcatgagttggtcctgtccttcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcgtcgtctcagccacaattccatcagccacatt gcggagggtgccttcaaggactcaggagcctgcgagcttggatctggaccataacgagatttcgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgttggaaacaagatc aagctctgtggctaagagagcattctcggggctggaaggcctggagcacctgaaccttggagggaatgcgata agatctgtccagtttgatgccttctgaagatgaagaatcttaagagctccatcagcagcgcagacgtctc ctgtgtgactgccagctgaagtggtgcccgcgtggctaatggcaggatgctgcaggccttctgagagcc acctgtgccaccagagatcactgaagggtcagagcatttctctgtgccaccagagagttctgtgtgcat gacttctgaagccacagatcatcacccagccagaaaccacctggctatggtgggcaaggacatccggttt acatgctcagcagccagcagcagcagctccccatgaccttgcctggaagaagacaatgaagctcctgacc aatgcagacatggagaacttctccacgtccacgcgagggaggggaagtgatggagtacaccacctcctg cacctcctgaggtcacttccgggcacgagggcgctaccaatgtgtcatcaccaaccttggctccacc tattacataaagccaggtcaccgtgaatgtgtgccatcatcaccaaaacgcccacgacataaacatc cggaccaccacctggcccgcctggaatgtgctgccacaggtcaccacaacctcagattgctggcagaag gatggaggcacggatttccccgctgcccgtgagcagcagcatgcatgcatgcggatgacgacgtgttttca atcactgatgtgaaatagatgacgcagggtttacagctgtactgctcagaactcagccggttctatttca gctaatgccacctgactgtcctagagacctccttgggtggtccccttggagaccgtgtggtatctgtg ggagaacagtgccctccaatgcaaagccacgggaacctccgcccgcgcatcacctggttcaagggggac cgcccgtgagcctcactgagcggcaccacctgacctgacaaccagctcctggtggttcagaacctggtg gcagaggatgcggccgataacctgtgagatgtccaacacctgggcacggagcgagctcacagccagctg agcgtcctgccgcagcaggctgcaggaaggatgggaccacggtaggcatcttc GGATCC GAGCCAAAGTCTCTGATAAGACACACCTCTCCACCATGCCAGCACCAGAGCTGCTGGGAGGACCAAGC GTGTTCC CTGTTTCTCCAAAGCCCAAGGACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGAC GTGAGCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAAAGACCC AAGCCAGAGAGGAGCAGTACAACCTACTCTATAGGGTGGTGAGCGTGTGACAGTGTGACACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTACGTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 42	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCCTGGACCCGGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggcgtgcttcacacatgtcgtctctctcttctcagcacaacaagattcgcagcgtg gaggggagccagctgaaggcctaccttccctagaagtgttagatctgagtttgaacaacatcacggaagtg cggaacacctgctttccacacggaccgctataaaggagctcaacctggcaggcaatcggaattggcaccctg gagttgggagcatttgatggctgtcacggctcgtgctaactcttcgctgagcaaaaacaggatcaccag cttctgtgaagagcattcaagctaccaggtgacacaactggacctcaatcggaacaggatctggctgata gagggcctcaccttcaggggctcaacagcttggaggtgctgaagcttcagcgaaacaacatcagcaaatg acagatggggccttctggggactgtccaagatgcatgtgctgcacctggagtacaacagcctggtagaagtg aacagcggctcgtctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgctt caccgcaagggtggagcttctgccagaagctgcatgagttggtcctgtccttcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcctgctctcagccacaattccatcagccacatt gcggagggtgccttcaaggagctcaggagcctgcgagcttggtatggacctaacagagatttcgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgtttggaaacaagatc aagctctgtggctaagagagcattctcggggctggaaggcctggagcacctgaaccttggagggaatgcgatc agatctgtccagtttgatgcctttgtgaagatgaagaatcttaaagagctccatcagcagcgacagcttc ctgtgtgactgccagctgaagtggtgccccctggctaatggcaggatgctgcagccttctgtgacagcc acctgtgcccaccagaatcactgaagggtcagagcatttctctgtgccaccagagagttctgtgtgcat gacttctgaagccacagatcatcaccagccagaaccaccatggctatggtgggcaaggacatccggttt acatgctcagcagccagcagcagcagctccccatgacctttgcctggaagaaagacaatgaagtcctgacc aatgcagacatggagaactttgtccacgtccacgcgcaggacggggaagtgatggagtacaccaccatcctg cacctccgtcaggtcacttccgggcacgaggccgctaccaatgtgtcatcaccaaccacttggctccacc tattacataaaggccaggtcaccgtgaatgtgttgccatcattcaccaaaacgccccacagacataaccatc cggaccaccaccgtggcccgctcgaatgtgctgccacaggtcacccaaacctcagattgcctggcagaag gatggaggcacggatttccccgctgcccgtagcgacgcatgcatgtcatgccggatgacgacgtgttttc atcactgatgtgaaaatagatgacgcagggtttacagctgtactgctcagaactcagccggttctatttca gctaagtgccaccctgactgtcctagagaccccatccttggtggtcccttgggaagaccgttggtatctgtg ggagaaacagtggccctccaatgcaaagccacggggaacctccgccccgcatcacctggttcaagggggac cgcccgctgagcctcactgagcggcaccacctgaccttgacaaccagctcctggtggttcagaacgtggtg gcagaggatgcgggccgatatacctgtgagatgtccaacacctgggcacggagcagctcacagccagctg agcgtcctgcccgcagcaggctgcaggaaggatgggaccacggtaggcatcttc GGATCC Gagcctcggggccctaccatcaagccctgcccccttgcaagtgcctgcccctaatctgctgggcggaccc tccgtgttc CTGTTTCCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGGAC GTGAGCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTACCTATAGGGTGGTGAGCGTGCTGACAGTGCTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTACGTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 43	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCCTGGACCCGGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggcgtgcttcatcacatgtcgtctctctcttctcagcacaacaagattcgcagcgtg gaggggagccagctgaaggcctaccttcccttagaagtgttagatctgagtttgaacaacatcacggaagtg cggaacacctgctttccacacggaccgcctataaaggagctcaacctggcaggcaatcggaattggcaccttg gagttgggagcatttgatggctgtcacggctcgtgctaactcttcgctgagcaaaaacaggatcaccag cttctgtgaagagcattcaagctaccaggtgacacaactggacctcaatcggaacaggatctggctgata gagggcctcaccttccaggggctcaacagcttggaggtgctgaagcttcagcgaacaacatcagcaaatg acagatggggccttctggggactgtccaagatgcatgtgctgcacctggagtacaacagcctggtagaagtg aacagcggctcgtctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgctt caccgcaagggtggagcttctgccagaagctgcatgagttggtcctgtccttcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcctgcgtctcagccacaattccatcagccacatt gcggagggtgccttcaaggagctcaggagcctgcgagcttggatctggaccataacagagatttcgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgttggaaacaagatc aagctctgtggctaagagagcattctcggggctggaaggcctggagcacctgaaccttggagggaatgcgac agatctgtccagtttgatgccttctgaagatgaagaatctaaagagctccatcagcagcgacagcttct ctgtgtgactgccagctgaagtggtgccccgtggctaatggcaggatgctgcagccttctgtgacagcc acctgtgcccaccagaatcactgaagggtcagagcatttctctgtgccaccagagagttctgtgtgcat gacttctgaagccacagatcatcaccagccagaaccaccatggctatggtgggaaggacatccggtt acatgctcagcagccagcagcagcagctccccatgaccttgcctggaagaaagacaatgaagtcctgacc aatgcagacatggagaacttctccacgtccacgcgcaggacggggaagtgatggagtacaccaccatcctg cacctccgtcaggtcacttccgggcacgagggcctaccaatgtgtcatcaccaaccacttggctccacc tattacataaaggccaggtcaccgtgaatgtgttgccatcattcacaaaaagccccacagacataaccatc cggaccaccaccgtggcccgctcgaatgtgctgccacaggtcacccaaacctcagattgcctggcagaag gatggaggcacggatttccccgtgcccgtgagcgacgcatgcatgtcatgccggatgacgacgtgtttt atcactgatgtgaaaatagatgacgcagggtttacagctgtactgctcagaactcagccggttctattca gctaagtgccacctgactgtcctagagaccccatccttgggtggtcccttgggaagaccgttggtatctgtg ggagaaacagtggccctccaatgcaaagccacggggaacctcgcgcccgcatcacctggttcaagggggac cgcccgctgagcctcactgagcggcaccacctgaccttgacaaccagctcctgggtggttcagaacgtgggtg gcagaggatgcgggccgatatacctgtgagatgtccaacacctgggcacggagcagctcacagccagctg agcgtcctgcccgcagcaggctgcaggaaggatgggaccacggtaggcatcttc GGATCC cgcaacaccggccgcgccggcgaggagaagaagaaggagaaggagaaggaggagcaggaggagcgcgagacc aagacccccgagtgccccagccacaccagccccctgggcgtgttc CTGTTTCCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGAC GTGAGCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTACCTATAGGGTGGTGAGCGTGCTGACAGTGCTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTACGTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 44	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCCTGGACCCGGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggctgcttcatcacatgtcgtctctctcttctcagcacaacaagat tgcagcgtg gaggggagccagctgaaggcctaccttcccttagaagtgttagatctgagtttgaacaacatcacggaagt cggaacacctgcttccacacggaccgctataaaggagctcaacctggcaggcaatcggaatggcaccctg gagttgggagcatttgatggctgtcacggctcgtgctaactctcgccctgagcaaaaaacaggatcaccag cttctgtgaagagcattcaagctaccaggtgacacaactggacctcaatcggaacaggat tggctgata gagggcctcaccttccaggggtcaacagcttggaggtgctgaagcttcagcgaacaacatcagcaactg acagatggggccttctggggactgtccaagatgcatgtgctgcacctggagtacaacagcctggtagaagt aacagcggctcgtctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgctt caccgcaagggtggagcttctgccagaagctgcatgagtggctcctgtccttcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcctgctctcagccacaattccatcagccacct gaggagggtgccttcaaggagctcaggagcctgcgagcttggatctggacctaacagagatttctgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgttggaaacaagatc aagctctgtggctaagagagcattctcggggctggaaggcctggagcacctgaaccttggagggaatgcgatc agatctgtccagtttgatgccttctgaagatgaagaatcttaagagctccatcagcagcgacagcttct ctgtgtgactgccagctgaagtggctgccccctggctaatggcaggatgctgcagccttctgtgacagcc acctgtgccaccagaatcactgaagggtcagagcatttctctgtgccaccagagagttctgtgtgcat gacttctgaagccacagatcatcaccagccagaaccacctggctatggtgggaaggacatccggtt acatgctcagcagccagcagcagcagctccccatgaccttgcctggaagaaagacaatgaagctcctgacc aatgcagacatggagaacttctccacgtccacgcgcaggacggggaagtgtgagtagtaccaccatcctg cacctccgtcaggtcacttccgggcacgagggcctaccaatgtgtcatcaccaaccttggctccacc tattacataaaggccagctcaccgtgaatgtgttgccatcattcaccaaaacgccccacagataaacatc cggaccaccacctggcccgctcgaatgtgctgccacaggtcaccaaacctcagattgcctggcagaag gatggaggcacggatttccccctgcccgtgagcgacgcatgcatgtcatgccggatgacgacgtgtttt atcactgatgtgaaaatagatgacgcagggtttacagctgtactgctcagaactcagccggttctattca gctaattgccacctgactgtcctagagaccccatccttggtggtcccttgggaagaccgtgtggtatctgtg ggagaaacagtggccctccaatgcaaagccacggggaacctcgcgcccgcatcacctggttcaagggggac cgcccgctgagcctcactgagcggcaccacctgaccttgacaaccagctcctggtggttcagaactggtg gcagaggatgcgggcccgatatacctgtgagatgtccaacacctgggcacggagcagctcacagccagctg agcgtcctgcccgcagcaggctgcaggaaggatgggaccacggtaggcatcttc GGATCC gaaccgaaatcttctgacaaaacccacacctctccgctgtcctggctccggaactgctgggtggttcttct gttttc CTGTTTCCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGGAC GTGAGCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTTACCTATAGGGTGGTGAGCGTGCTGACAGTGCTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTACGTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAA

[0076] 본 발명에서 제공하는 융합 단백질의 또 다른 일 예시는 상기 서열번호 3으로 표시되는 Lrig-1 단백질의 세포 외 도메인; 서열번호 11로 표시되는 링커; 서열번호 7 내지 10 중 어느 하나로 표시되는 힌지 영역; 서열번호 5로 표시되는 인간 IgG1 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함하는 융합 단백질일 수 있다(하기 표 14 참조). 하기 표 14의 서열번호 45 내지 48로 표시되는 융합 단백질은 각각 하기 표 15의 서열번호 49 내지 52로 표시되는 핵산 서열에 의해 코딩될 수 있다(하기 표 15 참조).

표 14

[0078]

서열목록	서열정보
서열번호 45	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RLEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSFVSLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDVFFITDVKIDDMGVYSCTAQNSAGS VSANATLTVLETPSLAVPLEDRVVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GS EPKSSDKTHT SPPCPAPELL GGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
서열번호 46	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RLEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSFVSLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDVFFITDVKIDDMGVYSCTAQNSAGS VSANATLTVLETPSLAVPLEDRVVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GS EPRGPTIKPCPPCKCPAPNLLGGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
서열번호 47	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RLEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSFVSLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDVFFITDVKIDDMGVYSCTAQNSAGS VSANATLTVLETPSLAVPLEDRVVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GS RNTGRGGEKKKEKEKEEQEERETKTPECSHTQPLGVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK

서열번호 48	AQAGPRAPCAAACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSDVGSQKLSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRLLTLRLSKNRIITQLPVKAFKLPRLTQLDLNRNRIRLIEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNISIRIQRDGWSFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNLKSLTLFGN KIKSVAKRAFSGLSEHLNLGENAIRSVQFADFAMKMKNLKELYISSESFLCDCQLKWLPPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDFFPKPQIIITQPETTMVAVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGDTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQNAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRIITWLKGGRLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GS EPKSSDKTHTSPPSPAPELLGGSSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNYHTQKSLSLSPGK

표 15

[0080]

서열목록	서열정보
서열번호 49	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGACCTGCCTTCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCGCCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGCGCTGGTGAGCCTGTCTCTGCAGCACAAAGATCCTG AGCGTGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCTGCGGATCAGAGAGCTGAACCTGGCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCTGAGCAGATCCCTGCTGACACTGCGCCTGTCCAAGAACCAGATC ACCCAGCTGCGCGTGAAGGCCTTTAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCTGGATAGCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCTGCAGACGAGCATTGTTGGGCTGTCTAAGATGCACGTGCTGCACCTGAGTACAATAGCCTGGTG GAGGTGAACCTCTGGCAGCTGTATGGCTGACCGCCTGCACAGCTGACCTGTCTCAACAATAGCCTGAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCTGGCAGAGCTGTCTCTGTCCATCTGCGCTGTCTCACAATGCCATCAGC CACATCGCCGAGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGCTGGATCTGGACCACACAGAGATCTCT GGCACCATCGAGGATACAAGCGCGCCTTCACAGCCTGGACAATCTGTCCAAGCTGACCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGCCTTCTCTGGCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTTGCCAAGATGAAGAATCTGAAGGAGCTGTACATCAGCTCCGAG AGCTTCTGTGCGACTGTGACGTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGCAGGCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGCTGCCGATAGCTTCGTG TGCGACGATTTCTTAAGCCACAGATCATCCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTCTAGCCCCATGACCTTCGCTGGAAGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCCACGTGAGAGCCAGGATGGCGAAGTGATGGAGTATACCACA ATCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACAGTGATCATCACAAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGGCGTGTACTCCTGCACCCACAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTTCCAACACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCCGAGCCTGACAGAGCGCCACCTTCACCCCTGGCAATCAGCTGCTGGTGGTGACAGAAC GTGATGATCGATGACGCGGCAGGTATACATGCGAGATGAGCAATCCTCTGGGACCGAGAGGGCACACTCC CAGCTGTCTATCCTGCTACCCAGGCTGCGGAAGGATGGCACCACA GGATCC GAGCCAAAGTCTCTGATAAGACACACCTCTCCACCATGCCAGCACCAGAGCTGCTGGGAGGACCAAGC GTGTTT CTGTTTCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGAC GTGAGCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACATGCCAAGACC AAGCCAGAGAGGAGCAGTACAATCTACCTATAGGGTGGTGAGCGTGTGACAGTGTGACACAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAAGAGAGCCCCAGGTGTACACCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTACGTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 50	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTTGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTCTTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCCTGAGCAGATCCCTGTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCCGTGAAGGCCTTTAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGAATAGAATCAGG CTGATCGAGGGCCTGACCTTCCAGGGCCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAATCTGGCAGCCTGTATGGCCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTGTCCATCCTGCGCCTGTCTACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAGCCACAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCCTTCTTGCCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTGCCAAGATGAAGAATCTGAAGGAGCTGATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGCTGCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCACCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTTAGCCCCATGACCTTGCCTTGGGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCACGTGAGAGCCAGGATGGCGAAGTATGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAACTACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCACAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGAGC GTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCCTGAGCCTGACAGAGCGCCACCACTTACCCTGGCAATCAGCTGCTGGTGGTGACAAC GTGATGATCGATACGCGGCGAGGTATACATGCGAGATGAGCAATCCTTGGGACCGAGAGGGCACACTCC CAGCTGTCTATCTGCCTACCCAGGCTGCCGGAAGGATGGCACCACA GGATCC Gagcctcgggccctaccatcaagccctgcccccttgcaagtgcctgcccctaatctgctgggcggaccc tcggtgttc CTGTTTCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGAC GTGAGCCACGAGGACCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTACCTATAGGGTGGTGAGCGTGTGACAGTGTGCACACGAGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTAGCTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 51	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTTGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTCTTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGGCGCCTTCGATGGCCTGAGCAGATCCCTGTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCCGTGAAGGCCTTTAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCCTGACCTTCCAGGGCCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAATCTTGGCAGCCTGTATGGCCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCCTGCGCCTGTCTCACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAGCCACAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCCTTCTTGCCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTGGCAAGATGAAGAATCTGAAGGAGCTACATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGCAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCACCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTTAGCCCCATGACCTTGCCTTGGGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCACGTGAGAGCCAGGATGGCGAAGTGATGGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCACAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCACAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGAGC GTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCCTGAGCCTGACAGAGCGCCACCACTTCAACCTGGCAATCAGCTGCTGGTGGTGACAAC GTGATGATCGATACGCCGCGCAGGTATACATGCGAGATGAGCAATCCTTGGGACCGAGAGGGCACACTCC CAGCTGTCTATCTGCCTACCCAGGCTGCCGGAAGGATGGCACCACA GGATCC cgcaacaccggccgcgcgaggagagaagaaggagaaggagaaggaggagcaggaggagcgcgagacc aagacccccgagtgccccagccacaccagccccctggcggtgttc CTGTTTCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGAC GTGAGCCACGAGGACCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAATCTACCTATAGGGTGGTGAGCGTGTGACAGTGTGCACACGAGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTAGCTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 52	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCCAGGGACCTGCCTTCTTGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCTGAGCAGATCCCTGTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCCGTGAAGGCCTTAAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAATCTTGGCAGCCTGTATGGCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTGTCCATCCTGCGCTGTCTCACAATGCCATCAGC CACATCGCCGAGGGCGCCTTAAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAGCCACAACGAGATCTCT GGCACCATCGAGGATACAAGCGCGCCTTACAGGCCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCTTCTTGGCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTGGCAAGATGAAGAATCTGAAGGAGCTGATACAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGTATGGGAAGGATGCTGAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCACCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTTAGCCCCATGACCTTGCCTTGGGAAGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCCGCCACGTGAGAGCCAGGATGGCGAAGTGTGGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAACTACTTGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCACAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGAGC GTGTCCGCCAACGCCACCTTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTTCCAACACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCCGAGCCTGACAGAGCGCCACCTTACCCCTGGCAATCAGCTGCTGGTGGTGCAGAAC GTGATGATCGATGACGCGGCAGGTATACATGCGAGATGAGCAATCCTTGGGACCGAGAGGGCACACTCC CAGCTGTCTATCTGCTACCCAGGCTGCCGAAGGATGGCACCACA GGATCC gaaccgaaatcttctgacaaaacccacacctctccgctctccgctccggaactgctgggtggttcttct gttttc CTGTTTCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGGAC GTGAGCCACGAGGACCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTACCTATAGGGTGGTGAGCGTGTGACAGTGTGCACACGAGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTAGCTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

[0082] 본 발명에서 제공하는 융합 단백질의 또 다른 일 예시는 상기 서열번호 3으로 표시되는 Lrig-1 단백질의 세포 외 도메인; 서열번호 11로 표시되는 링커; 서열번호 7 내지 10 중 어느 하나로 표시되는 힌지 영역; 서열번호 6로 표시되는 마우스 IgG2 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함하는 융합 단백질일 수 있다(하기 표 16 참조). 하기 표 16의 서열번호 53 내지 56으로 표시되는 융합 단백질은 각각 하기 표 17의 서열번호 57 내지 60으로 표시되는 핵산 서열에 의해 코딩될 수 있다(하기 표 17 참조).

표 16

[0084]

서열목록	서열정보
서열번호 53	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RLEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSFQCQLHELILSFNNLT RLDEESLAELESSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQII TQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCI ITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDVFFITDVKIDDMGVYSCTAQNSAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRI TWLKGGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GS EPKSSDKTHTSPPCPAPELLGGPSVF IFPPKIKDVLMI SLSPITVCVVVDSEDDPDVQISWVFNNEVHTAQQTTHREDYNSTLRVVSALPIQHODW MSGKEFKCKVNNKDLPAIERTISKPKGSVRAPQVYVLPPEEEMTKKQVLTTCMVTDMPEDIYVEWTNNG KTELNYKNTEPVLDSGYSYFMYSKLRVEKKNWVERNSYSCSVVHEGLHNHHTTKSF SRTPGK
서열번호 54	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RLEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSFQCQLHELILSFNNLT RLDEESLAELESSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQII TQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCI ITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDVFFITDVKIDDMGVYSCTAQNSAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRI TWLKGGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GS EPRGPTIKPCPPCKCPAPNLLGGPSVF IFPPKIKDVLMI SLSPITVCVVVDSEDDPDVQISWVFNNEVHTAQQTTHREDYNSTLRVVSALPIQHODW MSGKEFKCKVNNKDLPAIERTISKPKGSVRAPQVYVLPPEEEMTKKQVLTTCMVTDMPEDIYVEWTNNG KTELNYKNTEPVLDSGYSYFMYSKLRVEKKNWVERNSYSCSVVHEGLHNHHTTKSF SRTPGK
서열번호 55	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RLEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSFQCQLHELILSFNNLT RLDEESLAELESSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQII TQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCI ITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDVFFITDVKIDDMGVYSCTAQNSAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRI TWLKGGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GS RNTGRGGEKKKEKEKEEQEERETKTPECSHTQPLGVF IFPPKIKDVLMI SLSPITVCVVVDSEDDPDVQISWVFNNEVHTAQQTTHREDYNSTLRVVSALPIQHODW MSGKEFKCKVNNKDLPAIERTISKPKGSVRAPQVYVLPPEEEMTKKQVLTTCMVTDMPEDIYVEWTNNG KTELNYKNTEPVLDSGYSYFMYSKLRVEKKNWVERNSYSCSVVHEGLHNHHTTKSF SRTPGK

서열번호 56	AQAGPRAPCAAACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRLLTLRLSKNRIITQLPVKAFKLPRLTQLDLNRNRIRLIEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNISIRIQRDGWSFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLHNEISGTIEDTSGAFTGLDNLKSLTLFGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFADFAMKMKNLKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDFFPKPQIIITQPETTMVAVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSTFKIPHDI AIRTGTTARLECAATGHPNPQIAWQKDGDTFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQNAGS VSANATLTVLETPSLAVPLEDRVTVGETVAFQCKATGSPTPRIITWLKGGRPPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGGT GS EPKSSDKTHTSPPSPAPELLGGSSVF IFPPKIKDVLMSLSPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQQTTHREDYNSTLRVVSALPIQHQDW MSGKEFKCKVNNKDLPAPIERTISKPKGSRAPQVYVLPPEEEMTKKQVTLTCMVTDMPEDIIVYEWNTNG KTELNYKNTEPVLDSGSYFMYSKLRVEKKNWVERNSYSCSVHEGLHNHHTTKSFSTRTPGK

표 17

[0086]

서열목록	서열정보
서열번호 57	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGACCTGCCTTCTGGACAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCGCCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGCGCTGGTGAGCCTGTTCCTGCAGCACAAAGATCTCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCTGCGGATCAGAGAGCTGAACCTGGCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCTGAGCAGATCCCTGCTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCGCGTGAAGGCCTTTAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGCGCTGACCTTCCAGGGCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCTGCAGACGAGCATTGTTGGGCTGTCTAAGATGCACGTGCTGCACCTGAGGTACAATAGCCTGGTG GAGGTGAACCTCTGGCAGCTGTATGGCTGACCGCCTGCACAGCTGCACCTGTCTCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGCTCTTCTGCCAGAAGCTGCACGAGCTGATCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCTGGCAGAGCTGTCTCTGTCCATCCTGCGCTGTCTCACAATGCCATCAGC CACATCGCCGAGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGCTGGATCTGGACCACACAGAGATCTCT GGCACCATCGAGGATACAAGCGCGCCTTCACAGCCTGGACAATCTGTCCAAGCTGACCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGCCTTCTCTGGCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTTGCCAAGATGAAGAATCTGAAGGAGCTGTACATCAGCTCCGAG AGCTTCTGTGCGACTGTGACGTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGCAGGCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCGGTGCTGCCGATAGCTTCGTG TGCGACGATTTCTTAAGCCACAGATCATCCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTCTAGCCCCATGACCTTCGCTGGAAGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCCACGTGAGAGCCAGGATGGCGAAGTGATGGAGTATACCACA ATCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGCGAGATACAGTGATCATCACAAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCCACACGACATC GCCATCAGAACAGGCACACAGCAAGGCTGAGGTGTCAGCAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGGCGTGTACTCCTGCACCCACAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCCTGAGCTGACAGAGCGCCACCTTCACCCCTGGCAATCAGCTGCTGGTGGTGACAGAAC GTGATGATCGATGACGCGGCGAGGTATACATGCGAGATGAGCAATCCTCTGGGACCGAGAGGGCACACTCC CAGCTGTCTATCCTGCTACCCAGGCTGCGGAAGGATGGCACCACA GGATCC GAGCCAAAGTCTCTGATAAGACACACCTCTCCACCATGCCAGCACCAGAGCTGCTGGGAGGACCAAGC GTGTTT atcttcccacccaagatcaaggacgtgctgatgatctccctgtcccccatcgtgacctgcgtgggtggac gtgtccgaggacgaccccgacgtgcagatcagttggttcgtgaacaacgtggaagtgcacaccgcccagacc cagaccacagagaggactacaactccacctcggggtggtgtccgacctgccccatccagaccaggactgg atgtccggcaagaattcaagtgcaaaagtgaacaacaaggacctgctgcccccatcgagcggaccatctcc aagcccaagggtccgtcggggtccccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgcccaggacatctacgtggaatggaccaacaatggc aagaccgagctgaactacaagaacaccgagcctgtgctggactccgacggctcctacttcatgtactccaag ctgcggtggaaaagaagaactgggtcgagcggaaactcctactcctgctcggtggtgcacagggcgctgcac aaccaccacaccaccaagtcttctccggacccccggcaaa

서열번호 58	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTGTAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCCTGAGCAGATCCCTGTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCGTGAAGGCCTTAAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAATCTTGGCAGCCTGTATGGCCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCATCCTGCGCCTGTCTACAATGCCATCAGC CACATCGCCGAGGGCGCCTTAAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAGCCACAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTACAGGCCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCTTCTTGGCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTGGCAAGATGAAGAATCTGAAGGAGCTGATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGCTGCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCACCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTTAGCCCCATGACCTTGCCTTGGGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTGCCCACGTGAGAGCCAGGATGGCGAAGTATGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAACTACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCACAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGACGGCCCTGAGCCTGACAGAGCGCCACCTTACCCCTGGCAATCAGCTGCTGGTGGTGACAAC GTGATGATCGATACGCGGCGAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCC CAGCTGTCTATCTGCCTACCCAGGCTGCCGGAAGGATGGCACCACA GGATCC Gagcctcggggccctaccatcaagccctgcccccttgcaagtgcctgcccctaatctgctgggcggaccc tcctgttc atcttcccacccaagatcaaggacgtgctgatgatctccctgtcccccatcgtgacctgcgtggtggtggac gtgtccgaggacgaccccgacgtgcagatcagttggttcgtgaacaacgtggaagtgcacaccgcccagacc cagaccacagagaggactacaactccacctgcgggtggtgtccgacctgcccacagaccaggactgg atgtccggcaaagaattcaagtgcgaagtgaacaacaaggacctgcctgccccatcgagcggaccatctcc aagcccaagggtccgtgcgggctccccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgcccaggacatctacgtggaattggaccaacaatggc aagaccgagctgaactacaagaacaccgagcctgtgctggactccgacggctcctacttcatgtactccaag ctgcgggtggaaaagaagaactgggtcgagcggaactcctactcctgctccgtggtgcacgaggcctgcac aaccaccacaccaccaagtcttctccggacccccggcaaa

서열번호 59	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTGTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTCTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTTCGATGGCCTGAGCAGATCCCTGTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCCGTGAAGGCCTTAAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCCTGACCTTCCAGGGCCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAATCTTGGCAGCCTGTATGGCCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCATCCTGCGCCTGTCTACAATGCCATCAGC CACATCGCCGAGGGCGCCTTAAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAGCCACAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTACAGGCCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCCTTCTTGGCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTGGCAAGATGAAGAATCTGAAGGAGCTGATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGCTGCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCACCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTTAGCCCCATGACCTTGCCTTGGGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTGCCCACGTGAGAGCCAGGATGGCGAAGTGATGGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGATCATCACAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCACAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGACAGCCCCCTGAGCCTGACAGAGCGCCACCCTTACCCTGGCAATCAGCTGCTGGTGGTGACAAC GTGATGATCGATGACGCGGCAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCC CAGCTGTCTATCTGCCTACCCAGGCTGCCGGAAGGATGGCACCACA GGATCC cgcaacaccggccgcgcgaggagaagaagaaggagaaggagaaggaggagcaggaggagcgcgagacc aagacccccgagtgccccagccacaccagccccctgggctgttc atcttcccacccaagatcaaggacgtgctgatgatctccctgtccccatcgtgacctgcgtggtggtggac gtgtccgaggacgaccccgacgtgcagatcagttggttcgtgaacaacgtggaagtgcacaccgcccagacc cagaccacagagaggactacaactccacctgcgggtggtgtccgacctgcccacagaccaggactgg atgtccggcaaagaattcaagtgcgaagtgaacaacaaggacctgcctgccccatcgagcggacctctcc aagcccaagggtccgtgcgggctccccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgcccaggacatctacgtggaatggaccaacaatggc aagaccgagctgaactacaagaacaccgagcctgtgctggactccgacggctcctacttcatgtactccaag ctgcgggtggaaaagaagaactgggtcgagcggaactcctactcctgctccgtggtgcacagggcctgcac aaccaccacaccaccaagtcttctccggacccccggcaaa

서열번호 60	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTTGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTCTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCTGAGCAGATCCCTGTGACACTGCGCCTGTCCAAGAACCAGATC ACCCAGCTGCCCGTGAAGGCTTTAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACAATAGCCTGGTG GAGGTGAATCTGGCAGCCTGTATGGCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCATCCTGCGCTGTCTCACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAGCACAAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCTTCTTGCCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTGCCAAGATGAAGAATCTGAAGGAGCTACATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGTATGGGAAGGATGCTGCAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCACCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTTCTAGCTCCTTAGCCCCATGACCTTGCCTGGAAGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCACGTGAGAGCCAGGATGGCGAAGTGTGGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCACAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCCACAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCCCTGAGCCTGACAGAGCGCCACCACTTCAACCCCTGGCAATCAGCTGCTGGTGGTGACAAC GTGATGATCGATACGCGGCGAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCC CAGCTGTCTATCTGCTACCCAGGCTGCCGGAAGGATGGCACCACA GGATCC gaaccgaaatcttctgacaaaacccacacctctccgccgtctccggctccggaactgctgggtggttcttct gttttc atcttcccacccaagatcaaggacgtgctgatgatctccctgtcccccatcgtgacctgcgtggtgggtggac gtgtccgaggacgacccccgacgtgcagatcagttggttcgtgaacaacgtggaagtgcacaccgcccagacc cagaccacagagaggactacaactccacctgcgggtggtgtccgacctgcccacagcaccaggactgg atgtccggcaaagaattcaagtgcgaagtgaacaacaaggacctgcctgccccatcgagcggacctctcc aagcccaagggtccgtgcgggtccccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgcccaggacatctacgtggaatggaccaacaatggc aagaccgagctgaactacaagaacaccgagcctgtgctggactccgacggctcctacttcatgtactccaag ctgcggtggaaaagaagaactgggtcgagcggaactcctactcctgctccgtggtgcacgagggcctgcac aaccaccacaccaccaagtcttctcccgacccccggcaaa

[0088] 본 발명에서 제공하는 융합 단백질의 또 다른 일 예시는 상기 서열번호 1로 표시되는 Lrig-1 단백질의 세포 외 도메인; 서열번호 12로 표시되는 링커; 서열번호 11로 표시되는 링커; 서열번호 7 내지 10 중 어느 하나로 표시되는 힌지 영역; 서열번호 5로 표시되는 인간 IgG1 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함하는 융합 단백질일 수 있다(하기 표 18 참조). 하기 표 18의 서열번호 61 내지 64로 표시되는 융합 단백질은 하기 표 19의 서열번호 65 내지 68로 표시되는 핵산 서열에 의해 코딩될 수 있다(하기 표 19 참조).

표 18

[0090]

서열목록	서열정보
서열번호 61	AGPRAPCAAACCTCAGDSLDCGGRGLAALPGDLPSWTRSLNLSYNKLSEIDPAGFEDLPNLQEVYLNNNNELTA VPSLGAASSHVSLFLQHNLIRSVEGSQLKAYLSLEVLDLNLNNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVLKLQRNNISKL TDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNNSIARIHRKGWSFCQKLHELVL SFNNLTRL DEESLAELSSLVLRLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDLSKLTFLGINKI KSAKRAFSGLEGLEHLNLGGNAIRSVQDAFVKMKNLKELHISSDSFLCDCQLKWLPWWIGRMLQAFVTA TCAHPESLKGQSIFSVPPESFVCDDFLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKKDNEVLT NADMENFVHVHAQDGEVMEYTTILHLRQVTFGHEGGRYQCVITNHFSTYSHKARLTNNVLPSTFTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGDTDFPAARERRMHVMPDDDVFFITDVKIDDAGVYSCTAQSAGSIS ANATLTVLETPSLVPLEDRVSVGETVALQCKATGNPPPRIITWFKGDRPLSLTERHHLTPDNQLLVQNVV AEDAGRYTCEMSNTLGTERAHSQSVLPAAGCRKDGTTVGIF GGG GS EPKSSDKTHT SPCCAPELL GGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
서열번호 62	AGPRAPCAAACCTCAGDSLDCGGRGLAALPGDLPSWTRSLNLSYNKLSEIDPAGFEDLPNLQEVYLNNNNELTA VPSLGAASSHVSLFLQHNLIRSVEGSQLKAYLSLEVLDLNLNNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVLKLQRNNISKL TDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNNSIARIHRKGWSFCQKLHELVL SFNNLTRL DEESLAELSSLVLRLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDLSKLTFLGINKI KSAKRAFSGLEGLEHLNLGGNAIRSVQDAFVKMKNLKELHISSDSFLCDCQLKWLPWWIGRMLQAFVTA TCAHPESLKGQSIFSVPPESFVCDDFLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKKDNEVLT NADMENFVHVHAQDGEVMEYTTILHLRQVTFGHEGGRYQCVITNHFSTYSHKARLTNNVLPSTFTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGDTDFPAARERRMHVMPDDDVFFITDVKIDDAGVYSCTAQSAGSIS ANATLTVLETPSLVPLEDRVSVGETVALQCKATGNPPPRIITWFKGDRPLSLTERHHLTPDNQLLVQNVV AEDAGRYTCEMSNTLGTERAHSQSVLPAAGCRKDGTTVGIF GGG GS EPRGPTIKPCPPCKCPAPNLLGGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
서열번호 63	AGPRAPCAAACCTCAGDSLDCGGRGLAALPGDLPSWTRSLNLSYNKLSEIDPAGFEDLPNLQEVYLNNNNELTA VPSLGAASSHVSLFLQHNLIRSVEGSQLKAYLSLEVLDLNLNNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVLKLQRNNISKL TDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNNSIARIHRKGWSFCQKLHELVL SFNNLTRL DEESLAELSSLVLRLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDLSKLTFLGINKI KSAKRAFSGLEGLEHLNLGGNAIRSVQDAFVKMKNLKELHISSDSFLCDCQLKWLPWWIGRMLQAFVTA TCAHPESLKGQSIFSVPPESFVCDDFLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKKDNEVLT NADMENFVHVHAQDGEVMEYTTILHLRQVTFGHEGGRYQCVITNHFSTYSHKARLTNNVLPSTFTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGDTDFPAARERRMHVMPDDDVFFITDVKIDDAGVYSCTAQSAGSIS ANATLTVLETPSLVPLEDRVSVGETVALQCKATGNPPPRIITWFKGDRPLSLTERHHLTPDNQLLVQNVV AEDAGRYTCEMSNTLGTERAHSQSVLPAAGCRKDGTTVGIF GGG GS RNTGRGGEEKKEKEKEEQEERETKTPECPSHTQPLGVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK

서열번호 64	AGPRAPCAAACTCAGDSLDCGGRLAALPGDLPSWTRSLNLSYNKLSEIDPAGFEDLPNLQEVYLNNNELTA VPSLGAASSHVVSFLQHNKIRSVEGSQLKAYLSLEVLDLSLNNITEVRNTCFPHGPPIKELNLAGNRIGTL ELGAFDGLSRSLTLRLSKNRITQLPVRAFKLPRLTQLDLNRNRIRLIEGLTFQGLNSLEVCLKQRNNISKL TDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSIARIHRKGWSFCQKLHELVL SFNNLTRL DEESLAELSSLVLRLSHNSISHIAEGAFKGLRSLRVLDLDHNEISGTIEDTSGAFSGLDSL SKLTLFGNKI KSAKRAFSGLEGLEHLNLGGNAIRSVQFADFVKMKNLKEHLISSDSFLCDCQLKWLPWLIGRMLQAFVTA TCAHPESLKGQSIFSVPPESFVCDDFLKPQIIITQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKKDNEVLT NADMENFVHVHAQDGEVMEYTTILHLRQVTFGHEGRYQCVITNHFGSTYSHKARLTVNVLPSTKTPHDITI RTTTVARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDAGVYSCTAQN SAGSIS ANATLTVLETPSLVPLEDRVVSGETVALQCKATGNPPPRITWFKGDRPLSLTERHHLTPDNQLLVVQNVV AEDAGRYTCEMSNTLGTERRAHSQSVLPAAGCRKDGTTVGIF GGG GS EPKSSDKTHTSPPSPAPELLGGSSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK

표 19

[0092]

서열목록	서열정보
서열번호 65	GCTGGGCCTCGGGCTCCTTGTGTGTCGCCCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCCTGGACCCGGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggcgctgcttcatcacatgtcgtctctctcttctgcagcacaacaagattcgcagcgtg gaggggagccagctgaaggcctacctttccttagaagtgttagatctgagtttgaacaacatcacggaagtg cggaacacctgctttccacacggaccgctataaaggagctcaacctggcaggcaatcggtatggcacctg gagttgggagcatttgatggctgtcacggctcgtgctaactcttcgctgagcaaaaacaggatcaccag cttctgtgaagagcattcaagctaccaggctgacacaactggacctcaatcggaacaggattcggtgata gagggcctcaccttccaggggctcaacagcttggaggtgctgaagcttcagcgaaacaacatcagcaactg acagatggggccttctggggactgtccaagatgcatgtctgcacctggagtacaacagcctggtagaagtg aacagcggctcgtctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgatt caccgcaagggtggagcttctgccagaagctgcatgagttggtcctgtccttcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcgtcgtctcagccacaattccatcagccacatt gaggagggtgcttcaagggaactcaggagcctgcagtgcttggtatggaccataacgagatttcgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgttggaaacaagatc aagctctgtggctaagagagcattctcggggctggaaggcctggagcactgaaccttggagggaatgcgac agatctgtccagtttgatgcctttgtgaagatgaagaatcttaagagctccatcagcagcgacagcttc ctgtgtgactgccagctgaagtggctgccccgtggctaattggcaggatgctgcaggcctttgtgacagcc acctgtgccaccaggaatcactgaagggtcagagcatttctctgtgccaccagagagtttctgtgagat gacttctgaagccacagatcatcaccagccagaaaccacatggctatggtgggcaaggacatccggttt acatgctcagcagccagcagcagcagctccccatgacctttgcctggaagaagacaatgaagtcctgacc aatgcagacatggagaactttgtccagctccacgcagcagggggaagtgatggagtacaccacatcctg cacctcgtcaggtcacttccggcagcagggcgctaccaatgtgcatcaccaaccactttggctccacc tattcacataaggccaggtcacctgaatgtgttgccatcatcaccaaaacgccccacgacataaccatc cggaccaccaccgtggcccgctcgaatgtgtgccacaggtcaccaaacctcagattgcctggcagaag gatggaggcacggatttccccgtgcccgtgagcgacgcatgcatgtcgcggatgacgacgtgttttc atcactgatgtgaaatagatgagcaggggtttacagctgactgctcagaactcagccggttctatttca gctaatgccacctgactgtcctagagaccctccttgggtggctcccttggagaccgtgtggtatctgtg ggagaacagtgccctccaatgcaaagccacggggaacctccgccccgcatcacctggttcaagggggac cgcccgctgagcctcactgagcggcaccacctgacccctgacaaccagctcctgggtggttcagaacgtggg gcagaggatgcgggccgatatacctgtgagatgtccaacacctgggcacggagcgagctcacagccagctg agcgtcctgcccgcagcaggtgcaggaaggatgggaccacggtaggcatctc GGCGGTGGC GGATCC GAGCCAAAGTCTCTGATAAGACACACCTCTCCACCATGCCAGCACCAGAGCTGCTGGGAGGACCAAGC GTGTTC CTGTTTCCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGGAC GTGAGCCACGAGGACCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTTACCTATAGGGTGGTGAGCGTGCTGACAGTGCTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTAGCTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 66	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCCTGGACCCGGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggcgtgcttcatcacatgtcgtctctctcttctcagcacacaagaattcgcagcgtg gaggggagccagctgaaggcctaccttcccttagaagtgttagatctgagtttgaacaacatcacggaagt cggaacacctgcttccacacggaccgctataaaggagctcaacctggcaggcaatcggaattggcaccctg gagttgggagcatttgatggctgtcacggctcgtgctaactcttcgctgagcaaaaacaggatcacccag cttctgtgaagagcattcaagctaccaggtgacacaaactggacctcaatcggaacaggatctggctgata gagggcctcaccttccaggggctcaacagcttggaggtgctgaagcttcagcgaaacaacatcagcaaatg acagatggggccttctggggactgtccaagatgcatgtcgtgcacctggagtacaacagcctggtagaagt aacagcggctcgtctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgctt caccgcaagggtggagcttctgccagaagctgcatgagttggtcctgtccttcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcgtgctcagccacaattccatcagccacct gaggagggtgccttcaaggagctcaggagcctgcgagcttggatctggagataacagagatttcgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgttggaaacaagatc aagctctgtggctaagagagcattctcggggctggaaggcctggagcacctgaaccttggagggaatgcgatc agatctgtccagtttgatgccttctgaagatgaagaatctaaagagctccatcagcagcgacagcttct ctgtgtgactgccagctgaagtggtgccccgtggctaatggcaggatgctgcagggccttctgacagcc acctgtgcccaccagaatcactgaagggtcagagcatttctctgtgccaccagagagttctgtgtgcat gacttctgaagccacagatcatcaccagccagaaccaccatggctatggtgggaaggacatccggtt acatgctcagcagccagcagcagcagctccccatgaccttgcctggaagaaagacaatgaagtcctgacc aatgcagacatggagaacttctccacgtccacgcgcaggacggggaagtgatggagtacaccaccatcctg cacctccgtcaggtcacttccgggcacgaggccgctaccaatgtgtcatcaccaaccacttggctccacc tattacataaaggccaggtcaccgtgaatgtgttgccatcattcaccaaaacgccccacagataaacatc cggaccaccaccgtggcccgctcgaatgtgctgccacaggtcaccaaacctcagattgcctggcagaag gatggaggcacggatttccccgtgcccgtgagcgacgcatgcatgtcatgccggatgacgacgtgttttc atcactgatgtgaaaatagatgacgcagggtttacagctgtactgctcagaactcagccggttctattca gctaagtcaccctgactgtcctagagaccctccttgggtggctcccttgggaagaccgtgtggtatctgtg ggagaacacgtggcctccaatgcaaagccacggggaacctcgcgccgcatcacctggttcaagggggac cgcccgctgagcctcactgagcggcaccacctgaccttgacaaccagctcctggtggttcagaacgtggtg gcagaggatgcgggccgatatacctgtgagatgtccaacacctgggcacggagcagctcacagccagctg agcgtcctgcccgcagcaggctgcaggaaggatgggaccacggtaggcatcttc GGCGGTGGC GGATCC Gagccteggggacctaccatcaagccctgcccccttgcaagtgcctgcccctaatctgctgggcggacc tccgtgttc CTGTTTCCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGGAC GTGAGCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTTACCTATAGGGTGGTGAAGCTGCTGACAGTGTGCACACGAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTAGCTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 67	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCCTGGACCCGGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggcgtgcttcatcacatgtcgtctctctcttctcagcacacaagaattcgcagcgtg gaggggagccagctgaaggcctaccttcccttagaagtgttagatctgagtttgaacaacatcacggaagtg cggaacacctgcttccacacggaccgctataaaggagctcaacctggcaggcaatcggaattggcaccctg gagttgggagcatttgatggctgtcacggctcgtgctaactcttcgctgagcaaaaacaggatcacccag cttctgtgaagagcattcaagctaccaggtgacacaactggacctcaatcggaacaggatctggctgata gagggcctcaccttccaggggctcaacagcttggaggtgctgaagcttcagcgaaacaacatcagcaaatg acagatggggccttctggggactgtccaagatgcatgtcgtgcacctggagtacaacagcctggtagaagtg aacagcggctcgtctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgctt caccgaagggtggagcttctgccagaagctgcatgagtggctcctgtccttcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcgtgctcagccacaattccatcagccacatt gcggagggtgccttcaaggagctcaggagcctgcgagcttggatctggacataacagagatttcgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgttggaaacaagatc aagctctgtggctaagagagcattctcggggctggaaggcctggagcacctgaaccttggagggaatgcgac agatctgtccagtttgatgccttctgaagatgaagaatctaaagagctccatcagcagcgacagcttct ctgtgtgactgccagctgaagtggctgccccgtggctaatggcaggatgctgcagccttctgtgacagcc acctgtgcccaccagaatcactgaagggtcagagcatttctctgtgccaccagagagttctgtgtgcat gacttctgaagccacagatcatcaccagccagaaccaccatggctatggtgggaaggacatccggtt acatgctcagcagccagcagcagcagctccccatgaccttgcctggaagaagacaatgaagtcctgacc aatgcagacatggagaacttctccacgtccacgcgcaggacggggaagtgatggagtacaccaccatcctg cacctccgtcaggtcacttccgggcacgaggccgctaccaatgtgtcatcaccaaccacttggctccacc tattacataaaggccaggtcaccgtgaatgtgttgccatcattcaccaaaacgccccacgacataaccatc cggaccaccaccgtggcccgctcgaatgtgctgccacaggtcaccaaacctcagattgcctggcagaag gatggaggcacggatttccccgtgcccgtgagcgacgcatgcatgtcatgccggatgacgacgtgttttc atcactgatgtgaaaatagatgacgcagggtttacagctgtactgctcagaactcagccggttctattca gctaagtgccacctgactgtcctagagaccctccttgggtggctcccttggaaagaccgtgtggtatctgtg ggagaaacagtggcctccaatgcaaagccacggggaacctccgccccgcatcacctggttcaagggggac cgcccgctgagcctcactgagcggcaccacctgaccttgacaaccagctcctggtggttcagaacgtggtg gcagaggatgcgggccgatatacctgtgagatgtccaacacctgggcacggagcagctcacagccagctg agcgtcctgcccgcagcaggctgcaggaaggatgggaccacggtaggcatcttc GGCGGTGGC GGATCC cgcaacaccggccgcgccggcgaggagaagaagaaggagaaggagaaggaggagcaggaggagcgcgagacc aagacccccgagtgccccagccacccagccccctgggcgtgttc CTGTTTCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGGAC GTGAGCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTTACCTATAGGGTGGTGAAGCTGCTGACAGTGTGCACACGAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTAGCTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 68	GCTGGGCCTCGGGCTCCTTGTGCTGCCGCCTGCACATGTGCAGGCGATTCCCTGGACTGCGGCGGCAGAGGC CTGGCCGCCCTGCCTGGCGATCTGCCATCCTGGACCCGAGCCTGAACCTGAGCTACAACAAGCTGAGCGAG ATCGATCCCCGCCGCTTTGAGGACCTGCCTAACCTGCAGGAGGTGTATCTGAACAATAACGAGCTGACCGCG GTACCatccctgggcgtgcttcatcacatgtcgtctctctcttctcagcacacaagaattcgcagcgtg gaggggagccagctgaaggcctaccttcccttagaagtgttagatctgagtttgaacaacatcacggaagt cggaacacctgcttccacacggaccgctataaaggagctcaacctggcaggcaatcggatggcaccctg gagttgggagcatttgatggctgtcacggctcgtgctaactctcgccctgagcaaaaacaggatcacccag cttctgtgaagagcattcaagctaccagagctgacacaactggacctcaatcggaacaggatcggctgata gagggcctcaccttccaggggctcaacagcttggaggtgctgaagcttcagcgaacaacatcagcaactg acagatggggccttctggggactgtccaagatgcatgtcgtgcacctggagtacaacagcctggtagaagt aacagcggctcgtctacggcctcacggcctgcatcagctccacctcagcaacaattccatcgctcgctt caccgaagggtggagcttctgccagaagctgcatgagtggctcctgcttcaacaacctgacacggctg gacgaggagagcctggccgagctgagcagcctgagtgctcgtcgtcagccacaattccatcagccacct gaggagggtgccttcaaggagctcaggagcctgcgagcttggatctggacctaacagagatttcgggcaca atagaggacacgagcggcgcttctcagggtcgacagcctcagcaagctgactctgttggaaacaagatc aagctctgtggctaagagagcattctcggggctggaaggcctggagcacctgaaccttggagggaatgcgatc agatctgtccagtttgatgccttctgaagatgaagaatctaaagagctccatcagcagcgacagcttct ctgtgtgactgccagctgaagtggctgccccctggctaatggcaggatgctgcagggccttctgacagcc acctgtgcccaccagaatcactgaagggtcagagcatttctctgtgccaccagagagttcgtgtgcgat gacttctgaagccacagatcatcaccagccagaaccaccatggctatggtgggaaggacatccggtt acatgctcagcagccagcagcagcagctcccccatgaccttgcctggaagaagacaatgaagctcctgacc aatgcagacatggagaacttctccacgtccacgcgcaggacggggaagtgatggagtacaccaccatcctg cacctccgtcaggtcacttccgggcacgagggcctaccaatgtgtcatcaccaaccacttggctccacc tattacataaaggccagctcacctgaatgtgttgccatcattcaccaaaacgccccacagataaccatc cggaccaccaccgtggcccgctcgaatgtgctgccacaggtcaccaaacctcagattgcctggcagaag gatggaggcacggatttccccctgcccgtgagcgacgcatgcatgtcatgccggatgacgacgtgttttc atcactgatgtgaaaatagatgacgcagggtttacagctgtactgctcagaactcagccggttctattca gctaagtcaccctgactgtcctagagaccctccttgggtggctcccttgggaagaccgtgtggtatctgtg ggagaacacagtggccctccaatgcaaagccacggggaacctccgccccgcatcacctggttcaagggggac cgcccgctgagcctcactgagcggcaccacctgaccttgacaaccagctcctgggtggttcagaacgtggtg gcagaggatgcgggcccgatatacctgtgagatgtccaacacctgggcacggagcgagctcacagccagctg agcgtcctgcccgcagcaggctgcaggaaggatgggaccacggtaggcatcttc GGCGGTGGC GGATCC gaaccgaaatcttctgacaaaaccacacctctccgctcctcggtcctcggaactgctgggtggttcttct gttttc CTGTTTCCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGGAC GTGAGCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAAATGCCAAGACC AAGCCCAGAGAGGAGCAGTACAACCTACCTATAGGGTGGTGAAGCTGCTGACAGTGCTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTTACGTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

[0094] 본 발명에서 제공하는 융합 단백질의 또 다른 일 예시는 상기 서열번호 3으로 표시되는 Lig-1 단백질의 세포 외 도메인; 서열번호 12로 표시되는 링커; 서열번호 11로 표시되는 링커; 서열번호 7 내지 10 중 어느 하나로 표시되는 힌지 영역; 서열번호 5로 표시되는 인간 IgG1 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3) 을 포함하는 융합 단백질일 수 있다(하기 표 20 참조). 하기 표 20의 서열번호 69 내지 72로 표시되는 융합 단백질은 각각 하기 표 21의 서열번호 73 내지 76으로 표시되는 핵산 서열에 의해 코딩될 수 있다(하기 표 21 참조).

표 20

[0096]

서열목록	서열정보
서열번호 69	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRIITQLPVKAFKLPRLTQLDLNRNRIRLIEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNLKSLTLFGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKLKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDIA AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQNSAGS VSANATLTVLETPSLAVPLEDRVVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GGG GS EPKSSDKTHT SPCCAPELL GGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
서열번호 70	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRIITQLPVKAFKLPRLTQLDLNRNRIRLIEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNLKSLTLFGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKLKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDIA AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQNSAGS VSANATLTVLETPSLAVPLEDRVVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GGG GS EPRGPTIKPCPPCKCPAPNLLGGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
서열번호 71	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRIITQLPVKAFKLPRLTQLDLNRNRIRLIEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNLKSLTLFGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMNKLKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDIA AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQNSAGS VSANATLTVLETPSLAVPLEDRVVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GGG GS RNTGRGGEKKKEKEKEEQEERETKTPECPSHTQPLGVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK

서열번호 72	AQAGPRAPCAAACACTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESGAFDGLSRLLTLRLSKNRITQLPVKAFKLPRLTQLDLNRNRIRLIEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNLSKLTLFGN KIKSVAKRAFSGLESLEHLNLGENAIRSVQFDAFAKMKNLKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMNAVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSTFKIPHDI AIRTGTTARLECAATGHPNPQIAWQKGGTDFPAARERRMHVMPDDVFFITDVKIDDMGVYSCTAQNSAGS VSANATLTVLETPSLAVPLEDRVVTGETVAFQCKATGSPTPRI TWLKGGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCMSNPLGTERAHSQLSILPTPGCRKDGT GGG GS EPKSSDKTHTSPPSPAPELLGGSSVF LFPPKPKDTLMSRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK

표 21

[0098]

서열목록	서열정보
서열번호 73	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCCAGGGACCTGCCTTCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCCTGCCGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGGCGCCTTCGATGGCCTGAGCAGATCCCTGCTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCGTGAAGGCCTTTAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCCTGGATAGCCTGGAGGTGCTGCGCCTGCAGCGGAACAATATCTCC CGCCTGACAGACGGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACAATAGCCTGGTG GAGGTGAATCTTGACAGCTGTATGGCTGACCGCCTGCACAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCTGTCTTTTAAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCCTGCGCCTGTCTCACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCCTGAAGAGCCTGAGGGTGTGGATCTGGACCACAACGAGATCTCT GGCACCATCGAGGATACAAGCGCGCCTTCACAGGCCTGGACAATCTTCCAAGCTGACCTGTTTGGCAAC AAGATCAAGTCTGTGGCCAAGCGGGCCTTCTTGCCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTTGCCAAGATGAAGAATCTGAAGGAGCTGTACATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGATGGAAAGGATGCTGCAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGCCAGAGCATCTTCTCGTGCTGCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATACCCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTCTAGCCCCATGACCTTCGCCTGGAAGAAGGATAACGAGGTG CTGGCCAATGCGCATGGAGAACTTCGCCCACGTGAGAGCCAGGATGGCGAAGTGTAGGATATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCACAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGGCAGC GTGTCCGCCAACGCCACCCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACACCAAGGATCAGCTGGCTAAG GGCGGCAGGCCCCTGAGCCTGACAGAGCGCCACCCTTCAACCCCTGGCAATCAGCTGCTGGTGGTGCAGAAC GTGATGATCGATGACGCCGGCAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCC CAGCTGTCTATCCTGCCTACCCAGGCTGCCGGAAGGATGGCACCACA GGCGGTGGC GGATCC GAGCCAAAGTCTCTGATAAGACACACACCTCTCCACCATGCCAGCACCAGAGCTGCTGGGAGGACCAAGC GTGTTC CTGTTTCTCTCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGAC GTGAGCCACGAGGACCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTACCTATAGGGTGGTGAGCGTGTGACAGTGTGCACAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCCTGCCCCCTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTAGCTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 74	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTTGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCTGAGCAGATCCCTGCTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCGTGAAGGCCTTAAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAATCTGGCAGCCTGTATGGCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCCTGCGCCTGTCTCACAATGCCATCAGC CACATCGCCGAGGGCGCCTTAAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAACACAAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTACAGGCCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCTTCTTGCCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTGCCAAGATGAAGAATCTGAAGGAGCTGATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGCTGCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCAGCCAGCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTTAGCCCCATGACCTTGCCTTGGAGCAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCACGTGAGAGCCAGGATGGCGAAGTATGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAACTACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGCAGC GTGTCCGCCAAGCCACCCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCTGAGCCTGACAGAGCGCCACCTTACCCCTGGCAATCAGCTGCTGGTGGTGAGAAC GTGATGATCGATGACGCGGCAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCC CAGCTGTCTATCCTGCCTACCCAGGCTGCCGGAAGGATGGCACCACA GGCGGTGGC GGATCC Gagccteggggeccetaccatcaagccctgcccccttgcaagtgcctgcccctaatctgetggcgaggacc tcctgttc CTGTTTCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGAC GTGAGCCACGAGGACCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAATCTACCTATAGGGTGGTGAGCGTGTGACAGTGTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCTGCCCTTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTTCTGCTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAA

서열번호 75	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCCAGGGACCTGCCTTCTTGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCTGAGCAGATCCCTGTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCGTGAAGGCCTTAAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAATCTGGCAGCCTGTATGGCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCCTGCGCCTGTCTACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAGCCACAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTACAGGCCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCTTCTTGCCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCCTTGCCAAGATGAAGAATCTGAAGGAGCTGATACAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGATGGGAAGGATGCTGCAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGCTGCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCAGCCAGCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTTAGCCCCATGACCTTGCCTTGGAGCAAGGAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCACGTGAGAGCCAGGATGGCGAAGTATGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAACTACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCTGAGCCTGACAGAGCGCCACCACTTACCCCTGGCAATCAGCTGCTGGTGGTGACAAC GTGATGATCGATGACGCCGCGAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCC CAGCTGTCTATCCTGCCTACCCAGGCTGCCGGAAGGATGGCACCACA GGCGGTGGC GGATCC cgcaacaccggccgcgccggcgaggagaagaagaaggagaaggagaaggaggagcaggaggagcgcgagacc aagacccccgagtccccagccaccccagccccctggcggtgttc CTGTTTCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGAC GTGAGCCACGAGGACCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAATCTACCTATAGGGTGGTGAGCGTGTGACAGTGTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCTGCCCTTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTTACGTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

서열번호 76	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTCTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCTGAGCAGATCCCTGCTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCGTGAAGGCCTTAAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAACCTCTGGCAGCCTGTATGGCCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCATCCTGCGCCTGTCTCACAATGCCATCAGC CACATCGCCGAGGGCGCCTTAAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAGCCACAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTACAGGCCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCCAAGCGGGCTTCTTGGCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTGGCCAAGATGAAGAATCTGAAGGAGCTGTACATCAGCTCCGAG AGCTTCTGTGCGACTGTGACGTGAAGTGGCTGCCACCTTGGCTGTATGGGAAGGATGCTGCAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCACCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCTGAGCCCATGACCTTGCCTTGAAGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCCGCCACGTGAGAGCCAGGATGGCGAAGTGTGGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAACTACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGCAGCAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCACAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGCAGC GTGTCCGCCAAGCCACCTTGACCGTCTGGAGACACCATCCCTGGCCGTGCCCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGAGGCCCCCTGAGCCTGACAGAGCGCCACCTTACCCCTGGCAATCAGCTGCTGGTGGTGACAAC GTGATGATCGATGACGCGGCAGGTATACATGCGAGATGAGCAATCCTCTGGGACCGAGAGGGCACACTCC CAGCTGTCTATCCTGCCTACCCAGGCTGCCGAAGGATGGCACCACA GGCGGTGGC GGATCC gaaccgaaatcttctgacaaaaccacacctctccgctctccgctccggaactgctgggtggttcttct gttttc CTGTTTCCTCCAAAGCCCAAGGACACACTGATGATCTCCAGGACACCAGAGGTGACCTGCGTGGTGGTGAC GTGAGCCACGAGGACCCGAGGTGAAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCACAATGCCAAGACC AAGCCAGAGAGGAGCAGTACAACCTTACCTATAGGGTGGTGAGCGTGTGACAGTGTGCACCAGGACTGG CTGAACGGCAAGGAGTATAAGTGCAAGGTGAGCAATAAGGCCCTGCCTGCCCAATCGAGAAGACAATCTCC AAGGCCAAGGGCCAGCCAAGAGAGCCCCAGGTGTACACCTGCCCTTAGCAGGGATGAGCTGACAAAGAAC CAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTTTATCCCTCCGACATCGCCGTGGAGTGGGAGTCTAATGGC CAGCCTGAGAATAACTACAAGACAACCCACCCGTGCTGGATTCTGACGGCAGCTTCTTTCTGTATTCTAAG CTGACCGTGGACAAGAGCAGGTGGCAGCAGGGCAACGTGTTTACGTGCTCCGTGATGCACGAAGCACTGCAC AATCACTACACCCAGAAATCACTGTCACTGAGCCCTGGCAAA

[0100]

본 발명에서 제공하는 융합 단백질의 또 다른 일 예시는 상기 서열번호 3으로 표시되는 Lrig-1 단백질의 세포 외 도메인; 서열번호 12로 표시되는 링커; 서열번호 11로 표시되는 링커; 서열번호 7 내지 10 중 어느 하나로 표시되는 힌지 영역; 서열번호 6으로 표시되는 마우스 IgG2 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3)을 포함하는 융합 단백질일 수 있다(하기 표 22 참조). 하기 표 22의 서열번호 77 내지 80로 표시되는 융합 단백질은 하기 표 23의 서열번호 81 내지 84로 표시되는 핵산 서열에 의해 코딩될 수 있다(하기 표 23 참조).

표 22

[0102]

서열목록	서열정보
서열번호 77	AQAGPRAPCAAACCTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RL IEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNSISRIQRDGSFQCQLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLSLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDIA AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQSAGS VSANATLTVLETPSLAVPLEDRVVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GGG GS EPKSSDKTHTSPPCAPELLGGPSVF IFPPKIKDVLMI SLSPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQQTTHREDYNSTLRVVSALPIQHODW MSGKEFKCKVNNKDLPAPIERTISKPKGSRAPQVYVLPPEEEMTKKQVLTTCMVTDMPEDIYVEWTNNG KTELNYKNTEPVLDSGYSYFMSKLRVEKKNWVERNSYSCSVVHEGLHNHHTTKSF SRTPGK
서열번호 78	AQAGPRAPCAAACCTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RL IEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNSISRIQRDGSFQCQLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLSLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDIA AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQSAGS VSANATLTVLETPSLAVPLEDRVVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GGG GS EPRGPTIKPCPPCKCPAPNLLGGPSVF IFPPKIKDVLMI SLSPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQQTTHREDYNSTLRVVSALPIQHODW MSGKEFKCKVNNKDLPAPIERTISKPKGSRAPQVYVLPPEEEMTKKQVLTTCMVTDMPEDIYVEWTNNG KTELNYKNTEPVLDSGYSYFMSKLRVEKKNWVERNSYSCSVVHEGLHNHHTTKSF SRTPGK
서열번호 79	AQAGPRAPCAAACCTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQLKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESAGFDGLSRSLTLRLSKNRI TQLPVKAFKL PRLTQLDLNRNRI RL IEGLTFQGLDSLEVLRLQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLNNSISRIQRDGSFQCQLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNL SKLTLFGN KIKSVAKRAFSGLSLEHLNLGENAIRSVQFDAFAKMNKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDIA AIRTGTTARLECAATGHPNPQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDMGVYSCTAQSAGS VSANATLTVLETPSLAVPLEDRVVTVGETVAFQCKATGSPTPRIITWLKGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCEMSPLGTERAHSQSLILPTPGCRKDGT GGG GS RNTGRGGEKKKEKEKEEQEERETKTPECSHTQPLGVF IFPPKIKDVLMI SLSPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQQTTHREDYNSTLRVVSALPIQHODW MSGKEFKCKVNNKDLPAPIERTISKPKGSRAPQVYVLPPEEEMTKKQVLTTCMVTDMPEDIYVEWTNNG KTELNYKNTEPVLDSGYSYFMSKLRVEKKNWVERNSYSCSVVHEGLHNHHTTKSF SRTPGK

서열번호 80	AQAGPRAPCAAACCTCAGDSLDCSGRGLATLPRDLPSWTRSLNLSYNRLSEIDSAAFEDLTNLQEVYLSNEL TAIPSLGAASIGVVSFLQHNKILSVDGSQKSYLSLEVLDLSSNNITEIRSSCFPNGLRIRELNLASNRIS ILESGAFDGLSRLLTLRLSKNRITQLPVKAFKLPRLTQLDLNRNRIRLIEGLTFQGLDSLEVLRQRNNIS RLTDGAFWGLSKMHVLHLEYNSLVEVNSGSLYGLTALHQLHLSNNSISRIQRDGSWFCQKLHELILSFNNLT RLDEESLAELSSLSILRLSHNAISHIAEGAFKGLKSLRVLDLDHNEISGTIEDTSGAFTGLDNLKSLTLFGN KIKSVAKRAFSGLSEHLNLGENAIRSVQFDAFAKMKNLKELYISSESFLCDCQLKWLPWLMGRMLQAFV TATCAHPESLKGQSIFSVLPDSFVCDDFPKPQIIITQPETTMVVGKDIRFTCSAASSSSSPMTFAWKDNEV LANADMENFAHVRAQDGEVMEYTTILHLRHVTFGHEGRYQCIITNHFGSTYSHKARLTVNVLPSFTKIPHDI AIRTGTTARLECAATGHPNPQIAWQKGGTDFPAARERRMHVMPDDVFFITDVKIDDMGVYSCTAQNSAGS VSANATLTVLETPSLAVPLEDRVVTGETVAFQCKATGSPTPRI TWLKGGRPLSLTERHHFTPGNQLLVVQN VMIDDAGRYTCMSNPLGTERAHSQLSILPTPGCRKDGT GGG GS EPKSSDKTHTSPPSPAPELLGGSSVF IFPPKIKDVLMSLSPIVTCVVVDVSEDDPDVQISWVFVNNVEVHTAQTQTHREDYNSTLRVVSALPIQHQDW MSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVTDMPEDIYVEWTNNG KTELNYKNTEPVLDSGSYFMYSKLRVEKKNWVERNSYSCSVVHEGLHNHHTTKSFRTPGK

표 23

[0104]

서열목록	서열정보
서열번호 81	GCTCAGGCTGGACCTAGGGCTCCTTGCGCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCCAGGGACCTGCCTTCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCTGCCGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCTGAGCAGATCCCTGCTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCGTGAAGGCCTTTAAGCTGCCAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACAATAGCCTGGTG GAGGTGAATCTTGACAGCTGTATGGCTGACCGCCTGCACAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCTGTCTTTTAAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTGTCCATCCTGCGCTGTCTCACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGACCACAACGAGATCTCT GGCACCATCGAGGATACAAGCGCGCCTTACAGGCCTGGACAATCTGCCAAGCTGACCTGTTTGGCAAC AAGATCAAGTCTGTGGCCAAGCGGGCTTCTTGCCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTTGCCAAGATGAAGAATCTGAAGGAGCTGTACATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGTGAAGTGGCTGCCACCTTGCGTGTGGAAAGGATGCTGAGGGCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCTGAAGGCCAGAGCATCTTCTCGTGCTGCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATACCCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTTAGCCCCATGACCTTCGCTGGAAGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAATTCGCCCACGTGAGAGCCCAGGATGGCGAAGTGATGGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACAGTGCATCATCACAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGGCAGC GTGTCCGCCAACGCCACCCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTGAAGGCCACCGGCTCTCCAACACCAAGGATCAGCTGGCTGAAG GGCGGCAGGCCCCTGAGCCTGACAGAGCGCCACCCTTCAACCCCTGGCAATCAGCTGCTGGTGGTGCAGAAC GTGATGATCGATGACGCCGGCAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCC CAGCTGTCTATCTGCCTACCCAGGCTGCCGAAGGATGGCACCACA GGCGGTGGC GGATCC GAGCCAAAGTCTCTGATAAGACACACCTCTCCACCATGCCAGCACCAGAGCTGCTGGGAGGACCAAGC GTGTTC atcttcccacccaagatcaaggacgtgctgatgatctccctgtcccccatcgtgacctgcgtggtggaggac gtgtccgaggacgaccccgacgtgcagatcagttggttcgtgaacaacgtggaagtgcacaccgcccagacc cagaccacagagaggactacaactccaccctgcgggtggtgtccgacctgcccatccagcaccaggactgg atgtccggcaaagaattcaagtgcgaagtgaacaacaaggacctgcctgcccccatcgagcggacctctcc aagcccaagggtccgtgcgggctccccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgcccaggacatctacgtggaatggaccaacaatggc aagaccgagctgaactacaagaacaccgacctgtgctggactccgacggctcctacttcatgtactccaag ctgcgggtggaaaagaagaactgggtcgagcggaactcctactcctgctccgtggtgcacgagggcctgcac aaccaccacaccaccaagtcttctcccggacccccggcaaa

서열번호 82	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTTCTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGGCGCCTTCGATGGCTGAGCAGATCCCTGTGACACTGCCGCTTCCAAGAACCGGATC ACCCAGCTGCCCGTGAAGGCCTTAAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCCTGACCTTCCAGGGCCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAATCTGGCAGCCTGTATGGCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCCTGCGCTGTCTCACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAGCCACAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCCTTCTTGCCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTGCCAAGATGAAGAATCTGAAGGAGCTGATACAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGTATGGGAAGGATGCTGAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCACCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTCTAGCCCCATGACCTTGGCTTGAAGCAAGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCACGTGAGAGCCAGGATGGCGAAGTGATGGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCACAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCCCTGGAGGACAGGGTGGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGCTGAAG GGCGGACAGCCCCCTGAGCCTGACAGAGCGCCACCCTTACCCTGGCAATCAGCTGCTGGTGGTGAGAAC GTGATGATCGATGACGCGGCAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCC CAGCTGTCTATCCTGCCTACCCAGGCTGCCGGAAGGATGGCACCACA GGCGGTGGC GGATCC Gagccteggggcectaccatcaagccctgcccccttgcaagtgcctgccctaatctgetggcgggaccc tcctgttc atcttcccacccaagatcaaggacgtgctgatgatctccctgtccccatcgtgacctgcgtggtggtggac gtgtccgaggacgaccccgacgtgcagatcagttggttcgtgaacaacgtggaagtgcacaccgcccagacc cagaccacagagaggactacaactccacctgcgggtggtgtccgacctgccatccagcaccaggactgg atgtccggcaaagaattcaagtgcgaagtgaacaacaaggacctgectgcccccatcgagcggaccatctcc aagcccaagggtccgtgcgggctccccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgcccaggacatctacgtggaatggaccaacaatggc aagaccgagctgaactacaagaacaccgagcctgtgctggactccgacggctcctacttcatgtactccaag ctgcgggtggaaaagaagaactgggtcgagcggaactcctactcctgctccgtggtgcacagggcctgcac aaccaccacaccaccaagtccttctccggacccccggcaaa

서열번호 83	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTGTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTCTTAATGGCCTGCGGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGGCGCCTTCGATGGCTGAGCAGATCCCTGTGACACTGCGCCTGCCAAGAACCGGATC ACCCAGCTGCCGTGAAGGCCTTAAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCCTGACCTTCCAGGGCCTGGATAGCCTGGAGGTGCTGCGCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAATCTGGCAGCCTGTATGGCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCCATCCTGCGCCTGTCTCACAAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGTGGATCTGGAACACAAACGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCCTTCTTGCCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTTGCCAAGATGAAGAATCTGAAGGAGCTGATACAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGTGGGAAGGATGCTGAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGTGCCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCAGCCAGCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTCTAGCTCCTCTAGCCCCATGACCTTGCCTTGGGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCACGTGAGAGCCAGGATGGCGAAGTGATGGAGTATACCACA ATCCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAAATCACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCCGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCACAGATGTGAAGATCGATGACATGGCGTGTACTCCTGCACCGCACAGAACAGCGCCGCGCAGC GTGTCCGCCAACGCCACCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCCCTGGAGGACAGGGTGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACACCAAGGATCACCTGGCTGAAG GGCGGCAGGCCCTGAGCCTGACAGAGCGCCACCACTTACCCTGGCAATCAGCTGCTGGTGGTGACAAC GTGATGATCGATGACGCCGCGAGGTATACATGCGAGATGAGCAATCCTCTGGGCACCGAGAGGGCACACTCC CAGCTGTCTATCCTGCCTACCCAGGCTGCCGGAAGGATGGCACCACA GGCGGTGGC GGATCC cgcaacaccggccgcgggcgaggagaagaagaaggagaaggagaaggaggagcaggaggagcgcgagacc aagacccccgagtccccagccaccccagccccctgggctgttc atcttcccacccaagatcaaggacgtgctgatgatctccctgtccccatcgtgacctgctggtggtggac gtgtccgaggacgaccccgacgtgcagatcagttggttcgtgaacaacgtggaagtgcacaccgcccagacc cagaccacagagaggactacaactccacctgcggtggtgtccgacctgcccacagcaccaggactgg atgtccggcaaagaattcaagtgcgaagtgaacaacaaggacctgectgcccccatcgagcggacctctcc aagcccaagggtccgtgcggtctcccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgcccaggacatctacgtggaatggaccaacaatggc aagaccgagctgaactacaagaacaccgagcctgtgctggactccgacggtctacttcatgtactccaag ctgcggtggaaaagaagaactgggtcgagcggaactctactcctgctcgtggtgcacagggcctgcac aaccaccacaccaccaagtccttctccggacccccggcaaa

서열번호 84	GCTCAGGCTGGACCTAGGGCTCCTTGCCTGCCGCTGCACCTGTGCAGGCGATTCTCTGGACTGCAGCGGC CGGGGCTGGCCACACTGCCAGGGACCTGCCTTCTGGACCAGATCTCTGAACCTGAGCTACAATCGGCTG TCCGAGATCGATTCTGCCGCTTTGAGGACCTGACAAATCTGCAGGAGGTGTATCTGAACAGCAATGAGCTG ACCGCAATCCCTCCCTGGGAGCAGCTCTATCGGCGTGGTGAGCCTGTTCTGCAGCACAAAGATCCTG AGCGTGGATGGCTCCAGCTGAAGAGCTACCTGTCTCTGGAGGTGCTGGACCTGAGCTCCAACAATATCACC GAGATCAGATCTAGCTGTTTCTAATGGCCTGCCGATCAGAGAGCTGAACCTGGCCTCTAATCGGATCAGC ATCCTGGAGTCCGCGCCTTCGATGGCTGAGCAGATCCCTGCTGACACTGCGCCTGTCCAAGAACCGGATC ACCCAGCTGCCCGTGAAGGCTTTAAGCTGCCTAGGCTGACACAGCTGGACCTGAACCGGAATAGAATCAGG CTGATCGAGGGCTGACCTTCCAGGGCTGGATAGCCTGGAGGTGCTGCCCTGCAGCGGAACAATATCTCC CGCCTGACAGACGAGCATTTTGGGGCTGTCTAAGATGCACGTGCTGCACCTGGAGTACATAGCCTGGTG GAGGTGAACCTCTGGCAGCCTGTATGGCTGACCGCCTGCACCAGCTGCACCTGTCCAACAATAGCATCAGC AGAATCCAGAGGGATGGCTGGTCTTCTGCCAGAAGCTGCACGAGCTGATCCTGTCTTTAACAATCTGACC AGGCTGGACGAGGAGAGCCTGGCAGAGCTGTCTCTCTGTCATCCTGCGCCTGTCTACAATGCCATCAGC CACATCGCCGAGGGCGCCTTTAAGGGCTGAAGAGCCTGAGGGTGTGTGGACCAACAGAGATCTCT GGCACCATCGAGGATACAAGCGGCGCCTTCACAGGCTGGACAATCTGTCCAAGCTGACCCTGTTTGGCAAC AAGATCAAGTCTGTGGCAAGCGGGCTTCTTGGCCTGGAGAGCCTGGAGCACCTGAACCTGGGCGAGAAT GCCATCAGATCCGTGCAGTTCGATGCCTTTCGCAAGATGAAGAATCTGAAGGAGCTGATCAGCTCCGAG AGCTTCTGTGCGACTGTGAGCTGAAGTGGCTGCCACCTTGGCTGTATGGGAAGGATGCTGCAGGCCTTTGTG ACCGCCACATGCGCCACCCAGAGAGCCTGAAGGGCCAGAGCATCTTCTCCGTGCTGCCGATAGCTTCGTG TGCGACGATTTTCTAAGCCACAGATCATCACCAGCCAGAGACAACAATGGCCGTGGTGGGCAAGGACATC CGGTTTACATGTTCCGCGCCTTAGCTCTTAGCCCCATGACCTTGCCTTGAAGAAGGATAACGAGGTG CTGGCCAATGCCGACATGGAGAACTTCGCCACGTGAGAGCCAGGATGGCGAAGTGTGAGTATACCACA ATCTGCACCTGCGGCACGTGACCTTTGGCCACGAGGGCAGATACCAGTGCATCATCAAACTACTTCGGC TCTACCTATAGCCACAAGGCCAGGCTGACAGTGAACGTGCTGCCTAGCTTTACCAAGATCCACACGACATC GCCATCAGAACAGGCACCACAGCAAGGCTGGAGTGTGACGAACCGGACACCCAAACCTCAGATCGCATGG CAGAAGGATGGAGGCACAGACTTCCCTGCAGCCCGCAGAGGAGAATGCACGTGATGCCAGACGATGACGTG TTCTTTATCAGATGTGAAGATCGATGACATGGCGTGTACTCTGCACCCACAGAACAGCGCCGCGCAGC GTGTCCGCAACGCCACCCTGACCGTGTGGAGACACCATCCCTGGCCGTGCCCTGGAGGACAGGCTGTG ACCGTGGGCGAGACAGTGGCCTTTCAGTGTAAAGGCCACCGGCTCTCCAACCAAGGATCACCTGGTGAAG GGCGGCGAGCCCTGAGCCTGACAGAGCGCCACCTTCAACCCCTGGCAATCAGCTGCTGGTGGTGCAGAAC GTGATGATCGATACGCGGCGAGGTATACATGCGAGATGAGCAATCCTCTGGGACCGAGAGGGCACACTCC CAGCTGTCTATCTGCTACCCAGGCTGCCGGAAGGATGGCACCACA GGCGGTGGC GGATCC gaaccgaaatcttctgacaaaaccacacctctcgccgtctcgggtcctgggaactgctgggtggttcttct gttttc atcttcccacccaagatcaaggacgtgctgatgatctcctgtccccatcgtgacctgcgtggtggtggac gtgtccgaggacgaccccgacgtgcagatcagttggttcgtgaacaactggaagtgcacaccgcccagacc cagaccacagagaggactacaactccacctgcggtggtgtcgccctgccccatccagaccaggactgg atgtcggcaagaattcaagtgaagtgaacaacaaggacctgctgccccatcgagcggacctctcc aagcccaagggtccgtgcggtgctccccaggtgtacgtgctgccccctccagaggaagagatgaccaagaag caggtcacactgacctgcatggtcaccgacttcatgcccaggacatctacgtggaatggaccaacaatggc aagaccgagctgaactacaagaacaccgagcctgtgctggactccgacggtcctacttcatgtactccaag ctcggttggaagaagaactgggtcgagcggaactcctactcctgctccgtggtgcacgagggcctgcac aaccaccacaccaccaagtcttctccgggacccccggcaaa

- [0106] 본 발명에서 제공하는 상기의 융합 단백질은 이펙터 T 세포(effector T cell)에 존재하는 Lrig-1 단백질에 대한 리간드와 상호 작용하여, Lrig-1 단백질을 표면에 포함하고 있는 조절 T 세포(regulatory T cell, Treg cell)와 이펙터 T 세포간의 상호 작용을 저해함에 따라 조절 T 세포의 활성을 억제하고 이펙터 T 세포의 활성은 유지 혹은 상승시켜 암 세포 중에서도 특히 고형암 세포의 성장을 효과적으로 억제할 수 있다.
- [0108] 본 발명의 다른 구현 예에 따르면, 본 발명에서 제공하는 상기 융합 단백질을 코딩하는 핵산 분자를 제공한다.
- [0109] 본 발명의 핵산 분자는 본 발명에서 제공하는 융합 단백질의 아미노산 서열을 당업자에게 알려진 바와 같이 폴리뉴클레오티드 서열로 번역된 핵산 분자 모두를 포함한다. 그러므로 ORF(open reading frame)에 의한 다양한 폴리뉴클레오티드 서열이 제조될 수 있으며 이 또한 모두 본 발명의 핵산 분자에 포함된다.
- [0110] 본 발명의 바람직한 일 예시로, 상기 핵산 분자는 서열번호 17 내지 20, 25 내지 28, 33 내지 36, 41 내지 44, 49 내지 52, 57 내지 60, 65 내지 68, 73 내지 76 및 81 내지 84 중 어느 하나로 표시될 수 있으나, 이에 제한되는 것은 아니다.
- [0111] 본 발명의 또 다른 구현 예에 따르면, 본 발명에서 제공하는 상기 단리된 핵산 분자가 삽입된 발현 벡터를 제공한다.

- [0112] 본 발명에서 상기 "벡터"는 어떤 핵산 분자가 연결된 또 다른 핵산을 수송할 수 있는 상기 핵산 분자이다. 벡터의 한 가지 유형은, 추가적인 DNA 세그먼트가 결합될 수 있는 원형 이중가닥 DNA를 가리키는 "플라스미드"이다. 또 다른 유형의 벡터는 파지 벡터이다. 또 다른 유형의 벡터는 바이러스성 벡터로, 추가적인 DNA 세그먼트가 바이러스 게놈에 결합될 수 있다. 어떤 벡터들은 그들이 유입된 숙주세포에서 자율적인 복제를 할 수 있다(예컨대, 박테리아성 벡터는 박테리아성 복제 기원을 갖는 예피솜 포유류 벡터). 기타 벡터(예컨대, 비-예피솜 포유류 벡터)는 숙주세포에 유입되면서 숙주세포의 게놈에 통합될 수 있고, 그럼으로써, 숙주 게놈과 함께 복제된다. 뿐만 아니라, 어떤 벡터는 이들이 작동차원에서 연결된 유전자의 발현을 지시할 수 있다. 이와 같은 벡터는 본원에서 "제조합 발현 벡터" 또는 단순히 "발현 벡터"라 명명된다. 일반적으로 제조합 DNA 기법에서 유용한 발현 벡터는 종종 플라스미드의 형태로 존재한다. 본 명세서에서, "플라스미드"와 "벡터"는, 플라스미드가 벡터 중 가장 통상적으로 사용되는 형태이기 때문에, 상호 교환하여 사용될 수 있다.
- [0113] 본 발명에서 상기 발현 벡터의 구체적인 예시로는 상업적으로 널리 사용되는 pCDNA 벡터, F, R1, RP1, Col, pBR322, ToL, Ti 벡터; 코스미드; 람다, 람다도이드(lambdoid), M13, Mu, p1 P22, Q μ , T-even, T2, T3, T7 등의 파아지; 식물 바이러스로 이루어진 군으로부터 선택될 수 있으나, 이에 제한되는 것은 아니며, 당업자에게 발현 벡터로 알려진 모든 발현 벡터는 본 발명에 사용 가능하고, 발현 벡터를 선택할 때에는 목적으로 하는 숙주 세포의 성질에 따른다. 숙주세포로의 벡터 도입 시 인산칼슘 트랜스펙션, 바이러스 감염, DEAE-텍스트란 조절 트랜스펙션, 리포펙타민 트랜스펙션 또는 전기천공법에 의해 수행될 수 있으나 이에 한정되는 것은 아니며 당업자는 사용하는 발현 벡터 및 숙주 세포에 알맞은 도입 방법을 선택하여 이용할 수 있다. 바람직하게 벡터는 하나 이상의 선별 마커를 함유하나 이에 한정되지 않으며, 선별 마커를 포함하지 않은 벡터를 이용하여 생산물 생산 여부에 따라 선별이 가능하다. 선별 마커의 선택은 목적하는 숙주 세포에 의해 선별되며, 이는 이미 당업자에게 알려진 방법을 이용하므로 본 발명은 이에 제한을 두지 않는다.
- [0114] 본 발명의 핵산 분자를 정제를 용이하게 하기 위하여 태그 서열을 발현 벡터 상에 삽입하여 융합시킬 수 있다. 상기 태그로는 핵사-히스티딘 태그, 헤마글루티닌 태그, myc 태그 또는 flag 태그를 포함하나 이에 한정되는 것은 아니며 당업자에게 알려진 정제를 용이하게 하는 태그는 모두 본 발명에서 이용 가능하다.
- [0116] 본 발명의 또 다른 구현 예에 따르면, 본 발명에서 제공하는 상기 발현 벡터가 형질 감염된 숙주 세포주를 제공한다.
- [0117] 본 발명에서 상기 "숙주 세포"에는 폴리펩타이드 삽입물의 편입을 위한 벡터(들)의 수령자(recipient)일 수 있거나 또는 수령자였던 개별적인 세포 또는 세포배양물이 포함된다. 숙주 세포에는 단일 숙주 세포의 자손이 포함되고, 상기 자손은 자연적인, 우발적인 또는 고의의 돌연변이 때문에 반드시 원래 모세포와 완전히 동일(형태 학상 또는 게놈 DNA 보완체에서)하지 않을 수 있다. 숙주 세포에는 본원의 폴리펩타이드(들)로 체내에서 형질주입된 세포가 포함된다.
- [0118] 본 발명에 있어서, 상기 숙주 세포로는 포유동물, 식물, 곤충, 균류 또는 세포성 기원의 세포를 포함할 수 있고, 예를 들면 대장균, 스트렙토미세스, 살모넬라 티피뮤리움 등의 박테리아 세포; 효모 세포, 피치아 파스토리스 등의 균류세포; 드로조필라, 스포도프테라 Sf9 세포 등의 곤충 세포; CHO(중국 햄스터 난소 세포, Chinese hamster ovary cells), SP2/0(생쥐 골수종), 인간 림프아구(Human lymphoblastoid), COS, NSO(생쥐 골수종), 293T, 보우 멜라노마 세포, HT-1080, BHK(베이비 햄스터 신장세포, Baby Hamster Kidney cells), HEK(인간 배아신장 세포, Human Embryonic Kidney cells) 또는 PERC.6(인간 망막 세포)의 동물 세포; 또는 식물 세포일 수 있으나, 이에 제한되는 것은 아니며, 당업자에게 알려진 숙주 세포주로 사용 가능한 세포는 모두 이용 가능하다.
- [0120] 본 발명의 또 다른 구현 예에 따르면, 본 발명에서 제공하는 융합 단백질을 유효 성분으로 포함하는 암의 예방 또는 치료용 약학 조성물을 제공한다.
- [0121] 본 발명에서 상기 "암" 포유류에서 전형적으로 조절되지 않는 세포 성장으로 특징 지어진 생리적 상태를 나타내거나 가리킨다. 본 발명에서 예방, 개선 또는 치료의 대상이 되는 암은 고형 장기(solid organ)에서 비정상적으로 세포가 성장하여 발생한 덩어리로 이루어진 고형암(solid tumor)일 수 있고, 고형 장기의 부위에 따라 위암, 간암, 교세포종, 난소암, 대장암, 두경부암, 방광암, 신장세포암, 유방암, 전이암, 전립선암, 췌장암, 흑색종 또는 폐암 등일 수 있으며, 바람직하게는 흑색종 또는 대장암일 수 있으나, 이에 제한되는 것은 아니다.
- [0122] 한편, 본 발명에서, "예방"은 본 발명의 약학 조성물을 이용하여 질환의 증상을 차단하거나, 그 증상을 억제 또는 지연시키는 모든 행위라면 제한없이 포함할 수 있다.

- [0123] 또한, 본 발명에서, "치료"는 본 발명의 약학 조성물을 이용하여 질환의 증상이 호전되거나 이롭게 되는 모든 행위라면 제한없이 포함할 수 있다.
- [0124] 본 발명에서 상기 약학 조성물은 캡슐, 정제, 과립, 주사제, 연고제, 분말 또는 음료 형태임을 특징으로 할 수 있으며, 상기 약학 조성물은 인간을 대상으로 하는 것을 특징으로 할 수 있다.
- [0125] 본 발명에서 상기 약학 조성물은 이들로 한정되는 것은 아니지만, 각각 통상의 방법에 따라 산제, 과립제, 캡슐, 정제, 수성 현탁액 등의 경구형 제형, 외용제, 좌제 및 멸균 주사 용액의 형태로 제형화하여 사용될 수 있다. 본 발명의 약학 조성물은 약학적으로 허용 가능한 담체를 포함할 수 있다. 약학적으로 허용되는 담체는 경구 투여 시에는 결합제, 활택제, 붕해제, 부형제, 가용화제, 분산제, 안정화제, 현탁화제, 색소, 향료 등을 사용할 수 있으며, 주사제의 경우에는 완충제, 보존제, 무통화제, 가용화제, 등장제, 안정화제 등을 혼합하여 사용할 수 있으며, 국소투여용의 경우에는 기제, 부형제, 윤활제, 보존제 등을 사용할 수 있다. 본 발명의 약학 조성물의 제형은 상술한 바와 같은 약제학적으로 허용되는 담체와 혼합하여 다양하게 제조될 수 있다. 예를 들어, 경구 투여시에는 정제, 트로키, 캡슐, 엘릭서(elixir), 서스펜션, 시럽, 웨이퍼 등의 형태로 제조할 수 있으며, 주사제의 경우에는 단위 투약 앰플 또는 다수회 투약 형태로 제조할 수 있다. 기타, 용액, 현탁액, 정제, 캡슐, 서방형 제제 등으로 제형화할 수 있다.
- [0126] 한편, 제제화에 적합한 담체, 부형제 및 희석제의 예로는, 락토즈, 텍스트로즈, 수크로즈, 솔비톨, 만니톨, 자일리톨, 에리스리톨, 말디톨, 전분, 아카시아 고무, 알지네이트, 젤라틴, 칼슘 포스페이트, 칼슘 실리케이트, 셀룰로즈, 메틸 셀룰로즈, 미정질 셀룰로즈, 폴리비닐피롤리돈, 물, 메틸하이드록시벤조에이트, 프로필하이드록시벤조에이트, 탈크, 마그네슘 스테아레이트 또는 광물유 등이 사용될 수 있다. 또한, 충전제, 향 응집제, 윤활제, 습윤제, 향료, 유화제, 방부제 등을 추가로 포함할 수 있다.
- [0127] 본 발명에 상기 약학 조성물의 투여 경로는 이들로 한정되는 것은 아니지만 구강, 정맥내, 근육내, 동맥내, 골수내, 경막내, 심장내, 경피, 피하, 복강내, 비강내, 장관, 국소, 설하 또는 직장이 포함된다. 경구 또는 비경구 투여가 바람직하다.
- [0128] 본 발명에서 상기 "비경구"란, 피하, 피내, 정맥내, 근육내, 관절내, 활액낭내, 흉골내, 경막내, 병소내 및 두개골내 주사 또는 주입기술을 포함한다. 본 발명의 약학 조성물은 또한 직장 투여를 위한 좌제의 형태로 투여될 수 있다.
- [0129] 본 발명의 상기 약학 조성물은 사용된 특정 화합물의 활성, 연령, 체중, 일반적인 건강, 성별, 정식, 투여 시간, 투여 경로, 배출율, 약물 배합 및 예방 또는 치료될 특정 질환의 중증도를 포함한 여러 요인에 따라 다양하게 변할 수 있고, 상기 약학 조성물의 투여량은 환자의 상태, 체중, 질병의 정도, 약물 형태, 투여 경로 및 기간에 따라 다르지만 당업자에 의해 적절하게 선택될 수 있고, 1일 0.0001 내지 50mg/kg 또는 0.001 내지 50mg/kg으로 투여할 수 있다. 투여는 하루에 한번 투여할 수도 있고, 수회 나누어 투여할 수도 있다. 상기 투여량은 어떠한 면으로든 본 발명의 범위를 한정하는 것은 아니다. 본 발명에 따른 의약 조성물은 환제, 당의정, 캡슐, 액제, 겔, 시럽, 슬러리, 현탁제로 제형화될 수 있다.
- [0131] 본 발명의 또 다른 구현 예에 따르면, 본 발명에 따른 융합 단백질 또는 이를 포함하는 조성물을 개체에 투여하는 단계를 포함하는 암의 예방 또는 치료 방법에 관한 것이다.
- [0132] 본 발명의 융합 단백질은 이펙터 T 세포(effector T cell)에 존재하는 Lrig-1 단백질에 대한 리간드와 상호 작용하여, Lrig-1 단백질을 표면에 포함하고 있는 조절 T 세포(Treg cell)와 이펙터 T 세포간의 상호 작용을 저해함에 따라 조절 T 세포의 활성을 억제하고 이펙터 T 세포의 활성은 유지 혹은 상승시켜 암 세포 중에서도 특히 고형암 세포의 성장을 효과적으로 억제할 수 있다.
- [0133] 본 발명에서 상기 "개체"는 암의 발병이 의심되는 개체로서, 상기 암 발병의 의심 개체는 해당 질환이 발병하였거나 발병할 수 있는 인간을 포함한 쥐, 가축 등을 포함하는 포유동물을 의미하나, 본 발명의 융합 단백질 또는 이를 포함하는 상기 조성물로 치료 가능한 개체는 제한 없이 포함된다.
- [0134] 본 발명의 방법은 융합 단백질 또는 이를 포함하는 조성물을 약학적 유효량으로 투여하는 것을 포함할 수 있다. 적합한 총 1일 사용량은 올바른 의학적 판단범위 내에서 처치의에 의해 결정될 수 있으며, 1회 또는 수회로 나누어 투여할 수 있다. 그러나 본 발명의 목적상, 특정 환자에 대한 구체적인 치료적 유효량은 달성하고자 하는 반응의 종류와 정도, 경우에 따라 다른 제제가 사용되는지의 여부를 비롯한 구체적 조성물, 환자의 연령, 체중, 일반 건강 상태, 성별 및 식이, 투여 시간, 투여 경로 및 조성물의 분비율, 치료기간, 구체적 조성물과 함께 사

용되거나 동시 사용되는 약물을 비롯한 다양한 인자와 의약 분야에 잘 알려진 유사 인자에 따라 다르게 적용하는 것이 바람직하다.

[0135] 한편, 이에 제한되지 않으나, 상기 암의 예방 또는 치료 방법은 하나 이상의 암 질환에 대한 치료적 활성을 가지는 화합물 또는 물질을 투여하는 것을 더 포함하는 병용 요법일 수 있다.

[0136] 본 발명에서 상기 "병용"은 동시, 개별 또는 순차 투여를 나타내는 것으로 이해되어야 한다. 상기 투여가 순차 또는 개별적인 경우, 2차 성분 투여의 간격은 상기 병용의 이로운 효과를 잃지 않도록 하는 것이어야 한다.

[0137] 본 발명에서 상기 융합 단백질의 투여 용량은 환자 체중 1 kg당 약 0.0001 μ g 내지 500 mg일 수 있으나, 이에 제한되는 것은 아니다.

발명의 효과

[0138] 본 발명에서 제공하는 융합 단백질은 이펙터 T 세포(effector T cell)에 존재하는 Lrig-1 단백질에 대한 리간드와 상호 작용하여, Lrig-1 단백질을 표면에 포함하고 있는 조절 T 세포(Treg cell)와 이펙터 T 세포간의 상호 작용을 저해함에 따라 조절 T 세포의 활성을 억제하고 이펙터 T 세포의 활성은 유지 혹은 상승시켜 암 세포 중에서도 특히 고형암 세포의 성장을 효과적으로 억제할 수 있다.

도면의 간단한 설명

- [0139] 도 1은 본 발명의 일 실시예에 따른 Lrig-1 단백질의 구조를 나타낸 것이다.
- 도 2는 본 발명의 일 실시예에 따른 Lrig-1 단백질의 구조를 나타낸 것이다.
- 도 3은 본 발명의 일 실시예에 따른 Lrig-1 단백질의 항원 결정기(epitope)를 예측한 결과를 나타낸 것이다.
- 도 4는 본 발명의 일 실시예에 따른 Lrig-1 단백질의 항원 결정기(epitope)를 예측한 결과를 나타낸 것이다.
- 도 5는 본 발명의 일 실시예에 따른 Lrig-1 mRNA의 발현 정도를 나타낸 것이다.
- 도 6은 본 발명의 일 실시예에 따른 Lrig-1 mRNA의 발현 정도를 나타낸 것이다.
- 도 7은 본 발명의 일 실시예에 따른 Lrig-1 mRNA의 발현 정도를 나타낸 것이다.
- 도 8은 본 발명의 일 실시예에 따른 Lrig-1, Lrig-2 및 Lrig-3 mRNA의 발현 정도를 나타낸 것이다.
- 도 9는 본 발명의 일 실시예에 따른 조절 T 세포와 비-조절 T 세포 내 Lrig-1 단백질의 발현량 비교 결과를 나타낸 것이다.
- 도 10은 본 발명의 일 실시예에 따른 조절 T 세포의 표면에 Lrig-1 단백질의 발현을 나타낸 것이다.
- 도 11은 본 발명의 일 실시예에 따른 융합 단백질의 이펙터 T 세포에 대한 조절 T 세포의 억제능을 저해하는 효과를 나타낸 것이다.
- 도 12는 본 발명의 일 실시예에 따른 융합 단백질에 의해 인식되는 리간드가 존재하는 T 세포 서브세트(subset)를 나타낸 것이다.
- 도 13은 본 발명의 일 실시예에 따른 융합 단백질을 이용한 암 치료 실험의 설계도를 나타낸 것이다.
- 도 14은 본 발명의 일 실시예에 따른 융합 단백질을 이용한 암 치료 효과를 분석한 결과를 나타낸 것이다.
- 도 15는 본 발명의 일 실시예에 따른 융합 단백질을 이용한 암 치료 효과를 분석한 결과를 나타낸 것이다.

발명을 실시하기 위한 구체적인 내용

[0140] 이하, 실시예를 통하여 본 발명을 더욱 상세히 설명하고자 한다. 이들 실시예는 오로지 본 발명을 보다 구체적으로 설명하기 위한 것으로서, 본 발명의 요지에 따라 본 발명의 범위가 이들 실시예에 의해 제한되지 않는다는 것은 당업계에서 통상의 지식을 가진 자에게 있어서 자명할 것이다.

[0142] 실시예

[0144] [준비예 1] T 세포 아형 세포 배양

[0145] 조절 T 세포(Treg)에서만 Lrig-1 단백질이 발현되는지 확인하기 위하여, T 세포의 아형(subset)인 Th0, Th1,

Th2, Th17 및 iTreg을 준비하였다. 상기 iTreg은 자연적으로 분리한 nTreg과는 달리 하기 조성을 포함하는 배지에서 분화를 인공적으로 유도한 세포를 의미한다.

[0146] T 세포의 아형은 우선, 쥐의 비장으로부터 얻은 나이브(naive) T 세포를 분리한 뒤, 우태아혈청(FBS; hyclone, logan, UT) 10%를 포함하는 RPMI1640(Invitrogen Gibco, Grand Island, NY) 영양배지에 하기 표 24의 성분을 각각 더 포함하도록 하여, 37°C, 5 % CO₂ 배양기 내에서 72시간 배양을 통해 각각의 세포로 분화 유도하였다.

표 24

분화 세포	조성
Th0	anti-CD3, anti-CD28
Th1	IL-12, anti-IL-4 항체
Th2	IL-4, anti-IFN β
Th17	IL-6, TGF β , anti-IFN β , anti-IL-4
iTreg	IL-2, TGF β

[실시예 1] Lrig-1 구조 분석

[0151] 조절 T 세포의 표면 단백질인 Lrig-1 단백질의 세포 외 도메인을 포함하는 융합 단백질을 제작하기 위하여 Lrig-1 단백질의 세포 외 도메인의 3차원 입체 구조를 예측하였다.

[0152] 우선, 항원 결정기(Epitope) 염기서열 예측을 위해 Lrig-1 단백질의 세포 외 도메인(Extracellular domain; ECD)의 구조를 확인하기 위하여 Uniprot(<http://www.uniprot.org>)과 RCSB Protein Data Bank (<http://www.rcsb.org/pdb>) 툴을 이용하여 3차원 입체 구조를 예측한 뒤, 그 결과를 도 1 및 2에 나타내었다.

[0153] 도 1에서 보는 바와 같이, Lrig-1 단백질의 세포 외 도메인 중 Lrig-LRR 도메인(아미노산 서열 41 ~ 494번) 내에는 LRR1 내지 LRR15의 총 15개의 류신 리치 부위(Leucine rich region)가 존재하였다. 상기 LRR 도메인 각각은 23 내지 27개의 아미노산으로 구성되고, 류신은 3 내지 5개가 존재하였다.

[0154] 또한, 도 2에서 보는 바와 같이, Lrig-1 단백질의 세포외 도메인 중 Lrig-1 단백질의 아미노산 서열 494 내지 781번에는 면역글로불린-유사 도메인(Immunoglobulin-like domain)이 3개 존재하였다.

[실시예 2] Lrig-1 항원 결정기(epitope) 아미노산 서열 예측

[0157] 상기 염기서열의 예측은 Lrig-1 단백질의 구조를 기반으로 하는 항원 결정기 예측 소프트웨어(epitope prediction software)인 Ellipro 서버(<http://tools.iedb.org/ellipro/>)를 이용하였다. 상기 Ellipro 검색 엔진은 현존하는 항원 결정기를 예측하는 알고리즘 중에서 가장 신뢰도가 높다고 알려진 검색엔진에 해당하여 이를 이용하였다.

[0158] 항원 결정기 예측 소프트웨어에 상기 실시예 1에서 분석된 세포의 도메인을 입력한 뒤, 예측된 항원 결정기의 예측된 연속 또는 불연속 아미노산 서열을 도 3 및 4에 나타내었다.

[0159] 도 3 및 4에서 보는 바와 같이, 연속된 항원 결정기 아미노산 서열은 총 22개가 예측되었고, 불연속된 항원 결정기 아미노산 서열은 총 8개가 예측되었다.

[실시예 3] Lrig-1 mRNA의 조절 T 세포에서의 특이적 발현 확인

[0162] Lrig-1 단백질이 조절 T 세포에 특이적인 바이오마커(biomarker)로 작용할 수 있는지 검증하였다.

[0163] 상기 검증을 위하여, 쥐의 비장으로부터 CD4 비드를 통해 자석 활성 세포 분류기(magnet-activated cell sorting; MACS)를 이용하여 CD4⁺ T 세포를 분리하였다. 이후, CD25 항체를 이용하여 형광 활성 세포 분류기(FACS)를 이용해 조절 T (CD4⁺CD25⁺ T) 세포 및 비 조절 T (CD4⁺CD25⁻ T) 세포를 분리하였다. 각각의 세포 및 상기 준비예 1에서 분화된 세포는 트리졸(Trizol)을 이용하여 mRNA를 추출한 뒤, 게노믹 RNA는 gDNA 추출 키트(Qiagen)를 이용하여 업체에서 제공한 프로토콜에 의해 gDNA를 제거하였다. gDNA가 제거된 mRNA는 BDsprint cDNA 합성 키트(Clonetech)를 통해 cDNA로 합성하였다.

[0164] 상기 cDNA에서 Lrig-1 mRNA의 발현량을 정량적으로 확인하기 위하여 실시간 중합효소연쇄반응(real time PCR)을 수행하였다.

[0165] 상기 실시간 중합효소연쇄반응은 SYBR Green (Molecular Probes)을 이용하여 업체에서 제공한 프로토콜에 의해 95℃에서 3분, 61℃에서 15초, 72℃에서 30초씩 40 사이클의 조건으로, 하기 표 25의 프라이머를 이용하여 수행하였고, 상대적인 유전자 발현량은 ΔCT 방법을 이용하여 계산하였으며, HPRT를 이용하여 일반화(normalization) 하여, 그 결과를 도 5 내지 8에 나타내었다.

표 25

프라이머	서열
쥐 Lrig-1	Forward 5' - GAC GGA ATT CAG TGA GGA GAA CCT - 3'
	Reverse 5' - CAA CTG GTA GTG GCA GCT TGT AGG - 3'
쥐 Lrig-2	forward 5' - TCA CAA GGA ACA TTG TCT GAA CCA- 3'
	reverse 5' - GCC TGA TCT AAC ACA TCC TCC TCA- 3'
쥐 Lrig-3	forward 5' - CAG CAC CTT GAG CTG AAC AGA AAC - 3'
	reverse 5' - CCA GCC TTT GGT AAT CTC GGT TAG - 3'
쥐 FOXP3	forward 5' - CTT TCA CCT ATC CCA CCC TTA TCC - 3'
	reverse 5' - ATT CAT CTA CGG TCC ACA CTG CTC - 3'
ACTG1	forward 5' - GGC GTC ATG GTG GGC ATG GG - 3'
	reverse 5' - ATG GCG TGG GGA AGG GCG TA - 3'

[0168] 도 5에서 보는 바와 같이, 비-조절 T 세포($CD4^+CD25^-$ T cell)에 비하여 조절 T 세포($CD4^+CD25^+$ T cell)에서 Lrig-1의 발현이 18.1배 높은 것을 알 수 있다. 이는, 기존에 알려져 있는 조절 T 세포의 마커인 Lag3 및 Ikzf4와 비교하였을 때 약 10배 정도 발현량이 높은 수준이었다.

[0169] 또한, 도 6 및 7에서 보는 바와 같이, 다른 종류의 면역 세포에 비하여 조절 T 세포, 특히 유도된 조절 T 세포(iTreg)에 비해 자연적으로 분리한 조절 T 세포(nTreg)에서 Lrig-1 mRNA의 발현이 현저하게 높았다.

[0170] 또한, 도 8에서 보는 바와 같이, Lrig 패밀리에 해당하는 Lrig-1, Lrig-2 및 Lrig-3 중에서 Lrig-1의 발현이 가장 높았다.

[0171] 상기 결과를 통해 본 발명에 따른 Lrig-1 단백질은 조절 T 세포, 특히 자연적으로 존재하는 조절 T 세포에서 특이적으로 발현하는 것을 알 수 있다.

[실시예 4] Lrig-1 단백질의 조절 T 세포에서의 특이적 발현 확인

[0174] Lrig-1 mRNA로부터 발현된 Lrig-1 단백질이 조절 T 세포에서만 특이적으로 발현되는지 확인하였다.

[0175] 조절 T 세포 특이적인 전사 인자인 FOXP3 프로모터에 RFP(Red fluorescence protein)이 결합된 FOXP3-RFP 주입(Knock-in) 쥐를 이용하여, 상기 쥐의 비장으로부터 $CD4^+$ 비드로 자석 활성 세포 분류기(magnet-activated cell sorting; MACS)를 이용하여 $CD4^+$ T 세포를 분리하였다. 이후, RFP 단백질을 이용하여, 형광 활성 세포 분류기(FACS)를 통해 조절 T 세포($CD4^+RFP^+$ T cell) 및 비-조절 T 세포($CD4^+RFP^-$ T cell)를 분리하여 얻었다. 각각의 상기 세포는 구입한 Lrig-1 항체 및 음성 대조군은 아이소타입(isotype)을 통해 염색하여 형광 활성 세포 분류기로 Lrig-1의 발현량을 측정하여, 그 결과를 도 9에 나타내었다.

[0176] 도 9에서 보는 바와 같이, 점선으로 표시되는 비-조절 T 세포의 경우 음성 대조군과 거의 동일한 Lrig-1의 발현 수준을 보였지만, 조절 T 세포의 경우 Lrig-1의 발현 수준이 높은 세포가 다수 존재하였다.

[0177] 상기 결과를 통해 본 발명에 따른 Lrig-1 단백질은 조절 T 세포에서 특이적으로 발현하는 것을 알 수 있다.

[실시예 5] 조절 T 세포 표면에서의 Lrig-1 단백질 특이적 발현 확인

[0180] Lrig-1 단백질이 세포 치료의 타겟이 되기 위해서는 조절 T 세포의 표면에서 발현되어야 더욱 효과적으로 타겟 치료를 할 수 있으므로, Lrig-1 단백질이 표면에서의 발현 여부를 확인하였다.

[0181] 상기 준비예 1의 각각의 분화된 T 세포 아형을 항- $CD4$ -APC 및 항 Lrig-1-PE 항체로 염색하고, 형광 이용 세포 분류기(Fluorescence-Activated Cell Sorter; FACS)를 이용하여 각각의 세포 표면에서 Lrig-1의 발현량을 측정하여, 그 결과를 도 10에 나타내었다.

[0182] 도 10에서 보는 바와 같이, 활성화된 T 세포(activated T cell), Th1 세포, Th2 세포, Th17 세포 및 나이브

(Naive) T 세포에서는 Lrig-1의 발현이 0.77 내지 15.3의 양으로 발현되는 반면, 분화가 유도된 T 세포(iTreg)에서는 83.9로 높게 발현되었다.

[0183] 상기 결과를 통해 본 발명에 따른 Lrig-1 단백질은 조절 T 세포(Treg) 세포에서 특이적으로 발현될 뿐만 아니라, 특히 상기 조절 T 세포의 표면에서 더욱 높게 발현되는 것을 알 수 있다.

[0185] **[제조예] 융합 단백질의 제작**

[0186] 1. 발현 벡터의 제작

[0187] 본 발명에 따른 융합 단백질을 제조하기 위하여, 하기 표 26의 각각의 융합 단백질을 코딩하는 각 핵산 서열을 합성하였다. 핵산 서열의 5' 말단과 3' 말단에 각각 NheI과 EcoRI 제한효소 서열을 첨가하였고, 5' 말단의 제한효소 서열 뒤에 코작 서열(Kozak's sequence)(GCCACC)과, 단백질 번역을 위한 시작 코돈과 발현된 단백질을 세포 밖으로 분비하게 하는 마우스 IgG 카파 경쇄 시그널 펩타이드(Mouse kappa light chain signal peptide)(ATGGAAACCGATACTCTGCTGCTGTGGGTGCTGCTGTGGGTGCCAGGCTCTACCGGG)를 삽입하였다. 이후 하기 표 26의 각각의 융합 단백질을 코딩하는 핵산 서열로, 인간 유래 Lrig-1 단백질의 세포 외 도메인; 선택적으로 링커; 힌지 영역; 인간 IgG1 유래의 중쇄 불변영역 2(CH2) 및 중쇄 불변영역 3(CH3);을 코딩화하는 핵산 서열 뒤에는 종결 코돈을 삽입하였다. NheI 과 EcoRI 두 제한효소 서열을 이용하여 본 발명의 융합 단백질을 코딩하는 핵산 서열을 pcDNA3.1(+) 발현 벡터에 클로닝하였다.

표 26

연번	융합 단백질의 아미노산 서열	융합 단백질의 핵산 서열
제조예 1	서열번호 13	서열번호 17
제조예 2	서열번호 14	서열번호 18
제조예 3	서열번호 15	서열번호 19
제조예 4	서열번호 16	서열번호 20
제조예 5	서열번호 21	서열번호 25
제조예 6	서열번호 22	서열번호 26
제조예 7	서열번호 23	서열번호 27
제조예 8	서열번호 24	서열번호 28
제조예 9	서열번호 29	서열번호 33
제조예 10	서열번호 30	서열번호 34
제조예 11	서열번호 31	서열번호 35
제조예 12	서열번호 32	서열번호 36
제조예 13	서열번호 37	서열번호 41
제조예 14	서열번호 38	서열번호 42
제조예 15	서열번호 39	서열번호 43
제조예 16	서열번호 40	서열번호 44
제조예 17	서열번호 45	서열번호 49
제조예 18	서열번호 46	서열번호 50
제조예 19	서열번호 47	서열번호 51
제조예 20	서열번호 48	서열번호 52
제조예 21	서열번호 53	서열번호 57
제조예 22	서열번호 54	서열번호 58
제조예 23	서열번호 55	서열번호 59
제조예 24	서열번호 56	서열번호 60
제조예 25	서열번호 61	서열번호 65
제조예 26	서열번호 62	서열번호 66
제조예 27	서열번호 63	서열번호 67
제조예 28	서열번호 64	서열번호 68
제조예 29	서열번호 69	서열번호 73
제조예 30	서열번호 70	서열번호 74
제조예 31	서열번호 71	서열번호 75
제조예 32	서열번호 72	서열번호 76
제조예 33	서열번호 77	서열번호 81
제조예 34	서열번호 78	서열번호 82
제조예 35	서열번호 79	서열번호 83
제조예 36	서열번호 80	서열번호 84

- [0191] 2. 융합 단백질의 정제
- [0192] 293F 세포에 폴리에틸렌이민(Polyethylenimine)을 이용하여 상기 1.에서 제작한 발현 벡터를 형질 전환시킨 뒤 37 °C 및 8% CO₂ 조건 하에서 6일 동안 배양하였다. 배양 상청액을 여과한 뒤 단백질 A 레진(Protein A resin)에 흘려준 후 1X PBS 로 세척하였다. pH 3.5의 0.1M 글리신(glycine) 용액을 이용하여 용출한 뒤 얻어진 용액에 pH 9.0의 1M TRIS 용액을 첨가하여 pH 중화하였다. 이후 용액을 투석하여 PBS 용액 상태로 만든 후 농축하여 사용하였다.
- [0194] **[실시예 6] 본 발명에 따른 융합 단백질에 의한, 조절 T 세포의 이펙터 T 세포에 대한 억제능(suppression activity) 저해 효과**
- [0195] 상기 제조예 5에서 제작된 본 발명에 따른 서열번호 21로 표시되는 융합 단백질(서열번호 25로 표시되는 핵산 서열을 이용한 제작)이 Lrig-1 단백질에 대한 리간드(ligand)와 결합하여, 상기 리간드와 조절 T 세포 사이의 상호 작용을 저해함에 따라 최종적으로 조절 T 세포의 이펙터 T 세포에 대한 증식 억제능을 감소시키는지 확인하기 위하여 하기의 실험을 수행하였다. 구체적으로는, 조절 T 세포와 이펙터 T 세포를 공동 배양(coculture)하는 조건에서 상기 제조예 5의 융합 단백질을 첨가하여, 조절 T 세포의 이펙터 T 세포에 대한 증식 억제능의 변화를 확인하였다. 그 결과는 도 11에 나타내었다.
- [0196] 도 11에서 보는 바와 같이, 본 발명에 따른 융합 단백질을 처리하자 이펙터 T 세포에 대한 조절 T 세포의 증식 억제능이 저하된 것을 확인할 수 있었다.
- [0197] 이를 통하여 본 발명에 따른 융합 단백질은 Lrig-1 단백질에 대한 리간드와 상호 작용하여, Lrig-1 단백질을 표면에 포함하고 있는 조절 T 세포와 상기 리간드 사이의 상호 작용을 저해함에 따라 조절 T 세포의 활성을 억제하고 이펙터 T 세포의 활성은 유지 혹은 상승시키는 것을 알 수 있었다.
- [0199] **[실시예 7] 본 발명에 따른 융합 단백질에 의해 인식되는 Lrig-1 리간드의 분포 확인**
- [0200] 상기 실시예 6에서 보는 바와 같이, 상기 제조예 5에서 제작된 본 발명에 따른 서열번호 21로 표시되는 융합 단백질(서열번호 25로 표시되는 핵산 서열을 이용한 제작)은 Lrig-1 리간드를 인식할 수 있는 것을 알 수 있으므로, 상기 Lrig-1의 리간드가 존재하는 면역 세포들을 발굴하기 위하여, 조절 T 세포의 타겟으로 생각되는 나이브 T 세포(naive T cell)로부터, 활성화된 T 세포, Th1 세포, Th2 세포 또는 Th17 세포로 분화를 유도시킨 뒤 이들 세포를 상기 제조예 5의 융합 단백질(1차 항체) 및 항-인간-PE 항체(2차 항체)로 염색(staining) 하였다. 형광 이용 세포 분류기(Fluorescence-Activated Cell Sorter; FACS)를 이용하여 각각의 세포 표면에서 상기 융합 단백질의 발현량을 측정하여, 그 결과를 도 12에 나타내었다.
- [0201] 도 12에서 보는 바와 같이, 본 발명에 따른 융합 단백질은 나이브 T 세포의 표면에 있는 항원(antigen)은 거의 염색시키지 않았고(0.71%), 활성화된 T 세포, Th1 세포, Th2 세포 및 Th17 세포의 표면에 있는 항원은 96% 이상을 염색시켰다.
- [0202] 이를 통하여 Lrig-1의 리간드는 T 세포 리셉터(receptor)의 자극에 의하여 유도되는 표면 단백질인 것을 알 수 있었다.
- [0204] **[실시예 8] 본 발명에 따른 융합 단백질의 암 치료 효과**
- [0205] 상기 제조예 5에서 제작된 본 발명에 따른 서열번호 21로 표시되는 융합 단백질(서열번호 25로 표시되는 핵산 서열을 이용한 제작)의 고형암에 대한 치료 효과를 확인하기 위하여, 도 13에서 보는 바와 같이, B16F10 흑색종 세포(melanoma cell)를 마우스 등에 3×10^5 세포의 양으로 피하 주사(subcutaneous injection)한 뒤, 4일, 8일, 12일 쯤에 상기 제조예 5의 융합 단백질을 200 ug의 양으로 복강 내 주사하였다. 상기 멜라노마 세포 이식 후 시간의 경과에 따른 종양의 부피 변화를 측정하여 그 결과를 도 14에 나타내었다.
- [0206] 도 14에서 보는 바와 같이, 본 발명에 따른 융합 단백질을 처리한 경우 아무런 처리하지 않은 음성 대조군에 비하여 흑색종 종양의 크기가 현저히 감소한 것을 확인할 수 있었다.
- [0208] **[실시예 9] 본 발명에 따른 융합 단백질의 암 치료 효과**
- [0209] 상기 제조예 34에서 제작된 본 발명에 따른 서열번호 78로 표시되는 융합 단백질(서열번호 82로 표시되는 핵산

서열을 이용한 제작)의 고형암에 대한 치료 효과를 확인하기 위하여, CT-26 대장암 세포를 마우스 등에 3×10^5 세포의 양으로 피하 주사(subcutaneous injection)한 뒤, 4일, 8일, 12일 후에 상기 제조예 34의 융합 단백질을 200 ug의 양으로 복강 내 주사하였다. 상기 대장암 세포 이식 후 시간의 경과에 따른 종양의 부피 변화를 측정하여 그 결과를 도 15에 나타내었다.

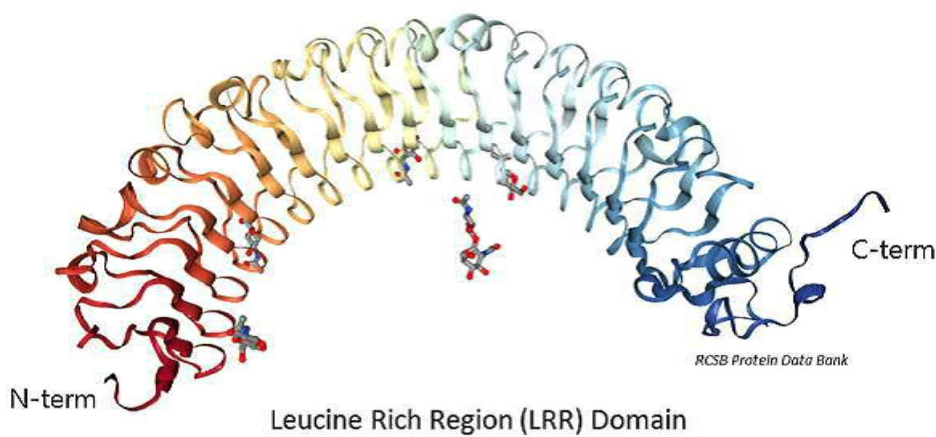
[0210] 도 15에서 보는 바와 같이, 본 발명에 따른 융합 단백질을 처리한 경우 아무런 처리하지 않은 음성 대조군에 비하여 대장암 종양의 크기가 현저히 감소한 것을 확인할 수 있었다.

[0212] 이를 통하여, 본 발명에 따른 Lrig-1 단백질의 세포 외 도메인 및 면역글로불린 Fc 영역을 포함하는 융합 단백질은 조절 T 세포와 이펙터 T 세포간의 상호 작용을 저해함에 따라 조절 T 세포의 활성을 억제하고 이펙터 T 세포의 활성을 유지 혹은 상승시켜 암 세포 중에서도 특히 고형암 세포의 성장을 효과적으로 억제할 수 있는 것을 알 수 있다.

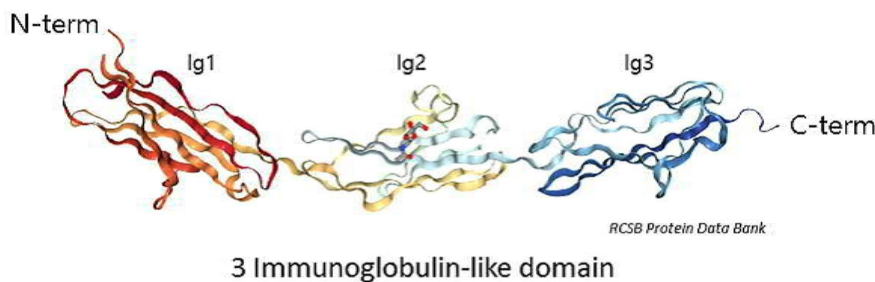
[0214] 이상에서 본 발명에 대하여 상세하게 설명하였지만 본 발명의 권리범위는 이에 한정되는 것은 아니고, 청구범위에 기재된 본 발명의 기술적 사상을 벗어나지 않는 범위 내에서 다양한 수정 및 변형이 가능하다는 것은 당 기술분야의 통상의 지식을 가진 자에게는 자명할 것이다.

도면

도면1



도면2



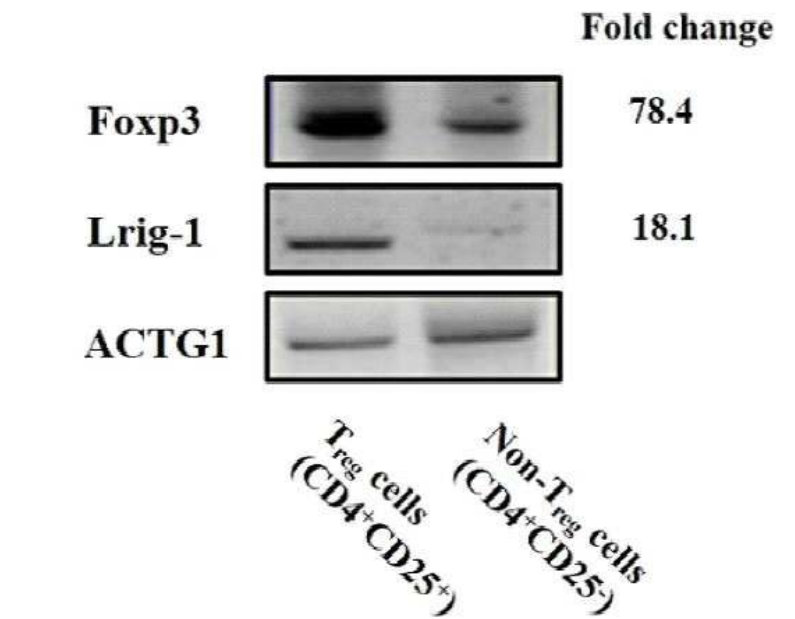
도면3

No.	Chain	Start	End	Peptide	Number of Residue	Score
1	A	9	56	GDSDCGGRGLALPGDLPSSTRSLNLSYNKLSIEDPA GFEDLRNLQE	48	0.86
2	A	399	455	SDSFLCQCQLKWLPFWLIGRMILQAFVTA TCAHPESLKGQSFSV/PRESFV/CDDRLKA	57	0.853
3	A	60	66	NNNELTA	7	0.814
4	A	376	393	NAIRSVQFDAPVKMINK	18	0.598
5	A	85	89	NKIRS	5	0.591
6	A	232	237	VE/NSG	6	0.541
7	A	266	281	ARIHRK	6	0.539
8	A	109	117	NNTEVRNT	9	0.52
9	A	183	196	IRLEGLTFQGLNS	14	0.52
10	A	207	220	ISKLTGAFWGLSK	14	0.514
11	A	158	170	NRITQLPVRAARKL	13	0.501
12	A	96	101	KAYLSL	6	0.5
13	A	531	559	KKDNELVTNADNENFVHVH/VMEYT	25	0.82
14	A	517	527	SAA SSSSRMT	11	0.817
15	A	727	744	FKGDRPLSLTERHHLTPD	18	0.781
16	A	777	786	QLSVLLENLY	10	0.772
17	A	494	501	KRQITQP	8	0.732
18	A	697	711	VFLDRVVS/GETVA	15	0.721
19	A	649	658	HVMPDDVFF	10	0.69
20	A	579	590	ITNHFGSTYSHK	12	0.678
21	A	746	760	QLLVVQNVVAEDAGR	15	0.669
22	A	563	570	HLRQVTFG	8	0.564

도면4

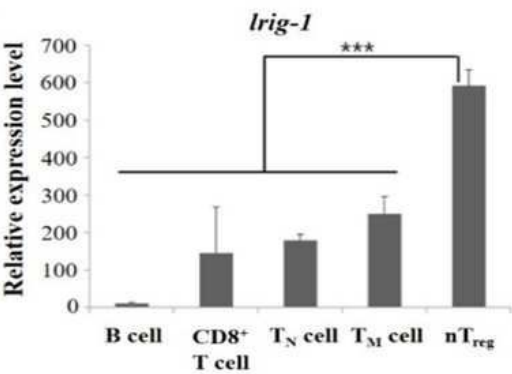
No.	Peptide	Number of Residue	Score
1	C1, P2, S3, R4, C5, T6, C7, S8, G9, D10, S11, L12, D13, C14, G15, G16, R17, G18, L19, A20, A21, L22, P23, G24, D25, L26, P27, S28, S29, T30, R31, S32, L33, N34, L35, S36, K39, L40, S41, E42, I43, D44, P45, A46, G47, F48, E49, D50, L51, P52, N53, L54, Q55, E56, L59, N60, N61, N62, E63, L64, T65, A66, P68, S69, L70, G71, A72, A73, S74, S75, H76, V78, H84, N85, K86, I87, R88, S89, K96, A97, Y98, L99, S100, L101, P120, H121, G122, P123, P124	91	0.747
2	N109, N110, I111, T112, E113, R115, N116, T117, N133, R134, I135, G136, T137, E139, L140, G141, A142, N158, R159, I160, T161, Q162, L163, P164, V165, R166, A167, K169, L170, P171, R182, I183, L185, E187, G188, L189, T190, Q192, G193, L194, N195, S196, I207, S208, K209, T211, D212, G213, A214, F215, W216, G217, L218, S219, K220, S230, L231, V232, E233, V234, N235, S236, G237, Y240, G241, L242, T243, A244, A256, R257, R260, K261, S264, F266, Q267, E284, E285, S286, L287, A288, E289, L290, S291, A307, E308, G309, K312, G313, R315, S316, S335, G336, S339, G340, L341, D342, S343, I354, K355, K359, G364, L365, E366, G367, E369, N376, A377, I378, R379, S380, V381, Q382, F383, D384, A385, V387, K388, M389, K390, N391, L392, K393, S399, D400, S401, F402, L403, C404, D405, C406, Q407, L408, K409, W410, L411, P412, P413, W414, L415, I416, G417, R418, L420, Q421, A422, F423, V424, T425, A426, T427, C428, A429, H430, P431, E432, S433, L434, K435, G436, Q437, S438, I439, F440, S441, V442, P443, F444, E445, S446, F447, V448, C449, D450, D451, F452, L453, K454, A455	178	0.628
1	N784, L785, Y786	3	0.877
2	K494, P495, Q496, I497, I498, T499, Q500, P501, S517, A518, A519, S520, S521, S522, S523, S524, P525, M526, T527, E543, N544, F546, V546, H547, V548, H549, V555, M556, E557, Y558, T559, E79, T580, N581, H582, F583, G584, S585, T586, Y587, S588, H589	42	0.788
3	V697, P698, L699, E700, D701, R702, V703, V704, S705, V706, G707, E708, T709, V710, A711, F727, K728, G729, D730, R731, P732, L733, S734, L735, T736, E737, R738, H739, H740, L741, T742, P743, D744, N745, L747, V749, V750, Q751, N752, V753, V754, A755, E756, D757, A758, R760, Q777, L778, S779, V780, L781, L782, E783	53	0.739
4	D511, K531, K532, D533, N534, E535, V536, L537, T538, N539, A540, D541, M542, H563, R565	15	0.699
5	T614, M615, H649, V650, M651, P662, D663, D664, D665, V666, F668, T660	12	0.669
6	V508, G509, K510, Q566, V567, T568, F569, G570	8	0.529

도면5

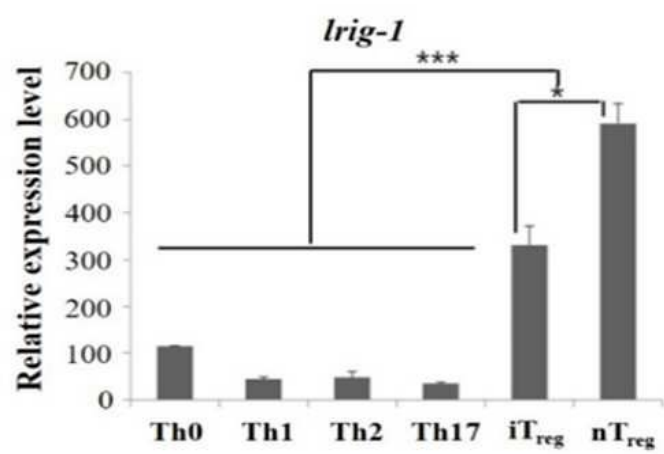


Gene	Fold change	Reference
GPR83	29.5	J. Immunol. 2006
Nrp1	23.7	Eur. J. Immunol. 2004
Lag3	3.1	Immunity. 2003
Ikzf4	4.2	Science. 2009

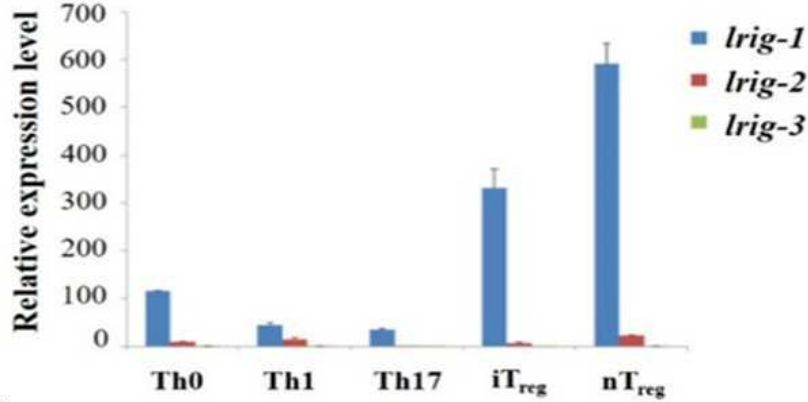
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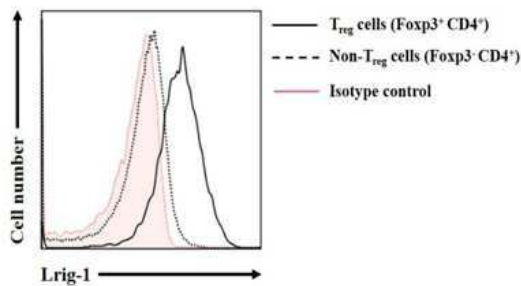
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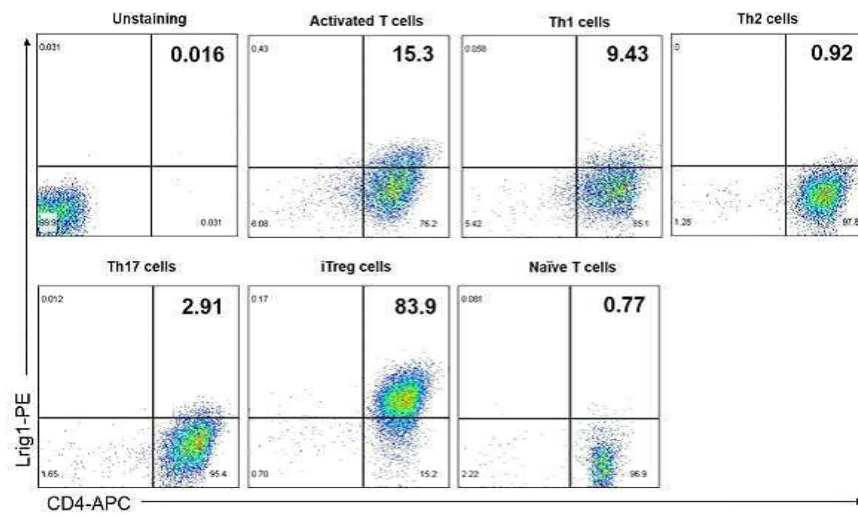
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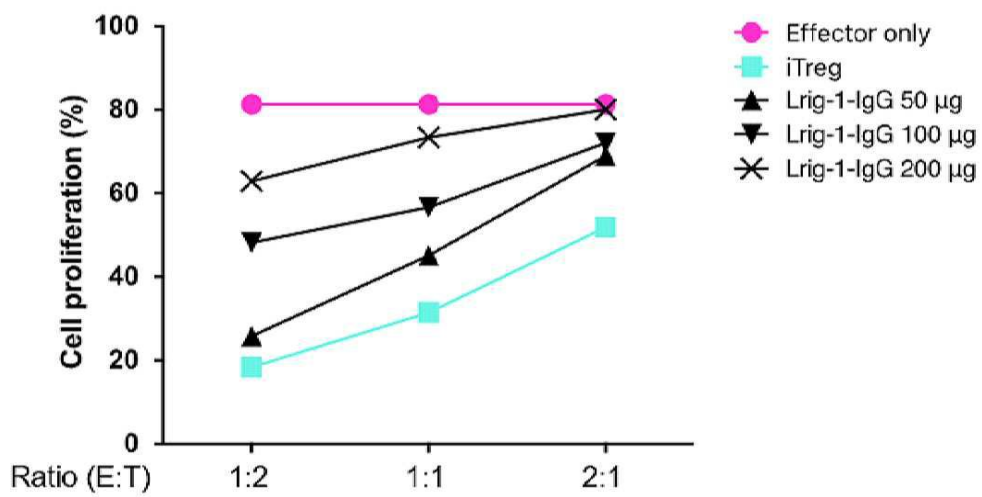
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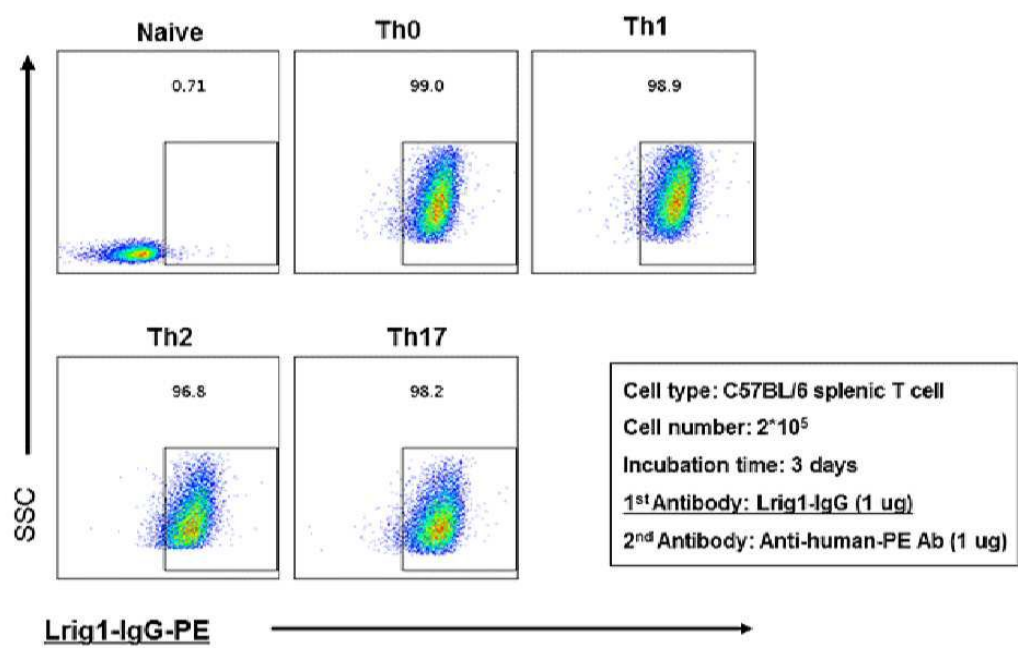
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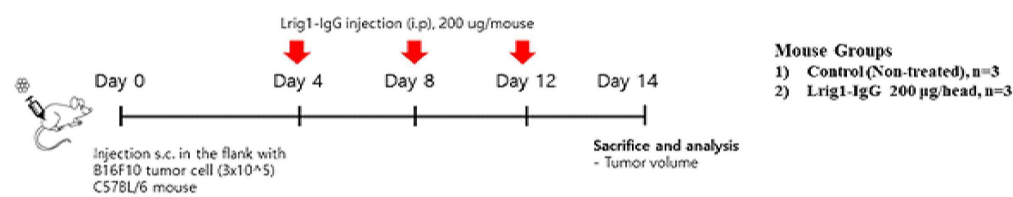
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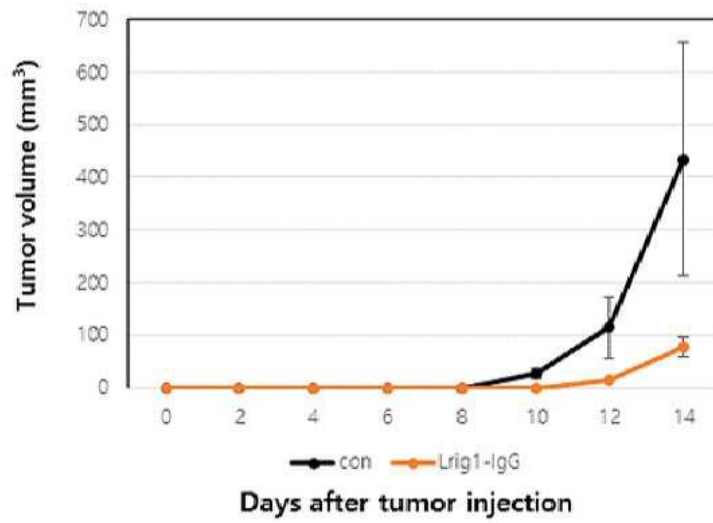
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도면13



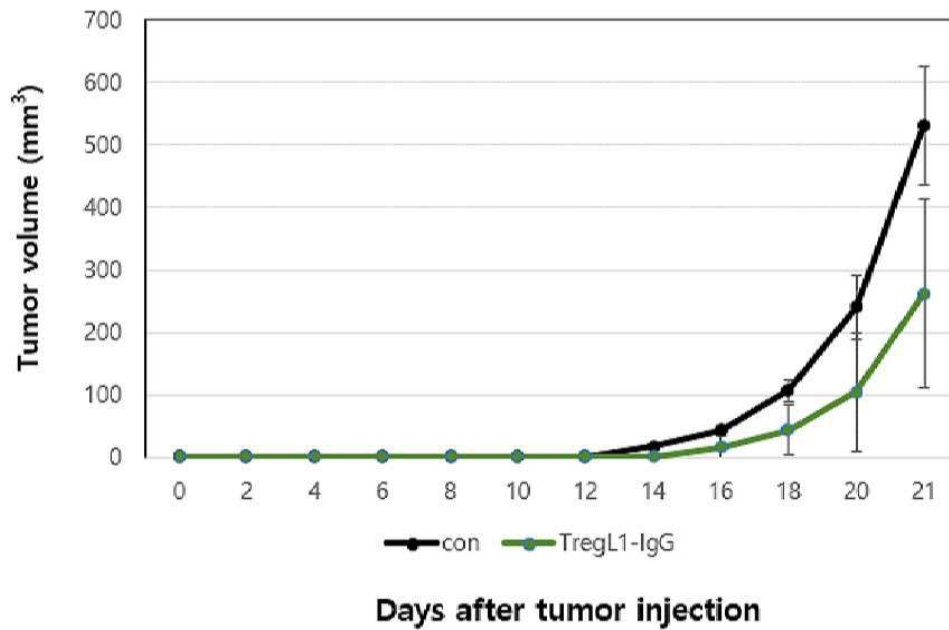
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- ✓ control 대비 암크기 감소 표시 (0~30 %: ---, 31~70 %: --, 71~100 %: -)
- ✓ control 대비 암크기 증가 표시 (100~130 %: +, 131~170 %: ++, 170 % 이상: +++)

도면15



서열 목록

<110> Good T Cells, Inc.

<120> NOVEL FUSION PROTEIN AND PHARMACEUTICAL COMPOSITION FOR

PREVENTING OR TREATING CANCER COMPRISING THE SAME

<130> PDPB187151k01

<150> KR 10-2018-0048343

<151> 2018-04-26

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Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr

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Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser

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Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val

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Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu

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Gln Arg Asn Asn Ile Ser Lys Leu Thr Asp Gly Ala Phe Trp Gly Leu		
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2280

<210> 5
<211> 206
<212> PRT
<213> Homo sapiens
<400> 5

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro

1 5 10 15

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val

20 25 30

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr

35 40 45

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val

50 55 60

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys

65 70 75 80

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser

85 90 95

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro

100 105 110
 Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
 115 120 125
 Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
 130 135 140
 Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
 145 150 155 160

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
 165 170 175
 Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
 180 185 190
 Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 195 200 205

<210> 6
 <211> 206
 <212> PRT
 <213> Mus musculus
 <400> 6

Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu Ser Pro
 1 5 10 15

Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro Asp Val
 20 25 30
 Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr Ala Gln Thr
 35 40 45
 Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg Val Val Ser Ala
 50 55 60
 Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys Glu Phe Lys Cys
 65 70 75 80
 Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu Arg Thr Ile Ser

85 90 95
 Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr Val Leu Pro Pro
 100 105 110

Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu Thr Cys Met Val
 115 120 125
 Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp Thr Asn Asn Gly
 130 135 140
 Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val Leu Asp Ser Asp
 145 150 155 160

Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu Lys Lys Asn Trp
 165 170 175
 Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu Gly Leu His
 180 185 190
 Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys
 195 200 205

<210> 7
 <211> 26
 <212> PRT
 <213> Homo sapiens
 <400> 7

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Ser Pro Pro Cys Pro Ala
 1 5 10 15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
 20 25

<210> 8
 <211> 27
 <212> PRT
 <213> Mus musculus
 <400> 8

Glu Pro Arg Gly Pro Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro
 1 5 10 15

Ala Pro Asn Leu Leu Gly Gly Pro Ser Val Phe
 20 25

<210> 9
 <211> 39
 <212> PRT

<213> Homo sapiens

<400> 9

Arg Asn Thr Gly Arg Gly Gly Glu Glu Lys Lys Lys Glu Lys Glu Lys

1 5 10 15

Glu Glu Gln Glu Glu Arg Glu Thr Lys Thr Pro Glu Cys Pro Ser His

20 25 30

Thr Gln Pro Leu Gly Val Phe

35

<210> 10

<211> 26

<212> PRT

<213> Artificial Sequence

<220><223> Abatacept hinge

<400> 10

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Ser Pro Pro Ser Pro Ala

1 5 10 15

Pro Glu Leu Leu Gly Gly Ser Ser Val Phe

20 25

<210> 11

<211> 2

<212> PRT

<213> Artificial Sequence

<220><223> linker

<400> 11

Gly Ser

1

<210> 12

<211> 3

<212> PRT

<213> Artificial Sequence

<220><223> linker

<400> 12

Gly Gly Gly

1

<210> 13

<211> 994

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 13

Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala Gly Asp

1 5 10 15

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

20 25 30

Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu Ser Glu

35 40 45

Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr

50 55 60

Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser

65 70 75 80

Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val

85 90 95

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

100 105 110

Ser Leu Asn Asn Ile Thr Glu Val Arg Asn Thr Cys Phe Pro His Gly

115 120 125

Pro Pro Ile Lys Glu Leu Asn Leu Ala Gly Asn Arg Ile Gly Thr Leu

130 135 140

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

145 150 155 160

Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu

165 170 175

Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg Leu Ile

180 185 190

Glu Gly Leu Thr Phe Gln Gly Leu Asn Ser Leu Glu Val Leu Lys Leu

195 200 205
 Gln Arg Asn Asn Ile Ser Lys Leu Thr Asp Gly Ala Phe Trp Gly Leu
 210 215 220
 Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val Glu Val

 225 230 235 240
 Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu His Leu
 245 250 255
 Ser Asn Asn Ser Ile Ala Arg Ile His Arg Lys Gly Trp Ser Phe Cys
 260 265 270
 Gln Lys Leu His Glu Leu Val Leu Ser Phe Asn Asn Leu Thr Arg Leu
 275 280 285
 Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Val Leu Arg Leu
 290 295 300

 Ser His Asn Ser Ile Ser His Ile Ala Glu Gly Ala Phe Lys Gly Leu
 305 310 315 320
 Arg Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser Gly Thr
 325 330 335
 Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys
 340 345 350
 Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg Ala Phe
 355 360 365
 Ser Gly Leu Glu Gly Leu Glu His Leu Asn Leu Gly Gly Asn Ala Ile

 370 375 380
 Arg Ser Val Gln Phe Asp Ala Phe Val Lys Met Lys Asn Leu Lys Glu
 385 390 395 400
 Leu His Ile Ser Ser Asp Ser Phe Leu Cys Asp Cys Gln Leu Lys Trp
 405 410 415
 Leu Pro Pro Trp Leu Ile Gly Arg Met Leu Gln Ala Phe Val Thr Ala
 420 425 430
 Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe Ser Val
 435 440 445

Pro Pro Glu Ser Phe Val Cys Asp Asp Phe Leu Lys Pro Gln Ile Ile
 450 455 460
 Thr Gln Pro Glu Thr Thr Met Ala Met Val Gly Lys Asp Ile Arg Phe
 465 470 475 480
 Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe Ala Trp
 485 490 495
 Lys Lys Asp Asn Glu Val Leu Thr Asn Ala Asp Met Glu Asn Phe Val
 500 505 510
 His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu
 515 520 525
 His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val
 530 535 540
 Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg Leu Thr
 545 550 555 560
 Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile
 565 570 575
 Arg Thr Thr Thr Val Ala Arg Leu Glu Cys Ala Ala Thr Gly His Pro
 580 585 590
 Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe Pro Ala
 595 600 605
 Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val Phe Phe
 610 615 620
 Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys Thr Ala
 625 630 635 640
 Gln Asn Ser Ala Gly Ser Ile Ser Ala Asn Ala Thr Leu Thr Val Leu
 645 650 655
 Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val Ser Val
 660 665 670
 Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro
 675 680 685
 Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg
 690 695 700

His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val
 705 710 715 720
 Ala Glu Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Thr Leu Gly
 725 730 735

 Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala Gly Cys
 740 745 750
 Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Glu Pro Lys Ser Ser Asp
 755 760 765
 Lys Thr His Thr Ser Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
 770 775 780
 Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 785 790 795 800
 Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu

 805 810 815
 Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 820 825 830
 Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
 835 840 845
 Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 850 855 860
 Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
 865 870 875 880

 Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 885 890 895
 Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
 900 905 910
 Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 915 920 925
 Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 930 935 940
 Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp

945 950 955 960
 Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
 965 970 975
 Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
 980 985 990
 Gly Lys

<210> 14
 <211> 995
 <212> PRT
 <213> Artificial Sequence
 <220><223> fusion protein
 <400> 14

Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala Gly Asp

1 5 10 15
 Ser Leu Asp Cys Gly Gly Arg Gly Leu Ala Ala Leu Pro Gly Asp Leu
 20 25 30
 Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu Ser Glu
 35 40 45
 Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr
 50 55 60
 Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser
 65 70 75 80

 Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val
 85 90 95
 Glu Gly Ser Gln Leu Lys Ala Tyr Leu Ser Leu Glu Val Leu Asp Leu
 100 105 110
 Ser Leu Asn Asn Ile Thr Glu Val Arg Asn Thr Cys Phe Pro His Gly
 115 120 125
 Pro Pro Ile Lys Glu Leu Asn Leu Ala Gly Asn Arg Ile Gly Thr Leu
 130 135 140
 Glu Leu Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr Leu Arg

145 150 155 160
 Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu
 165 170 175
 Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg Leu Ile
 180 185 190
 Glu Gly Leu Thr Phe Gln Gly Leu Asn Ser Leu Glu Val Leu Lys Leu
 195 200 205
 Gln Arg Asn Asn Ile Ser Lys Leu Thr Asp Gly Ala Phe Trp Gly Leu
 210 215 220

 Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val Glu Val
 225 230 235 240
 Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu His Leu
 245 250 255
 Ser Asn Asn Ser Ile Ala Arg Ile His Arg Lys Gly Trp Ser Phe Cys
 260 265 270
 Gln Lys Leu His Glu Leu Val Leu Ser Phe Asn Asn Leu Thr Arg Leu
 275 280 285
 Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Val Leu Arg Leu

 290 295 300
 Ser His Asn Ser Ile Ser His Ile Ala Glu Gly Ala Phe Lys Gly Leu
 305 310 315 320
 Arg Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser Gly Thr
 325 330 335
 Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys
 340 345 350
 Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg Ala Phe
 355 360 365

 Ser Gly Leu Glu Gly Leu Glu His Leu Asn Leu Gly Gly Asn Ala Ile
 370 375 380
 Arg Ser Val Gln Phe Asp Ala Phe Val Lys Met Lys Asn Leu Lys Glu
 385 390 395 400
 Leu His Ile Ser Ser Asp Ser Phe Leu Cys Asp Cys Gln Leu Lys Trp

405 410 415
 Leu Pro Pro Trp Leu Ile Gly Arg Met Leu Gln Ala Phe Val Thr Ala
 420 425 430
 Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe Ser Val

 435 440 445
 Pro Pro Glu Ser Phe Val Cys Asp Asp Phe Leu Lys Pro Gln Ile Ile
 450 455 460
 Thr Gln Pro Glu Thr Thr Met Ala Met Val Gly Lys Asp Ile Arg Phe
 465 470 475 480
 Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe Ala Trp
 485 490 495
 Lys Lys Asp Asn Glu Val Leu Thr Asn Ala Asp Met Glu Asn Phe Val
 500 505 510

 His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu
 515 520 525
 His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val
 530 535 540
 Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg Leu Thr
 545 550 555 560
 Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile
 565 570 575
 Arg Thr Thr Thr Val Ala Arg Leu Glu Cys Ala Ala Thr Gly His Pro

 580 585 590
 Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe Pro Ala
 595 600 605
 Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val Phe Phe
 610 615 620
 Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys Thr Ala
 625 630 635 640
 Gln Asn Ser Ala Gly Ser Ile Ser Ala Asn Ala Thr Leu Thr Val Leu
 645 650 655

Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val Ser Val
 660 665 670
 Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro
 675 680 685
 Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg
 690 695 700
 His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val
 705 710 715 720
 Ala Glu Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Thr Leu Gly
 725 730 735
 Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala Gly Cys
 740 745 750
 Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Glu Pro Arg Gly Pro Thr
 755 760 765
 Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu Gly
 770 775 780
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 785 790 795 800
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 805 810 815
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 820 825 830
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 835 840 845
 Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 850 855 860
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 865 870 875 880
 Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 885 890 895
 Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
 900 905 910

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 915 920 925
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 930 935 940

 Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 945 950 955 960
 Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 965 970 975
 His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 980 985 990
 Pro Gly Lys
 995
 <210> 15
 <211> 1007
 <212> PRT
 <213> Artificial Sequence
 <220><223> fusion protein

 <400> 15
 Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala Gly Asp
 1 5 10 15
 Ser Leu Asp Cys Gly Gly Arg Gly Leu Ala Ala Leu Pro Gly Asp Leu
 20 25 30
 Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu Ser Glu
 35 40 45
 Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr
 50 55 60
 Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser

 65 70 75 80
 Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val
 85 90 95
 Glu Gly Ser Gln Leu Lys Ala Tyr Leu Ser Leu Glu Val Leu Asp Leu
 100 105 110

Ser Leu Asn Asn Ile Thr Glu Val Arg Asn Thr Cys Phe Pro His Gly
 115 120 125
 Pro Pro Ile Lys Glu Leu Asn Leu Ala Gly Asn Arg Ile Gly Thr Leu
 130 135 140

 Glu Leu Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr Leu Arg
 145 150 155 160
 Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu
 165 170 175
 Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg Leu Ile
 180 185 190
 Glu Gly Leu Thr Phe Gln Gly Leu Asn Ser Leu Glu Val Leu Lys Leu
 195 200 205
 Gln Arg Asn Asn Ile Ser Lys Leu Thr Asp Gly Ala Phe Trp Gly Leu

 210 215 220
 Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val Glu Val
 225 230 235 240
 Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu His Leu
 245 250 255
 Ser Asn Asn Ser Ile Ala Arg Ile His Arg Lys Gly Trp Ser Phe Cys
 260 265 270
 Gln Lys Leu His Glu Leu Val Leu Ser Phe Asn Asn Leu Thr Arg Leu
 275 280 285

 Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Val Leu Arg Leu
 290 295 300
 Ser His Asn Ser Ile Ser His Ile Ala Glu Gly Ala Phe Lys Gly Leu
 305 310 315 320
 Arg Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser Gly Thr
 325 330 335
 Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys
 340 345 350
 Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg Ala Phe

355 360 365
 Ser Gly Leu Glu Gly Leu Glu His Leu Asn Leu Gly Gly Asn Ala Ile
 370 375 380
 Arg Ser Val Gln Phe Asp Ala Phe Val Lys Met Lys Asn Leu Lys Glu
 385 390 395 400
 Leu His Ile Ser Ser Asp Ser Phe Leu Cys Asp Cys Gln Leu Lys Trp
 405 410 415
 Leu Pro Pro Trp Leu Ile Gly Arg Met Leu Gln Ala Phe Val Thr Ala
 420 425 430

 Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe Ser Val
 435 440 445
 Pro Pro Glu Ser Phe Val Cys Asp Asp Phe Leu Lys Pro Gln Ile Ile
 450 455 460
 Thr Gln Pro Glu Thr Thr Met Ala Met Val Gly Lys Asp Ile Arg Phe
 465 470 475 480
 Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe Ala Trp
 485 490 495
 Lys Lys Asp Asn Glu Val Leu Thr Asn Ala Asp Met Glu Asn Phe Val

 500 505 510
 His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu
 515 520 525
 His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val
 530 535 540
 Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg Leu Thr
 545 550 555 560
 Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile
 565 570 575

 Arg Thr Thr Thr Val Ala Arg Leu Glu Cys Ala Ala Thr Gly His Pro
 580 585 590
 Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe Pro Ala
 595 600 605
 Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val Phe Phe

610	615	620	
Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys Thr Ala			
625	630	635	640
Gln Asn Ser Ala Gly Ser Ile Ser Ala Asn Ala Thr Leu Thr Val Leu			
	645	650	655
Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val Ser Val			
	660	665	670
Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro			
	675	680	685
Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg			
	690	695	700
His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val			
705	710	715	720
Ala Glu Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Thr Leu Gly			
	725	730	735
Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala Gly Cys			
	740	745	750
Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Arg Asn Thr Gly Arg Gly			
	755	760	765
Gly Glu Glu Lys Lys Lys Glu Lys Glu Lys Glu Glu Gln Glu Glu Arg			
	770	775	780
Glu Thr Lys Thr Pro Glu Cys Pro Ser His Thr Gln Pro Leu Gly Val			
785	790	795	800
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr			
	805	810	815
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu			
	820	825	830
Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys			
	835	840	845
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser			
	850	855	860

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
865 870 875 880
Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
885 890 895
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
900 905 910
Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
915 920 925
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn

930 935 940
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
945 950 955 960
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
965 970 975
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
980 985 990
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
995 1000 1005

<210> 16
<211> 994
<212> PRT
<213> Artificial Sequence
<220><223> fusion protein
<400> 16

Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala Gly Asp
1 5 10 15
Ser Leu Asp Cys Gly Gly Arg Gly Leu Ala Ala Leu Pro Gly Asp Leu
20 25 30
Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu Ser Glu
35 40 45
Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr

50 55 60

Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser
 65 70 75 80
 Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val
 85 90 95
 Glu Gly Ser Gln Leu Lys Ala Tyr Leu Ser Leu Glu Val Leu Asp Leu
 100 105 110
 Ser Leu Asn Asn Ile Thr Glu Val Arg Asn Thr Cys Phe Pro His Gly
 115 120 125

 Pro Pro Ile Lys Glu Leu Asn Leu Ala Gly Asn Arg Ile Gly Thr Leu
 130 135 140
 Glu Leu Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr Leu Arg
 145 150 155 160
 Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu
 165 170 175
 Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg Leu Ile
 180 185 190
 Glu Gly Leu Thr Phe Gln Gly Leu Asn Ser Leu Glu Val Leu Lys Leu

 195 200 205
 Gln Arg Asn Asn Ile Ser Lys Leu Thr Asp Gly Ala Phe Trp Gly Leu
 210 215 220
 Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val Glu Val
 225 230 235 240
 Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu His Leu
 245 250 255
 Ser Asn Asn Ser Ile Ala Arg Ile His Arg Lys Gly Trp Ser Phe Cys
 260 265 270

 Gln Lys Leu His Glu Leu Val Leu Ser Phe Asn Asn Leu Thr Arg Leu
 275 280 285
 Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Val Leu Arg Leu
 290 295 300
 Ser His Asn Ser Ile Ser His Ile Ala Glu Gly Ala Phe Lys Gly Leu
 305 310 315 320

Arg Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser Gly Thr
325 330 335

Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys
340 345 350

Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg Ala Phe
355 360 365

Ser Gly Leu Glu Gly Leu Glu His Leu Asn Leu Gly Gly Asn Ala Ile
370 375 380

Arg Ser Val Gln Phe Asp Ala Phe Val Lys Met Lys Asn Leu Lys Glu
385 390 395 400

Leu His Ile Ser Ser Asp Ser Phe Leu Cys Asp Cys Gln Leu Lys Trp
405 410 415

Leu Pro Pro Trp Leu Ile Gly Arg Met Leu Gln Ala Phe Val Thr Ala
420 425 430

Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe Ser Val
435 440 445

Pro Pro Glu Ser Phe Val Cys Asp Asp Phe Leu Lys Pro Gln Ile Ile
450 455 460

Thr Gln Pro Glu Thr Thr Met Ala Met Val Gly Lys Asp Ile Arg Phe
465 470 475 480

Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe Ala Trp
485 490 495

Lys Lys Asp Asn Glu Val Leu Thr Asn Ala Asp Met Glu Asn Phe Val
500 505 510

His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu
515 520 525

His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val
530 535 540

Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg Leu Thr
545 550 555 560

Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile

565 570 575
 Arg Thr Thr Thr Val Ala Arg Leu Glu Cys Ala Ala Thr Gly His Pro
 580 585 590
 Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe Pro Ala
 595 600 605
 Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val Phe Phe
 610 615 620
 Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys Thr Ala

 625 630 635 640
 Gln Asn Ser Ala Gly Ser Ile Ser Ala Asn Ala Thr Leu Thr Val Leu
 645 650 655
 Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val Ser Val
 660 665 670
 Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro
 675 680 685
 Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg
 690 695 700

 His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val
 705 710 715 720
 Ala Glu Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Thr Leu Gly
 725 730 735
 Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala Gly Cys
 740 745 750
 Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Glu Pro Lys Ser Ser Asp
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50 55 60

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

65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu

85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu

100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro

115 120 125

Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser

130 135 140

Ile Leu Glu Ser Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr
145 150 155 160
Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe
165 170 175
Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg
180 185 190
Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu
195 200 205
Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp
210 215 220
Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val
225 230 235 240
Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu
245 250 255
His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser
260 265 270
Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr
275 280 285
Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
290 295 300
Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
305 310 315 320
Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser
325 330 335
Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
340 345 350
Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
355 360 365
Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
370 375 380
Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
385 390 395 400

Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
 405 410 415

 Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
 420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
 435 440 445
 Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln
 450 455 460
 Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
 465 470 475 480
 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe

 485 490 495
 Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
 500 505 510
 Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
 515 520 525
 Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
 530 535 540
 Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
 545 550 555 560

 Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
 565 570 575
 Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
 580 585 590
 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
 595 600 605
 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
 610 615 620
 Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys

 625 630 635 640
 Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr

645 650 655
 Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
 660 665 670
 Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
 675 680 685
 Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
 690 695 700

 Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
 705 710 715 720
 Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
 725 730 735
 Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
 740 745 750
 Gly Cys Arg Lys Asp Gly Thr Thr Glu Pro Lys Ser Ser Asp Lys Thr
 755 760 765
 His Thr Ser Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser

 770 775 780
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 785 790 795 800
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 805 810 815
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 820 825 830
 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
 835 840 845

 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 850 855 860
 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
 865 870 875 880
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 885 890 895
 Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys

900 905 910
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser

915 920 925
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp

930 935 940
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser

945 950 955 960
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala

965 970 975
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

980 985 990

<210> 22

<211> 993

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 22

Ala Gln Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala

1 5 10 15

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

20 25 30

Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu

35 40 45

Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu

50 55 60

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

65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu

85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu

100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro

115	120	125	
Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser			
130	135	140	
Ile Leu Glu Ser Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr			
145	150	155	160
Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe			
165	170	175	
Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg			
180	185	190	
Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu			
195	200	205	
Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp			
210	215	220	
Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val			
225	230	235	240
Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu			
245	250	255	
His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser			
260	265	270	
Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr			
275	280	285	
Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu			
290	295	300	
Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys			
305	310	315	320
Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser			
325	330	335	
Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu			
340	345	350	
Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg			
355	360	365	

Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
370 375 380

Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
385 390 395 400

Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
405 410 415

Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
420 425 430

Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
435 440 445

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

Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
465 470 475 480

Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe
485 490 495

Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
500 505 510

Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
515 520 525

Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
530 535 540

Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
545 550 555 560

Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
565 570 575

Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
580 585 590

His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
595 600 605

Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
610 615 620

Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys

625 630 635 640

Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr

645 650 655

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

660 665 670

Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro

675 680 685

Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr

690 695 700

Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn

705 710 715 720

Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro

725 730 735

Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro

740 745 750

Gly Cys Arg Lys Asp Gly Thr Thr Glu Pro Arg Gly Pro Thr Ile Lys

755 760 765

Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu Gly Gly Pro

770 775 780

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser

785 790 795 800

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

805 810 815

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn

820 825 830

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val

835 840 845

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu

850 855 860

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys

865 870 875 880
 Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 885 890 895
 Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
 900 905 910
 Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu

 915 920 925
 Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 930 935 940
 Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 945 950 955 960
 Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 965 970 975
 Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 980 985 990

Lys

<210> 23
 <211> 1005
 <212> PRT
 <213> Artificial Sequence
 <220><223> fusion protein
 <400> 23

Ala Gln Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala
 1 5 10 15
 Gly Asp Ser Leu Asp Cys Ser Gly Arg Gly Leu Ala Thr Leu Pro Arg
 20 25 30
 Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu
 35 40 45
 Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu

 50 55 60
 Val Tyr Leu Asn Ser Asn Glu Leu Thr Ala Ile Pro Ser Leu Gly Ala

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

325 330 335
Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu

340 345 350
Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg

355 360 365
Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn

370 375 380
Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu

385 390 395 400
Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu

405 410 415

Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val

420 425 430
Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe

435 440 445
Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln

450 455 460
Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile

465 470 475 480
Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe

485 490 495
Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn

500 505 510
Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr

515 520 525
Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln

530 535 540
Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg

545 550 555 560

Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile

565 570 575

Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
580 585 590

His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
595 600 605

Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
610 615 620

Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys

625 630 635 640

Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
645 650 655

Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
660 665 670

Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
675 680 685

Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
690 695 700

Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
705 710 715 720

Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
725 730 735

Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
740 745 750

Gly Cys Arg Lys Asp Gly Thr Thr Arg Asn Thr Gly Arg Gly Gly Glu
755 760 765

Glu Lys Lys Lys Glu Lys Glu Lys Glu Glu Gln Glu Glu Arg Glu Thr

770 775 780

Lys Thr Pro Glu Cys Pro Ser His Thr Gln Pro Leu Gly Val Phe Leu
785 790 795 800

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
805 810 815

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
820 825 830

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
835 840 845

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
850 855 860

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
865 870 875 880

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
885 890 895

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
900 905 910

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys

915 920 925

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
930 935 940

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
945 950 955 960

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
965 970 975

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
980 985 990

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
995 1000 1005

<210> 24

<211> 992

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 24

Ala Gln Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala
1 5 10 15

Gly Asp Ser Leu Asp Cys Ser Gly Arg Gly Leu Ala Thr Leu Pro Arg
20 25 30

Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu

35 40 45

Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu

50 55 60

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

65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu

85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu

100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro

115 120 125

Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser

130 135 140

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

145 150 155 160

Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe

165 170 175

Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg

180 185 190

Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu

195 200 205

Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp

210 215 220

Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val

225 230 235 240

Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu

245 250 255

His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser

260 265 270

Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr

275 280 285
 Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
 290 295 300
 Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
 305 310 315 320
 Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser

 325 330 335
 Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
 340 345 350
 Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
 355 360 365
 Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
 370 375 380
 Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
 385 390 395 400

 Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
 405 410 415
 Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
 420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
 435 440 445
 Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln
 450 455 460
 Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile

 465 470 475 480
 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe
 485 490 495
 Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
 500 505 510
 Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
 515 520 525
 Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln

530 535 540
 Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
 545 550 555 560
 Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
 565 570 575
 Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
 580 585 590
 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
 595 600 605
 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val

 610 615 620
 Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys
 625 630 635 640
 Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
 645 650 655
 Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
 660 665 670
 Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
 675 680 685

 Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
 690 695 700
 Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
 705 710 715 720
 Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
 725 730 735
 Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
 740 745 750
 Gly Cys Arg Lys Asp Gly Thr Thr Glu Pro Lys Ser Ser Asp Lys Thr

 755 760 765
 His Thr Ser Pro Pro Ser Pro Ala Pro Glu Leu Leu Gly Gly Ser Ser
 770 775 780

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 785 790 795 800
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 805 810 815
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 820 825 830

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
 835 840 845
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 850 855 860
 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
 865 870 875 880
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 885 890 895
 Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys

900 905 910
 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 915 920 925
 Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 930 935 940
 Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
 945 950 955 960
 Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 965 970 975

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 980 985 990

<210> 25

<211> 2976

<212> DNA

<213> Artificial Sequence

<220><223> fusion protein

<400> 25

gctcaggctg gacctagggc tccttgcgct gccgcctgca cctgtgcagg cgattctctg	60
gactgcagcg gccggggcct ggccacactg cccagggacc tgccttcctg gaccagatct	120
ctgaacctga gctacaatcg gctgtccgag atcgattctg ccgcctttga ggacctgaca	180
aatctgcagg aggtgtatct gaacagcaat gagctgaccg caatcccctc cctgggagca	240
gcctctatcg gcgtggtgag cctgttcctg cagcacaaca agatcctgag cgtggatggc	300
tcccagctga agagctacct gtctctggag gtgctggacc tgagctcaa caatatcacc	360
gagatcagat ctagctgttt tcctaatggc ctgcggatca gagagctgaa cctggcctct	420
aatcgatca gcatcctgga gtccggcgcc ttcgatggcc tgagcagatc cctgctgaca	480
ctgcgcctgt ccaagaaccg gatcacccag ctgcccgtga aggcctttaa gctgcctagg	540
ctgacacagc tggacctgaa ccggaataga atcaggctga tcgagggcct gaccttcag	600
ggcctggata gcctggaggt gctgcgcctg cagcgggaaca atatctcccg cctgacagac	660
ggagcat tttt ggggcctgtc taagatgcac gtgctgcacc tggagtaca tagcctggtg	720
gaggtgaact ctggcagcct gtatggcctg accgcctgc accagctgca cctgtccaac	780
aatagcatca gcagaatcca gagggatggc tggctcttct gccagaagct gcacgagctg	840
atcctgtctt ttaacaatct gaccaggctg gacgaggaga gcctggcaga gctgtcctct	900
ctgtccatcc tgcgcctgtc tcacaatgcc atcagccaca tcgccgaggg cgcctttaag	960
ggcctgaaga gcctgagggg gctggatctg gaccacaacg agatctctgg caccatcgag	1020
gatacaagcg gcgccttcac aggcctggac aatctgtcca agctgaccct gtttggcaac	1080
aagatcaagt ctgtggccaa gcgggccttc tctggcctgg agagcctgga gcacctgaac	1140
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Val Tyr Leu Asn Ser Asn Glu Leu Thr Ala Ile Pro Ser Leu Gly Ala

65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu

85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu

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Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro

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 770 775 780
 Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu
 785 790 795 800
 Ser Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro
 805 810 815
 Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr Ala
 820 825 830
 Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg Val Val
 835 840 845

 Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys Glu Phe
 850 855 860
 Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu Arg Thr
 865 870 875 880
 Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr Val Leu
 885 890 895

Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu Thr Cys
 900 905 910
 Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp Thr Asn
 915 920 925
 Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val Leu Asp
 930 935 940
 Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu Lys Lys
 945 950 955 960
 Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu Gly
 965 970 975
 Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys
 980 985 990

<210> 30

<211> 993

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 30

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

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro
 115 120 125

 Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser
 130 135 140
 Ile Leu Glu Ser Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr
 145 150 155 160
 Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe
 165 170 175
 Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg
 180 185 190
 Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu

 195 200 205
 Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp
 210 215 220
 Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val
 225 230 235 240
 Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu
 245 250 255
 His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser
 260 265 270

 Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr
 275 280 285
 Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
 290 295 300
 Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
 305 310 315 320
 Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser
 325 330 335
 Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu

 340 345 350
 Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg

355 360 365
 Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
 370 375 380
 Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
 385 390 395 400
 Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
 405 410 415

 Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
 420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
 435 440 445
 Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln
 450 455 460
 Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
 465 470 475 480
 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe

 485 490 495
 Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
 500 505 510
 Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
 515 520 525
 Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
 530 535 540
 Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
 545 550 555 560

 Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
 565 570 575
 Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
 580 585 590
 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
 595 600 605
 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val

610 615 620
 Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys

 625 630 635 640
 Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
 645 650 655
 Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
 660 665 670
 Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
 675 680 685
 Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
 690 695 700

 Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
 705 710 715 720
 Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
 725 730 735
 Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
 740 745 750
 Gly Cys Arg Lys Asp Gly Thr Thr Glu Pro Arg Gly Pro Thr Ile Lys
 755 760 765
 Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu Gly Gly Pro

 770 775 780
 Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser
 785 790 795 800
 Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp Asp
 805 810 815
 Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr
 820 825 830
 Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg Val
 835 840 845

 Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys Glu
 850 855 860

Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu Arg
865 870 875 880
Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr Val
885 890 895
Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu Thr
900 905 910
Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp Thr
915 920 925
Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val Leu
930 935 940
Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu Lys
945 950 955 960
Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu
965 970 975
Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly
980 985 990

Lys

<210> 31

<211> 1005

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 31

Ala Gln Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala
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20 25 30
Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu
35 40 45
Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu
50 55 60

Val Tyr Leu Asn Ser Asn Glu Leu Thr Ala Ile Pro Ser Leu Gly Ala
65 70 75 80
Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu
85 90 95
Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu
100 105 110
Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro
115 120 125

Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser
130 135 140
Ile Leu Glu Ser Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr
145 150 155 160
Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe
165 170 175
Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg
180 185 190
Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu

195 200 205
Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp
210 215 220
Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val
225 230 235 240
Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu
245 250 255
His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser
260 265 270

Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr
275 280 285
Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
290 295 300
Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
305 310 315 320

Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser
325 330 335

Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
340 345 350

Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
355 360 365

Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
370 375 380

Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
385 390 395 400

Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
405 410 415

Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
420 425 430

Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
435 440 445

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

Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
465 470 475 480

Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe
485 490 495

Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
500 505 510

Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
515 520 525

Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
530 535 540

Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
545 550 555 560

Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile

565 570 575
 Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
 580 585 590
 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
 595 600 605
 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
 610 615 620
 Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys

 625 630 635 640
 Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
 645 650 655
 Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
 660 665 670
 Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
 675 680 685
 Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
 690 695 700

 Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
 705 710 715 720
 Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
 725 730 735
 Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
 740 745 750
 Gly Cys Arg Lys Asp Gly Thr Thr Arg Asn Thr Gly Arg Gly Gly Glu
 755 760 765
 Glu Lys Lys Lys Glu Lys Glu Lys Glu Glu Gln Glu Glu Arg Glu Thr

 770 775 780
 Lys Thr Pro Glu Cys Pro Ser His Thr Gln Pro Leu Gly Val Phe Ile
 785 790 795 800
 Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu Ser Pro Ile
 805 810 815
 Val Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro Asp Val Gln

820 825 830
Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr Ala Gln Thr Gln
835 840 845

Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg Val Val Ser Ala Leu
850 855 860
Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys Glu Phe Lys Cys Lys
865 870 875 880
Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu Arg Thr Ile Ser Lys
885 890 895
Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr Val Leu Pro Pro Pro
900 905 910
Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu Thr Cys Met Val Thr

915 920 925
Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp Thr Asn Asn Gly Lys
930 935 940
Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val Leu Asp Ser Asp Gly
945 950 955 960
Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu Lys Lys Asn Trp Val
965 970 975
Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu Gly Leu His Asn
980 985 990

His His Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys
995 1000 1005

<210> 32

<211> 992

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 32

Ala Gln Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala
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Gly Asp Ser Leu Asp Cys Ser Gly Arg Gly Leu Ala Thr Leu Pro Arg

20 25 30
 Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu

 35 40 45
 Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu
 50 55 60
 Val Tyr Leu Asn Ser Asn Glu Leu Thr Ala Ile Pro Ser Leu Gly Ala
 65 70 75 80
 Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu
 85 90 95
 Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu
 100 105 110

 Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro
 115 120 125
 Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser
 130 135 140
 Ile Leu Glu Ser Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr
 145 150 155 160
 Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe
 165 170 175
 Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg

 180 185 190
 Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu
 195 200 205
 Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp
 210 215 220
 Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val
 225 230 235 240
 Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu
 245 250 255

 His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser
 260 265 270

Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr
 275 280 285
 Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
 290 295 300
 Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
 305 310 315 320
 Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser
 325 330 335
 Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
 340 345 350
 Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
 355 360 365
 Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
 370 375 380
 Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
 385 390 395 400
 Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
 405 410 415
 Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
 420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
 435 440 445
 Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln
 450 455 460
 Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
 465 470 475 480
 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe
 485 490 495
 Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
 500 505 510
 Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
 515 520 525

Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
530 535 540

Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
545 550 555 560

Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
565 570 575

Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
580 585 590

His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
595 600 605

Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
610 615 620

Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys
625 630 635 640

Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
645 650 655

Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
660 665 670

Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
675 680 685

Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
690 695 700

Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
705 710 715 720

Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
725 730 735

Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
740 745 750

Gly Cys Arg Lys Asp Gly Thr Thr Glu Pro Lys Ser Ser Asp Lys Thr
755 760 765

His Thr Ser Pro Pro Ser Pro Ala Pro Glu Leu Leu Gly Gly Ser Ser

770 775 780
 Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu
 785 790 795 800
 Ser Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro
 805 810 815
 Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr Ala
 820 825 830

 Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg Val Val
 835 840 845
 Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys Glu Phe
 850 855 860
 Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu Arg Thr
 865 870 875 880
 Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr Val Leu
 885 890 895
 Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu Thr Cys

 900 905 910
 Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp Thr Asn
 915 920 925
 Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val Leu Asp
 930 935 940
 Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu Lys Lys
 945 950 955 960
 Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu Gly
 965 970 975

 Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys
 980 985 990

 <210> 33
 <211> 2976
 <212> DNA
 <213> Artificial Sequence
 <220><223> fusion protein

<400> 33

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aactgggtcg agcggaaact ctactcctgc tccgtggtgc acgagggcct gcacaaccac 2940
cacaccacca agtcttctc ccggaccccc ggcaaa 2976

<210> 34
<211> 2979
<212> DNA
<213> Artificial Sequence
<220><223> fusion protein
<400> 34

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tcccagctga agagctacct gtctctggag gtgctggacc tgagctccaa caatatcacc	360
gagatcagat ctagctgttt tcctaattggc ctgcggatca gagagctgaa cctggcctct	420
aatcggatca gcatcctgga gtccggcgcc ttcgatggcc tgagcagatc cctgctgaca	480
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<211> 996

<212> PRT

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<220><223> fusion protein

<400> 37

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Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu Ser Glu

35 40 45

Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr

50 55 60

Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser

65 70 75 80

Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val

85 90 95

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

100 105 110

Ser Leu Asn Asn Ile Thr Glu Val Arg Asn Thr Cys Phe Pro His Gly

115 120 125

Pro Pro Ile Lys Glu Leu Asn Leu Ala Gly Asn Arg Ile Gly Thr Leu

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Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu			
	165	170	175
Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg Leu Ile			
	180	185	190
Glu Gly Leu Thr Phe Gln Gly Leu Asn Ser Leu Glu Val Leu Lys Leu			
195	200	205	
Gln Arg Asn Asn Ile Ser Lys Leu Thr Asp Gly Ala Phe Trp Gly Leu			
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Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val Glu Val			
225	230	235	240
Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu His Leu			
	245	250	255
Ser Asn Asn Ser Ile Ala Arg Ile His Arg Lys Gly Trp Ser Phe Cys			
	260	265	270
Gln Lys Leu His Glu Leu Val Leu Ser Phe Asn Asn Leu Thr Arg Leu			
275	280	285	
Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Val Leu Arg Leu			
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Ser His Asn Ser Ile Ser His Ile Ala Glu Gly Ala Phe Lys Gly Leu			
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Arg Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser Gly Thr			
	325	330	335
Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys			
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Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg Ala Phe			
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Ser Gly Leu Glu Gly Leu Glu His Leu Asn Leu Gly Gly Asn Ala Ile			
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Arg Ser Val Gln Phe Asp Ala Phe Val Lys Met Lys Asn Leu Lys Glu			

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 Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe Ser Val
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 485 490 495
 Lys Lys Asp Asn Glu Val Leu Thr Asn Ala Asp Met Glu Asn Phe Val
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 His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu
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 His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val
 530 535 540
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 545 550 555 560

 Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile
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 580 585 590
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 625 630 635 640

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 Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val Ser Val
 660 665 670
 Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro
 675 680 685
 Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg
 690 695 700

 His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val
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 Ala Glu Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Thr Leu Gly
 725 730 735
 Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala Gly Cys
 740 745 750
 Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Gly Ser Glu Pro Lys Ser
 755 760 765
 Ser Asp Lys Thr His Thr Ser Pro Pro Cys Pro Ala Pro Glu Leu Leu

 770 775 780
 Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
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 Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 805 810 815
 His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 820 825 830
 Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
 835 840 845

 Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
 850 855 860
 Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
 865 870 875 880
 Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
 885 890 895

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
900 905 910

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val

915 920 925

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
930 935 940

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
945 950 955 960

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
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<212> PRT

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<220><223> fusion protein

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Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu Ser Glu
35 40 45

Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr
50 55 60

Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser
65 70 75 80

Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val
85 90 95

Glu Gly Ser Gln Leu Lys Ala Tyr Leu Ser Leu Glu Val Leu Asp Leu
 100 105 110
 Ser Leu Asn Asn Ile Thr Glu Val Arg Asn Thr Cys Phe Pro His Gly
 115 120 125
 Pro Pro Ile Lys Glu Leu Asn Leu Ala Gly Asn Arg Ile Gly Thr Leu
 130 135 140
 Glu Leu Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr Leu Arg
 145 150 155 160
 Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu
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 Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg Leu Ile
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 Glu Gly Leu Thr Phe Gln Gly Leu Asn Ser Leu Glu Val Leu Lys Leu
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 Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val Glu Val
 225 230 235 240
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 325 330 335
 Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys

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 370 375 380
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 His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu
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 His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val
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 Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg Leu Thr

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 Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile
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 Arg Thr Thr Thr Val Ala Arg Leu Glu Cys Ala Ala Thr Gly His Pro
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 Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe Pro Ala

595 600 605
 Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val Phe Phe
 610 615 620

 Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys Thr Ala
 625 630 635 640
 Gln Asn Ser Ala Gly Ser Ile Ser Ala Asn Ala Thr Leu Thr Val Leu
 645 650 655
 Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val Ser Val
 660 665 670
 Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro
 675 680 685
 Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg

 690 695 700
 His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val
 705 710 715 720
 Ala Glu Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Thr Leu Gly
 725 730 735
 Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala Gly Cys
 740 745 750
 Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Gly Ser Glu Pro Arg Gly
 755 760 765

 Pro Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu
 770 775 780
 Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 785 790 795 800
 Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 805 810 815
 Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 820 825 830
 Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser

 835 840 845

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
850 855 860
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
865 870 875 880
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
885 890 895
Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
900 905 910

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
915 920 925
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
930 935 940
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
945 950 955 960
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
965 970 975
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
980 985 990

Leu Ser Pro Gly Lys

995

<210> 39

<211> 1009

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 39

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Ser Leu Asp Cys Gly Gly Arg Gly Leu Ala Ala Leu Pro Gly Asp Leu
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Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu Ser Glu
35 40 45

Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr
50 55 60

Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser
65 70 75 80

Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val
85 90 95

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

Ser Leu Asn Asn Ile Thr Glu Val Arg Asn Thr Cys Phe Pro His Gly
115 120 125

Pro Pro Ile Lys Glu Leu Asn Leu Ala Gly Asn Arg Ile Gly Thr Leu
130 135 140

Glu Leu Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr Leu Arg
145 150 155 160

Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu
165 170 175

Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg Leu Ile
180 185 190

Glu Gly Leu Thr Phe Gln Gly Leu Asn Ser Leu Glu Val Leu Lys Leu
195 200 205

Gln Arg Asn Asn Ile Ser Lys Leu Thr Asp Gly Ala Phe Trp Gly Leu
210 215 220

Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val Glu Val
225 230 235 240

Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu His Leu
245 250 255

Ser Asn Asn Ser Ile Ala Arg Ile His Arg Lys Gly Trp Ser Phe Cys
260 265 270

Gln Lys Leu His Glu Leu Val Leu Ser Phe Asn Asn Leu Thr Arg Leu
275 280 285

Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Val Leu Arg Leu
290 295 300

Ser His Asn Ser Ile Ser His Ile Ala Glu Gly Ala Phe Lys Gly Leu
305 310 315 320
Arg Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser Gly Thr
325 330 335
Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys
340 345 350
Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg Ala Phe
355 360 365
Ser Gly Leu Glu Gly Leu Glu His Leu Asn Leu Gly Gly Asn Ala Ile
370 375 380
Arg Ser Val Gln Phe Asp Ala Phe Val Lys Met Lys Asn Leu Lys Glu
385 390 395 400
Leu His Ile Ser Ser Asp Ser Phe Leu Cys Asp Cys Gln Leu Lys Trp
405 410 415
Leu Pro Pro Trp Leu Ile Gly Arg Met Leu Gln Ala Phe Val Thr Ala
420 425 430
Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe Ser Val
435 440 445
Pro Pro Glu Ser Phe Val Cys Asp Asp Phe Leu Lys Pro Gln Ile Ile
450 455 460
Thr Gln Pro Glu Thr Thr Met Ala Met Val Gly Lys Asp Ile Arg Phe
465 470 475 480
Thr Cys Ser Ala Ala Ser Ser Ser Ser Pro Met Thr Phe Ala Trp
485 490 495
Lys Lys Asp Asn Glu Val Leu Thr Asn Ala Asp Met Glu Asn Phe Val
500 505 510
His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu
515 520 525
His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val
530 535 540
Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg Leu Thr

545 550 555 560
 Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile
 565 570 575
 Arg Thr Thr Thr Val Ala Arg Leu Glu Cys Ala Ala Thr Gly His Pro
 580 585 590
 Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe Pro Ala
 595 600 605
 Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val Phe Phe

 610 615 620
 Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys Thr Ala
 625 630 635 640
 Gln Asn Ser Ala Gly Ser Ile Ser Ala Asn Ala Thr Leu Thr Val Leu
 645 650 655
 Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val Ser Val
 660 665 670
 Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro
 675 680 685

 Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg
 690 695 700
 His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val
 705 710 715 720
 Ala Glu Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Thr Leu Gly
 725 730 735
 Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala Gly Cys
 740 745 750
 Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Gly Ser Arg Asn Thr Gly

 755 760 765
 Arg Gly Gly Glu Glu Lys Lys Lys Glu Lys Glu Lys Glu Glu Gln Glu
 770 775 780
 Glu Arg Glu Thr Lys Thr Pro Glu Cys Pro Ser His Thr Gln Pro Leu
 785 790 795 800
 Gly Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser

805 810 815
 Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
 820 825 830

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 835 840 845

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
 850 855 860

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 865 870 875 880

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 885 890 895

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr

900 905 910
 Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr

915 920 925
 Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu

930 935 940
 Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu

945 950 955 960
 Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys

965 970 975

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 980 985 990

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 995 1000 1005

Lys

<210> 40

<211> 996

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 40

Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala Gly Asp

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

20 25 30

Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu Ser Glu

35 40 45

Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr

50 55 60

Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser

65 70 75 80

Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val

85 90 95

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

100 105 110

Ser Leu Asn Asn Ile Thr Glu Val Arg Asn Thr Cys Phe Pro His Gly

115 120 125

Pro Pro Ile Lys Glu Leu Asn Leu Ala Gly Asn Arg Ile Gly Thr Leu

130 135 140

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

145 150 155 160

Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu

165 170 175

Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg Leu Ile

180 185 190

Glu Gly Leu Thr Phe Gln Gly Leu Asn Ser Leu Glu Val Leu Lys Leu

195 200 205

Gln Arg Asn Asn Ile Ser Lys Leu Thr Asp Gly Ala Phe Trp Gly Leu

210 215 220

Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val Glu Val

225 230 235 240

Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu His Leu
 245 250 255
 Ser Asn Asn Ser Ile Ala Arg Ile His Arg Lys Gly Trp Ser Phe Cys
 260 265 270
 Gln Lys Leu His Glu Leu Val Leu Ser Phe Asn Asn Leu Thr Arg Leu
 275 280 285
 Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Val Leu Arg Leu
 290 295 300
 Ser His Asn Ser Ile Ser His Ile Ala Glu Gly Ala Phe Lys Gly Leu
 305 310 315 320
 Arg Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser Gly Thr
 325 330 335
 Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys
 340 345 350
 Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg Ala Phe
 355 360 365
 Ser Gly Leu Glu Gly Leu Glu His Leu Asn Leu Gly Gly Asn Ala Ile
 370 375 380
 Arg Ser Val Gln Phe Asp Ala Phe Val Lys Met Lys Asn Leu Lys Glu
 385 390 395 400
 Leu His Ile Ser Ser Asp Ser Phe Leu Cys Asp Cys Gln Leu Lys Trp
 405 410 415
 Leu Pro Pro Trp Leu Ile Gly Arg Met Leu Gln Ala Phe Val Thr Ala
 420 425 430
 Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe Ser Val
 435 440 445
 Pro Pro Glu Ser Phe Val Cys Asp Asp Phe Leu Lys Pro Gln Ile Ile
 450 455 460
 Thr Gln Pro Glu Thr Thr Met Ala Met Val Gly Lys Asp Ile Arg Phe
 465 470 475 480
 Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe Ala Trp
 485 490 495

Lys Lys Asp Asn Glu Val Leu Thr Asn Ala Asp Met Glu Asn Phe Val
 500 505 510
 His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu
 515 520 525

 His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val
 530 535 540
 Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg Leu Thr
 545 550 555 560
 Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile
 565 570 575
 Arg Thr Thr Thr Val Ala Arg Leu Glu Cys Ala Ala Thr Gly His Pro
 580 585 590
 Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe Pro Ala

 595 600 605
 Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val Phe Phe
 610 615 620
 Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys Thr Ala
 625 630 635 640
 Gln Asn Ser Ala Gly Ser Ile Ser Ala Asn Ala Thr Leu Thr Val Leu
 645 650 655
 Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val Ser Val
 660 665 670

 Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro
 675 680 685
 Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg
 690 695 700
 His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val
 705 710 715 720
 Ala Glu Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Thr Leu Gly
 725 730 735
 Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala Gly Cys

740	745	750	
Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Gly Ser Glu Pro Lys Ser			
755	760	765	
Ser Asp Lys Thr His Thr Ser Pro Pro Ser Pro Ala Pro Glu Leu Leu			
770	775	780	
Gly Gly Ser Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu			
785	790	795	800
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser			
805	810	815	
His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu			
820	825	830	
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr			
835	840	845	
Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn			
850	855	860	
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro			
865	870	875	880
Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln			
885	890	895	
Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val			
900	905	910	
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val			
915	920	925	
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro			
930	935	940	
Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr			
945	950	955	960
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val			
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Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu			
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Ser Pro Gly Lys			

995

<210> 41

<211> 2988

<212> DNA

<213> Artificial Sequence

<220><223> fusion protein

<400> 41

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<210> 42

<211> 2991

<212> DNA

<213> Artificial Sequence

<220><223> fusion protein

<400> 42

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<210> 43
<211> 3027
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<211> 994

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 45

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Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu

35 40 45

Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu

50 55 60

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

65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu

85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu

100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro

115	120	125	
Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser			
130	135	140	
Ile Leu Glu Ser Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr			
145	150	155	160
Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe			
165	170	175	
Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg			
180	185	190	
Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu			
195	200	205	
Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp			
210	215	220	
Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val			
225	230	235	240
Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu			
245	250	255	
His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser			
260	265	270	
Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr			
275	280	285	
Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu			
290	295	300	
Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys			
305	310	315	320
Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser			
325	330	335	
Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu			
340	345	350	
Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg			
355	360	365	
Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn			

370 375 380
 Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu

 385 390 395 400
 Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu

 405 410 415
 Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val

 420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe

 435 440 445
 Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln

 450 455 460

 Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
 465 470 475 480
 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe

 485 490 495
 Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn

 500 505 510
 Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr

 515 520 525
 Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln

 530 535 540
 Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
 545 550 555 560
 Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile

 565 570 575
 Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly

 580 585 590
 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe

 595 600 605

 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
 610 615 620

Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys
 625 630 635 640
 Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
 645 650 655
 Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
 660 665 670
 Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro

 675 680 685
 Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
 690 695 700
 Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
 705 710 715 720
 Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
 725 730 735
 Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
 740 745 750

 Gly Cys Arg Lys Asp Gly Thr Thr Gly Ser Glu Pro Lys Ser Ser Asp
 755 760 765
 Lys Thr His Thr Ser Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
 770 775 780
 Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 785 790 795 800
 Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
 805 810 815
 Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His

 820 825 830
 Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
 835 840 845
 Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 850 855 860
 Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
 865 870 875 880

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
885 890 895

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
900 905 910

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
915 920 925

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
930 935 940

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
945 950 955 960

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His

965 970 975

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
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Gly Lys

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<211> 995

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 46

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20 25 30

Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu
35 40 45

Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu
50 55 60

Val Tyr Leu Asn Ser Asn Glu Leu Thr Ala Ile Pro Ser Leu Gly Ala
65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu
85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu
100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro
115 120 125

Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser
130 135 140

Ile Leu Glu Ser Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr
145 150 155 160

Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe
165 170 175

Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg
180 185 190

Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu
195 200 205

Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp
210 215 220

Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val
225 230 235 240

Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu
245 250 255

His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser
260 265 270

Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr
275 280 285

Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
290 295 300

Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
305 310 315 320

Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser

325 330 335
 Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
 340 345 350
 Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
 355 360 365
 Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
 370 375 380

 Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
 385 390 395 400
 Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
 405 410 415
 Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
 420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
 435 440 445
 Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln

 450 455 460
 Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
 465 470 475 480
 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe
 485 490 495
 Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
 500 505 510
 Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
 515 520 525

 Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
 530 535 540
 Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
 545 550 555 560
 Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
 565 570 575
 Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly

580 585 590
His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe

595 600 605
Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val

610 615 620
Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys

625 630 635 640
Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr

645 650 655
Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val

660 665 670

Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
675 680 685

Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
690 695 700

Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
705 710 715 720

Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
725 730 735

Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro

740 745 750
Gly Cys Arg Lys Asp Gly Thr Thr Gly Ser Glu Pro Arg Gly Pro Thr

755 760 765
Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu Gly

770 775 780
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met

785 790 795 800
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His

805 810 815

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
820 825 830

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr

835 840 845

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly

850 855 860

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile

865 870 875 880

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val

885 890 895

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser

900 905 910

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu

915 920 925

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro

930 935 940

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val

945 950 955 960

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met

965 970 975

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980 985 990

Pro Gly Lys

995

<210> 47

<211> 1007

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 47

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

Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
290 295 300

Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
305 310 315 320

Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser
325 330 335

Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
340 345 350

Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
355 360 365

Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn

370 375 380

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

145 150 155 160

Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe

165 170 175

Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg

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Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu

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Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp

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ctgtcactga gccctggcaa a 3021

<210> 52

<211> 2982

<212> DNA

<213> Artificial Sequence

<220><223> fusion protein

<400> 52

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ctgaacctga gctacaatcg gctgtccgag atcgattctg ccgcctttga ggacctgaca 180

aatctgcagg aggtgtatct gaacagcaat gagctgaccg caatcccctc cctgggagca 240

gcctctatcg gcgtggtgag cctgttctg cagcacaaca agatcctgag cgtggatggc 300

tcccagctga agagctacct gtctctggag gtgctggacc tgagctccaa caatatcacc 360

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acccaccgcc tgctggattc tgacggcagc ttttttctgt attctaagct gaccgtggac 2880

aagagcaggt ggcagcaggg caacgtgttc agctgctccg tgatgcacga agcactgcac 2940

aatactaca ccagaaatc actgtcactg agccctggca aa 2982

<210> 53

<211> 994

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 53

Ala Gln Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala

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

20 25 30

Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu

35 40 45

Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu

50 55 60

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

65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu

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

Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu

340 345 350

Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg

355 360 365

Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn

370 375 380

Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu

385 390 395 400

Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu

405 410 415

Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val

420 425 430

Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe

435 440 445

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

450 455 460

Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile

465 470 475 480

Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe

485 490 495

Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn

500 505 510

Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr

515 520 525

Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln

530 535 540

Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg

545 550 555 560

Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile

565 570 575

Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly

580 585 590
 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
 595 600 605
 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
 610 615 620
 Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys

 625 630 635 640
 Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
 645 650 655
 Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
 660 665 670
 Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
 675 680 685
 Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
 690 695 700

 Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
 705 710 715 720
 Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
 725 730 735
 Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
 740 745 750
 Gly Cys Arg Lys Asp Gly Thr Thr Gly Ser Glu Pro Lys Ser Ser Asp
 755 760 765
 Lys Thr His Thr Ser Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly

 770 775 780
 Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile
 785 790 795 800
 Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp
 805 810 815
 Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His
 820 825 830
 Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg

835 840 845

Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys

850 855 860

Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu

865 870 875 880

Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr

885 890 895

Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu

900 905 910

Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp

915 920 925

Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val

930 935 940

Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu

945 950 955 960

Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His

965 970 975

Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro

980 985 990

Gly Lys

<210> 54

<211> 995

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 54

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

20 25 30

Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu

35 40 45
Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu

50 55 60
Val Tyr Leu Asn Ser Asn Glu Leu Thr Ala Ile Pro Ser Leu Gly Ala
65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu
85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu
100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro
115 120 125

Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser
130 135 140

Ile Leu Glu Ser Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr
145 150 155 160

Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe
165 170 175

Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg
180 185 190

Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu

195 200 205
Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp

210 215 220
Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val

225 230 235 240
Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu

245 250 255
His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser

260 265 270
Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr

275 280 285

Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
290 295 300

Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
305 310 315 320

Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser
325 330 335

Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
340 345 350

Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
355 360 365

Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
370 375 380

Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
385 390 395 400

Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
405 410 415

Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
420 425 430

Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
435 440 445

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

Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
465 470 475 480

Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe
485 490 495

Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
500 505 510

Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
515 520 525

Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
530 535 540

Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
545 550 555 560

Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
565 570 575

Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
580 585 590

His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
595 600 605

Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
610 615 620

Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys

625 630 635 640
Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
645 650 655

Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
660 665 670

Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
675 680 685

Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
690 695 700

Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
705 710 715 720

Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
725 730 735

Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
740 745 750

Gly Cys Arg Lys Asp Gly Thr Thr Gly Ser Glu Pro Arg Gly Pro Thr
755 760 765

Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu Gly

770 775 780

Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met

785 790 795 800
 Ile Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu
 805 810 815
 Asp Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val
 820 825 830
 His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu
 835 840 845

 Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly
 850 855 860
 Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile
 865 870 875 880
 Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val
 885 890 895
 Tyr Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr
 900 905 910
 Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu

 915 920 925
 Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro
 930 935 940
 Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val
 945 950 955 960
 Glu Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val
 965 970 975
 His Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr
 980 985 990

 Pro Gly Lys
 995
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 <212> PRT
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 <220><223> fusion protein

<400> 55

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20 25 30

Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu

35 40 45

Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu

50 55 60

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

65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu

85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu

100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro

115 120 125

Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser

130 135 140

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

145 150 155 160

Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe

165 170 175

Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg

180 185 190

Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu

195 200 205

Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp

210 215 220

Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val

225 230 235 240

Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu

245 250 255
His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser

260 265 270
Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr

275 280 285
Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu

290 295 300
Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys

305 310 315 320
Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser

325 330 335

Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
340 345 350

Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
355 360 365

Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
370 375 380

Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
385 390 395 400

Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu

405 410 415

Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val

420 425 430

Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe

435 440 445

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

450 455 460

Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile

465 470 475 480

Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe

485 490 495

Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
500 505 510

Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
515 520 525

Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
530 535 540

Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg

545 550 555 560

Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
565 570 575

Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
580 585 590

His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
595 600 605

Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
610 615 620

Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys
625 630 635 640

Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
645 650 655

Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
660 665 670

Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
675 680 685

Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr

690 695 700

Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
705 710 715 720

Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
725 730 735

Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
740 745 750

Gly Cys Arg Lys Asp Gly Thr Thr Gly Ser Arg Asn Thr Gly Arg Gly
755 760 765

Gly Glu Glu Lys Lys Lys Glu Lys Glu Lys Glu Glu Gln Glu Glu Arg
770 775 780

Glu Thr Lys Thr Pro Glu Cys Pro Ser His Thr Gln Pro Leu Gly Val
785 790 795 800

Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu Ser
805 810 815

Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro Asp
820 825 830

Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr Ala Gln

835 840 845

Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg Val Val Ser
850 855 860

Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys Glu Phe Lys
865 870 875 880

Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu Arg Thr Ile
885 890 895

Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr Val Leu Pro
900 905 910

Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu Thr Cys Met
915 920 925

Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp Thr Asn Asn
930 935 940

Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val Leu Asp Ser
945 950 955 960

Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu Lys Lys Asn
965 970 975

Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu Gly Leu

980 985 990

His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys

995 1000 1005
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 <211> 994
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 Gly Asp Ser Leu Asp Cys Ser Gly Arg Gly Leu Ala Thr Leu Pro Arg
 20 25 30

 Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu
 35 40 45
 Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu
 50 55 60
 Val Tyr Leu Asn Ser Asn Glu Leu Thr Ala Ile Pro Ser Leu Gly Ala
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agcctgaagg gccagagcat cttctccgtg ctgcccata gcttcgtgtg cgacathtt	1380
cctaagccac agatcatcac ccagccagag acaacaatgg ccgtgggtggg caaggacatc	1440
cggtttacct gticcgcgc ctctagctcc tctagcccca tgaccttcgc ctggaagaag	1500
gataacgagg tcttgccaa tgcgacatg gagaacttcg ccacgtgag agcccaggat	1560
ggcgaagtga tggagtatac cacaatcctg cacctgcggc acgtgacctt tggccacgag	1620
ggcagatacc agtgcacat cacaatcac ttgggtctta cctatagcca caaggccagg	1680
ctgacagtga acgtgctgcc tagctttacc aagatccac acgacatgc catcagaaca	1740
ggcaccacag caaggctgga gtgtgcagca accggacacc caaacctca gatcgcatgg	1800
cagaaggatg gaggcacaga cttccctgca gccgcgaga ggagaatgca cgtgatgcca	1860
gacgatgacg tttctttat cacagatgtg aagatcgatg acatgggcgt gtactcctgc	1920
accgcacaga acagcgccgg cagcgtgtcc gccaaccca cctgaccgt gctggagaca	1980
ccatccctgg ccgtgccct ggaggacagg gtggtgaccg tgggcgagac agtggccttt	2040

cagtgtgaagg ccaccggctc tccaacacca aggatcacct ggctgaaggg cggcaggccc 2100

ctgagcctga cagagcgcca ccacttcacc cctggcaatc agctgctggt ggtgcagaac 2160

gtgatgatcg atgacgccgg caggtataca tgcgagatga gcaatcctct gggcaccgag 2220

agggcacact ccagctgtc tctcctgcct accccaggct gccggaagga tggcaccaca 2280

ggatccgaac cgaaatcttc tgacaaaacc cacacctctc cgccgtctcc ggctccggaa 2340

ctgctgggtg gttcttctgt ttctatcttc ccaccaaga tcaaggacgt gctgatgatc 2400

tccctgtccc ccatcgtgac ctgctgggtg gtggacgtgt ccgaggacga ccccgacgtg 2460

cagatcagtt ggttcgtgaa caacgtggaa gtgcacaccg ccagacca gaccacaga 2520

gaggactaca atccacacct gcgggtgggtg tccgcctgc ccatccagca ccaggactgg 2580

atgtccggca aagaattcaa gtgcaaagtg aacaacaagg acctgcctgc ccccatcgag 2640

cggaccatct ccaagcccaa gggctccgtg cgggtccccc aggtgtacgt gctgccccct 2700

ccagaggaag agatgaccaa gaagcaggtc aactgacct gcatggtcac cgacttcatg 2760

cccgaggaca tctacgtgga atggaccaac aatggcaaga ccgagctgaa ctacaagaac 2820

accgagcctg tcttggaact cgacggctcc tacttcatgt actccaagct gcgggtggaa 2880

aagaagaact gggctgagcg gaactcctac tctgtctccg tgggtcacga gggcctgcac 2940

aaccaccaca ccaccaagtc cttctcccg acccccgga aa 2982

<210> 61

<211> 999

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 61

Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala Gly Asp

1 5 10 15

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

20 25 30

Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu Ser Glu

35 40 45

Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr

50 55 60

Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser

65	70	75	80
Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val			
	85	90	95
Glu Gly Ser Gln Leu Lys Ala Tyr Leu Ser Leu Glu Val Leu Asp Leu			
	100	105	110
Ser Leu Asn Asn Ile Thr Glu Val Arg Asn Thr Cys Phe Pro His Gly			
	115	120	125
Pro Pro Ile Lys Glu Leu Asn Leu Ala Gly Asn Arg Ile Gly Thr Leu			
	130	135	140
Glu Leu Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr Leu Arg			
145	150	155	160
Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu			
	165	170	175
Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg Leu Ile			
	180	185	190
Glu Gly Leu Thr Phe Gln Gly Leu Asn Ser Leu Glu Val Leu Lys Leu			
	195	200	205
Gln Arg Asn Asn Ile Ser Lys Leu Thr Asp Gly Ala Phe Trp Gly Leu			
	210	215	220
Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val Glu Val			
225	230	235	240
Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu His Leu			
	245	250	255
Ser Asn Asn Ser Ile Ala Arg Ile His Arg Lys Gly Trp Ser Phe Cys			
	260	265	270
Gln Lys Leu His Glu Leu Val Leu Ser Phe Asn Asn Leu Thr Arg Leu			
	275	280	285
Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Val Leu Arg Leu			
	290	295	300
Ser His Asn Ser Ile Ser His Ile Ala Glu Gly Ala Phe Lys Gly Leu			
305	310	315	320

Arg Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser Gly Thr

325 330 335

Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys

340 345 350

Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg Ala Phe

355 360 365

Ser Gly Leu Glu Gly Leu Glu His Leu Asn Leu Gly Gly Asn Ala Ile

370 375 380

Arg Ser Val Gln Phe Asp Ala Phe Val Lys Met Lys Asn Leu Lys Glu

385 390 395 400

Leu His Ile Ser Ser Asp Ser Phe Leu Cys Asp Cys Gln Leu Lys Trp

405 410 415

Leu Pro Pro Trp Leu Ile Gly Arg Met Leu Gln Ala Phe Val Thr Ala

420 425 430

Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe Ser Val

435 440 445

Pro Pro Glu Ser Phe Val Cys Asp Asp Phe Leu Lys Pro Gln Ile Ile

450 455 460

Thr Gln Pro Glu Thr Thr Met Ala Met Val Gly Lys Asp Ile Arg Phe

465 470 475 480

Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe Ala Trp

485 490 495

Lys Lys Asp Asn Glu Val Leu Thr Asn Ala Asp Met Glu Asn Phe Val

500 505 510

His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu

515 520 525

His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val

530 535 540

Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg Leu Thr

545 550 555 560

Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile

565 570 575
 Arg Thr Thr Thr Val Ala Arg Leu Glu Cys Ala Ala Thr Gly His Pro
 580 585 590
 Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe Pro Ala
 595 600 605
 Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val Phe Phe

 610 615 620
 Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys Thr Ala
 625 630 635 640
 Gln Asn Ser Ala Gly Ser Ile Ser Ala Asn Ala Thr Leu Thr Val Leu
 645 650 655
 Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val Ser Val
 660 665 670
 Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro
 675 680 685

 Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg
 690 695 700
 His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val
 705 710 715 720
 Ala Glu Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Thr Leu Gly
 725 730 735
 Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala Gly Cys
 740 745 750
 Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Gly Gly Gly Gly Ser Glu

 755 760 765
 Pro Lys Ser Ser Asp Lys Thr His Thr Ser Pro Pro Cys Pro Ala Pro
 770 775 780
 Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
 785 790 795 800
 Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
 805 810 815
 Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp

820 825 830

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr

835 840 845

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp

850 855 860

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu

865 870 875 880

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg

885 890 895

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys

900 905 910

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp

915 920 925

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys

930 935 940

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser

945 950 955 960

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser

965 970 975

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser

980 985 990

Leu Ser Leu Ser Pro Gly Lys

995

<210> 62

<211> 1000

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 62

Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala Gly Asp

1 5 10 15

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

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

Gln Lys Leu His Glu Leu Val Leu Ser Phe Asn Asn Leu Thr Arg Leu
275 280 285

Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Val Leu Arg Leu
290 295 300

Ser His Asn Ser Ile Ser His Ile Ala Glu Gly Ala Phe Lys Gly Leu
305 310 315 320

Arg Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser Gly Thr
325 330 335

Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys
340 345 350

Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg Ala Phe
355 360 365

Ser Gly Leu Glu Gly Leu Glu His Leu Asn Leu Gly Gly Asn Ala Ile
370 375 380

Arg Ser Val Gln Phe Asp Ala Phe Val Lys Met Lys Asn Leu Lys Glu
385 390 395 400

Leu His Ile Ser Ser Asp Ser Phe Leu Cys Asp Cys Gln Leu Lys Trp
405 410 415

Leu Pro Pro Trp Leu Ile Gly Arg Met Leu Gln Ala Phe Val Thr Ala
420 425 430

Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe Ser Val
435 440 445

Pro Pro Glu Ser Phe Val Cys Asp Asp Phe Leu Lys Pro Gln Ile Ile
450 455 460

Thr Gln Pro Glu Thr Thr Met Ala Met Val Gly Lys Asp Ile Arg Phe
465 470 475 480

Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe Ala Trp
485 490 495

Lys Lys Asp Asn Glu Val Leu Thr Asn Ala Asp Met Glu Asn Phe Val
500 505 510

His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu
515 520 525

His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val

530

535

540

Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg Leu Thr

545

550

555

560

Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile

565

570

575

Arg Thr Thr Thr Val Ala Arg Leu Glu Cys Ala Ala Thr Gly His Pro

580

585

590

Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe Pro Ala

595

600

605

Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val Phe Phe

610

615

620

Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys Thr Ala

625

630

635

640

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

645

650

655

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

660

665

670

Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro

675

680

685

Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg

690

695

700

His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val

705

710

715

720

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

725

730

735

Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala Gly Cys

740

745

750

Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Gly Gly Gly Gly Ser Glu

755

760

765

Pro Arg Gly Pro Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala

770 775 780
 Pro Asn Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
 785 790 795 800
 Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
 805 810 815
 Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val

 820 825 830
 Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
 835 840 845
 Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
 850 855 860
 Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
 865 870 875 880
 Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
 885 890 895

 Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
 900 905 910
 Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
 915 920 925
 Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
 930 935 940
 Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
 945 950 955 960
 Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe

 965 970 975
 Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
 980 985 990
 Ser Leu Ser Leu Ser Pro Gly Lys
 995 1000

 <210> 63
 <211> 1012
 <212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 63

Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala Gly Asp

1 5 10 15

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

20 25 30

Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu Ser Glu

35 40 45

Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr

50 55 60

Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser

65 70 75 80

Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val

85 90 95

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

100 105 110

Ser Leu Asn Asn Ile Thr Glu Val Arg Asn Thr Cys Phe Pro His Gly

115 120 125

Pro Pro Ile Lys Glu Leu Asn Leu Ala Gly Asn Arg Ile Gly Thr Leu

130 135 140

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

145 150 155 160

Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu

165 170 175

Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg Leu Ile

180 185 190

Glu Gly Leu Thr Phe Gln Gly Leu Asn Ser Leu Glu Val Leu Lys Leu

195 200 205

Gln Arg Asn Asn Ile Ser Lys Leu Thr Asp Gly Ala Phe Trp Gly Leu

210 215 220

Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val Glu Val

225 230 235 240
 Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu His Leu
 245 250 255
 Ser Asn Asn Ser Ile Ala Arg Ile His Arg Lys Gly Trp Ser Phe Cys
 260 265 270
 Gln Lys Leu His Glu Leu Val Leu Ser Phe Asn Asn Leu Thr Arg Leu
 275 280 285
 Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Val Leu Arg Leu
 290 295 300
 Ser His Asn Ser Ile Ser His Ile Ala Glu Gly Ala Phe Lys Gly Leu

 305 310 315 320
 Arg Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser Gly Thr
 325 330 335
 Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys
 340 345 350
 Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg Ala Phe
 355 360 365
 Ser Gly Leu Glu Gly Leu Glu His Leu Asn Leu Gly Gly Asn Ala Ile
 370 375 380

 Arg Ser Val Gln Phe Asp Ala Phe Val Lys Met Lys Asn Leu Lys Glu
 385 390 395 400
 Leu His Ile Ser Ser Asp Ser Phe Leu Cys Asp Cys Gln Leu Lys Trp
 405 410 415
 Leu Pro Pro Trp Leu Ile Gly Arg Met Leu Gln Ala Phe Val Thr Ala
 420 425 430
 Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe Ser Val
 435 440 445
 Pro Pro Glu Ser Phe Val Cys Asp Asp Phe Leu Lys Pro Gln Ile Ile

 450 455 460
 Thr Gln Pro Glu Thr Thr Met Ala Met Val Gly Lys Asp Ile Arg Phe
 465 470 475 480

Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe Ala Trp
485 490 495

Lys Lys Asp Asn Glu Val Leu Thr Asn Ala Asp Met Glu Asn Phe Val
500 505 510

His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu
515 520 525

His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val
530 535 540

Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg Leu Thr
545 550 555 560

Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile
565 570 575

Arg Thr Thr Thr Val Ala Arg Leu Glu Cys Ala Ala Thr Gly His Pro
580 585 590

Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe Pro Ala
595 600 605

Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val Phe Phe
610 615 620

Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys Thr Ala
625 630 635 640

Gln Asn Ser Ala Gly Ser Ile Ser Ala Asn Ala Thr Leu Thr Val Leu
645 650 655

Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val Ser Val
660 665 670

Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro
675 680 685

Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg
690 695 700

His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val
705 710 715 720

Ala Glu Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Thr Leu Gly
725 730 735

Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala Gly Cys

740 745 750
Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Gly Gly Gly Gly Ser Arg
755 760 765
Asn Thr Gly Arg Gly Gly Glu Glu Lys Lys Lys Glu Lys Glu Lys Glu
770 775 780
Glu Gln Glu Glu Arg Glu Thr Lys Thr Pro Glu Cys Pro Ser His Thr
785 790 795 800
Gln Pro Leu Gly Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
805 810 815

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
820 825 830
His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
835 840 845
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
850 855 860
Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
865 870 875 880
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro

885 890 895
Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
900 905 910
Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
915 920 925
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
930 935 940
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
945 950 955 960

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
965 970 975
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val

980 985 990
 Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 995 1000 1005
 Ser Pro Gly Lys
 1010
 <210> 64
 <211> 999
 <212> PRT
 <213> Artificial Sequence
 <220><223> fusion protein

 <400> 64
 Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala Gly Asp
 1 5 10 15
 Ser Leu Asp Cys Gly Gly Arg Gly Leu Ala Ala Leu Pro Gly Asp Leu
 20 25 30
 Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu Ser Glu
 35 40 45
 Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu Val Tyr
 50 55 60
 Leu Asn Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala Ala Ser

 65 70 75 80
 Ser His Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Arg Ser Val
 85 90 95
 Glu Gly Ser Gln Leu Lys Ala Tyr Leu Ser Leu Glu Val Leu Asp Leu
 100 105 110
 Ser Leu Asn Asn Ile Thr Glu Val Arg Asn Thr Cys Phe Pro His Gly
 115 120 125
 Pro Pro Ile Lys Glu Leu Asn Leu Ala Gly Asn Arg Ile Gly Thr Leu
 130 135 140

 Glu Leu Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr Leu Arg
 145 150 155 160
 Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Arg Ala Phe Lys Leu

165	170	175	
Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg Leu Ile			
180	185	190	
Glu Gly Leu Thr Phe Gln Gly Leu Asn Ser Leu Glu Val Leu Lys Leu			
195	200	205	
Gln Arg Asn Asn Ile Ser Lys Leu Thr Asp Gly Ala Phe Trp Gly Leu			
210	215	220	
Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val Glu Val			
225	230	235	240
Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu His Leu			
245	250	255	
Ser Asn Asn Ser Ile Ala Arg Ile His Arg Lys Gly Trp Ser Phe Cys			
260	265	270	
Gln Lys Leu His Glu Leu Val Leu Ser Phe Asn Asn Leu Thr Arg Leu			
275	280	285	
Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Val Leu Arg Leu			
290	295	300	
Ser His Asn Ser Ile Ser His Ile Ala Glu Gly Ala Phe Lys Gly Leu			
305	310	315	320
Arg Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser Gly Thr			
325	330	335	
Ile Glu Asp Thr Ser Gly Ala Phe Ser Gly Leu Asp Ser Leu Ser Lys			
340	345	350	
Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg Ala Phe			
355	360	365	
Ser Gly Leu Glu Gly Leu Glu His Leu Asn Leu Gly Gly Asn Ala Ile			
370	375	380	
Arg Ser Val Gln Phe Asp Ala Phe Val Lys Met Lys Asn Leu Lys Glu			
385	390	395	400
Leu His Ile Ser Ser Asp Ser Phe Leu Cys Asp Cys Gln Leu Lys Trp			
405	410	415	
Leu Pro Pro Trp Leu Ile Gly Arg Met Leu Gln Ala Phe Val Thr Ala			

420 425 430
 Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe Ser Val
 435 440 445
 Pro Pro Glu Ser Phe Val Cys Asp Asp Phe Leu Lys Pro Gln Ile Ile
 450 455 460
 Thr Gln Pro Glu Thr Thr Met Ala Met Val Gly Lys Asp Ile Arg Phe
 465 470 475 480
 Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe Ala Trp
 485 490 495
 Lys Lys Asp Asn Glu Val Leu Thr Asn Ala Asp Met Glu Asn Phe Val
 500 505 510
 His Val His Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr Ile Leu
 515 520 525
 His Leu Arg Gln Val Thr Phe Gly His Glu Gly Arg Tyr Gln Cys Val
 530 535 540
 Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg Leu Thr
 545 550 555 560
 Val Asn Val Leu Pro Ser Phe Thr Lys Thr Pro His Asp Ile Thr Ile
 565 570 575
 Arg Thr Thr Thr Val Ala Arg Leu Glu Cys Ala Ala Thr Gly His Pro
 580 585 590
 Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe Pro Ala
 595 600 605
 Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val Phe Phe
 610 615 620
 Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys Thr Ala
 625 630 635 640
 Gln Asn Ser Ala Gly Ser Ile Ser Ala Asn Ala Thr Leu Thr Val Leu
 645 650 655
 Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val Ser Val
 660 665 670

Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro Pro Pro
 675 680 685
 Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr Glu Arg
 690 695 700
 His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn Val Val
 705 710 715 720

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

275 280 285
 Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
 290 295 300
 Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
 305 310 315 320
 Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser
 325 330 335
 Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu

 340 345 350
 Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
 355 360 365
 Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
 370 375 380
 Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
 385 390 395 400
 Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
 405 410 415

 Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
 420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
 435 440 445
 Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln
 450 455 460
 Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
 465 470 475 480
 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe

 485 490 495
 Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
 500 505 510
 Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
 515 520 525
 Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln

530 535 540
 Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
 545 550 555 560

 Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
 565 570 575
 Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
 580 585 590
 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
 595 600 605
 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
 610 615 620
 Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys

 625 630 635 640
 Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
 645 650 655
 Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
 660 665 670
 Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
 675 680 685
 Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
 690 695 700

 Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
 705 710 715 720
 Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
 725 730 735
 Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
 740 745 750
 Gly Cys Arg Lys Asp Gly Thr Thr Gly Gly Gly Gly Ser Glu Pro Lys
 755 760 765
 Ser Ser Asp Lys Thr His Thr Ser Pro Pro Cys Pro Ala Pro Glu Leu

 770 775 780

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
785 790 795 800
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
805 810 815
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
820 825 830
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
835 840 845

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
850 855 860
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
865 870 875 880
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
885 890 895
Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
900 905 910
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala

915 920 925
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
930 935 940
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
945 950 955 960
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
965 970 975
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
980 985 990

Leu Ser Pro Gly Lys
995

<210> 70

<211> 998

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 70

Ala Gln Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala

1 5 10 15

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

20 25 30

Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu

35 40 45

Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu

50 55 60

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

65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu

85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu

100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro

115 120 125

Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser

130 135 140

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

145 150 155 160

Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe

165 170 175

Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg

180 185 190

Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu

195 200 205

Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp

210 215 220

Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val

225 230 235 240

Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu
 245 250 255
 His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser
 260 265 270
 Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr
 275 280 285
 Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
 290 295 300
 Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
 305 310 315 320
 Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser
 325 330 335

 Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
 340 345 350
 Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
 355 360 365
 Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
 370 375 380
 Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
 385 390 395 400
 Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu

 405 410 415
 Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
 420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
 435 440 445
 Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln
 450 455 460
 Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
 465 470 475 480

 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe

485	490	495	
Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn			
500	505	510	
Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr			
515	520	525	
Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln			
530	535	540	
Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg			
545	550	555	560
Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile			
565	570	575	
Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly			
580	585	590	
His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe			
595	600	605	
Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val			
610	615	620	
Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys			
625	630	635	640
Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr			
645	650	655	
Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val			
660	665	670	
Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro			
675	680	685	
Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr			
690	695	700	
Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn			
705	710	715	720
Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro			
725	730	735	
Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro			

740	745	750
Gly Cys Arg Lys Asp Gly Thr Thr Gly Gly Gly Gly Ser Glu Pro Arg		
755	760	765
Gly Pro Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn		
770	775	780
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp		
785	790	795
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp		
805	810	815
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly		
820	825	830
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn		
835	840	845
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp		
850	855	860
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro		
865	870	875
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu		
885	890	895
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn		
900	905	910
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile		
915	920	925
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr		
930	935	940
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys		
945	950	955
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys		
965	970	975
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu		
980	985	990

Ser Leu Ser Pro Gly Lys

995

<210> 71

<211> 1010

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 71

Ala Gln Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala

1 5 10 15

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

20 25 30

Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu

35 40 45

Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu

50 55 60

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

65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu

85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu

100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro

115 120 125

Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser

130 135 140

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

145 150 155 160

Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe

165 170 175

Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg

180 185 190

Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu
 195 200 205
 Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp
 210 215 220
 Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val
 225 230 235 240
 Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu
 245 250 255

 His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser
 260 265 270
 Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr
 275 280 285
 Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
 290 295 300
 Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
 305 310 315 320
 Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser

 325 330 335
 Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
 340 345 350
 Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
 355 360 365
 Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
 370 375 380
 Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
 385 390 395 400

 Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
 405 410 415
 Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
 420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
 435 440 445

Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln
 450 455 460
 Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile

 465 470 475 480
 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe
 485 490 495
 Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
 500 505 510
 Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
 515 520 525
 Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
 530 535 540

 Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
 545 550 555 560
 Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
 565 570 575
 Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
 580 585 590
 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
 595 600 605
 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val

 610 615 620
 Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys
 625 630 635 640
 Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
 645 650 655
 Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
 660 665 670
 Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
 675 680 685

 Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr

690 695 700
 Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
 705 710 715 720
 Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
 725 730 735
 Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
 740 745 750
 Gly Cys Arg Lys Asp Gly Thr Thr Gly Gly Gly Gly Ser Arg Asn Thr

 755 760 765
 Gly Arg Gly Gly Glu Glu Lys Lys Lys Glu Lys Glu Lys Glu Glu Gln
 770 775 780
 Glu Glu Arg Glu Thr Lys Thr Pro Glu Cys Pro Ser His Thr Gln Pro
 785 790 795 800
 Leu Gly Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 805 810 815
 Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
 820 825 830

 Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 835 840 845
 Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
 850 855 860
 Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 865 870 875 880
 Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
 885 890 895
 Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr

 900 905 910
 Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
 915 920 925
 Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 930 935 940
 Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val

945 950 955 960
 Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
 965 970 975

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
 980 985 990
 Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
 995 1000 1005

Gly Lys

1010

<210> 72

<211> 997

<212> PRT

<213> Artificial Sequence

<220><223> fusion protein

<400> 72

Ala Gln Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala
 1 5 10 15
 Gly Asp Ser Leu Asp Cys Ser Gly Arg Gly Leu Ala Thr Leu Pro Arg

 20 25 30

Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu
 35 40 45

Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu
 50 55 60

Val Tyr Leu Asn Ser Asn Glu Leu Thr Ala Ile Pro Ser Leu Gly Ala
 65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu
 85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu
 100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro
 115 120 125

Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser

130	135	140	
Ile Leu Glu Ser Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr			
145	150	155	160
Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe			
	165	170	175
Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg			
	180	185	190
Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu			
	195	200	205
Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp			
	210	215	220
Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val			
225	230	235	240
Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu			
	245	250	255
His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser			
	260	265	270
Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr			
	275	280	285
Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu			
	290	295	300
Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys			
305	310	315	320
Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser			
	325	330	335
Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu			
	340	345	350
Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg			
	355	360	365
Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn			
	370	375	380

Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
385 390 395 400
Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
405 410 415
Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
420 425 430
Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
435 440 445
Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln
450 455 460
Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
465 470 475 480
Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe
485 490 495
Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
500 505 510
Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
515 520 525
Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
530 535 540
Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
545 550 555 560
Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
565 570 575
Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
580 585 590
His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
595 600 605
Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
610 615 620
Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys
625 630 635 640

Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
 645 650 655
 Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
 660 665 670
 Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
 675 680 685
 Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
 690 695 700
 Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
 705 710 715 720
 Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
 725 730 735
 Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
 740 745 750
 Gly Cys Arg Lys Asp Gly Thr Thr Gly Gly Gly Gly Ser Glu Pro Lys
 755 760 765
 Ser Ser Asp Lys Thr His Thr Ser Pro Pro Ser Pro Ala Pro Glu Leu
 770 775 780
 Leu Gly Gly Ser Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 785 790 795 800
 Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 805 810 815
 Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 820 825 830
 Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
 835 840 845
 Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
 850 855 860
 Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 865 870 875 880
 Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro

885	890	895
Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln		
900	905	910
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala		
915	920	925
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr		
930	935	940
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu		
945	950	955
		960
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser		
965	970	975
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser		
980	985	990
Leu Ser Pro Gly Lys		
995		
<210>	73	
<211>	2991	
<212>	DNA	
<213>	Artificial Sequence	
<220><223>	fusion protein	
<400>	73	
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gactgcagcg gccggggcct ggccacactg cccagggacc tgccttctg gaccagatct		120
ctgaacctga gctacaatcg gctgtccgag atcgattctg ccgcctttga ggacctgaca		180
aatctgcagg aggtgtatct gaacagcaat gagctgaccg caatcccctc cctgggagca		240
gcctctatcg gcgtggtgag cctgttctg cagcacaaca agatcctgag cgtggatggc		300
tcccagctga agagctacct gtctctggag gtgctggacc tgagctcaa caatatcacc		360
gagatcagat ctagtgttt tcctaattggc ctgcggatca gagagctgaa cctggcctct		420
aatcggatca gcatcctgga gtccggcgcc ttcatgggcc tgagcagatc cctgctgaca		480
ctgcgcctgt ccaagaaccg gatcacccag ctgcccgtga aggcctttaa gctgcctagg		540
ctgacacagc tggacctgaa ccggaataga atcaggctga tcgagggcct gaccttcag		600
ggcctggata gcctggaggt gctgcgcctg cagcgggaaca atatctccg cctgacagac		660

ggagcatttt ggggcctgtc taagatgcac gtgctgcacc tggagtacaa tagcctgggtg	720
gaggtgaact ctggcagcct gtatggcctg accgcctgc accagctgca cctgtccaac	780
aatagcatca gcagaatcca gagggatggc tggtccttct gccagaagct gcacgagctg	840
atcctgtctt ttaacaatct gaccaggctg gacgaggaga gcctggcaga gctgtcctct	900
ctgtccatcc tgcgcctgtc tcacaatgcc atcagccaca tcgccgaggg cgcctttaag	960
ggcctgaaga gcctgagggg gctggatctg gaccacaacg agatctctgg caccatcgag	1020
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755 760 765
 Ser Ser Asp Lys Thr His Thr Ser Pro Pro Cys Pro Ala Pro Glu Leu
 770 775 780
 Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val
 785 790 795 800
 Leu Met Ile Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val
 805 810 815
 Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val

 820 825 830
 Glu Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser
 835 840 845
 Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met
 850 855 860
 Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala
 865 870 875 880
 Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro
 885 890 895

 Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln
 900 905 910
 Val Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr
 915 920 925
 Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr
 930 935 940
 Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu
 945 950 955 960
 Arg Val Glu Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser

 965 970 975
 Val Val His Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser
 980 985 990
 Arg Thr Pro Gly Lys
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<400> 78

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Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Arg Leu

35 40 45

Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu

50 55 60

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

65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu

85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu

100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro

115 120 125

Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser

130 135 140

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

145 150 155 160

Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe

165 170 175

Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg

180 185 190

Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu

195 200 205

Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp

210 215 220
 Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val
 225 230 235 240

 Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu
 245 250 255
 His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser
 260 265 270
 Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr
 275 280 285
 Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
 290 295 300
 Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys

 305 310 315 320
 Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser
 325 330 335
 Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
 340 345 350
 Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg
 355 360 365
 Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
 370 375 380

 Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
 385 390 395 400
 Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
 405 410 415
 Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val
 420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
 435 440 445
 Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln

 450 455 460

Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
 465 470 475 480
 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe
 485 490 495
 Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
 500 505 510
 Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
 515 520 525

 Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
 530 535 540
 Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
 545 550 555 560
 Leu Thr Val Asn Val Leu Pro Ser Phe Thr Lys Ile Pro His Asp Ile
 565 570 575
 Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
 580 585 590
 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe

 595 600 605
 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
 610 615 620
 Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys
 625 630 635 640
 Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
 645 650 655
 Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val
 660 665 670

 Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
 675 680 685
 Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
 690 695 700
 Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
 705 710 715 720

Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
725 730 735

Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
740 745 750

Gly Cys Arg Lys Asp Gly Thr Thr Gly Gly Gly Gly Ser Glu Pro Arg
755 760 765

Gly Pro Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn
770 775 780

Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp
785 790 795 800

Val Leu Met Ile Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp
805 810 815

Val Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn
820 825 830

Val Glu Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn
835 840 845

Ser Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp
850 855 860

Met Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro
865 870 875 880

Ala Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala
885 890 895

Pro Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys
900 905 910

Gln Val Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile
915 920 925

Tyr Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn
930 935 940

Thr Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys
945 950 955 960

Leu Arg Val Glu Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys

965 970 975
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 35 40 45
 Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu
 50 55 60
 Val Tyr Leu Asn Ser Asn Glu Leu Thr Ala Ile Pro Ser Leu Gly Ala
 65 70 75 80
 Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu

 85 90 95
 Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu
 100 105 110
 Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro
 115 120 125
 Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser
 130 135 140
 Ile Leu Glu Ser Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr
 145 150 155 160

 Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe

165	170	175	
Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg			
180	185	190	
Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu			
195	200	205	
Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp			
210	215	220	
Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val			
225	230	235	240
Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu			
245	250	255	
His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser			
260	265	270	
Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr			
275	280	285	
Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu			
290	295	300	
Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys			
305	310	315	320
Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser			
325	330	335	
Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu			
340	345	350	
Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg			
355	360	365	
Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn			
370	375	380	
Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu			
385	390	395	400
Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu			
405	410	415	
Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val			

420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
 435 440 445

 Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln
 450 455 460
 Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
 465 470 475 480
 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe
 485 490 495
 Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
 500 505 510
 Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr

 515 520 525
 Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
 530 535 540
 Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
 545 550 555 560
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 565 570 575
 Ala Ile Arg Thr Gly Thr Thr Ala Arg Leu Glu Cys Ala Ala Thr Gly
 580 585 590

 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
 595 600 605
 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val
 610 615 620
 Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Met Gly Val Tyr Ser Cys
 625 630 635 640
 Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr
 645 650 655
 Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val

 660 665 670

Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro
675 680 685

Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr
690 695 700

Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn
705 710 715 720

Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro
725 730 735

Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro
740 745 750

Gly Cys Arg Lys Asp Gly Thr Thr Gly Gly Gly Gly Ser Arg Asn Thr
755 760 765

Gly Arg Gly Gly Glu Glu Lys Lys Lys Glu Lys Glu Lys Glu Glu Gln
770 775 780

Glu Glu Arg Glu Thr Lys Thr Pro Glu Cys Pro Ser His Thr Gln Pro
785 790 795 800

Leu Gly Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile
805 810 815

Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp
820 825 830

Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His
835 840 845

Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg
850 855 860

Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys
865 870 875 880

Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu
885 890 895

Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr
900 905 910

Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu
915 920 925

Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp
930 935 940

Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val

945 950 955 960

Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu
965 970 975

Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His
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<220><223> fusion protein

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35 40 45

Ser Glu Ile Asp Ser Ala Ala Phe Glu Asp Leu Thr Asn Leu Gln Glu
50 55 60

Val Tyr Leu Asn Ser Asn Glu Leu Thr Ala Ile Pro Ser Leu Gly Ala
65 70 75 80

Ala Ser Ile Gly Val Val Ser Leu Phe Leu Gln His Asn Lys Ile Leu
85 90 95

Ser Val Asp Gly Ser Gln Leu Lys Ser Tyr Leu Ser Leu Glu Val Leu
100 105 110

Asp Leu Ser Ser Asn Asn Ile Thr Glu Ile Arg Ser Ser Cys Phe Pro
 115 120 125
 Asn Gly Leu Arg Ile Arg Glu Leu Asn Leu Ala Ser Asn Arg Ile Ser
 130 135 140
 Ile Leu Glu Ser Gly Ala Phe Asp Gly Leu Ser Arg Ser Leu Leu Thr
 145 150 155 160
 Leu Arg Leu Ser Lys Asn Arg Ile Thr Gln Leu Pro Val Lys Ala Phe
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 Lys Leu Pro Arg Leu Thr Gln Leu Asp Leu Asn Arg Asn Arg Ile Arg
 180 185 190
 Leu Ile Glu Gly Leu Thr Phe Gln Gly Leu Asp Ser Leu Glu Val Leu
 195 200 205
 Arg Leu Gln Arg Asn Asn Ile Ser Arg Leu Thr Asp Gly Ala Phe Trp
 210 215 220
 Gly Leu Ser Lys Met His Val Leu His Leu Glu Tyr Asn Ser Leu Val
 225 230 235 240
 Glu Val Asn Ser Gly Ser Leu Tyr Gly Leu Thr Ala Leu His Gln Leu
 245 250 255
 His Leu Ser Asn Asn Ser Ile Ser Arg Ile Gln Arg Asp Gly Trp Ser
 260 265 270
 Phe Cys Gln Lys Leu His Glu Leu Ile Leu Ser Phe Asn Asn Leu Thr
 275 280 285
 Arg Leu Asp Glu Glu Ser Leu Ala Glu Leu Ser Ser Leu Ser Ile Leu
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 Arg Leu Ser His Asn Ala Ile Ser His Ile Ala Glu Gly Ala Phe Lys
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 Gly Leu Lys Ser Leu Arg Val Leu Asp Leu Asp His Asn Glu Ile Ser
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 Gly Thr Ile Glu Asp Thr Ser Gly Ala Phe Thr Gly Leu Asp Asn Leu
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 Ser Lys Leu Thr Leu Phe Gly Asn Lys Ile Lys Ser Val Ala Lys Arg

355 360 365
 Ala Phe Ser Gly Leu Glu Ser Leu Glu His Leu Asn Leu Gly Glu Asn
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 Ala Ile Arg Ser Val Gln Phe Asp Ala Phe Ala Lys Met Lys Asn Leu
 385 390 395 400
 Lys Glu Leu Tyr Ile Ser Ser Glu Ser Phe Leu Cys Asp Cys Gln Leu
 405 410 415
 Lys Trp Leu Pro Pro Trp Leu Met Gly Arg Met Leu Gln Ala Phe Val

 420 425 430
 Thr Ala Thr Cys Ala His Pro Glu Ser Leu Lys Gly Gln Ser Ile Phe
 435 440 445
 Ser Val Leu Pro Asp Ser Phe Val Cys Asp Asp Phe Pro Lys Pro Gln
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 Ile Ile Thr Gln Pro Glu Thr Thr Met Ala Val Val Gly Lys Asp Ile
 465 470 475 480
 Arg Phe Thr Cys Ser Ala Ala Ser Ser Ser Ser Ser Pro Met Thr Phe
 485 490 495

 Ala Trp Lys Lys Asp Asn Glu Val Leu Ala Asn Ala Asp Met Glu Asn
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 Phe Ala His Val Arg Ala Gln Asp Gly Glu Val Met Glu Tyr Thr Thr
 515 520 525
 Ile Leu His Leu Arg His Val Thr Phe Gly His Glu Gly Arg Tyr Gln
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 Cys Ile Ile Thr Asn His Phe Gly Ser Thr Tyr Ser His Lys Ala Arg
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 565 570 575
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 580 585 590
 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe
 595 600 605
 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val

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Thr Ala Gln Asn Ser Ala Gly Ser Val Ser Ala Asn Ala Thr Leu Thr			
	645	650	655
Val Leu Glu Thr Pro Ser Leu Ala Val Pro Leu Glu Asp Arg Val Val			
	660	665	670
Thr Val Gly Glu Thr Val Ala Phe Gln Cys Lys Ala Thr Gly Ser Pro			
	675	680	685
Thr Pro Arg Ile Thr Trp Leu Lys Gly Gly Arg Pro Leu Ser Leu Thr			
690	695	700	
Glu Arg His His Phe Thr Pro Gly Asn Gln Leu Leu Val Val Gln Asn			
705	710	715	720
Val Met Ile Asp Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Pro			
	725	730	735
Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Ile Leu Pro Thr Pro			
	740	745	750
Gly Cys Arg Lys Asp Gly Thr Thr Gly Gly Gly Gly Ser Glu Pro Lys			
	755	760	765
Ser Ser Asp Lys Thr His Thr Ser Pro Pro Ser Pro Ala Pro Glu Leu			
770	775	780	
Leu Gly Gly Ser Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val			
785	790	795	800
Leu Met Ile Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val			
	805	810	815
Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val			
	820	825	830
Glu Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser			
	835	840	845
Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met			
850	855	860	

Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala
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 Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro
 885 890 895
 Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln
 900 905 910
 Val Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr
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Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr
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 Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu
 945 950 955 960
 Arg Val Glu Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser
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 Val Val His Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser
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