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(54) **METHOD OF CLASSIFYING ANTIBODY, METHOD OF IDENTIFYING ANTIGEN, METHOD OF OBTAINING ANTIBODY OR ANTIBODY SET, METHOD OF CONSTRUCTING ANTIBODY PANEL AND ANTIBODY OR ANTIBODY SET AND USE OF THE SAME**

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C40B 60/10	(2006.01)

(52) **U.S. Cl.** **506/9**; 435/7.2; 435/7.23; 530/387.7; 506/18; 506/38

(57) **ABSTRACT**

It is intended to provide a method whereby a plural number of antibodies against cell surface antigens are quickly classified and to provide a method whereby antigens of the thus classified antibodies are quickly identified. Further, it is intended to provide a method of promoting the utilization of the useful data obtained by the above methods. Furthermore, it is intended to provide an antibody which is effective in treating or diagnosing cancer. Namely, a method of classifying antibodies which comprises: (1) the step of preparing a plural number of antibodies respectively recognizing cell surface antigens; (2) the step of bringing each of these antibodies into contact with a cell of the same species; (3) the step of analyzing each of the cells having been treated in the step (2) by flow cytometry and thus obtaining data indicating the reactivity of each antibody with its cell surface antigen; and (4) the step of comparing the thus obtained data and classifying the individual antibodies depending on the similarity. A method of identifying antigens which further comprises: (5) the step of selecting one to several antibodies from each antibody group formed in the step (4) and identifying antigens thereof; and (6) on the assumption that antigens of the antibodies belonging to a single antibody group are the same or highly related to one another, making relations between the antigens having been identified in the step (5) and the antibody groups to thereby identify the antigens. An antibody against HER1, an antibody against HER2, an antibody against CD46, an antibody against ITGA3, an antibody against ICAM1, an antibody against ALCAM, an antibody against CD147, an antibody against C1qR, an antibody against CD44, an antibody against CD73, an antibody against EpCAM and an antibody against HGFR, each obtained by using the above methods.

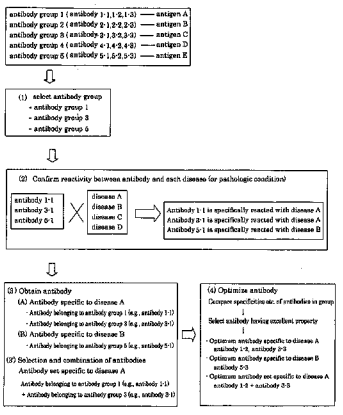


Fig.1

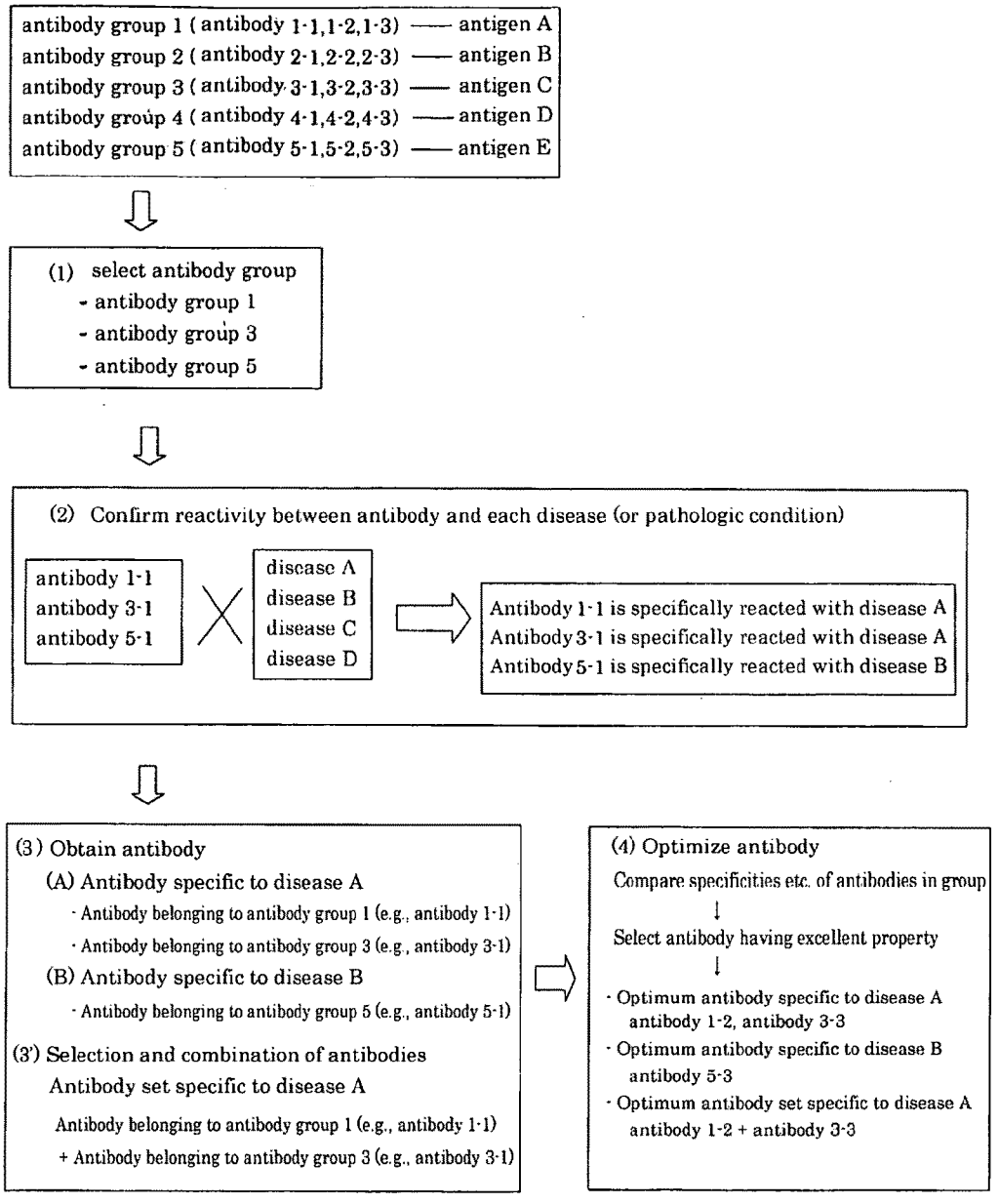

antibody group 1 (antibody 1-1,1-2,1-3) —— antigen A
antibody group 2 (antibody 2-1,2-2,2-3) —— antigen B
antibody group 3 (antibody 3-1,3-2,3-3) —— antigen C
antibody group 4 (antibody 4-1,4-2,4-3) —— antigen D
antibody group 5 (antibody 5-1,5-2,5-3) —— antigen E
(1) select antibody group
- antibody group 1
- antibody group 3
- antibody group 5
(2) Confirm reactivity between antibody and each disease (or pathologic condition)
antibody 1-1
antibody 3-1
antibody 5-1
disease A
disease B
disease C
disease D
Antibody 1-1 is specifically reacted with disease A
Antibody 3-1 is specifically reacted with disease A
Antibody 5-1 is specifically reacted with disease B
(3) Obtain antibody
(A) Antibody specific to disease A
· Antibody belonging to antibody group 1 (e.g., antibody 1-1)
· Antibody belonging to antibody group 3 (e.g., antibody 3-1)
(B) Antibody specific to disease B
· Antibody belonging to antibody group 5 (e.g., antibody 5-1)
(3') Selection and combination of antibodies
Antibody set specific to disease A
Antibody belonging to antibody group 1 (e.g., antibody 1-1)
+ Antibody belonging to antibody group 3 (e.g., antibody 3-1)
(4) Optimize antibody
Compare specificities etc. of antibodies in group
Select antibody having excellent property
· Optimum antibody specific to disease A
antibody 1-2, antibody 3-3
· Optimum antibody specific to disease B
antibody 5-3
· Optimum antibody set specific to disease A
antibody 1-2 + antibody 3-3

Fig.2

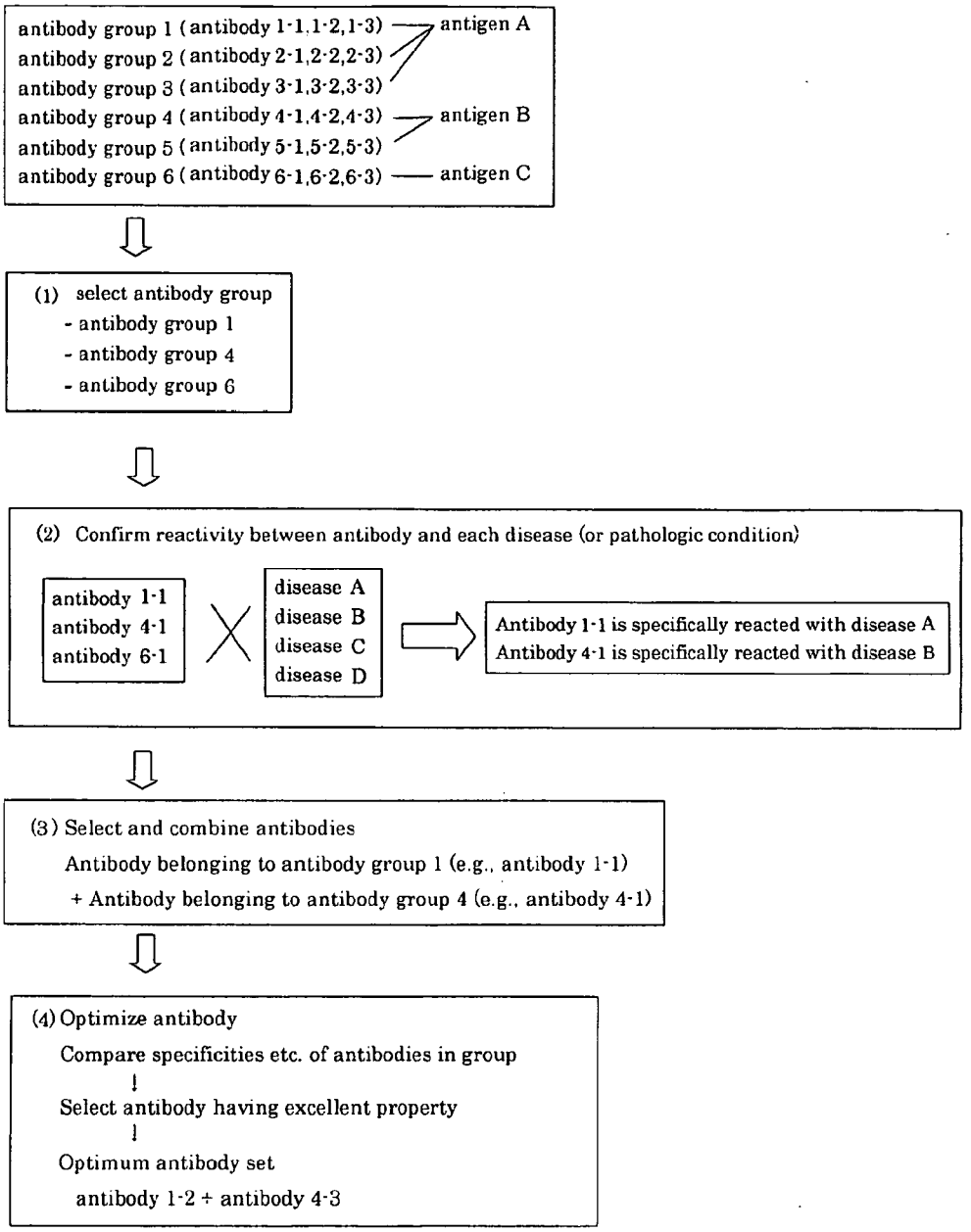

antibody group 1 (antibody 1-1,1-2,1-3)
antibody group 2 (antibody 2-1,2-2,2-3)
antibody group 3 (antibody 3-1,3-2,3-3)
antigen A
antibody group 4 (antibody 4-1,4-2,4-3)
antibody group 5 (antibody 5-1,5-2,5-3)
antigen B
antibody group 6 (antibody 6-1,6-2,6-3)
antigen C
(1) select antibody group
- antibody group 1
- antibody group 4
- antibody group 6
(2) Confirm reactivity between antibody and each disease (or pathologic condition)
antibody 1-1
antibody 4-1
antibody 6-1
disease A
disease B
disease C
disease D
Antibody 1-1 is specifically reacted with disease A
Antibody 4-1 is specifically reacted with disease B
(3) Select and combine antibodies
Antibody belonging to antibody group 1 (e.g., antibody 1-1)
+ Antibody belonging to antibody group 4 (e.g., antibody 4-1)
(4) Optimize antibody
Compare specificities etc. of antibodies in group
Select antibody having excellent property
Optimum antibody set
antibody 1-2 + antibody 4-3

Fig.3

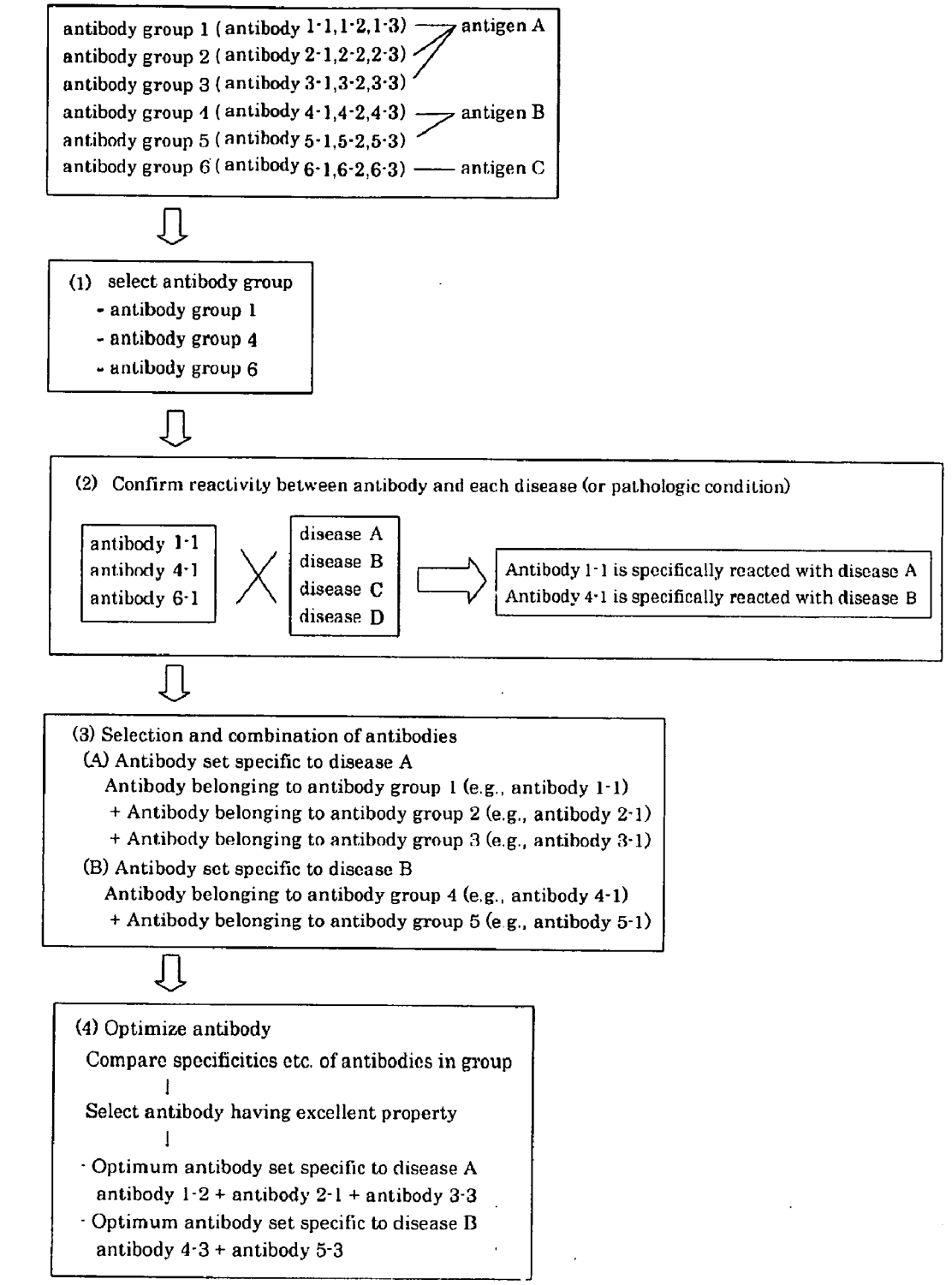

antibody group 1 (antibody 1-1,1-2,1-3)
antibody group 2 (antibody 2-1,2-2,2-3)
antibody group 3 (antibody 3-1,3-2,3-3)
antigen A
antibody group 4 (antibody 4-1,4-2,4-3)
antibody group 5 (antibody 5-1,5-2,5-3)
antigen B
antibody group 6 (antibody 6-1,6-2,6-3)
antigen C
(1) select antibody group
- antibody group 1
- antibody group 4
- antibody group 6
(2) Confirm reactivity between antibody and each disease (or pathologic condition)
antibody 1-1
antibody 4-1
antibody 6-1
disease A
disease B
disease C
disease D
Antibody 1-1 is specifically reacted with disease A
Antibody 4-1 is specifically reacted with disease B
(3) Selection and combination of antibodies
(A) Antibody set specific to disease A
Antibody belonging to antibody group 1 (e.g., antibody 1-1)
+ Antibody belonging to antibody group 2 (e.g., antibody 2-1)
+ Antibody belonging to antibody group 3 (e.g., antibody 3-1)
(B) Antibody set specific to disease B
Antibody belonging to antibody group 4 (e.g., antibody 4-1)
+ Antibody belonging to antibody group 5 (e g., antibody 5-1)
(4) Optimize antibody
Compare specificities etc. of antibodies in group
Select antibody having excellent property
- Optimum antibody set specific to disease A
antibody 1-2 + antibody 2-1 + antibody 3-3
- Optimum antibody set specific to disease B
antibody 4-3 + antibody 5-3

Fig.4

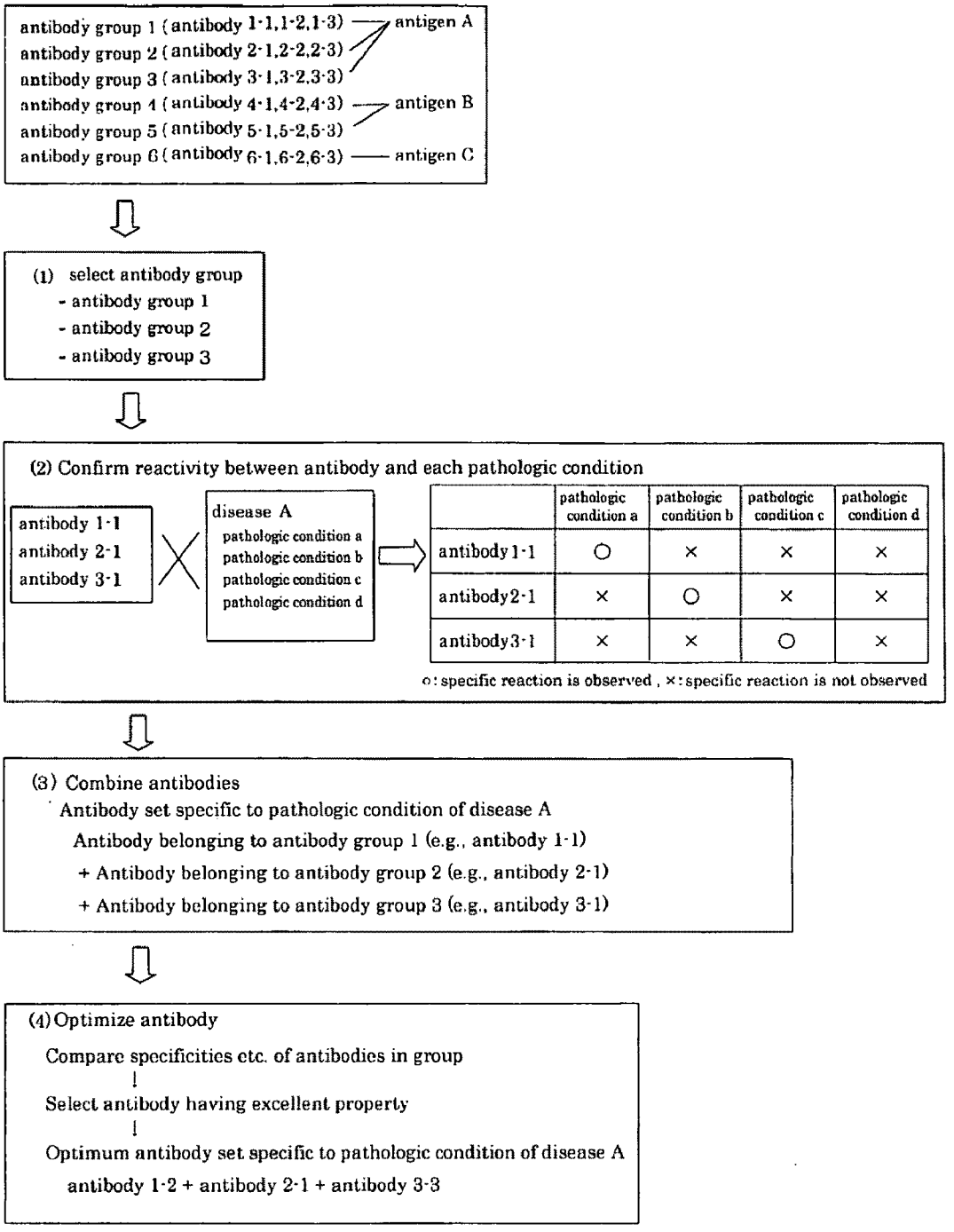
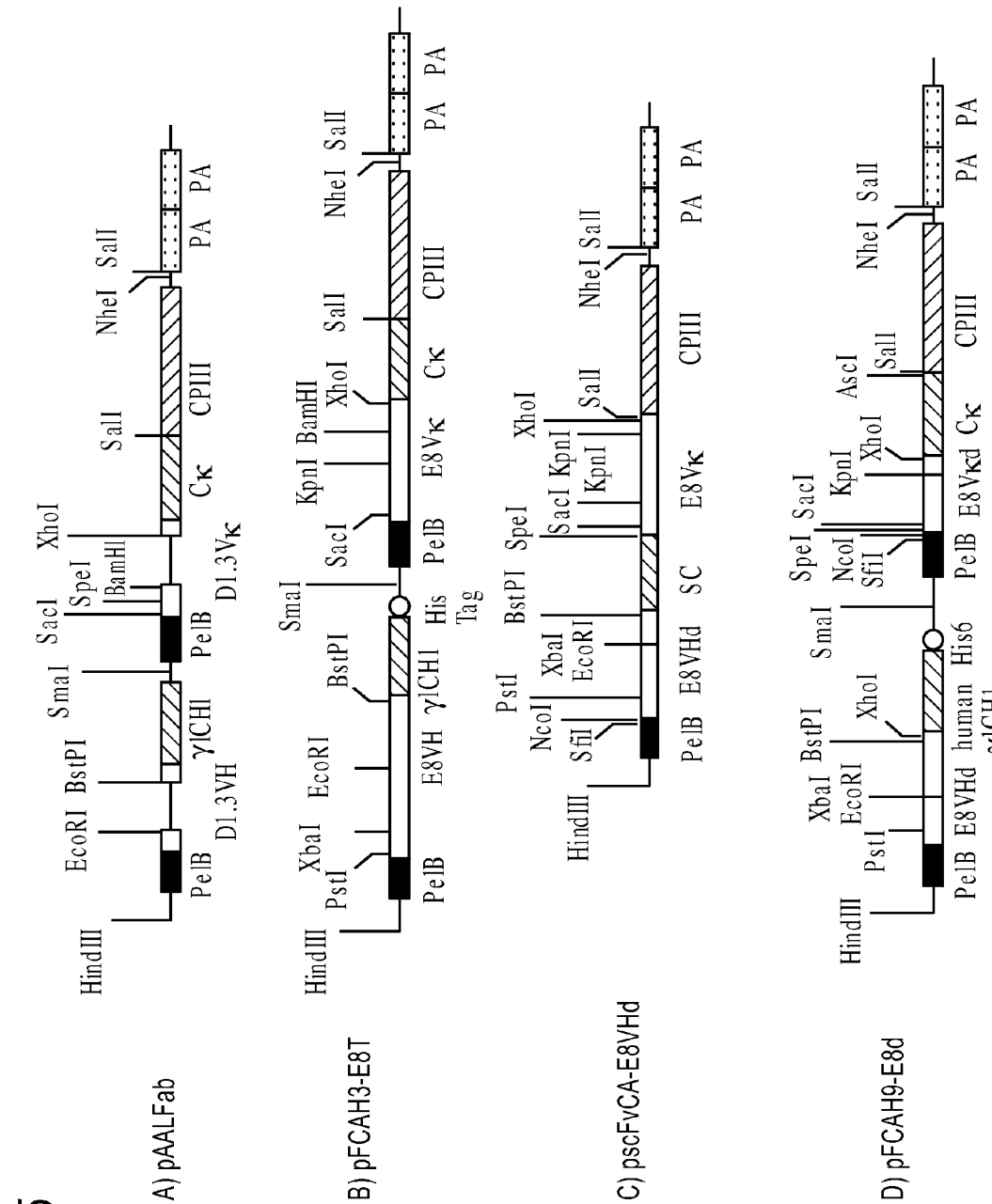

antibody group 1 (antibody 1-1,1-2,1-3) — antigen A
antibody group 2 (antibody 2-1,2-2,2-3)
antibody group 3 (antibody 3-1,3-2,3-3)
antibody group 4 (antibody 4-1,4-2,4-3) — antigen B
antibody group 5 (antibody 5-1,5-2,5-3)
antibody group 6 (antibody 6-1,6-2,6-3) — antigen C
(1) select antibody group
- antibody group 1
- antibody group 2
- antibody group 3
(2) Confirm reactivity between antibody and each pathologic condition
antibody 1-1
antibody 2-1
antibody 3-1
disease A
pathologic condition a
pathologic condition b
pathologic condition c
pathologic condition d
pathologic condition a | pathologic condition b | pathologic condition c | pathologic condition d
antibody1-1 | ○ | × | × | ×
antibody2-1 | × | ○ | × | ×
antibody3-1 | × | × | ○ | ×
○: specific reaction is observed , ×: specific reaction is not observed
(3) Combine antibodies
Antibody set specific to pathologic condition of disease A
Antibody belonging to antibody group 1 (e.g., antibody 1-1)
+ Antibody belonging to antibody group 2 (e.g., antibody 2-1)
+ Antibody belonging to antibody group 3 (e.g., antibody 3-1)
(4) Optimize antibody
Compare specificities etc. of antibodies in group
Select antibody having excellent property
Optimum antibody set specific to pathologic condition of disease A
antibody 1-2 + antibody 2-1 + antibody 3-3

Fig.5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D1.3VH
γ1CH1
PelB
Cκ
CPIII
PA
PA
D1.3Vκ
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HindIII
PstI
XbaI
EcoRI
BstPI
SmaI
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SalI
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Cκ
CPIII
PA
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Fig.6

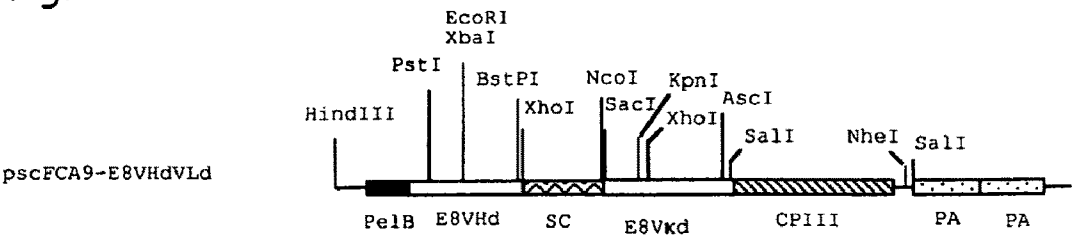
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Fig.7-1

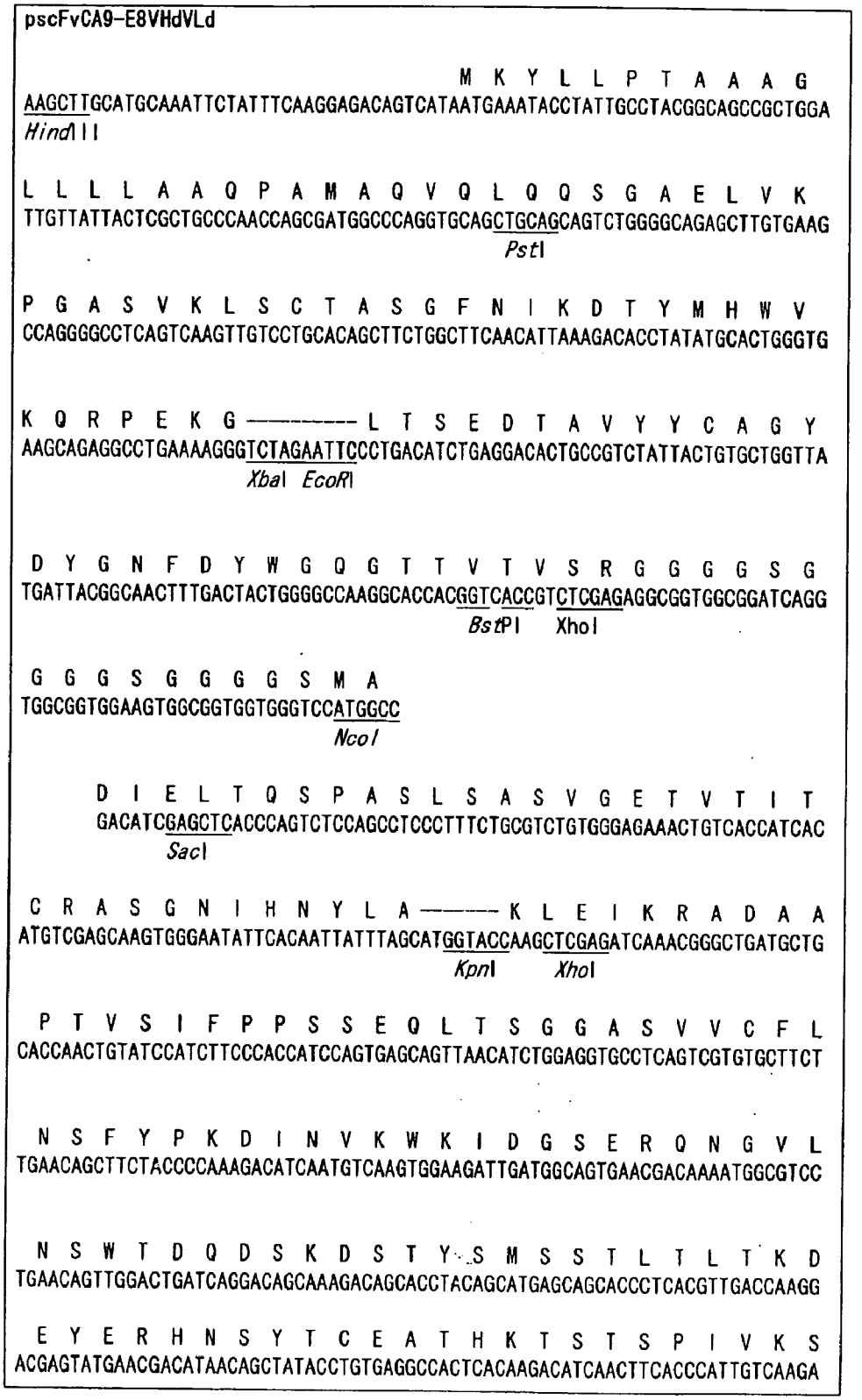
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Fig.7-2

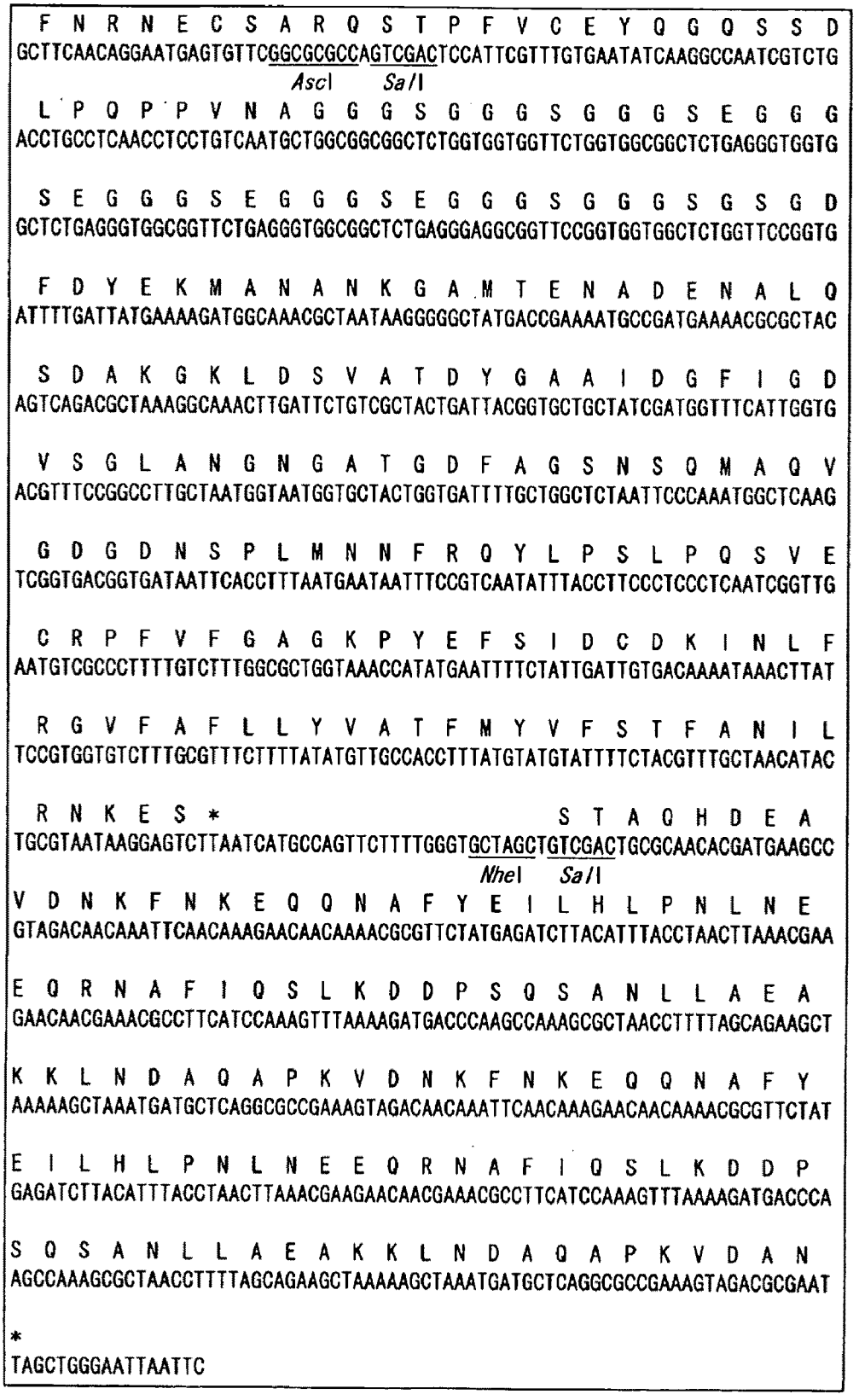
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Fig.8-1

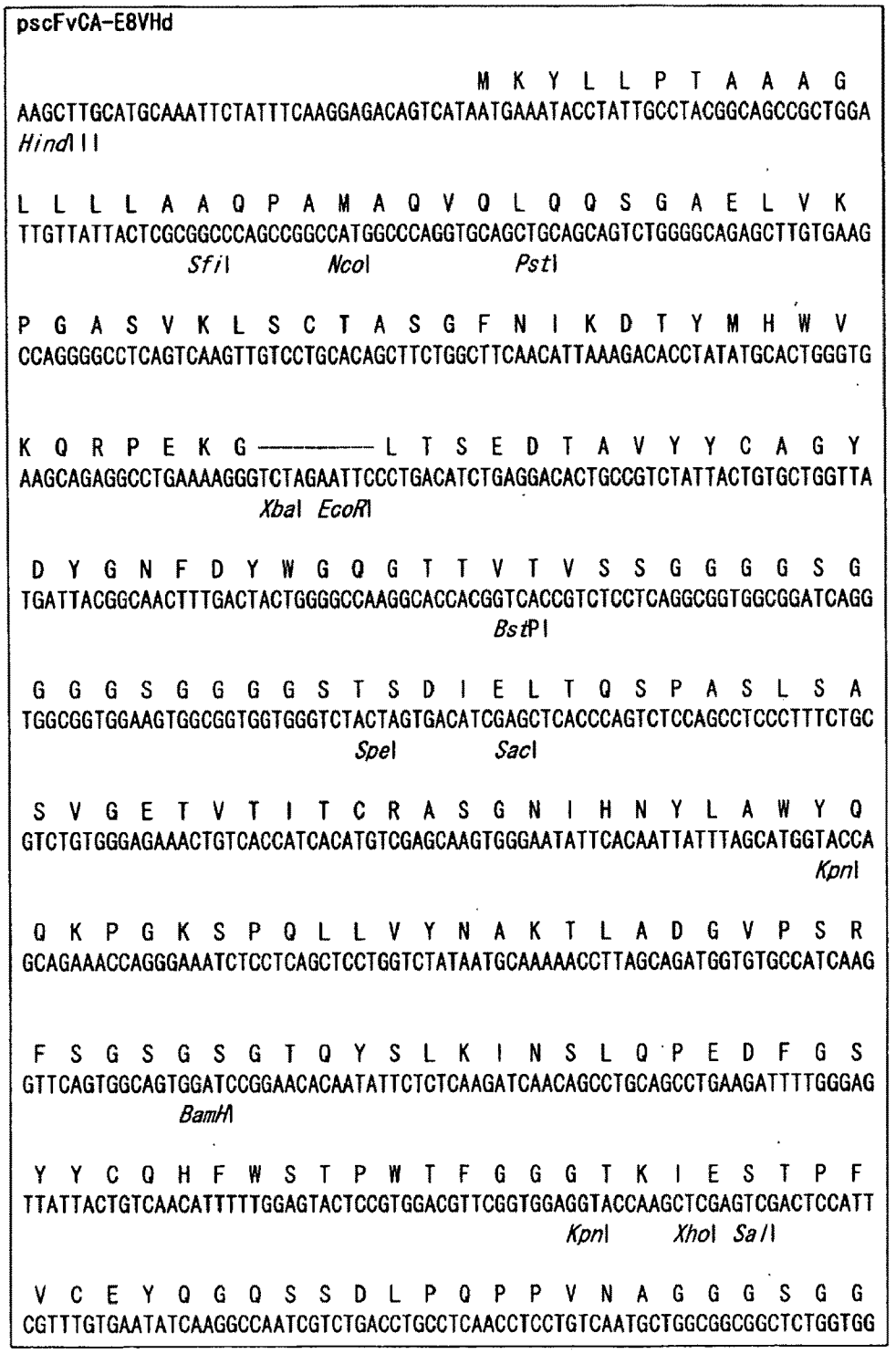
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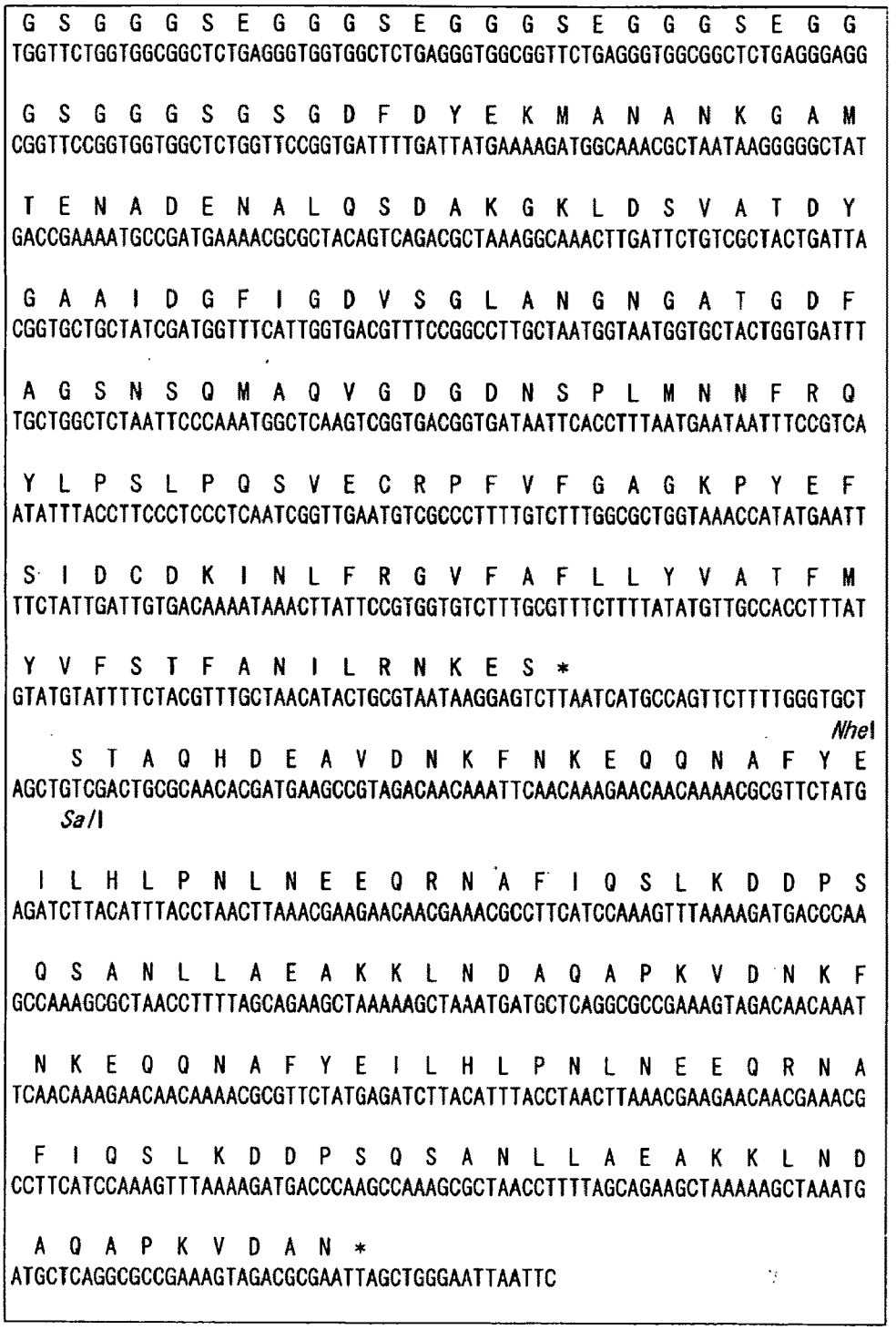
Fig.8-2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AGCTGTCGACTGCGCAACACGATGAAGCCGTAGACAACAAATTCAACAAAGAACAACAAAACGCGTTCTATG
SalI
I L H L P N L N E E Q R N A F I Q S L K D D P S
AGATCTTACATTTACCTAACTTAAACGAAGAACAACGAAACGCCTTCATCCAAAGTTTAAAAGATGACCCAA
Q S A N L L A E A K K L N D A Q A P K V D N K F
GCCAAAGCGCTAACCTTTTAGCAGAAGCTAAAAAGCTAAATGATGCTCAGGCGCCGAAAGTAGACAACAAAT
N K E Q Q N A F Y E I L H L P N L N E E Q R N A
TCAACAAAGAACAACAAAACGCGTTCTATGAGATCTTACATTTACCTAACTTAAACGAAGAACAACGAAACG
F I Q S L K D D P S Q S A N L L A E A K K L N D
CCTTCATCCAAAGTTTAAAAGATGACCCAAGCCAAAGCGCTAACCTTTTAGCAGAAGCTAAAAAGCTAAATG
A Q A P K V D A N *
ATGCTCAGGCGCCGAAAGTAGACGCGAATTAGCTGGGAATTAATTC

Fig.9

(A) HepG2 screening

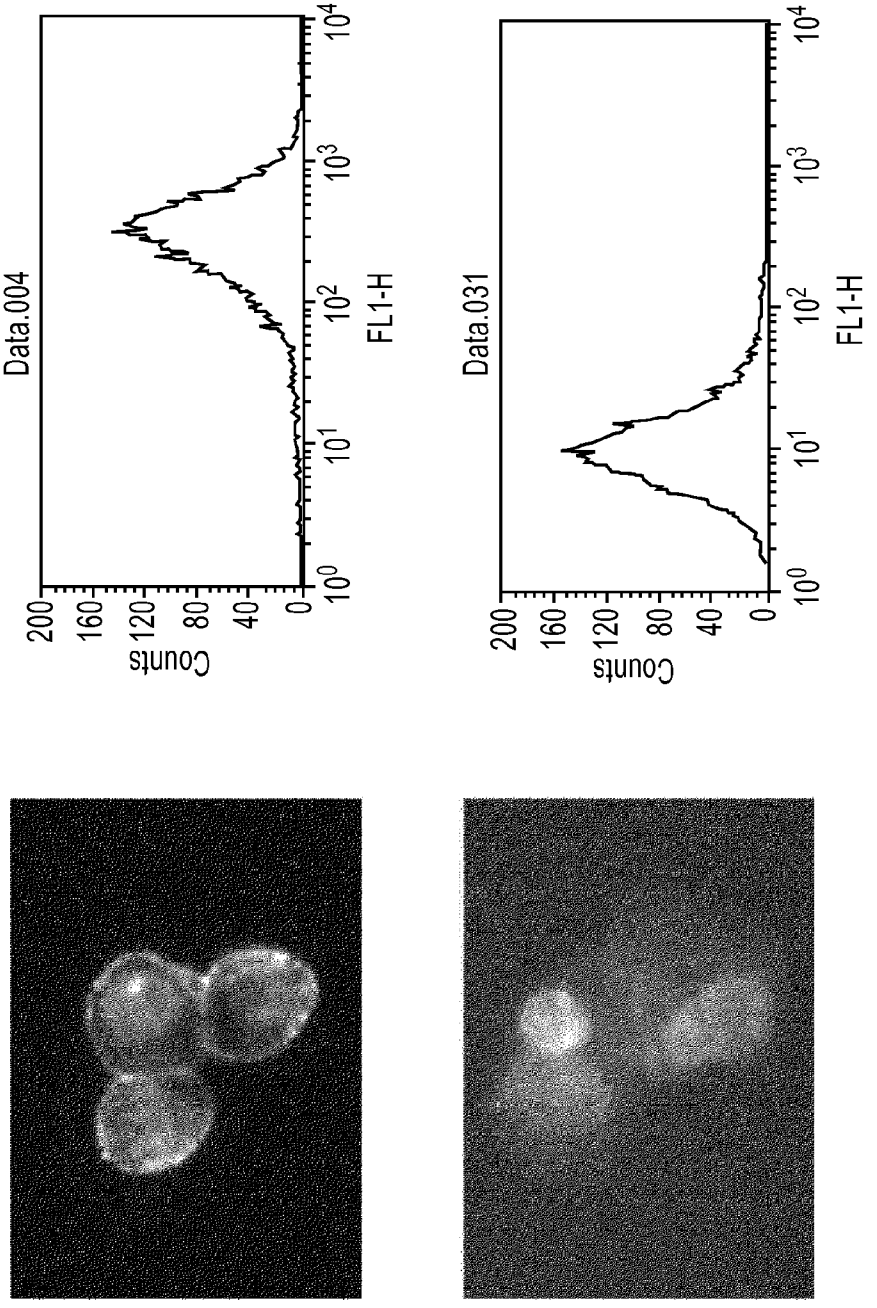
	input phage(cfu)	output phage(cfu)	recovery rate
1st screening	1×10^{13}	6.4×10^{8}	$1/1.6\times10^{5}$
2nd screening	1×10^{12}	3.9×10^{8}	$1/2.6\times10^{4}$
3rd screening	1×10^{9}	5.0×10^{6}	$1/2.0\times10^{3}$

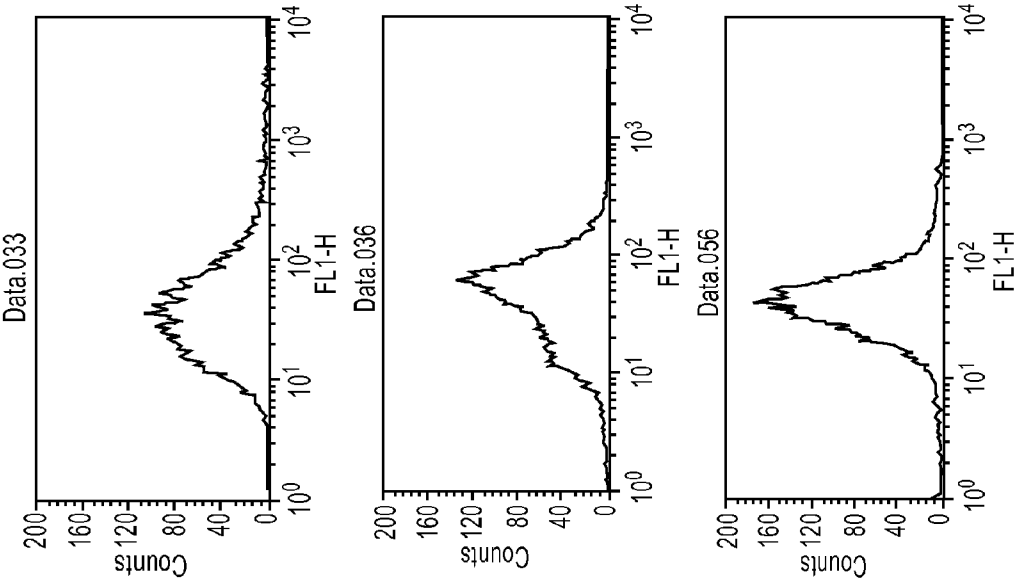
(B) Nuk-1 screening

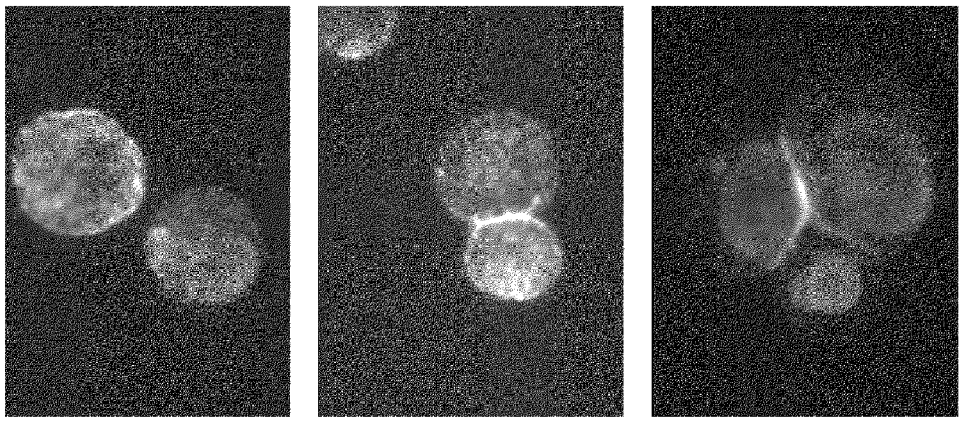
	input phage(cfu)	output phage(cfu)	recovery rate
1st screening	1×10^{13}	8.7×10^{7}	$1/1.1\times10^{6}$
2nd screening	2×10^{12}	2.1×10^{8}	$1/9.5\times10^{3}$
3rd screening	1×10^{9}	2.5×10^{5}	$1/4.0\times10^{3}$

Fig. 10

HLF, undifferentiated malignant liver cancer cell line







41-129 45-134 52-42

Fig. 11

Fig.12

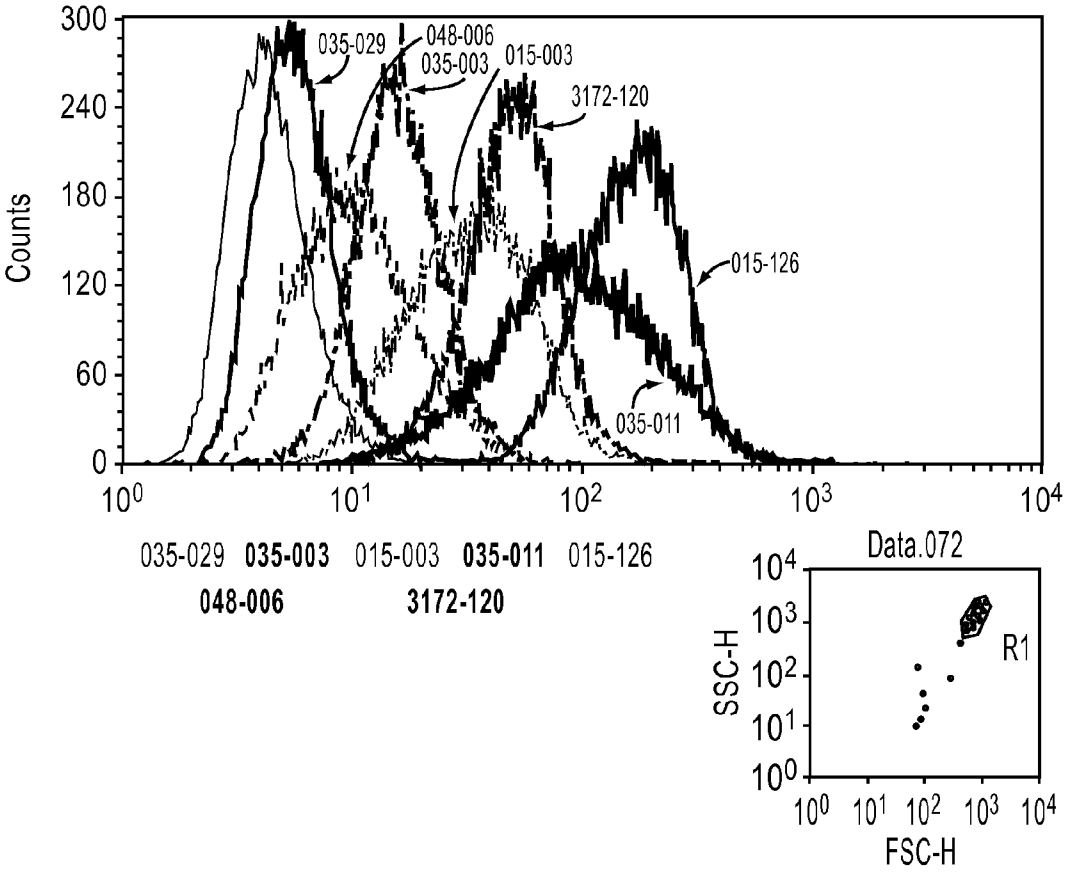

300
240
180
120
60
0
Counts
035-029
048-006
035-003
015-003
3172-120
015-126
035-011
10^0
10^1
10^2
10^3
10^4
035-029 035-003 015-003 035-011 015-126
048-006 3172-120
Data.072
SSC-H
FSC-H
R1

Fig.13

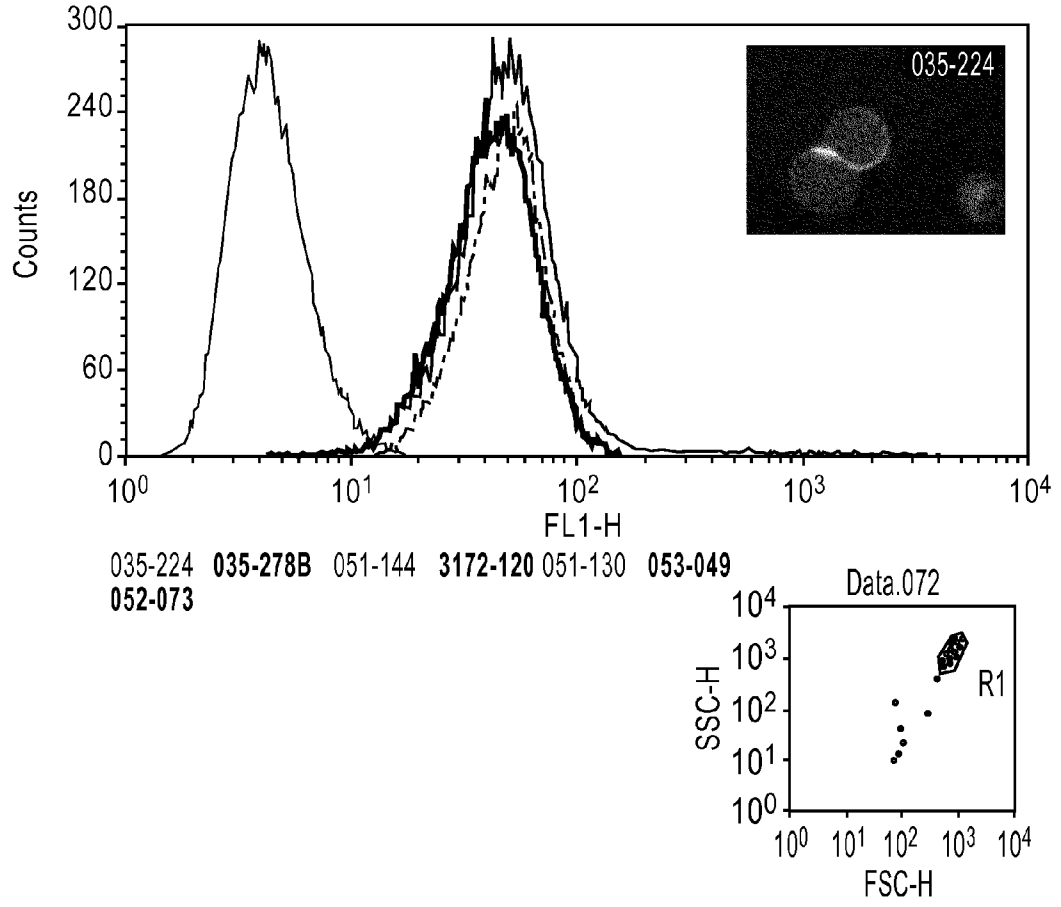

300
240
180
120
60
0
Counts
035-224
10^0
10^1
10^2
10^3
10^4
FL1-H
035-224 035-278B 051-144 3172-120 051-130 053-049
052-073
Data.072
10^4
10^3
10^2
10^1
10^0
SSC-H
R1
10^0 10^1 10^2 10^3 10^4
FSC-H

Fig.14

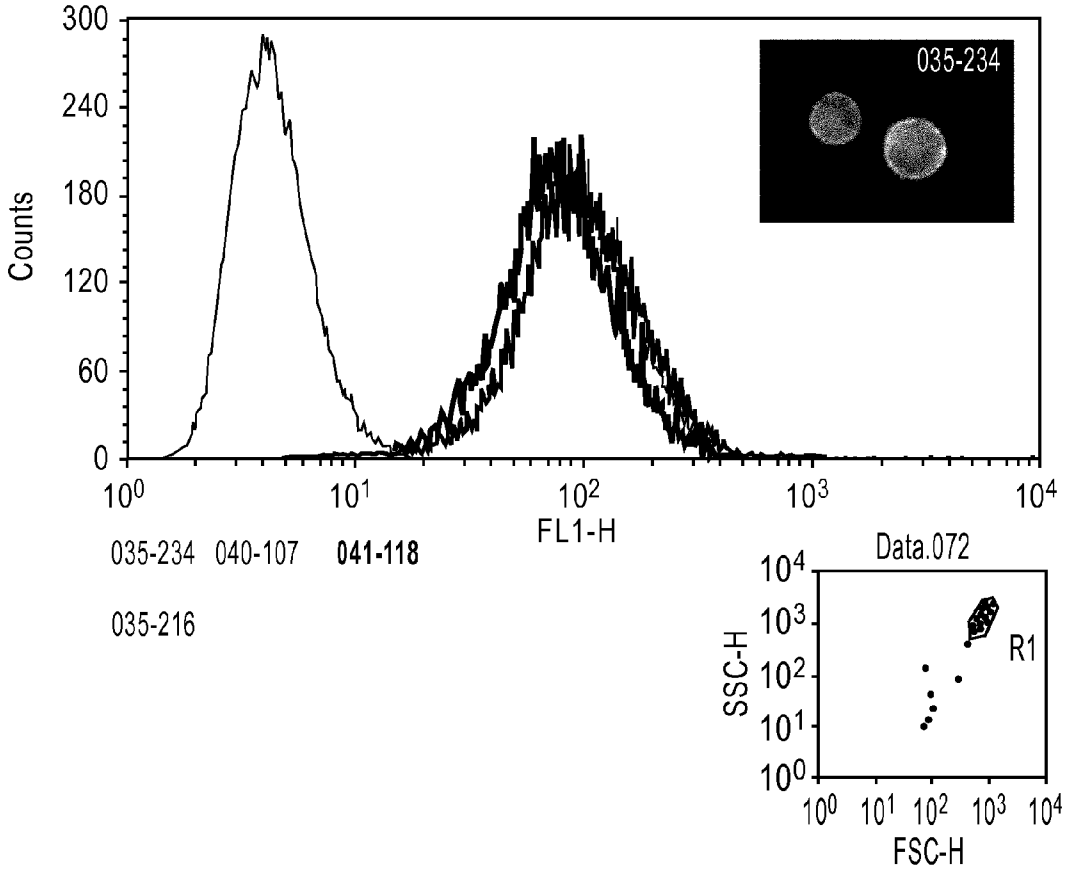

300
240
180
120
60
0
Counts
10^0
10^1
10^2
10^3
10^4
FL1-H
035-234
035-234 040-107 041-118
035-216
Data.072
10^4
10^3
10^2
10^1
10^0
SSC-H
R1
10^0 10^1 10^2 10^3 10^4
FSC-H

Fig.15

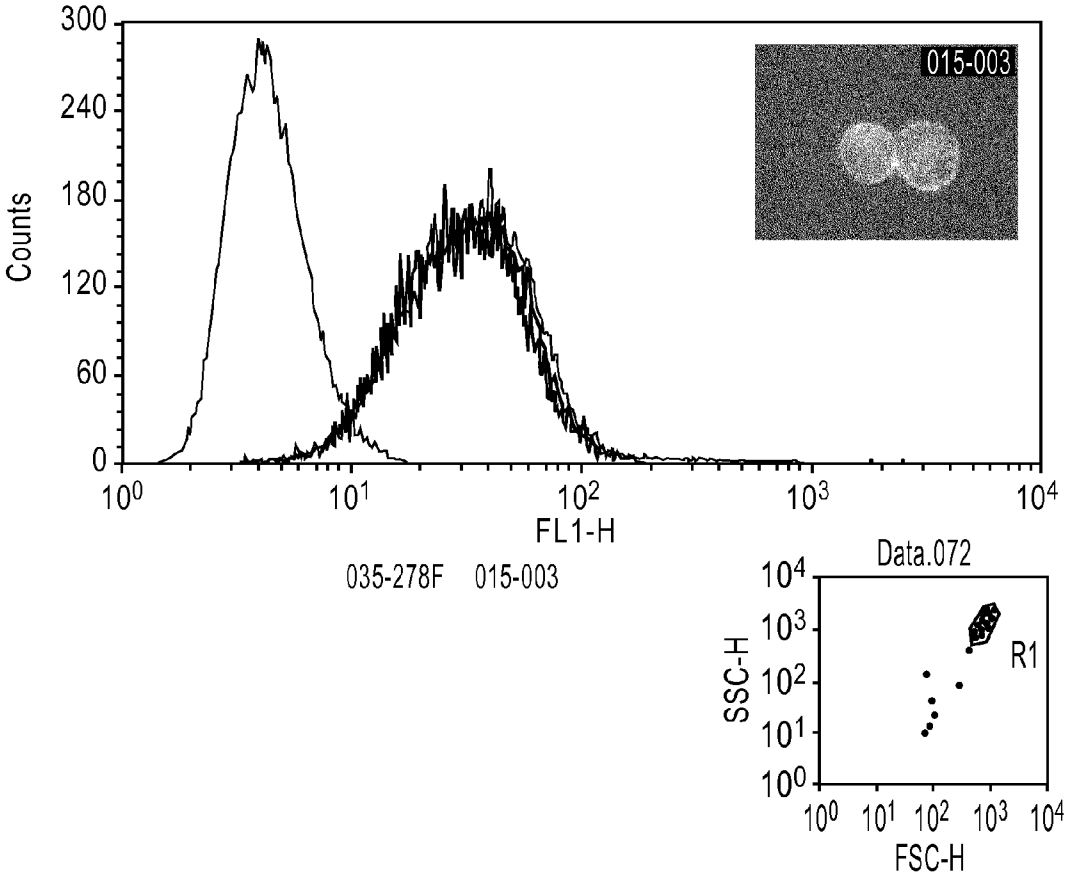
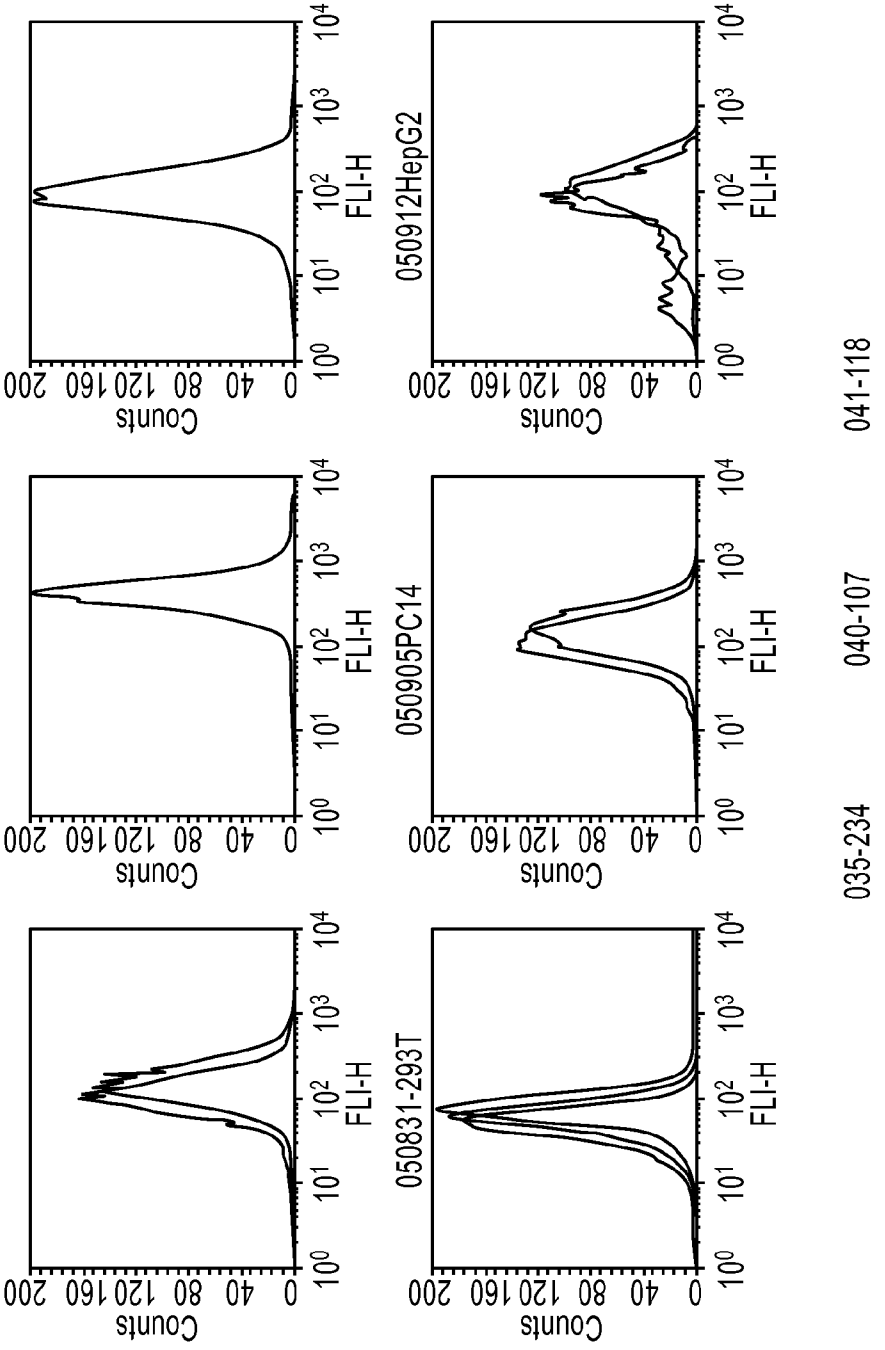

300
240
180
120
60
0
Counts
10^0
10^1
10^2
10^3
10^4
FL1-H
035-278F 015-003
015-003
Data.072
10^4
10^3
10^2
10^1
10^0
SSC-H
R1
10^0 10^1 10^2 10^3 10^4
FSC-H

Fig. 16


TypeL
050816HLF
050822SKOv3
050825BT474
050831-293T
050905PC14
050912HepG2
Counts
FLI-H
035-234
040-107
041-118

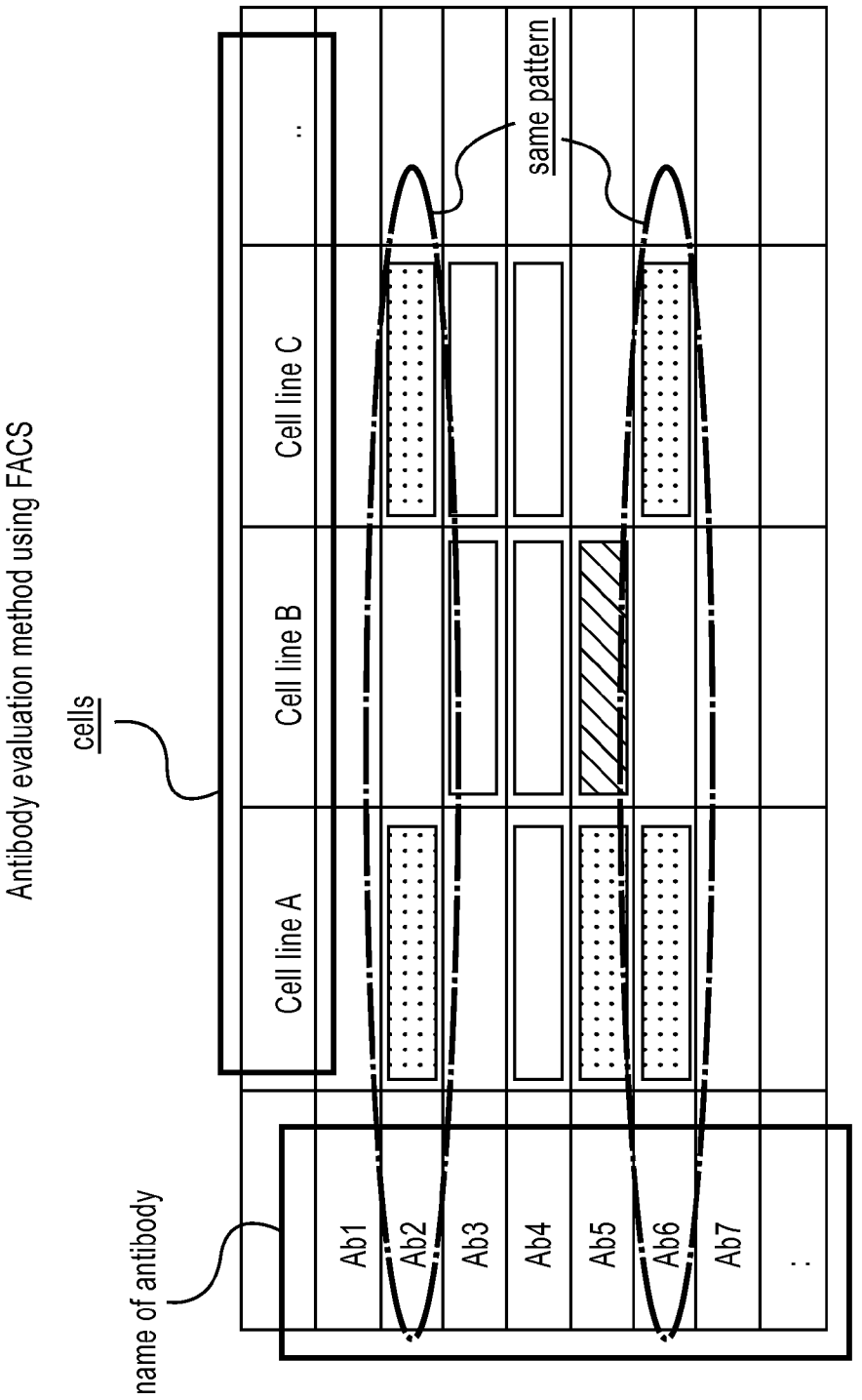

Antibody evaluation method using FACS
cells
name of antibody
Cell line A
Cell line B
Cell line C
..
same pattern
Ab1
Ab2
Ab3
Ab4
Ab5
Ab6
Ab7
..

Fig. 17

Fig.18

antigen	antibody	HLF	SKOv3	BT474	293T	PC-14	HepG2	ACHN	Caki-1	CCF-RC1	040520IT	CHOK1SV	EBC-1	A431	NCI-H1373
HER1	048-006	◎	◎	×	△	◎	△	◎	△	◎	○	×	◎	◎	◎
HER1	057-091	△	△	／	／	△	／	◎	×	◎	△	×	△	○	△
HER1	059-152	◎	○	／	／	○	／	／	／	◎	○	×	○	◎	○
HER2	015-126	×	◎	◎	×	×	△	×	×	×	×	×	／	／	／
CD46	035-224	○	◎	○	○	○	◎	○	○	○	△	×	／	／	／
CD46	045-011	○	◎	△	△	△	◎	○	○	○	△	×	／	／	／
CD46	051-144	○	◎	○	○	○	◎	／	／	／	／	／	／	／	／
CD46	052-053	／	○	△	○	△	○	／	／	／	／	／	／	／	／
CD46	052-073	○	◎	○	○	○	◎	／	／	／	／	／	／	／	／
CD46	053-049	◎	◎	○	○	○	◎	／	／	／	／	／	／	／	／
ITGA3	015-003	◎	◎	△	×	△	×	◎	◎	○	◎	×	／	／	／
ICAM1	052-033	×	×	×	×	△	◎	×	×	×	○	×	／	／	／
ICAM1	053-042	×	×	×	×	△	◎	／	／	／	／	／	／	／	／
ICAM1	053-051	×	×	×	×	△	◎	／	／	／	／	／	／	／	／
ICAM1	053-059	×	×	×	×	△	◎	／	／	／	／	／	／	／	／
ICAM1	053-085	×	×	×	×	△	◎	／	／	／	／	／	／	／	／
ALCAM	035-234	◎	◎	◎	◎	◎	◎	◎	◎	◎	○	◎	／	／	／
ALCAM	040-107	◎	◎	◎	○	◎	◎	／	／	／	／	／	／	／	／
ALCAM	041-118	◎	◎	◎	○	◎	◎	／	／	／	／	／	／	／	／
ALCAM	066-174	○	◎	／	／	△	／	／	／	／	／	／	△	×	○
ALCAM	083-040	／	／	／	／	／	／	／	／	／	／	／	／	／	／
CD147	059-053	／	／	／	／	△	／	○	○	◎	○	×	／	／	／
IgSF4	035-029	△	×	×	△	×	○	×	×	×	×	×	／	／	／
IgSF4	035-130	○	×	×	△	×	○	×	×	×	×	×	／	／	／
IgSF4	035-169	○	×	×	△	×	◎	／	／	／	／	／	／	／	／
IgSF4	035-212	○	×	×	△	×	◎	△	×	×	×	×	／	／	／
IgSF4	035-215	○	×	×	△	×	◎	／	／	／	／	／	／	／	／
IgSF4	035-273	◎	×	×	△	×	◎	／	／	／	／	／	／	／	／
IgSF4	035-283	○	△	×	△	×	◎	／	／	／	／	／	／	／	／
IgSF4	040-131	◎	×	×	○	×	◎	○	×	×	×	×	／	／	／
IgSF4	051-054	△	×	×	△	×	○	／	／	／	／	／	／	／	／
IgSF4	051-181	◎	×	×	○	×	◎	／	／	／	／	／	／	／	／

Fig.19

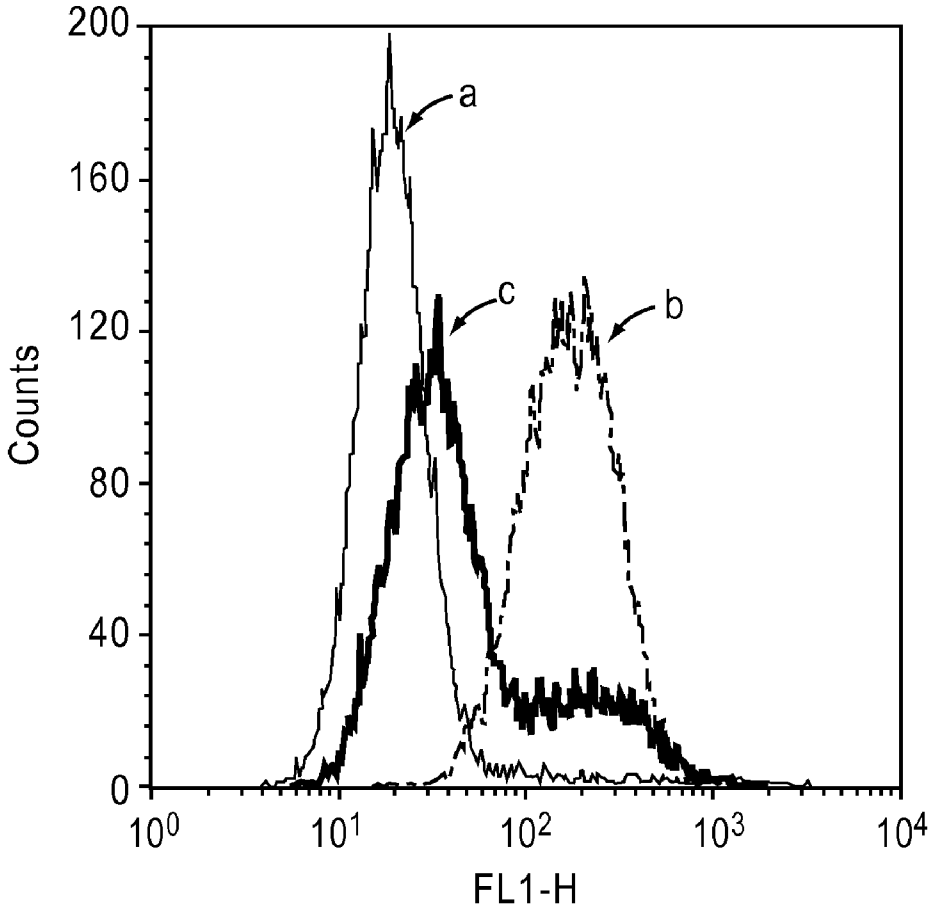


Fig.20

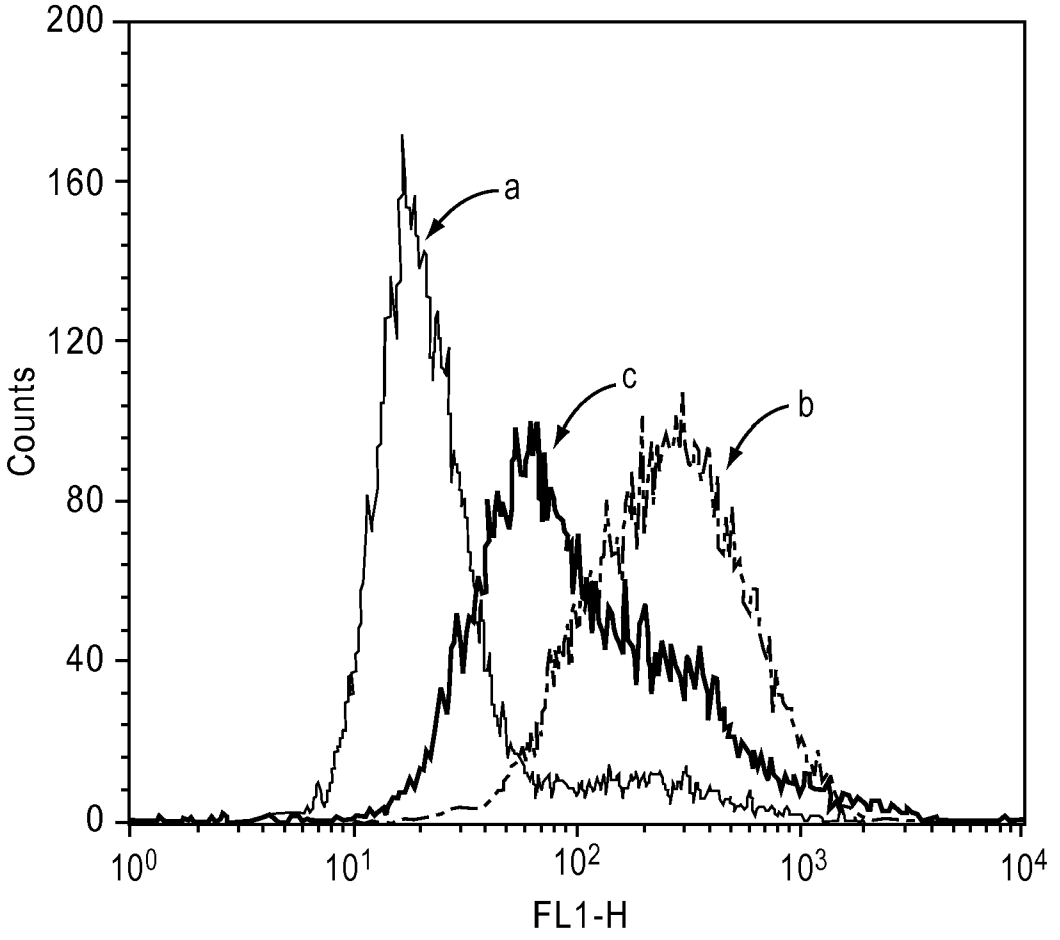


Fig.21

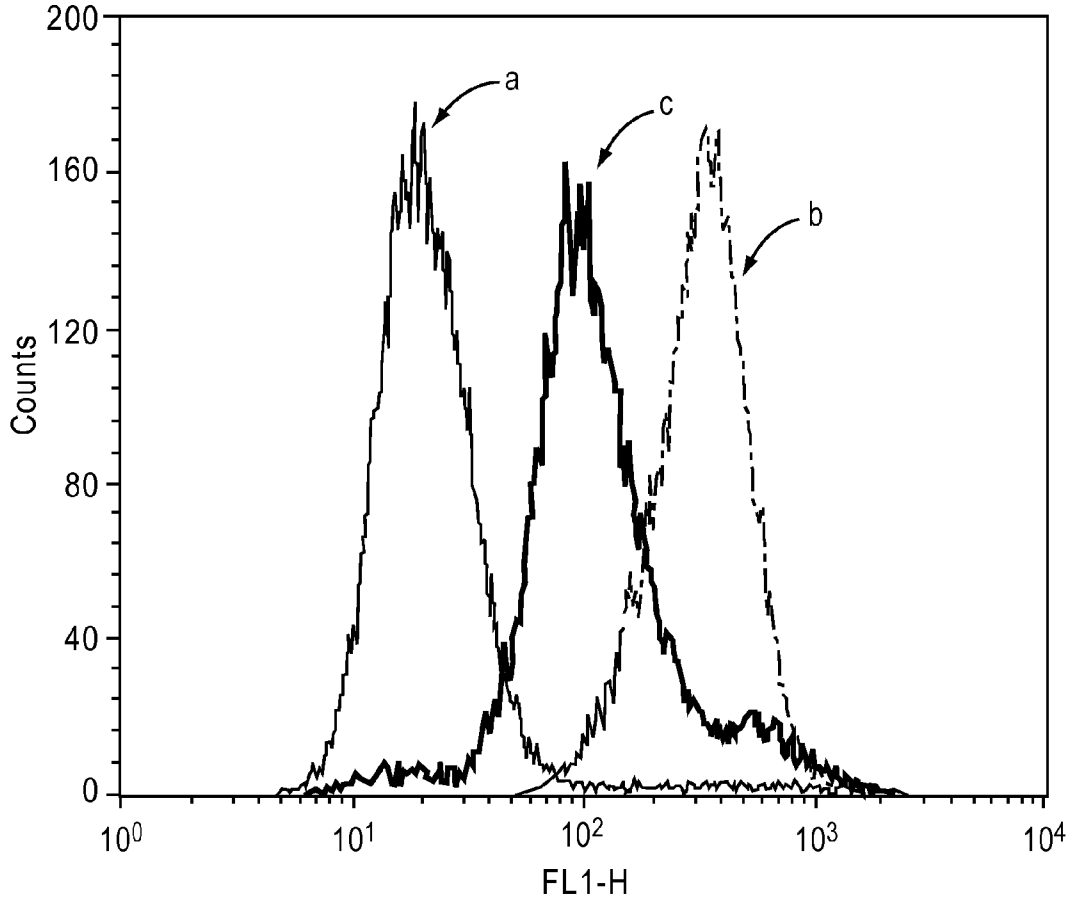


Fig.22

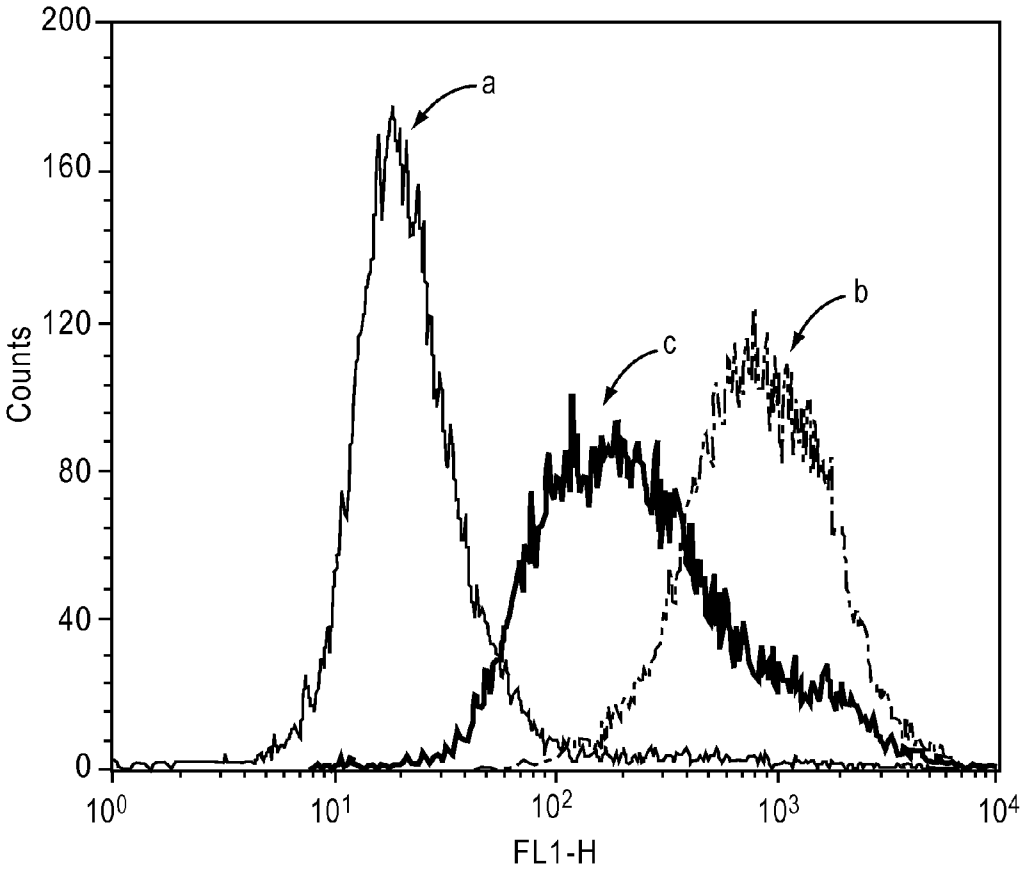


Fig.23

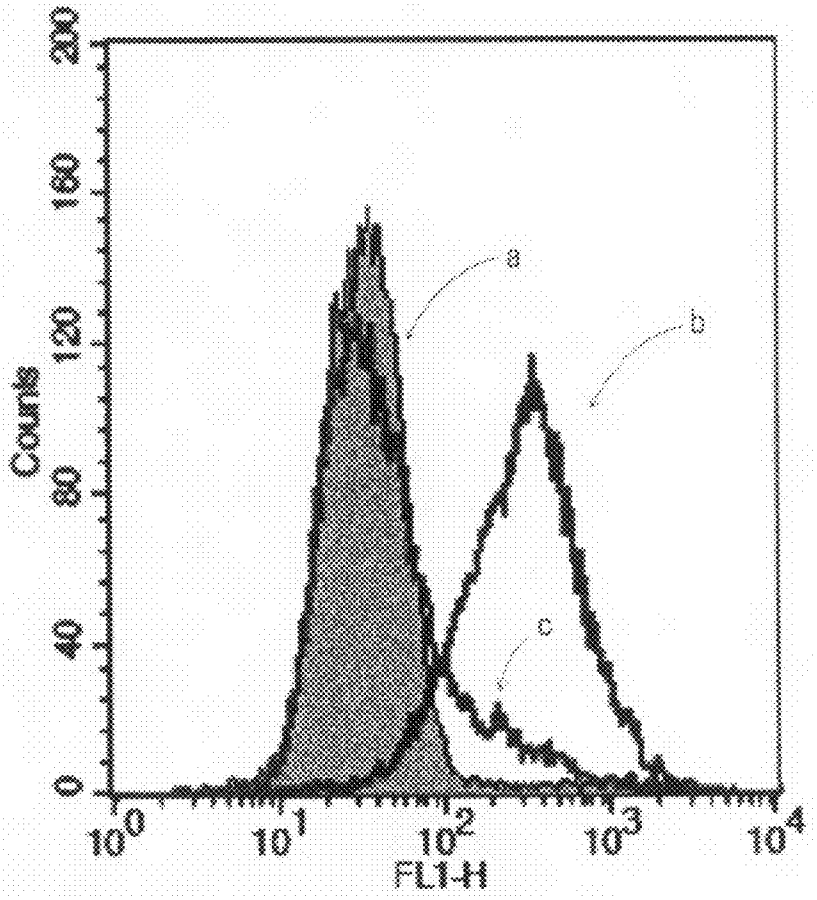
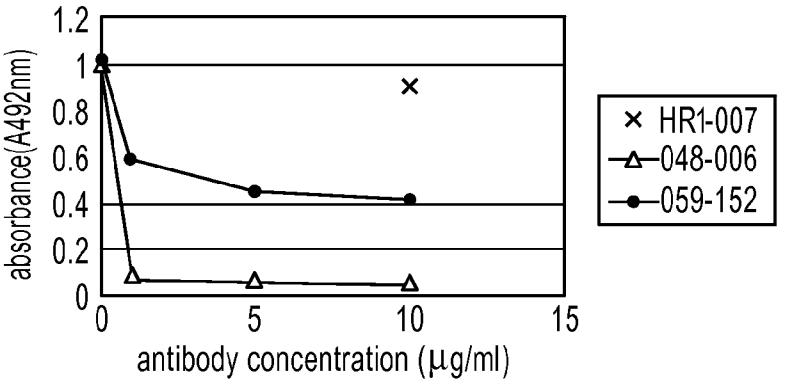
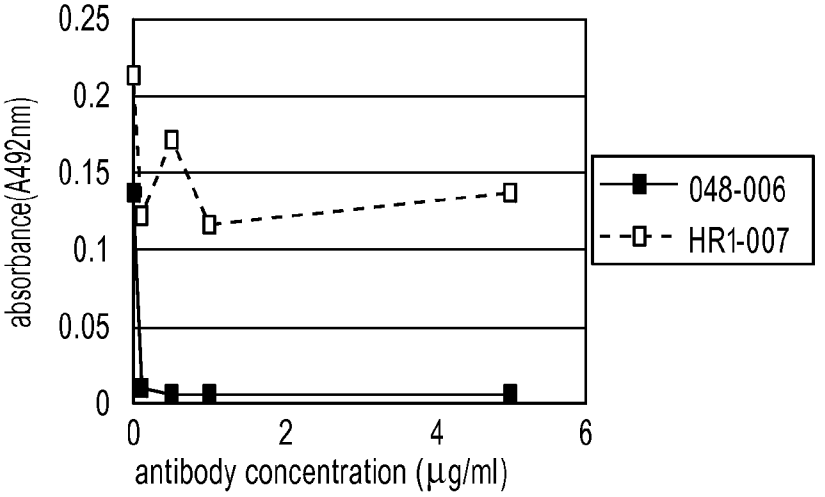


Fig.24

A


1.2
1
0.8
0.6
0.4
0.2
0
absorbance(A492nm)
0
5
10
15
antibody concentration (μg/ml)
HR1-007
048-006
059-152

B


0.25
0.2
0.15
0.1
0.05
0
absorbance(A492nm)
0
2
4
6
antibody concentration (μg/ml)
048-006
HR1-007

C

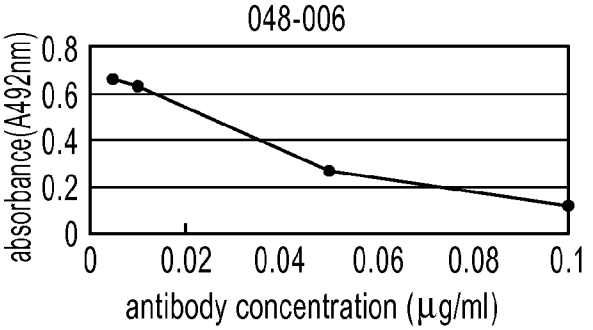
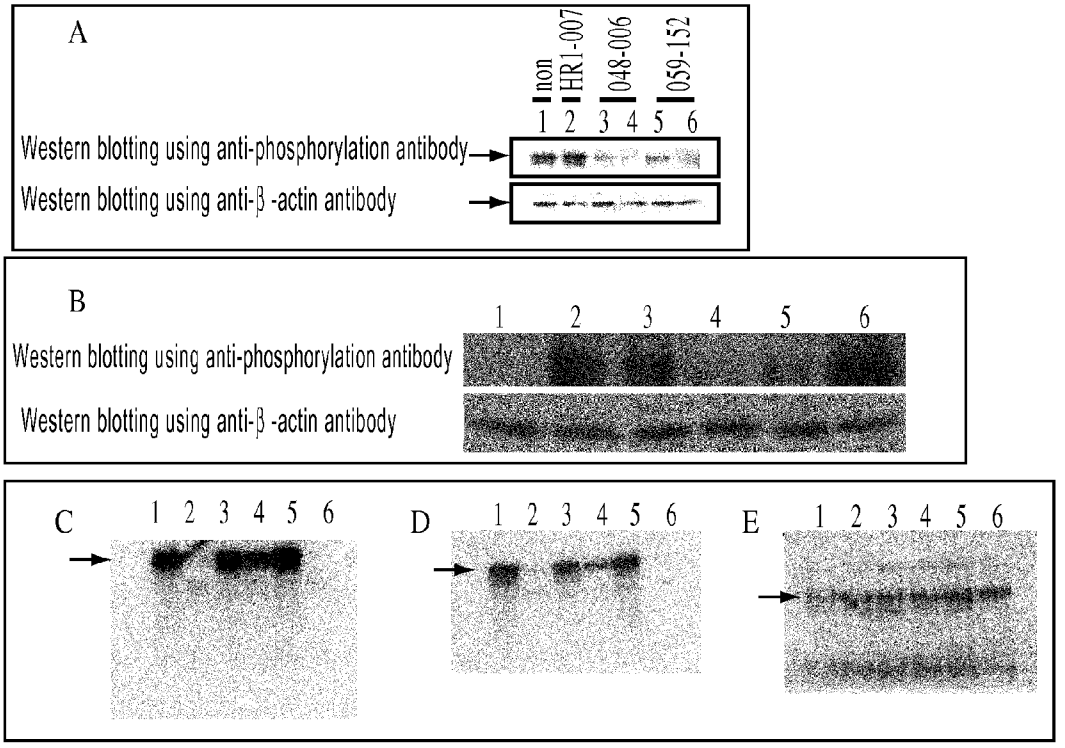

048-006
0.8
0.6
0.4
0.2
0
absorbance(A492nm)
0
0.02
0.04
0.06
0.08
0.1
antibody concentration (μg/ml)

Fig.25


A
non
HR1-007
048-006
059-152
1 2 3 4 5 6
Western blotting using anti-phosphorylation antibody
Western blotting using anti-β -actin antibody
B
1 2 3 4 5 6
Western blotting using anti-phosphorylation antibody
Western blotting using anti-β -actin antibody
C
1 2 3 4 5 6
D
1 2 3 4 5 6
E
1 2 3 4 5 6

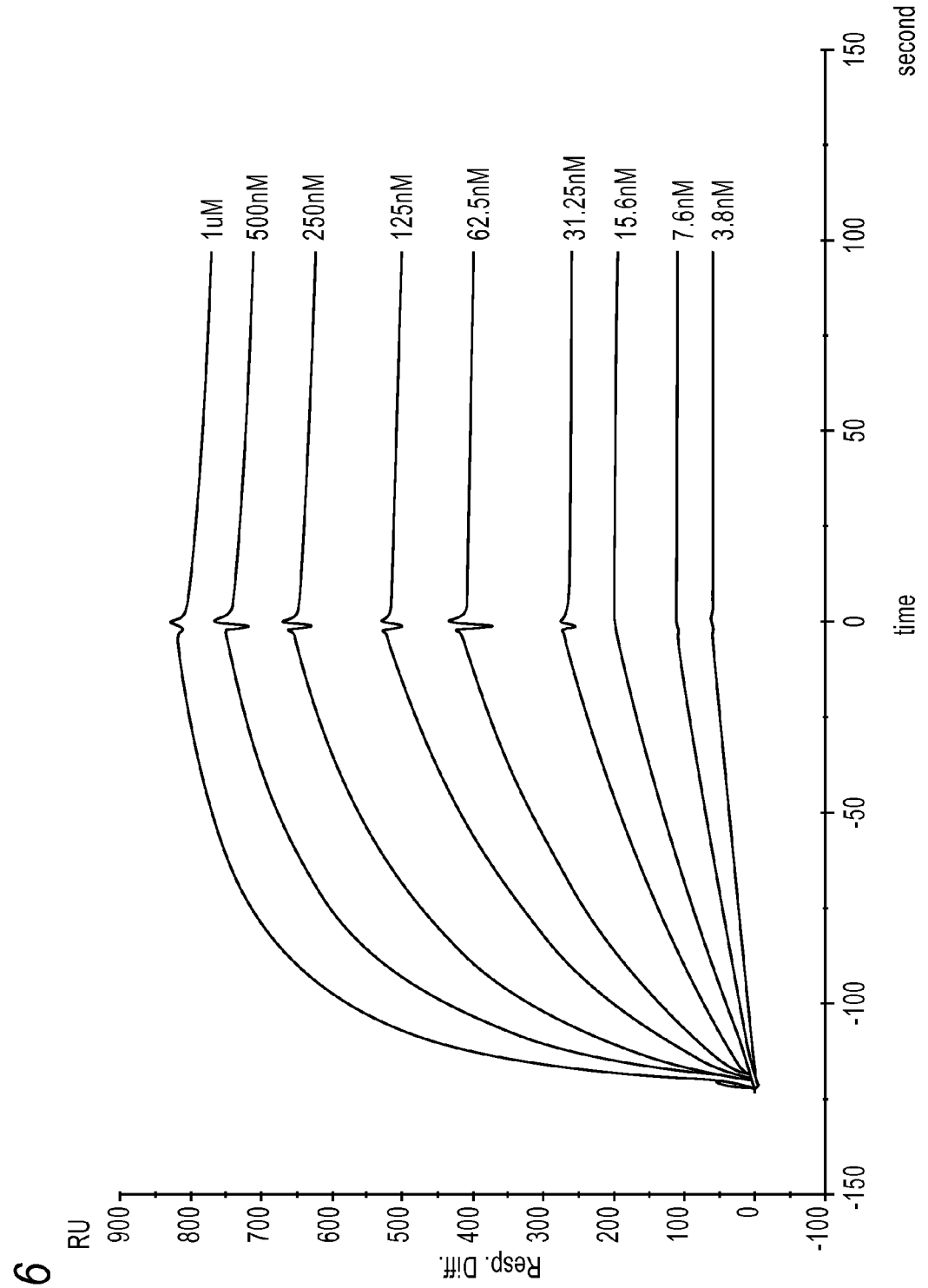

RU
900
800
700
600
500
400
300
200
100
0
-100
Resp. Diff.
-150
-100
-50
0
50
100
150
time
second
1uM
500nM
250nM
125nM
62.5nM
31.25nM
15.6nM
7.6nM
3.8nM

Fig.26

Fig.27

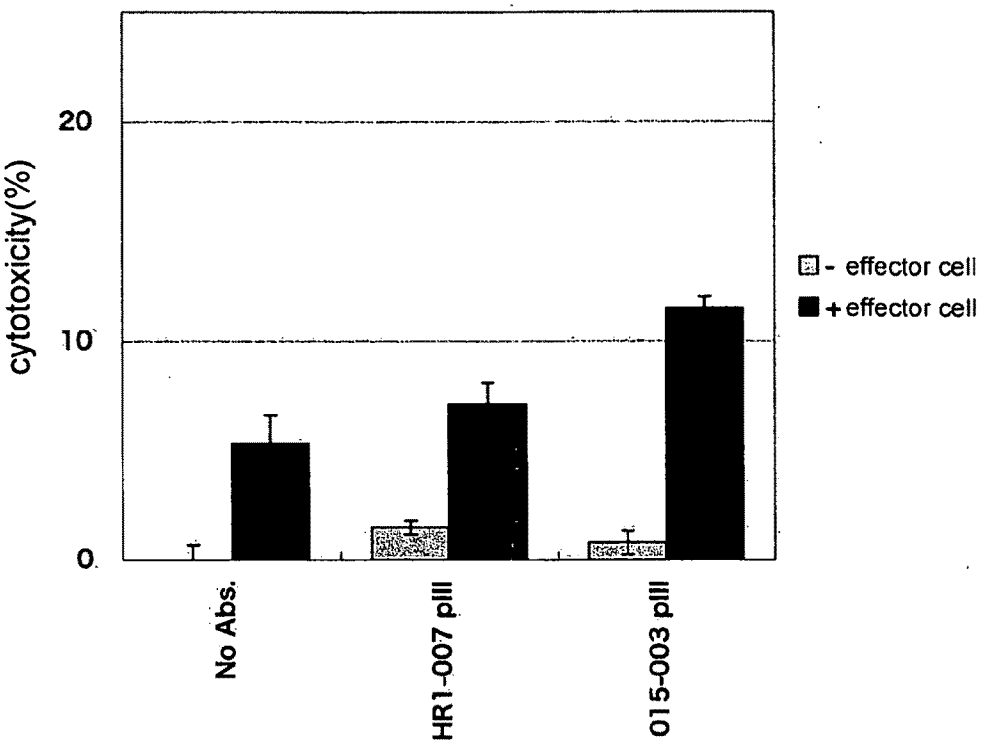

20
10
0
cytotoxicity(%)
- effector cell
+ effector cell
No Abs.
HR1-007 pIII
015-003 pIII

Fig.28

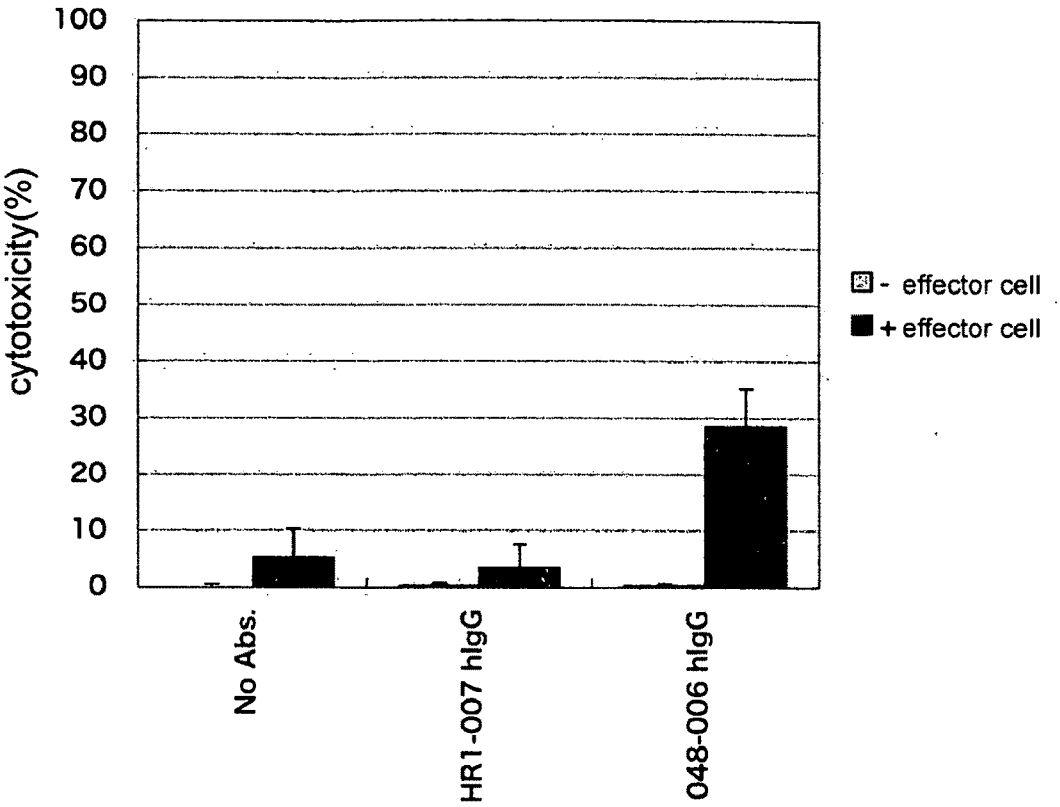

100
90
80
70
60
50
40
30
20
10
0
cytotoxicity(%)
- effector cell
+ effector cell
No Abs.
HR1-007 hIgG
048-006 hIgG

Fig.29

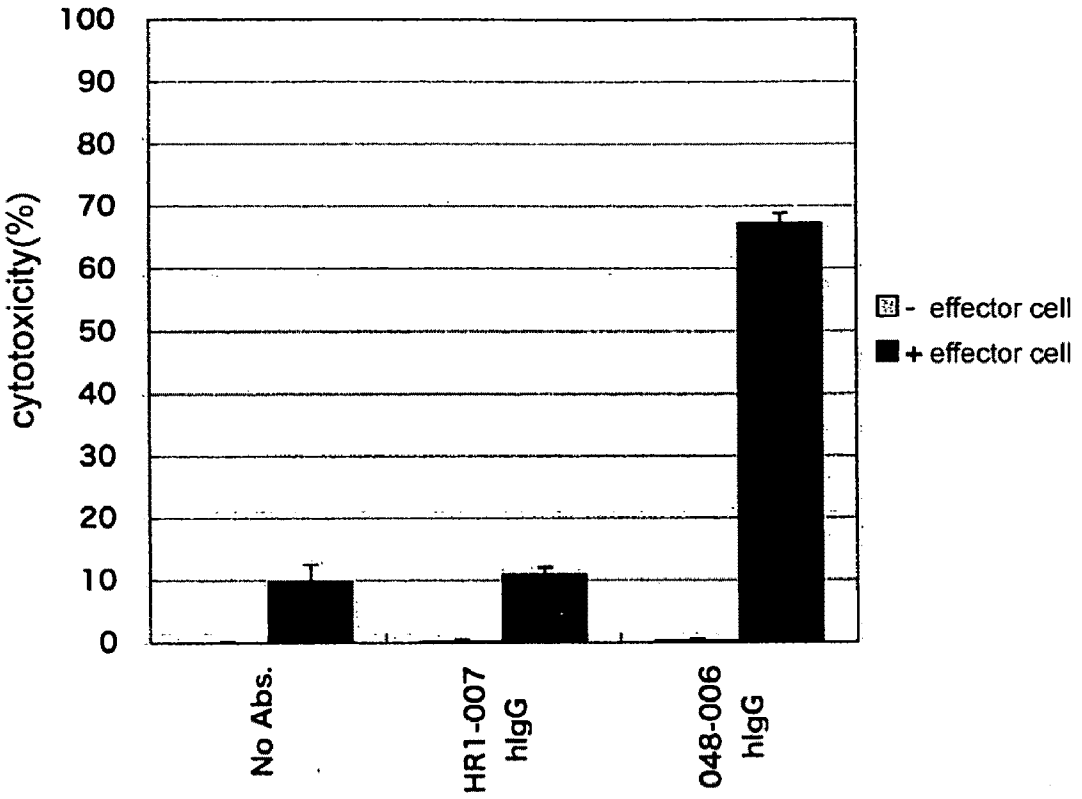

100
90
80
70
60
50
40
30
20
10
0
cytotoxicity(%)
- effector cell
+ effector cell
No Abs.
HR1-007 hIgG
048-006 hIgG

Fig.30

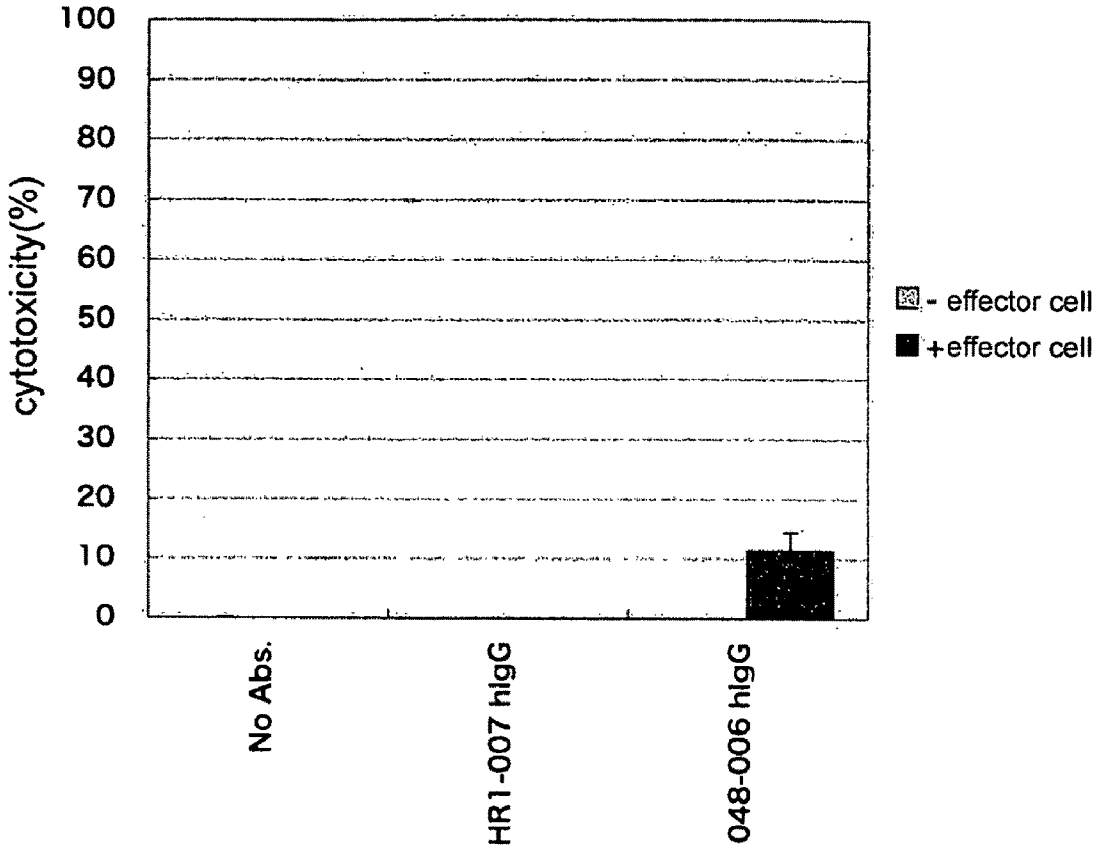

100
90
80
70
60
50
40
30
20
10
0
cytotoxicity(%)
- effector cell
+effector cell
No Abs.
HR1-007 hIgG
048-006 hIgG

Fig.31

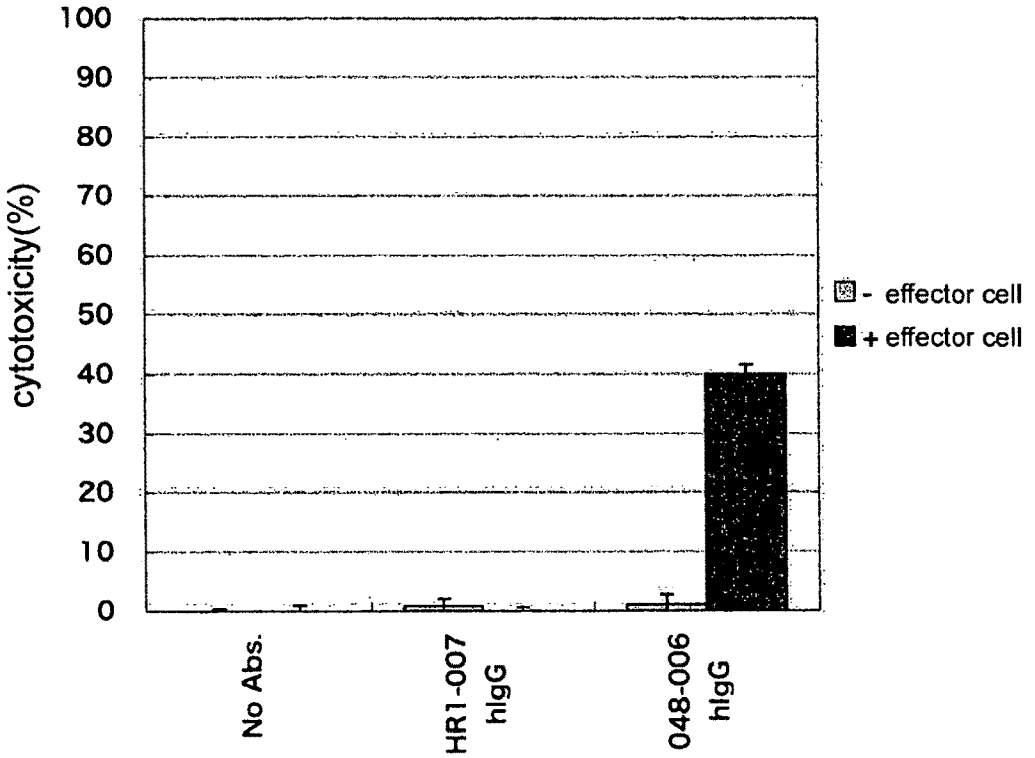

100
90
80
70
60
50
40
30
20
10
0
cytotoxicity(%)
- effector cell
+ effector cell
No Abs.
HR1-007 hIgG
048-006 hIgG

Fig.32

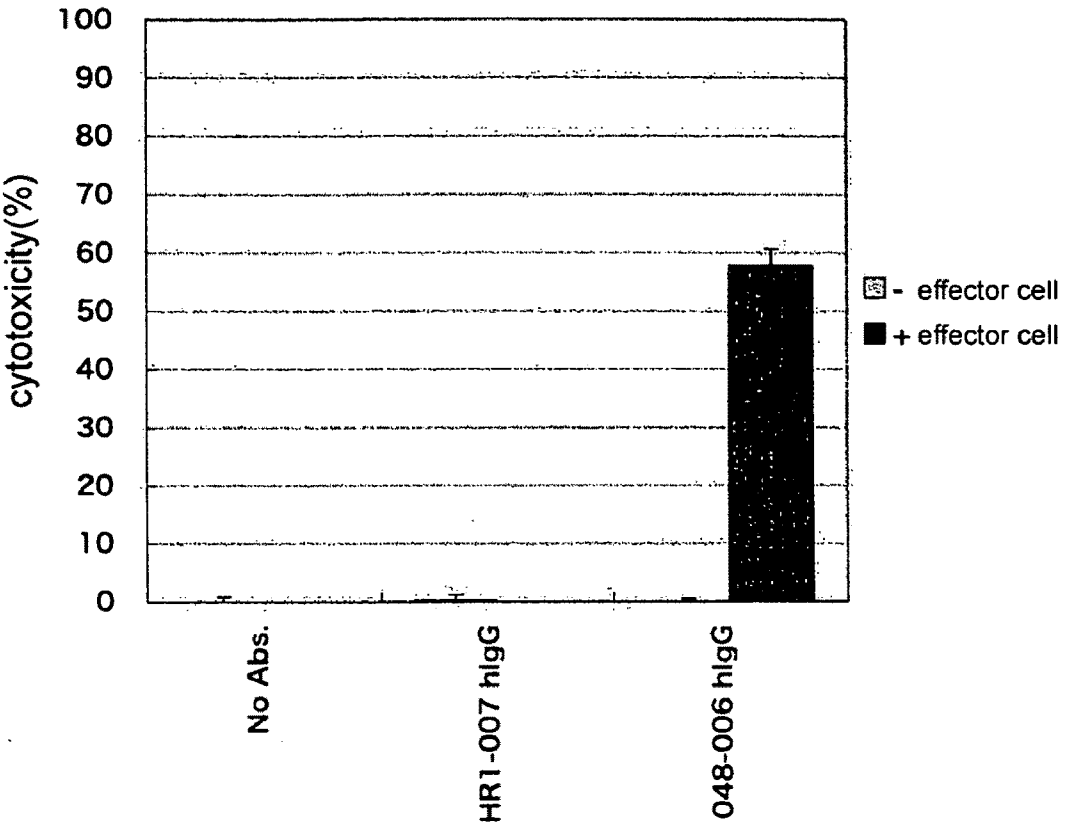

100
90
80
70
60
50
40
30
20
10
0
cytotoxicity(%)
- effector cell
+ effector cell
No Abs.
HR1-007 hIgG
048-006 hIgG

Fig.33

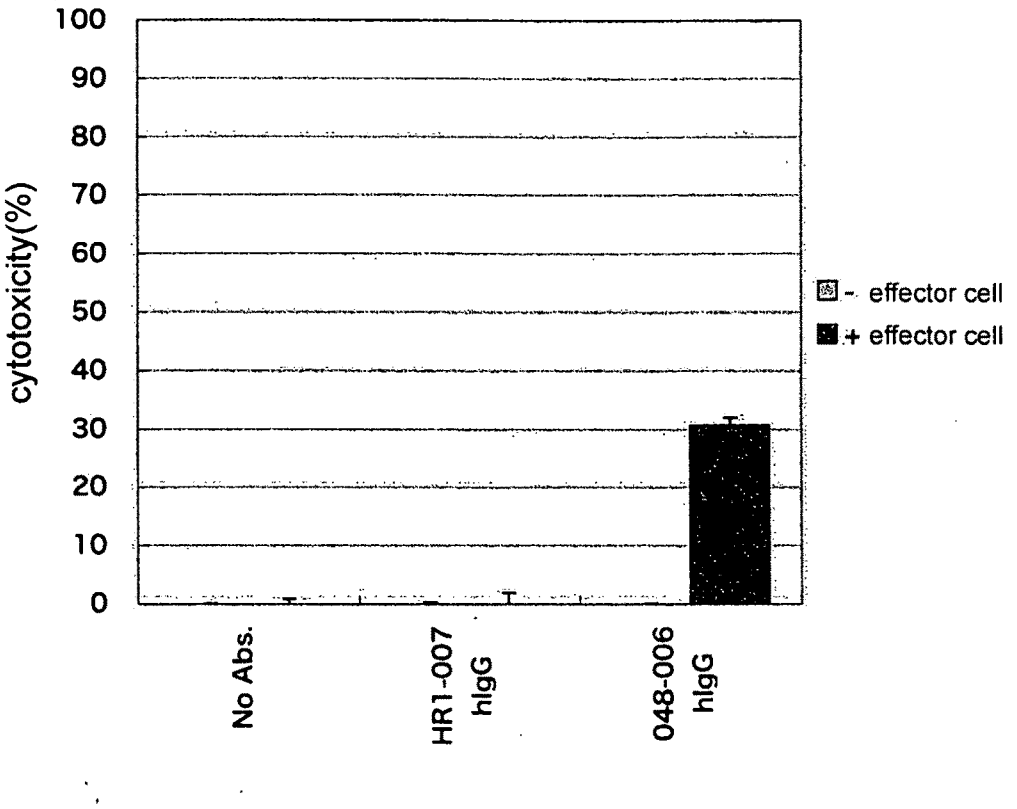

100
90
80
70
60
50
40
30
20
10
0
cytotoxicity(%)
- effector cell
+ effector cell
No Abs.
HR1-007 hIgG
048-006 hIgG

Fig.34

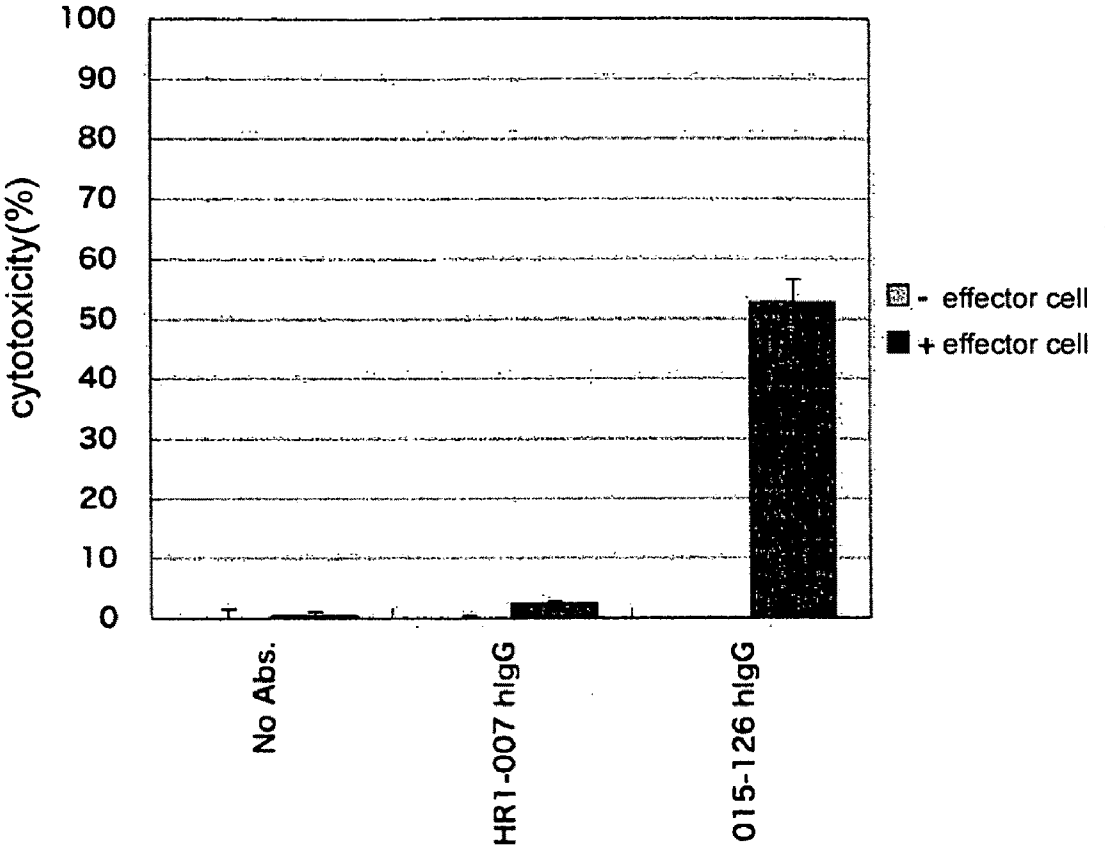

100
90
80
70
60
50
40
30
20
10
0
cytotoxicity(%)
- effector cell
+ effector cell
No Abs.
HR1-007 hIgG
015-126 hIgG

Fig.35

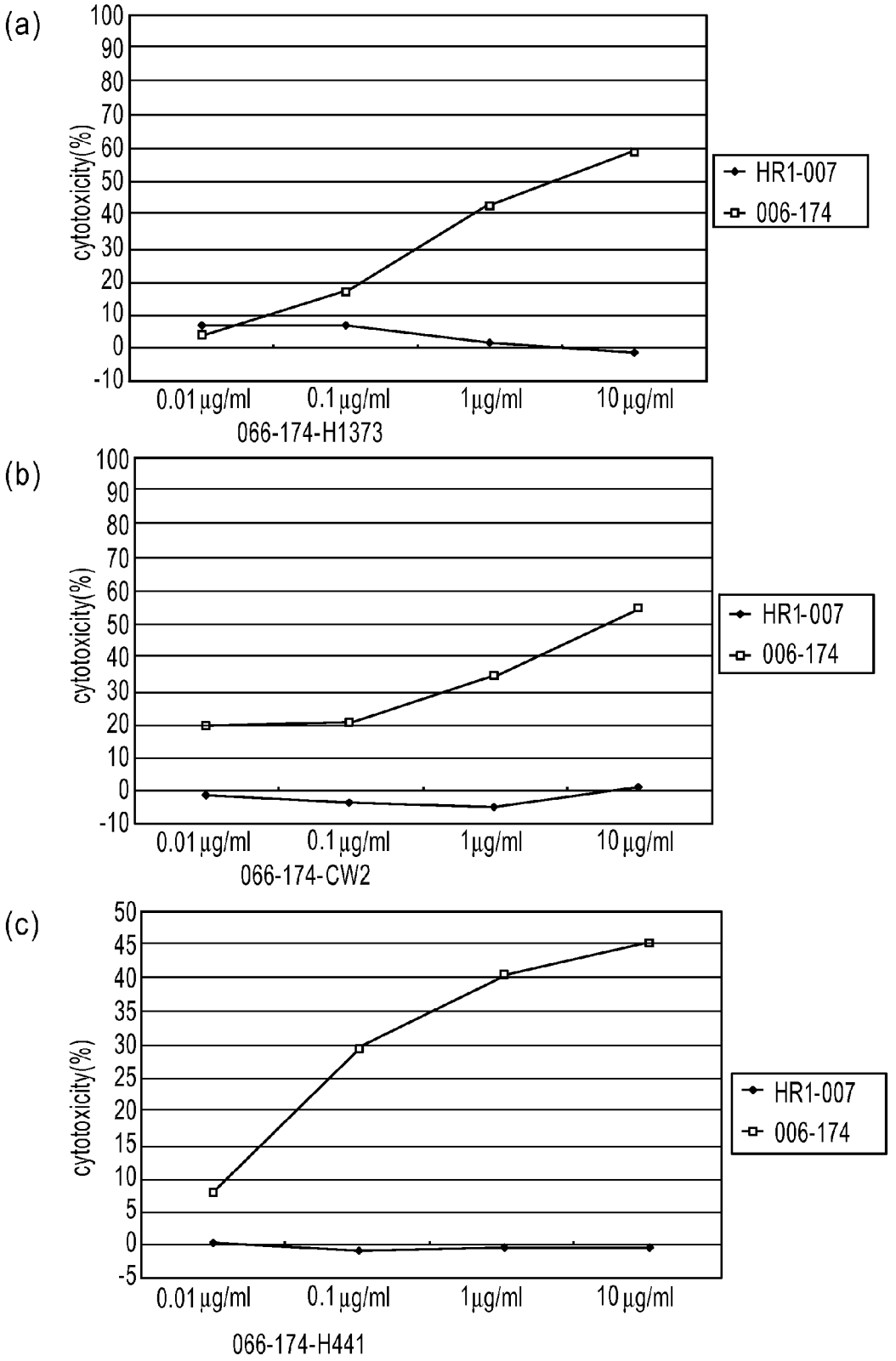

(a)
100
90
80
70
60
50
40
30
20
10
0
-10
cytotoxicity(%)
HR1-007
006-174
0.01μg/ml
0.1μg/ml
1μg/ml
10μg/ml
066-174-H1373
(b)
100
90
80
70
60
50
40
30
20
10
0
-10
cytotoxicity(%)
HR1-007
006-174
0.01μg/ml
0.1μg/ml
1μg/ml
10μg/ml
066-174-CW2
(c)
50
45
40
35
30
25
20
15
10
5
0
-5
cytotoxicity(%)
HR1-007
006-174
0.01μg/ml
0.1μg/ml
1μg/ml
10μg/ml
066-174-H441

Fig.36

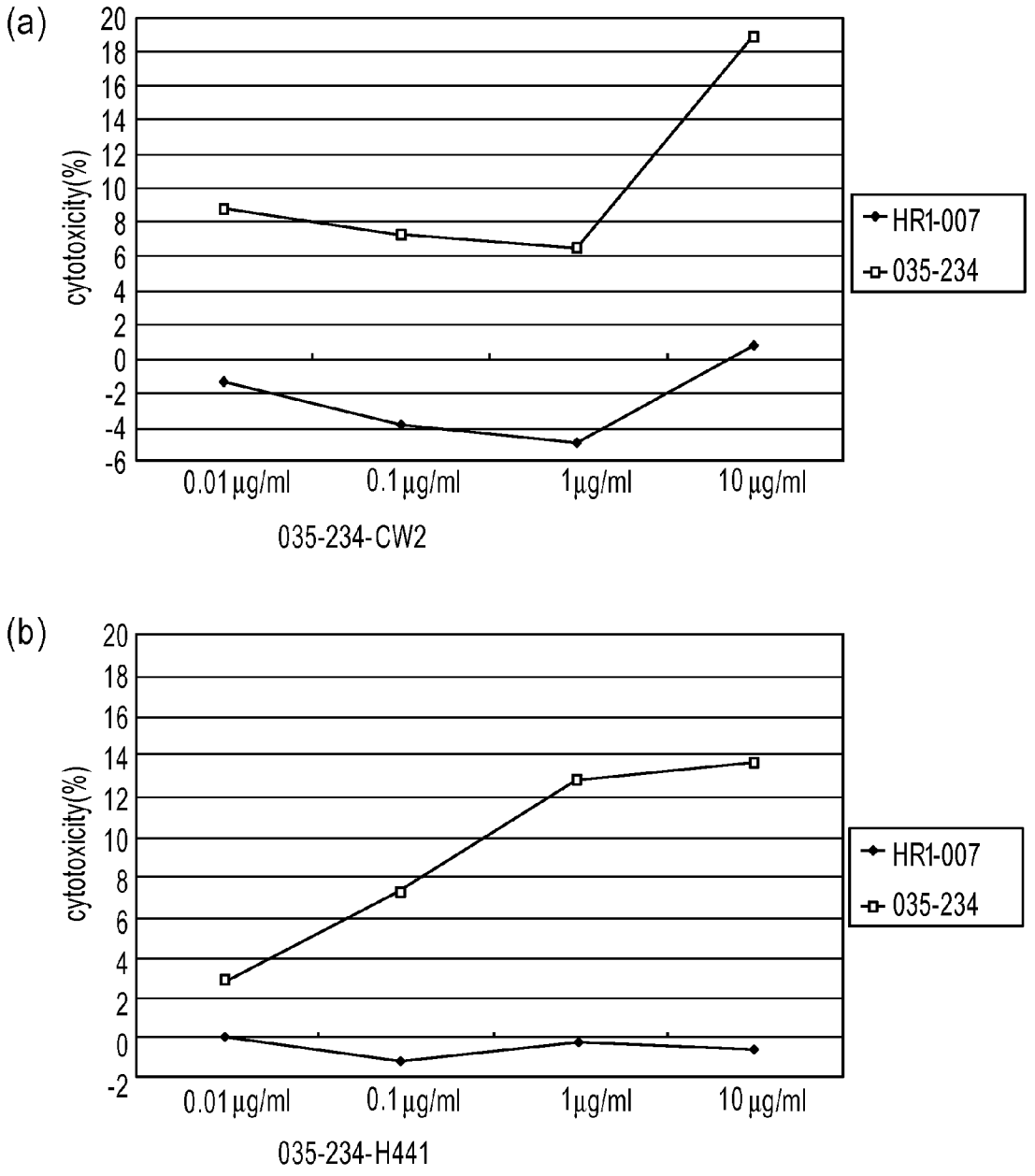

(a)
cytotoxicity(%)
20
18
16
14
12
10
8
6
4
2
0
-2
-4
-6
0.01μg/ml
0.1μg/ml
1μg/ml
10μg/ml
035-234-CW2
HR1-007
035-234
(b)
cytotoxicity(%)
20
18
16
14
12
10
8
6
4
2
0
-2
0.01μg/ml
0.1μg/ml
1μg/ml
10μg/ml
035-234-H441
HR1-007
035-234

Fig.37

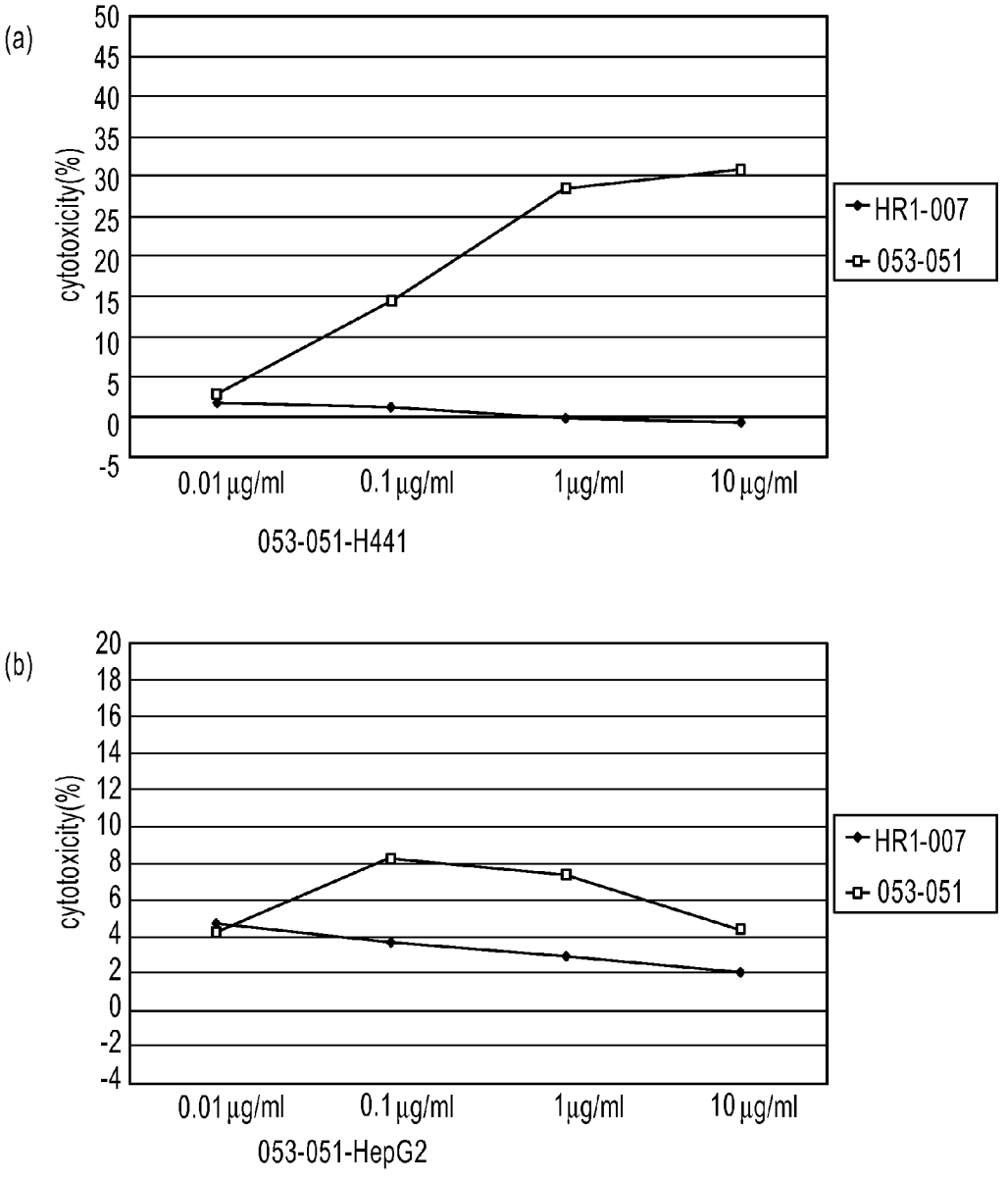

(a)
cytotoxicity(%)
50
45
40
35
30
25
20
15
10
5
0
-5
0.01μg/ml
0.1μg/ml
1μg/ml
10μg/ml
HR1-007
053-051
053-051-H441
(b)
cytotoxicity(%)
20
18
16
14
12
10
8
6
4
2
0
-2
-4
0.01μg/ml
0.1μg/ml
1μg/ml
10μg/ml
HR1-007
053-051
053-051-HepG2

Fig.38

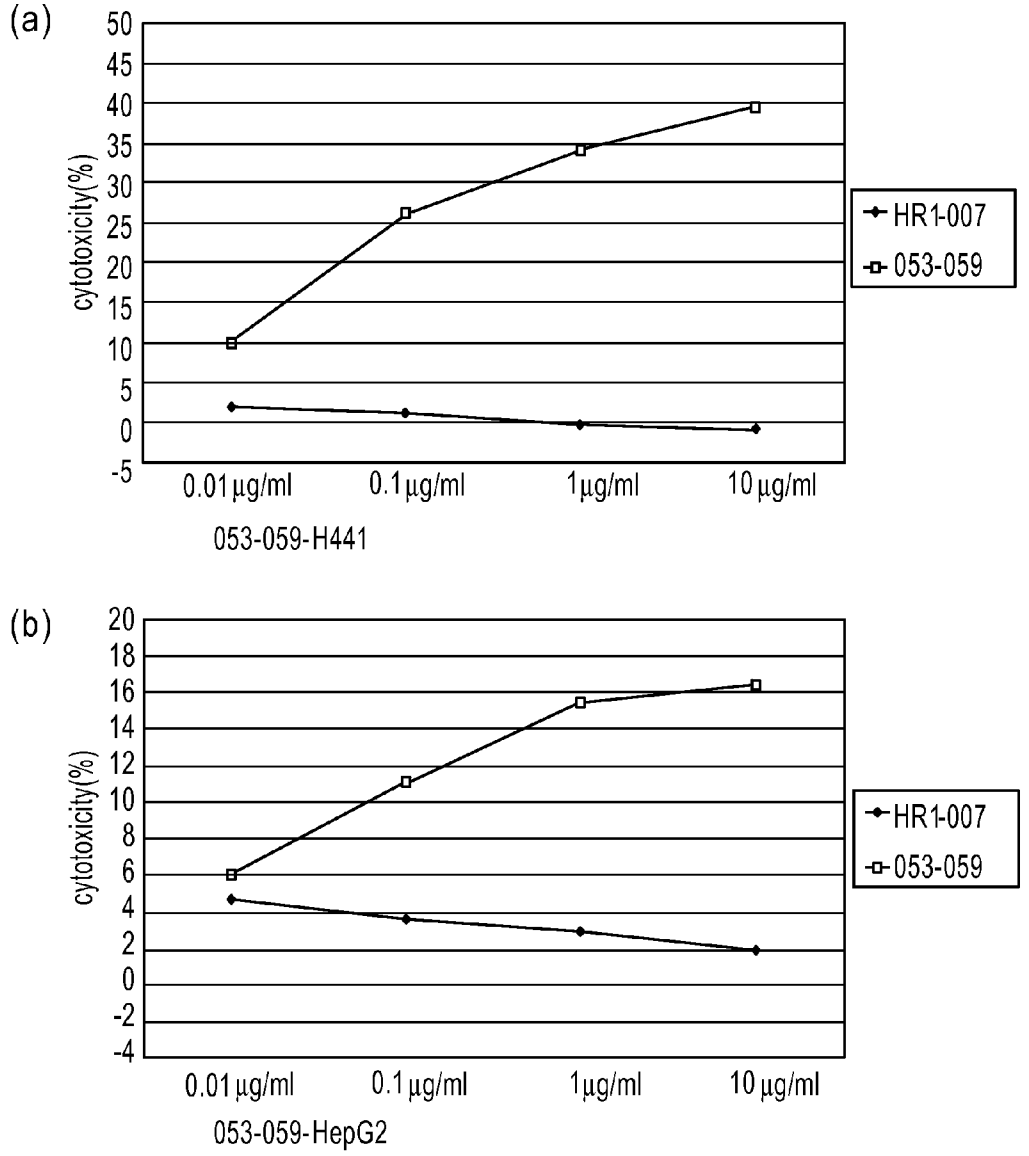

(a)
cytotoxicity(%)
50
45
40
35
30
25
20
15
10
5
0
-5
0.01μg/ml
0.1μg/ml
1μg/ml
10μg/ml
HR1-007
053-059
053-059-H441
(b)
cytotoxicity(%)
20
18
16
14
12
10
8
6
4
2
0
-2
-4
0.01μg/ml
0.1μg/ml
1μg/ml
10μg/ml
HR1-007
053-059
053-059-HepG2

Fig.39

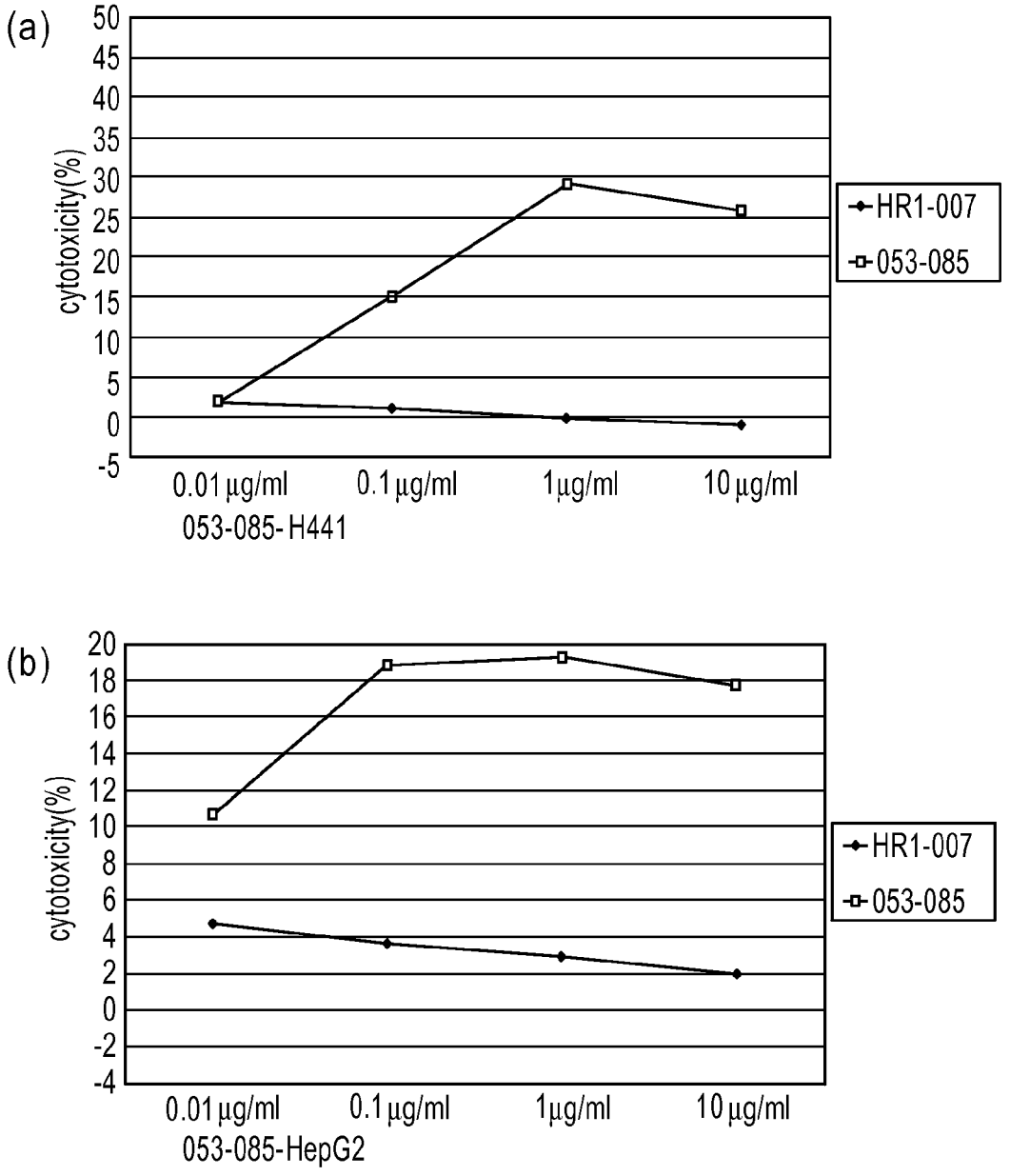

(a)
cytotoxicity(%)
50
45
40
35
30
25
20
15
10
5
0
-5
0.01μg/ml
0.1μg/ml
1μg/ml
10μg/ml
053-085-H441
HR1-007
053-085
(b)
cytotoxicity(%)
20
18
16
14
12
10
8
6
4
2
0
-2
-4
0.01μg/ml
0.1μg/ml
1μg/ml
10μg/ml
053-085-HepG2
HR1-007
053-085

Fig.40

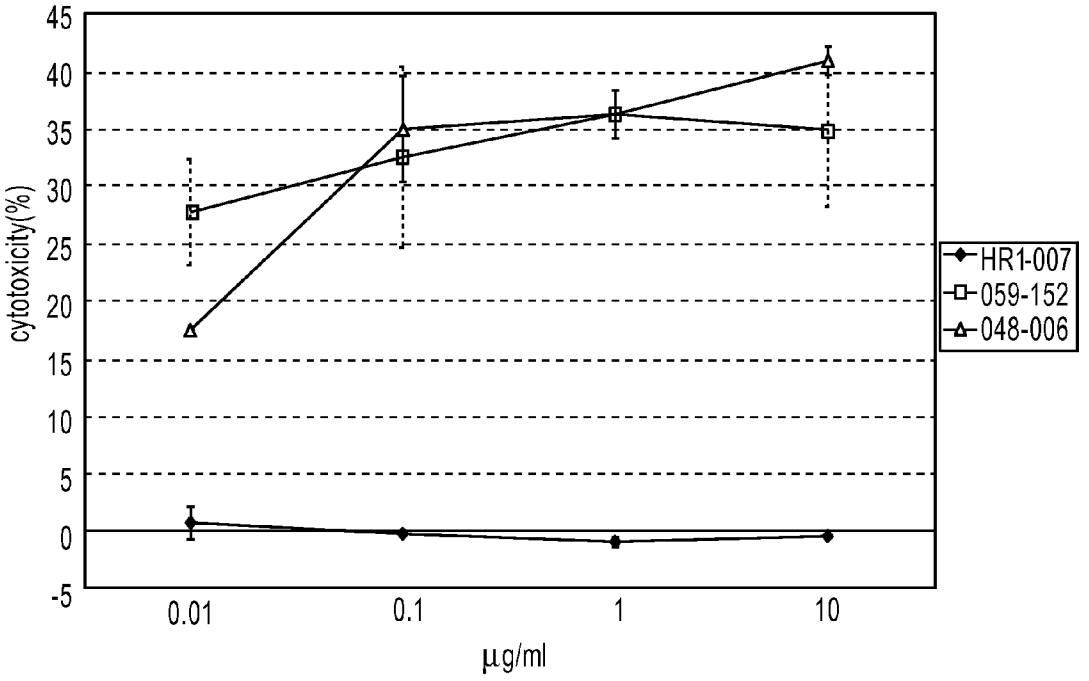

45
40
35
30
25
20
15
10
5
0
-5
cytotoxicity(%)
0.01
0.1
1
10
μg/ml
HR1-007
059-152
048-006

Fig.41

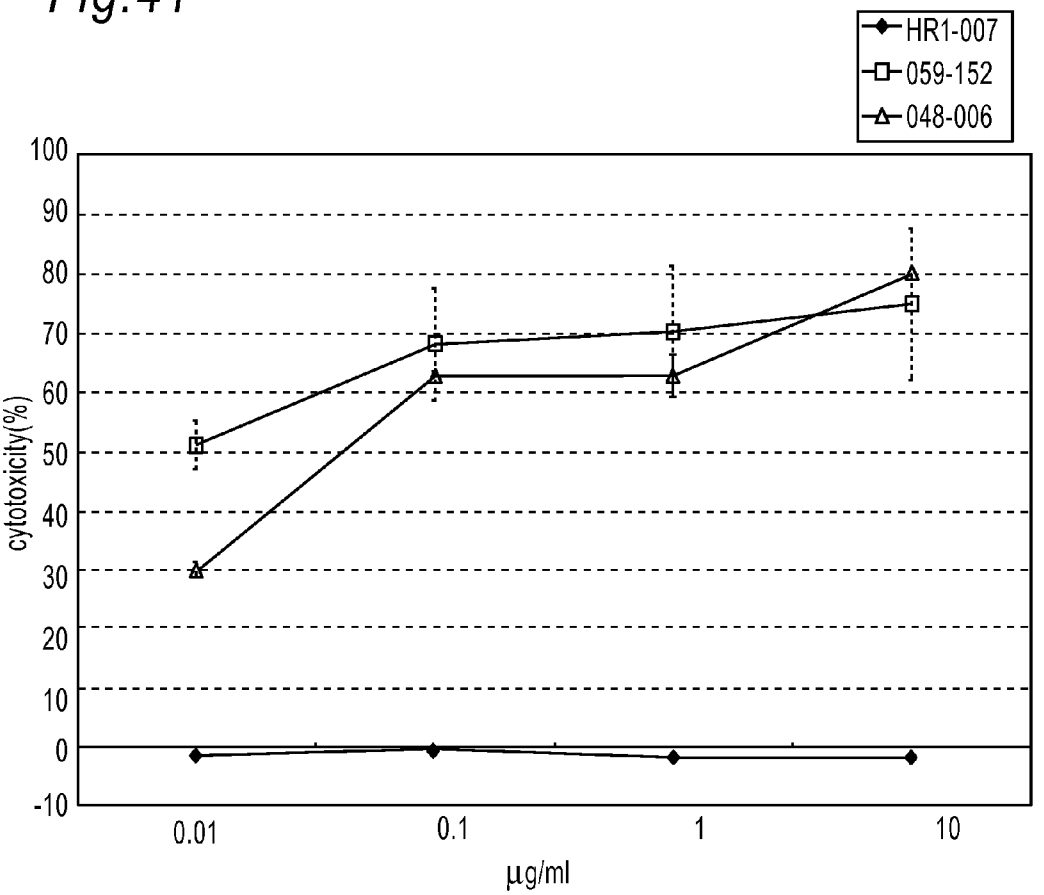
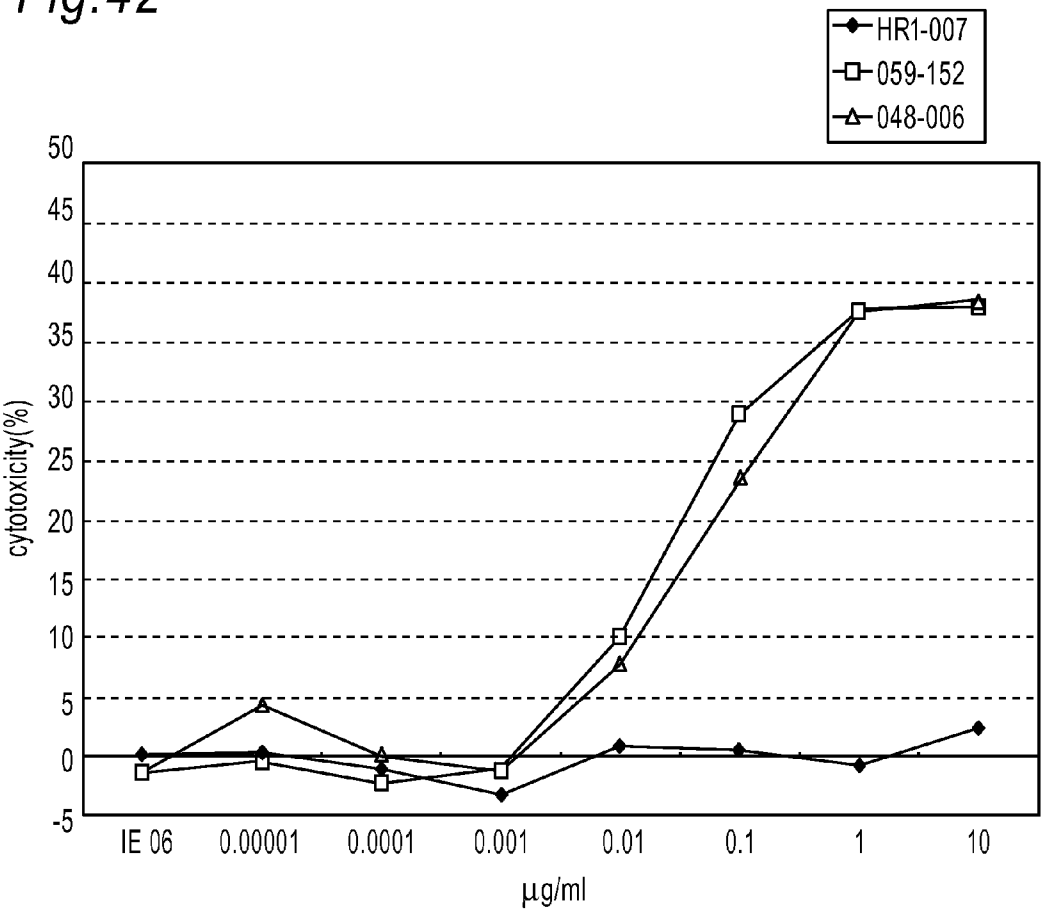

HR1-007
059-152
048-006
100
90
80
70
60
50
40
30
20
10
0
-10
cytotoxicity(%)
0.01
0.1
1
10
μg/ml

Fig.42


HR1-007
059-152
048-006
50
45
40
35
30
25
20
15
10
5
0
-5
cytotoxicity(%)
IE 06
0.00001
0.0001
0.001
0.01
0.1
1
10
μg/ml

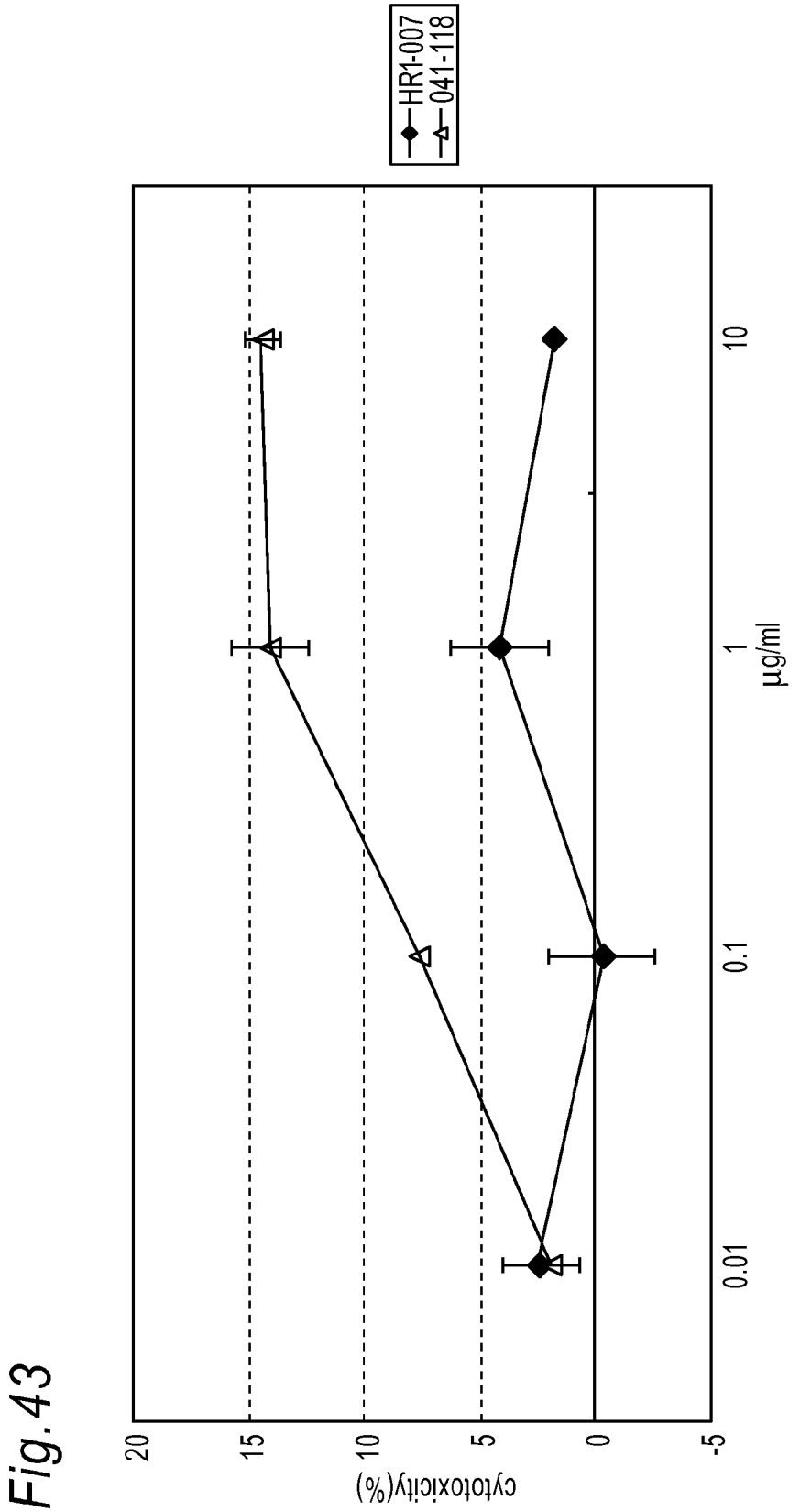


Fig. 43

Fig.44

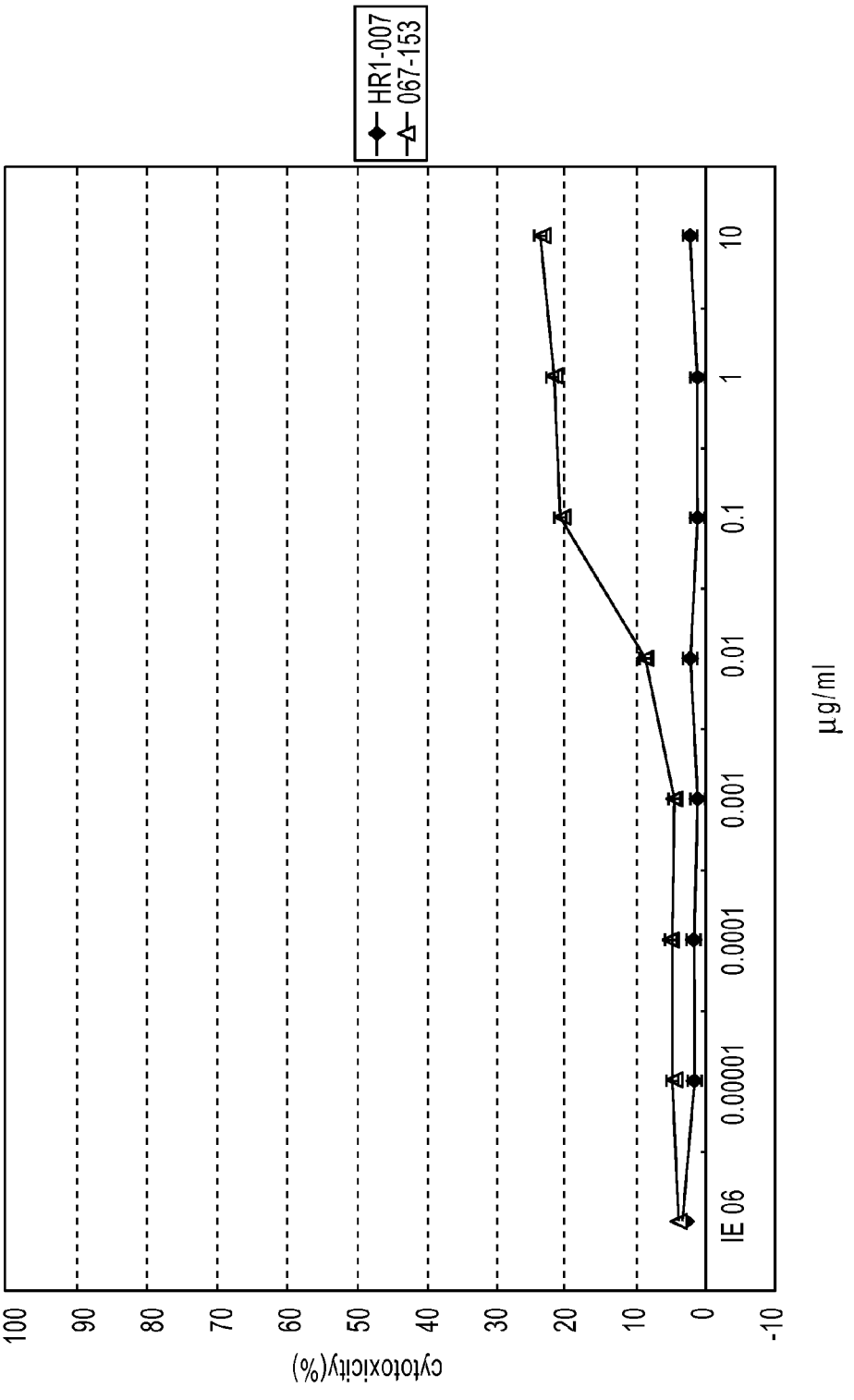

HR1-007
067-153
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
IE 06
0.00001
0.0001
0.001
0.01
0.1
1
10
μg/ml

Fig. 45

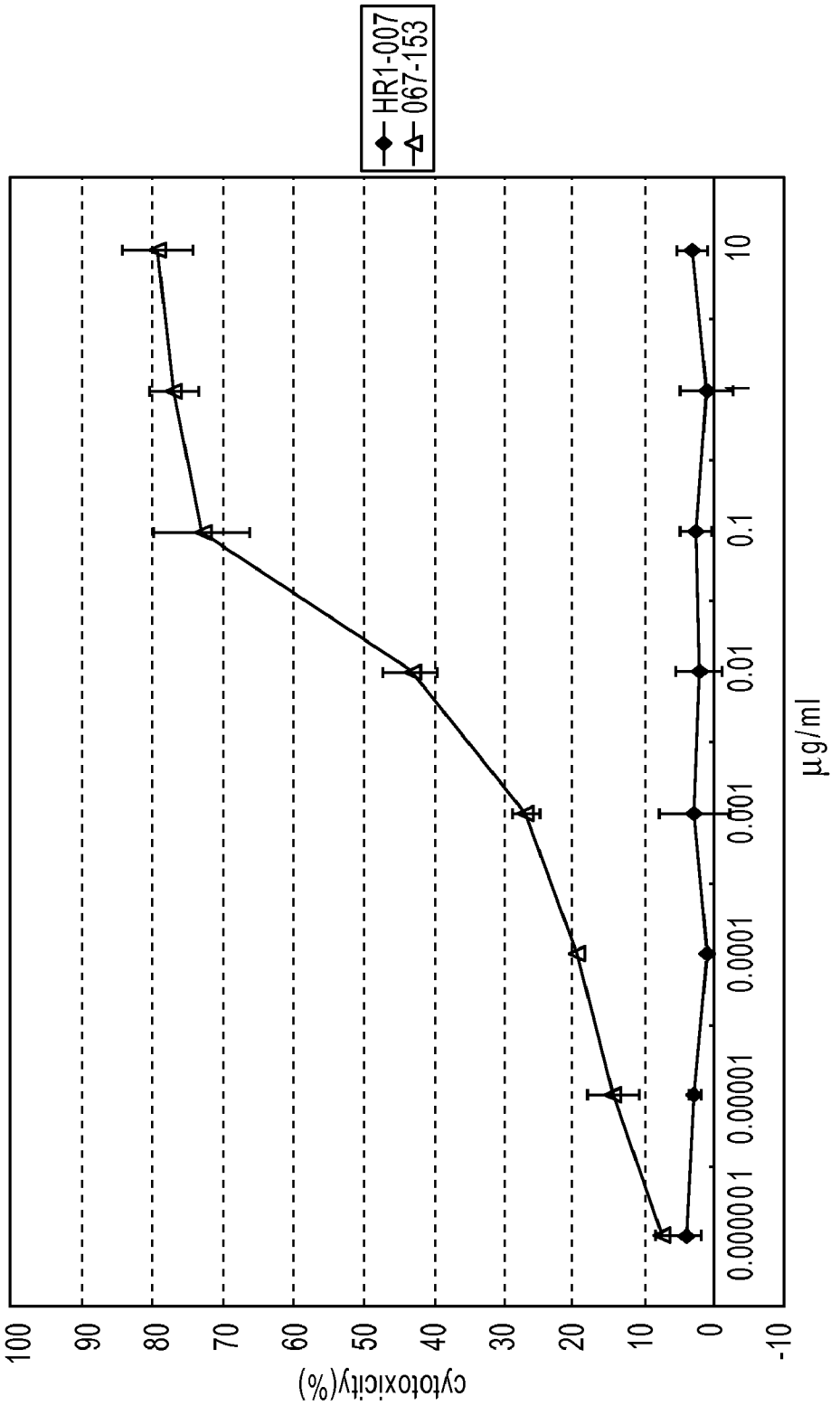
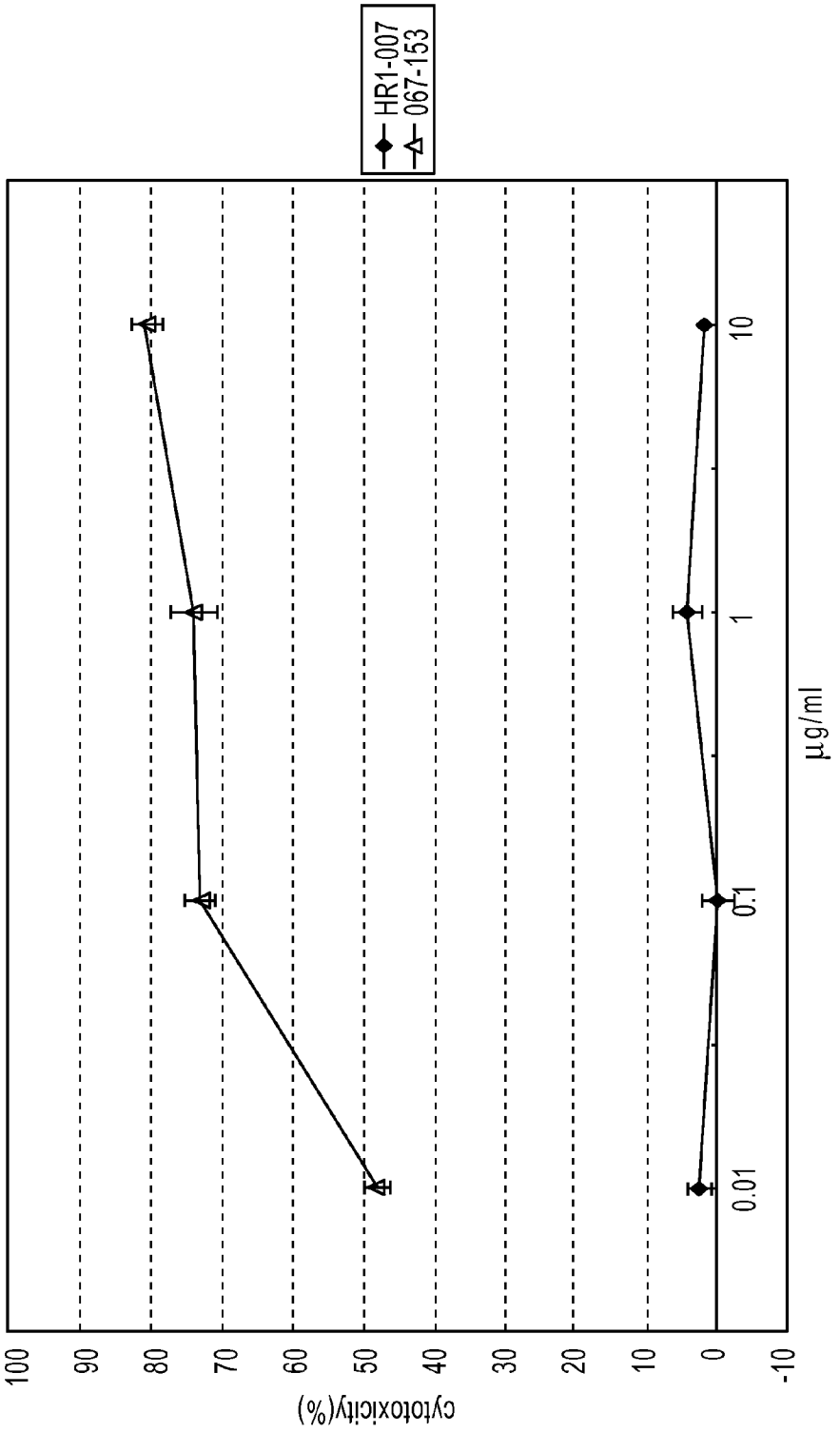

HR1-007
067-153
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
10
μg/ml

Fig.46


HR1-007
067-153
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
0.01
0.1
1
10
μg/ml

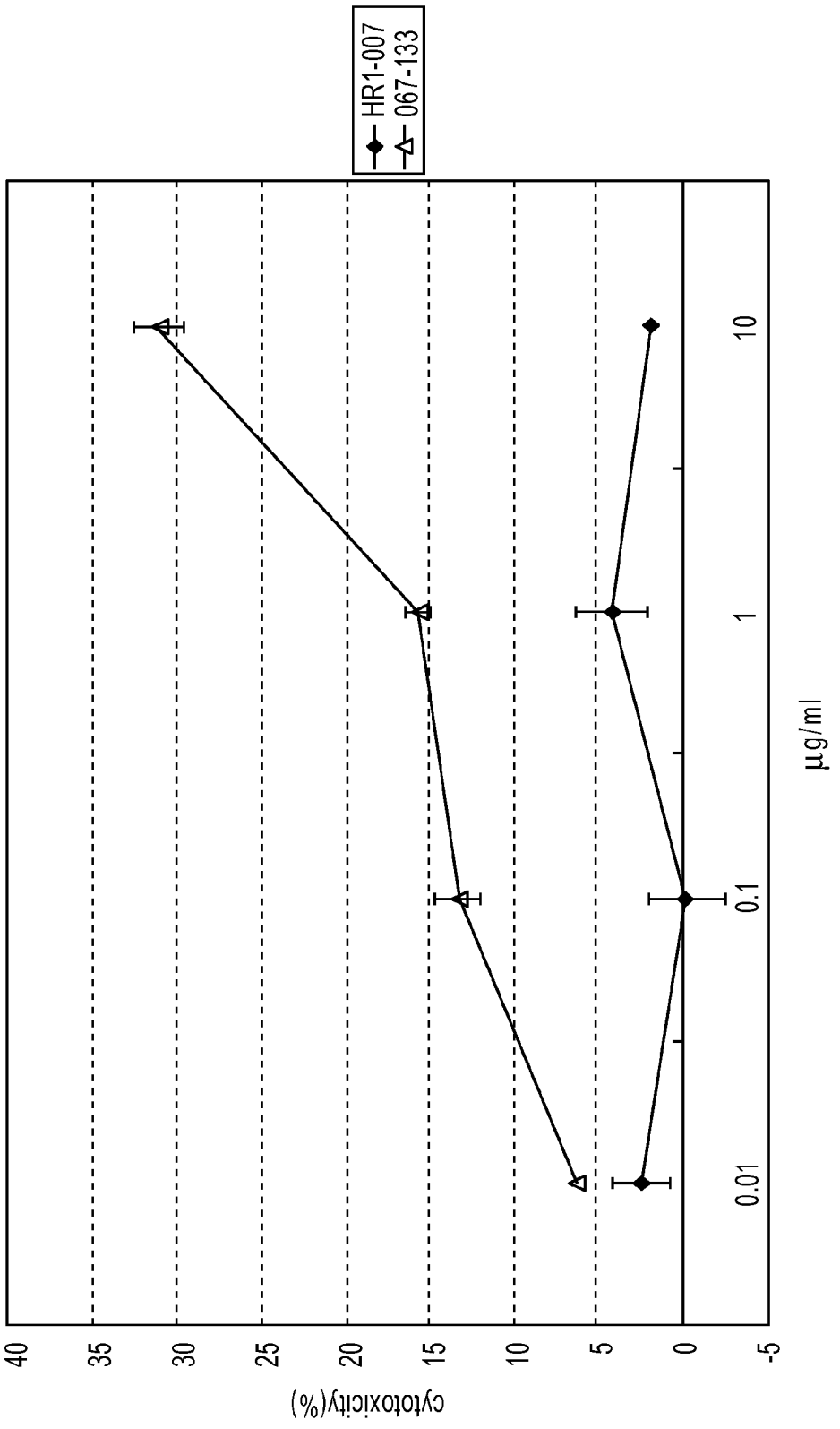
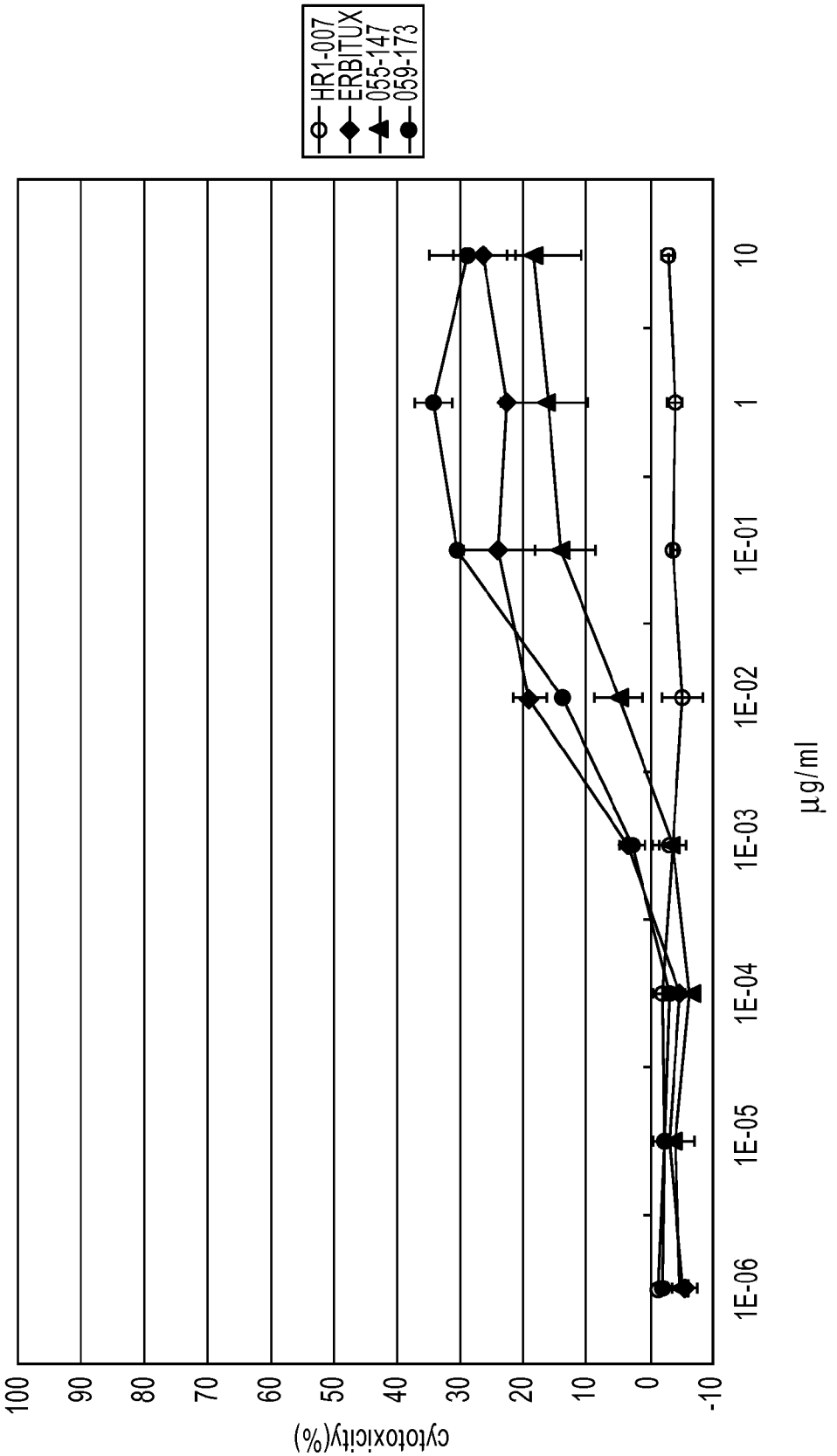

HR1-007
067-133
cytotoxicity(%)
40
35
30
25
20
15
10
5
0
-5
0.01
0.1
1
10
μg/ml

Fig.47

Fig.48


HR1-007
ERBITUX
055-147
059-173
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1E-06
1E-05
1E-04
1E-03
1E-02
1E-01
1
10
μg/ml

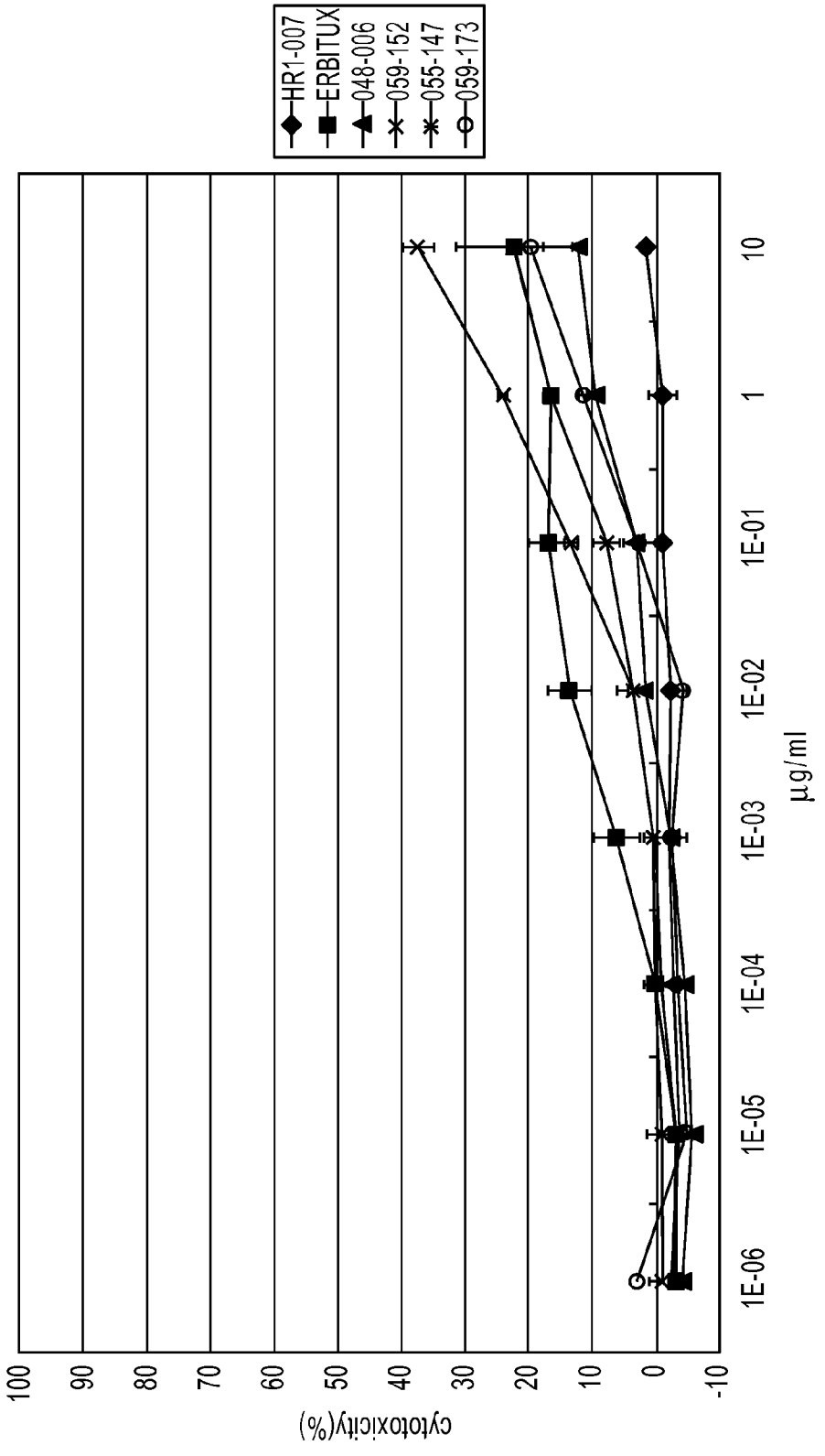

HR1-007
ERBITUX
048-006
059-152
055-147
059-173
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1E-06
1E-05
1E-04
1E-03
1E-02
1E-01
1
10
µg/ml

Fig. 49

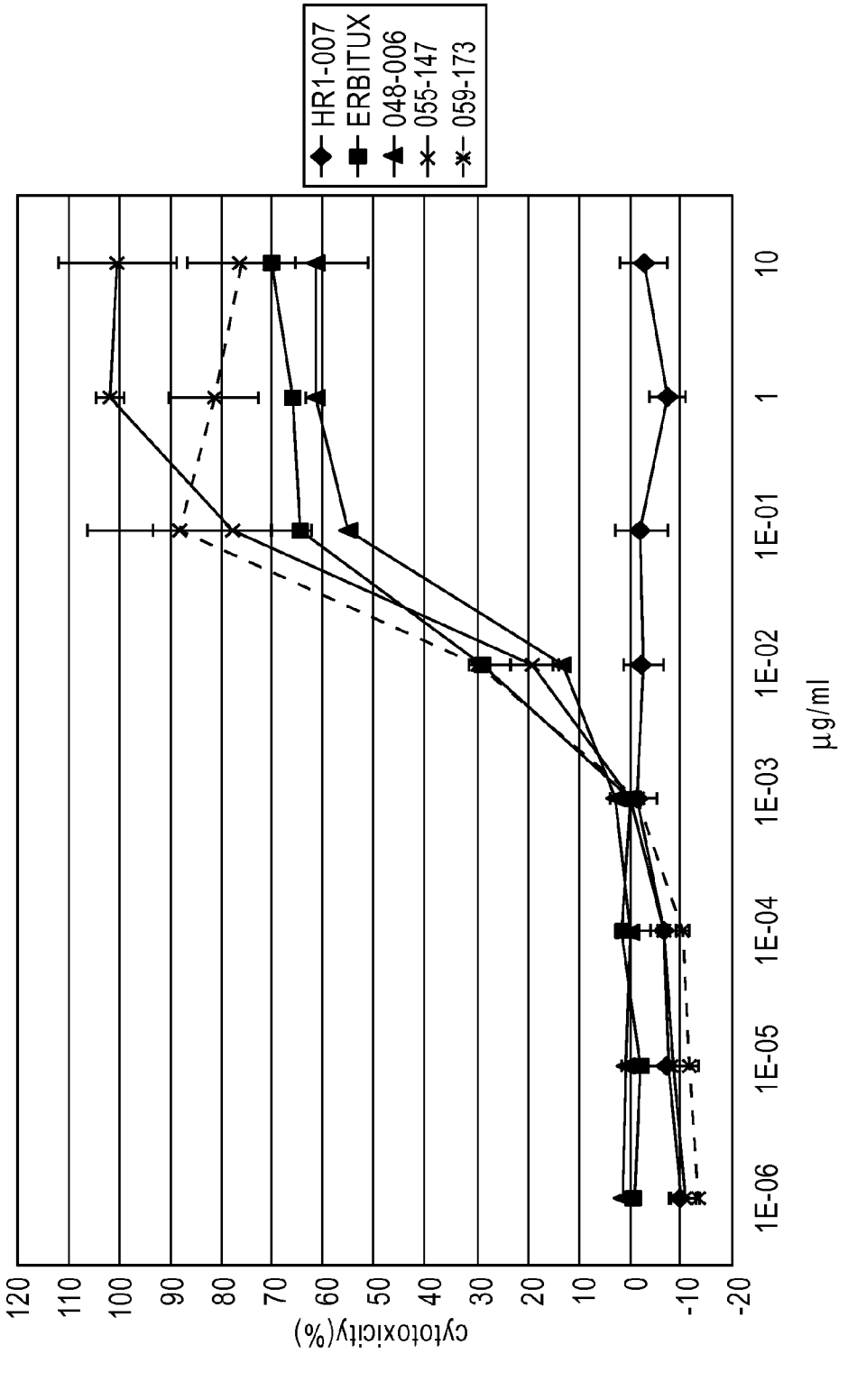

HR1-007
ERBITUX
048-006
055-147
059-173
cytotoxicity(%)
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
1E-06
1E-05
1E-04
1E-03
1E-02
1E-01
1
10
µg/ml

Fig.50

Fig.51

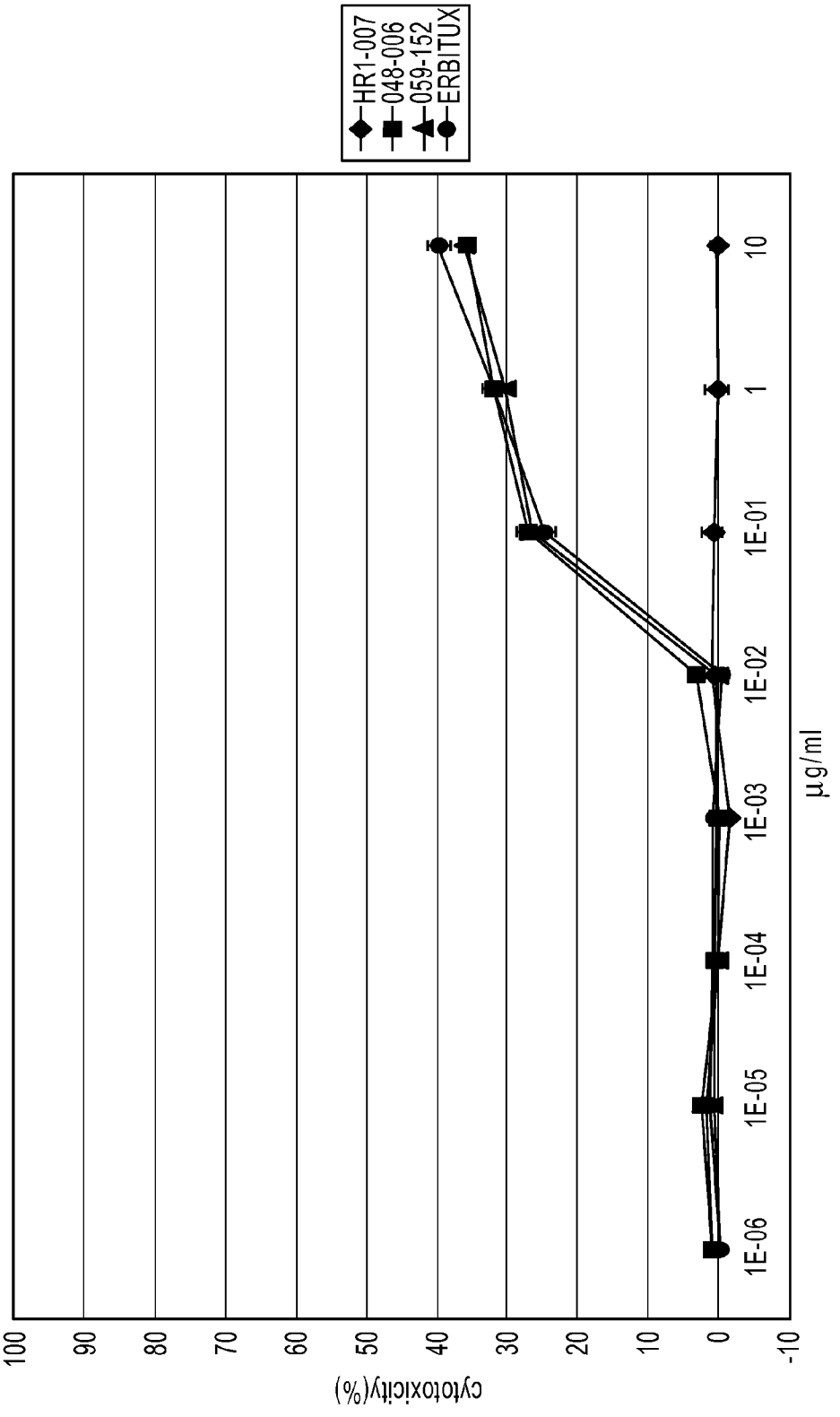

HR1-007
048-006
059-152
ERBITUX
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1E-06
1E-05
1E-04
1E-03
1E-02
1E-01
1
10
μg/ml

Fig.52

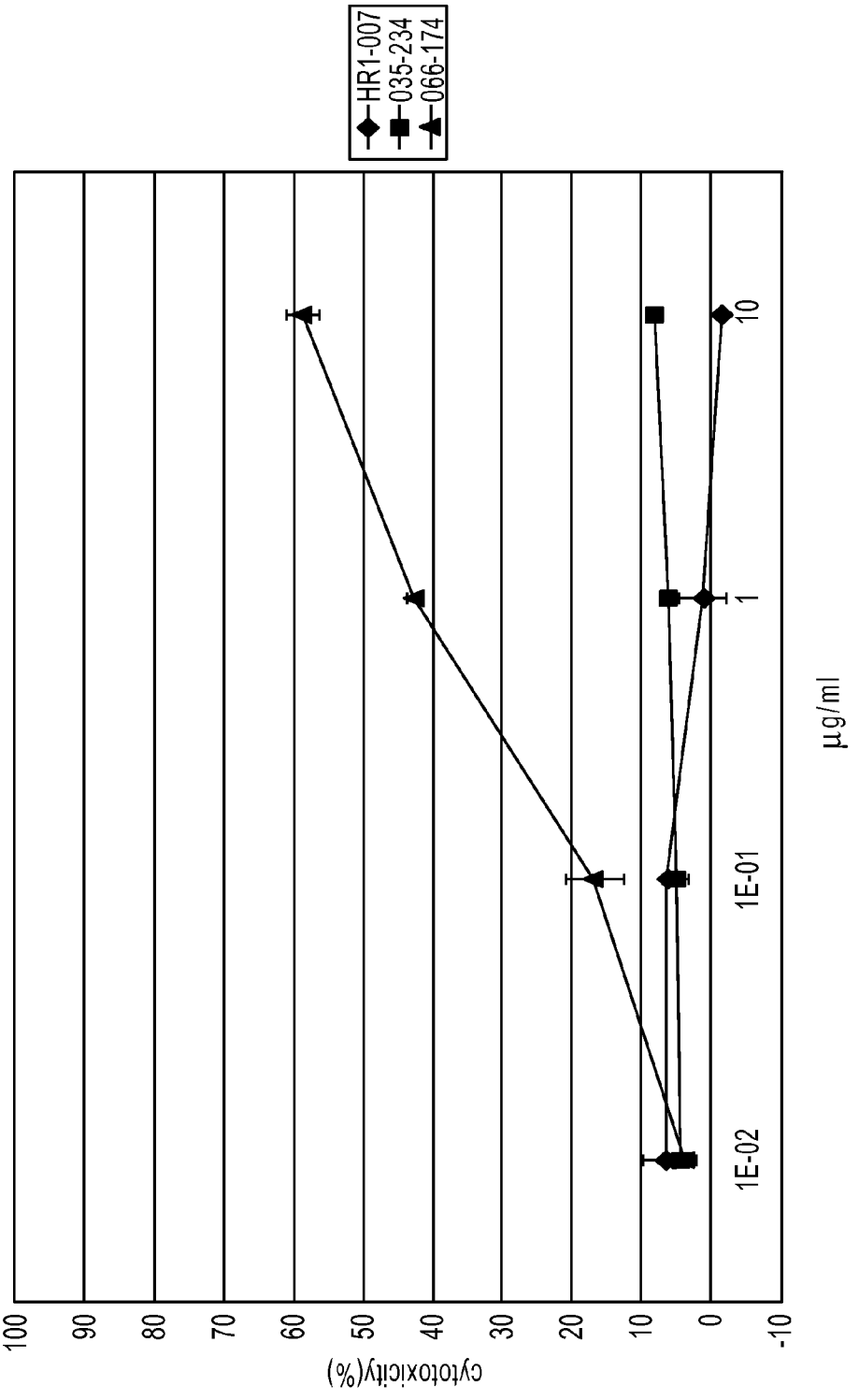

HR1-007
035-234
066-174
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1E-02
1E-01
1
10
μg/ml

Fig.53

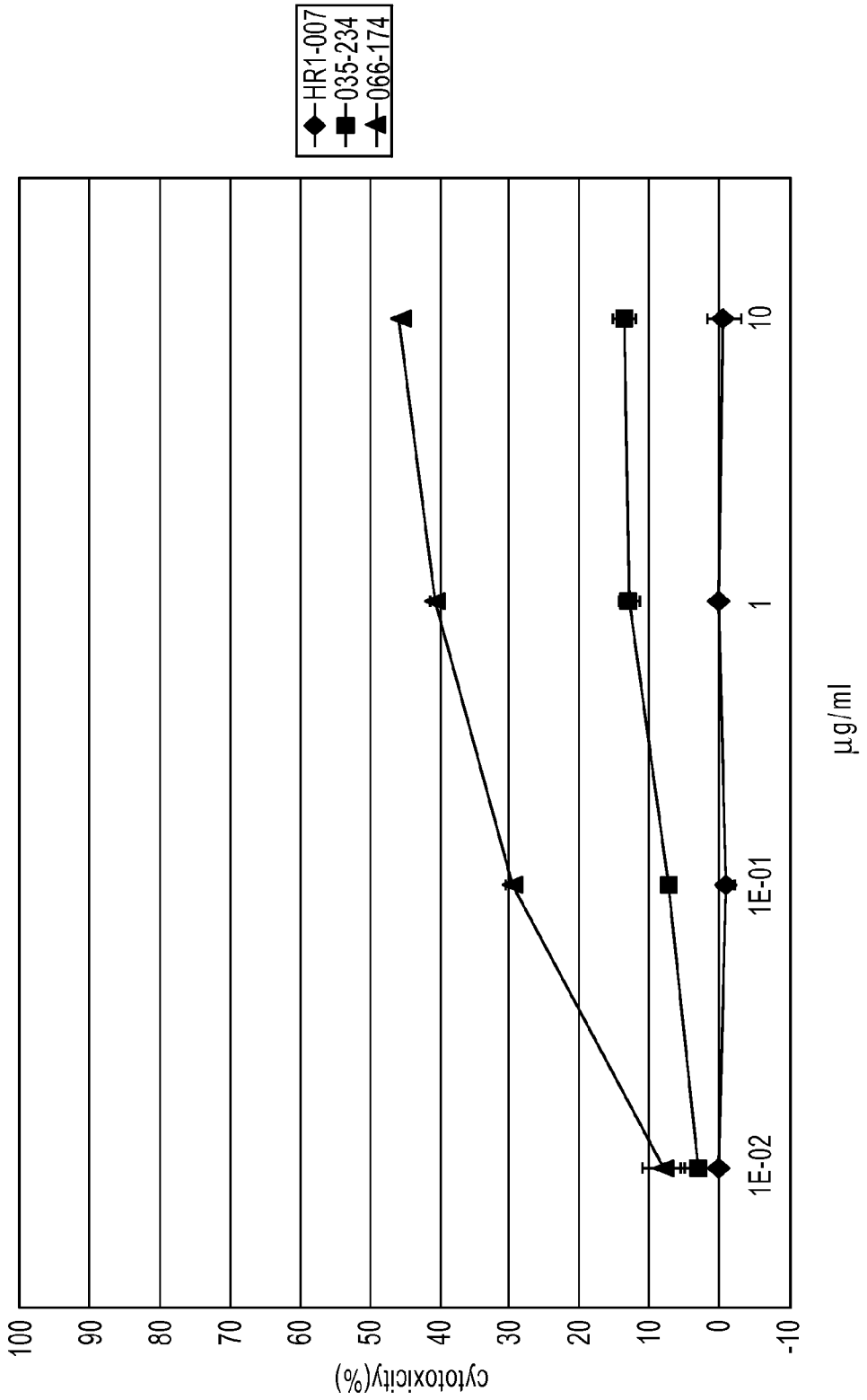

HR1-007
035-234
066-174
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1E-02
1E-01
1
10
μg/ml

Fig.54

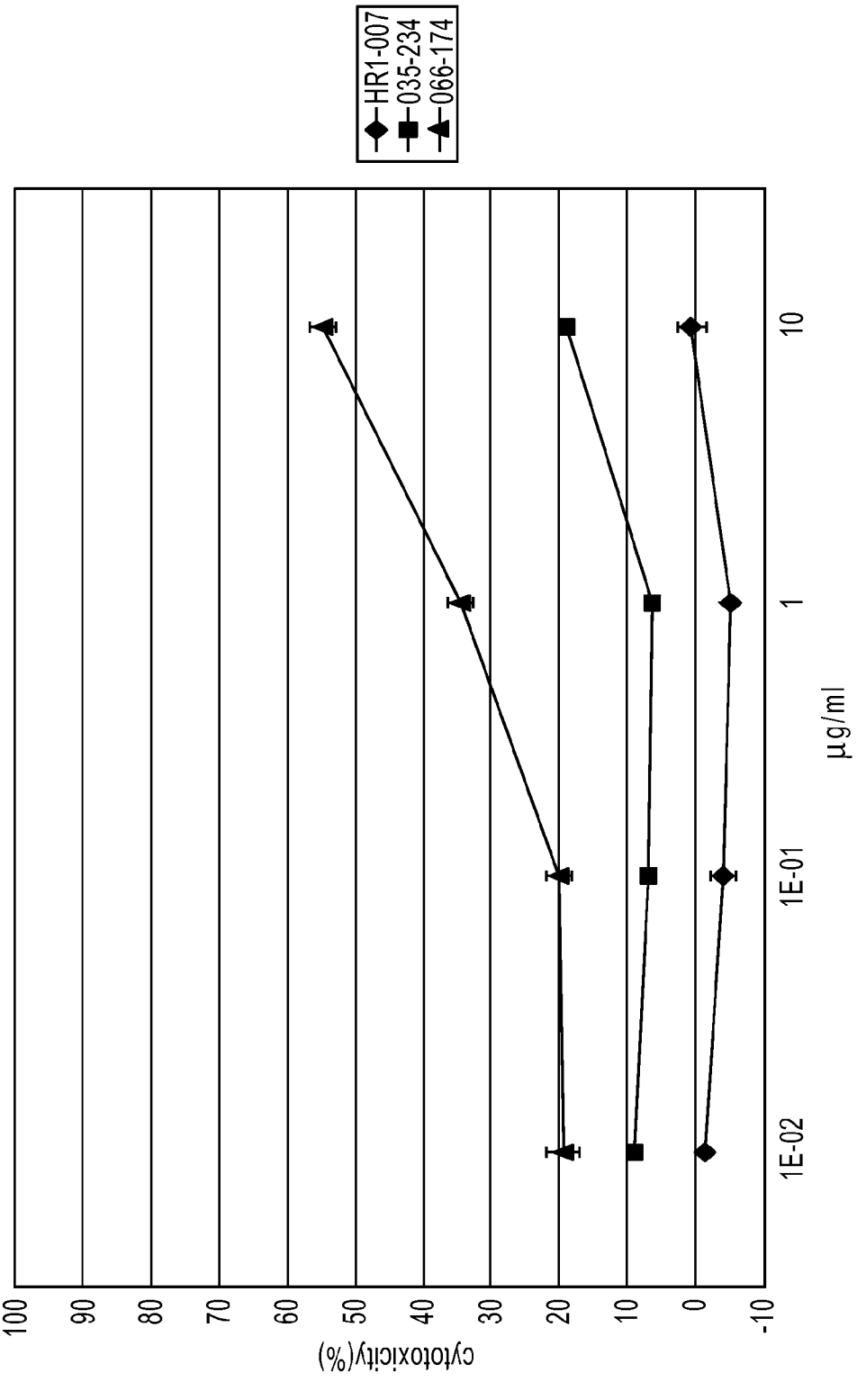

HR1-007
035-234
066-174
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1E-02
1E-01
1
10
μg/ml

Fig.55

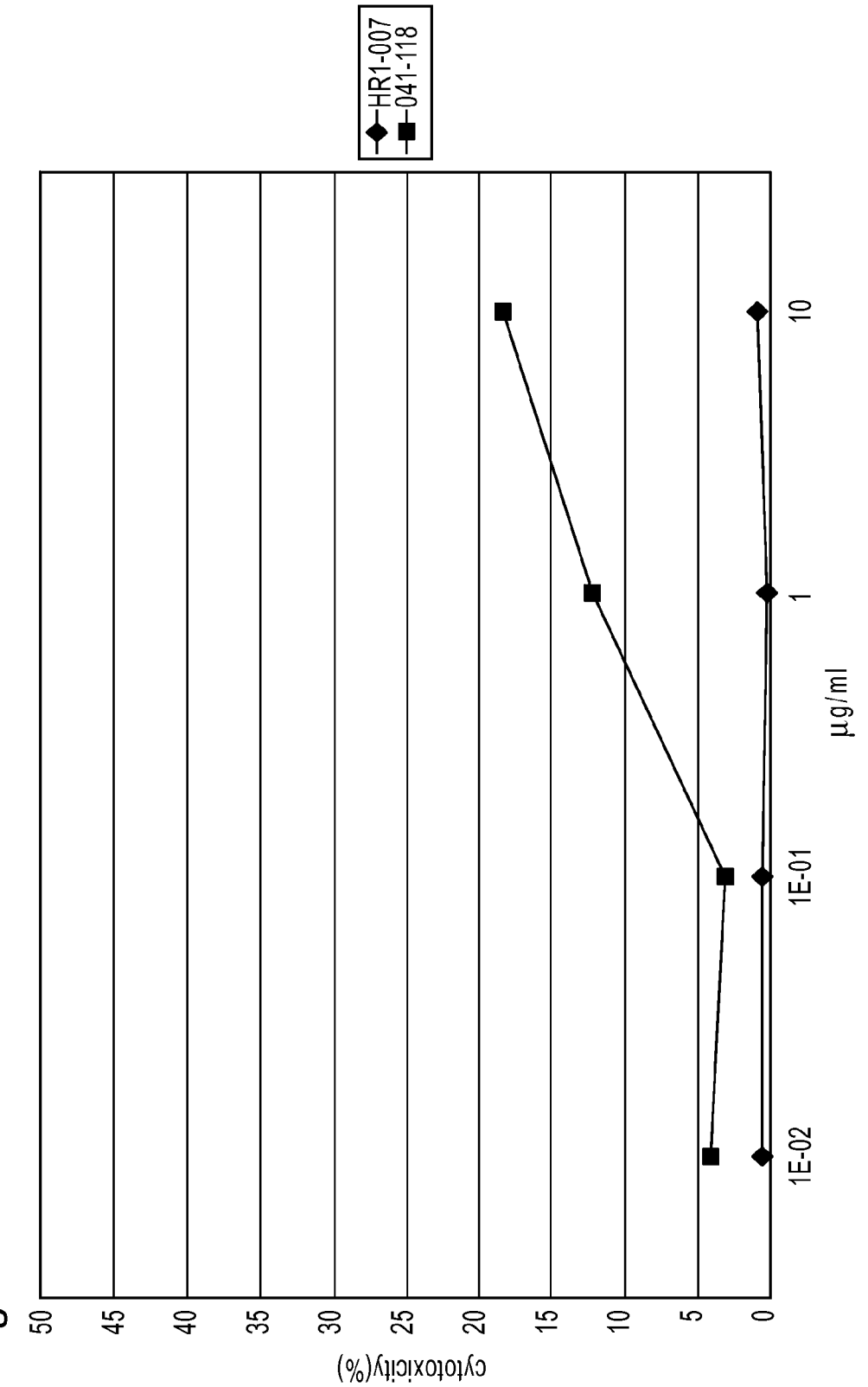

HR1-007
041-118
cytotoxicity(%)
50
45
40
35
30
25
20
15
10
5
0
1E-02
1E-01
1
10
μg/ml

Fig.56

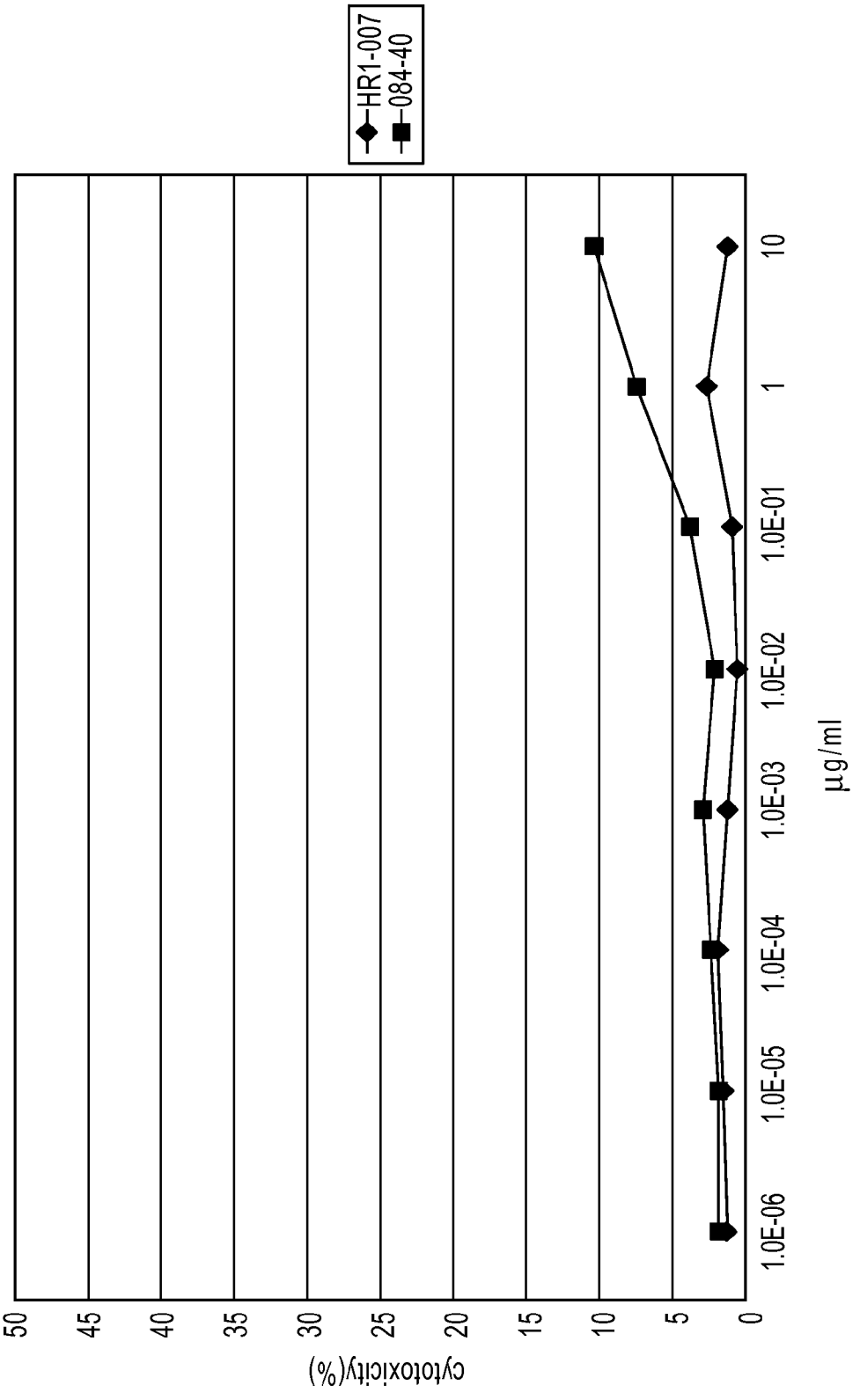

HR1-007
084-40
cytotoxicity(%)
0
5
10
15
20
25
30
35
40
45
50
1.0E-06
1.0E-05
1.0E-04
1.0E-03
1.0E-02
1.0E-01
1
10
μg/ml

Fig.57

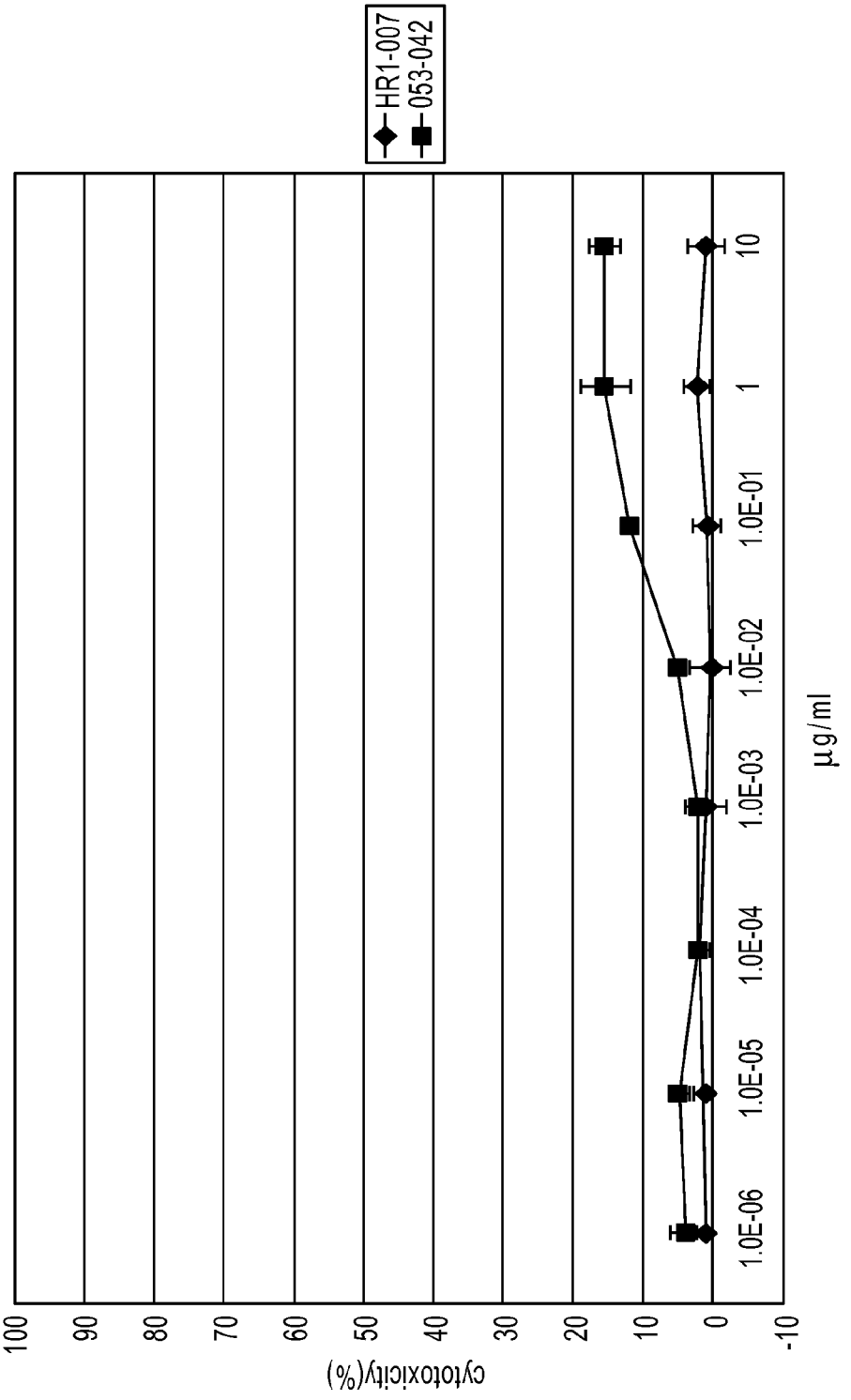

HR1-007
053-042
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1.0E-06
1.0E-05
1.0E-04
1.0E-03
1.0E-02
1.0E-01
1
10
μg/ml

Fig.58

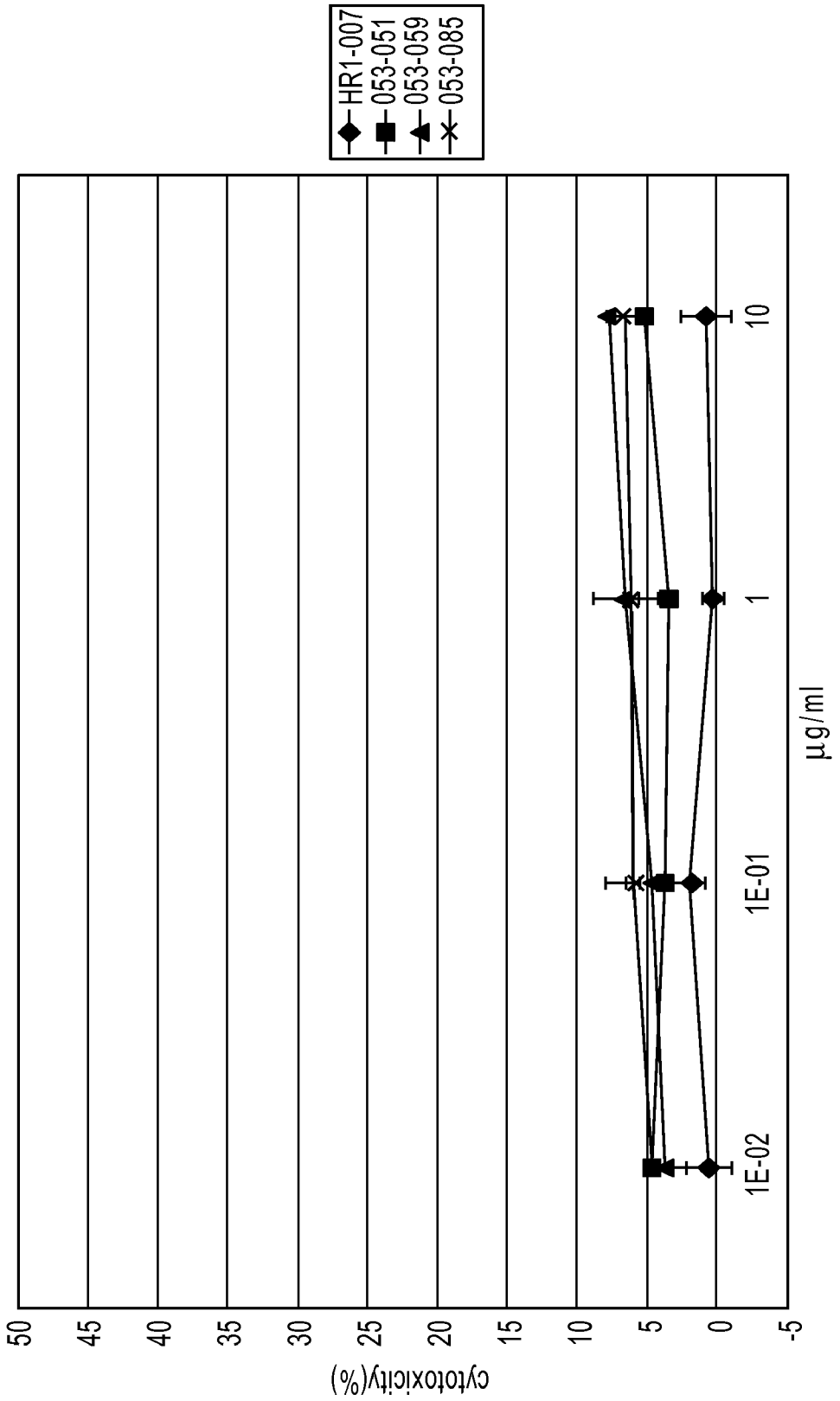

HR1-007
053-051
053-059
053-085
cytotoxicity(%)
50
45
40
35
30
25
20
15
10
5
0
-5
1E-02
1E-01
1
10
μg/ml

Fig.59

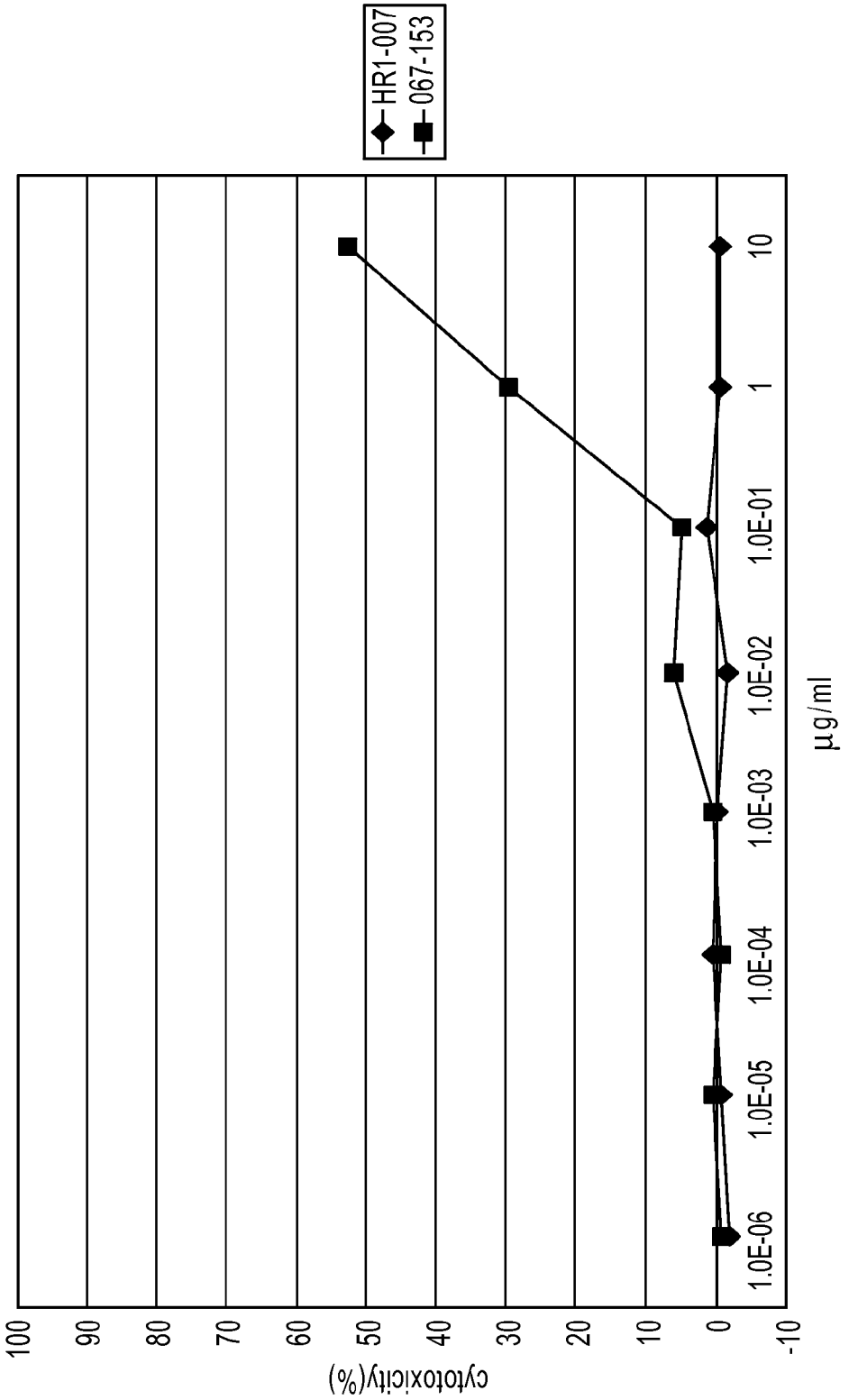

HR1-007
067-153
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1.0E-06
1.0E-05
1.0E-04
1.0E-03
1.0E-02
1.0E-01
1
10
μg/ml

Fig. 60

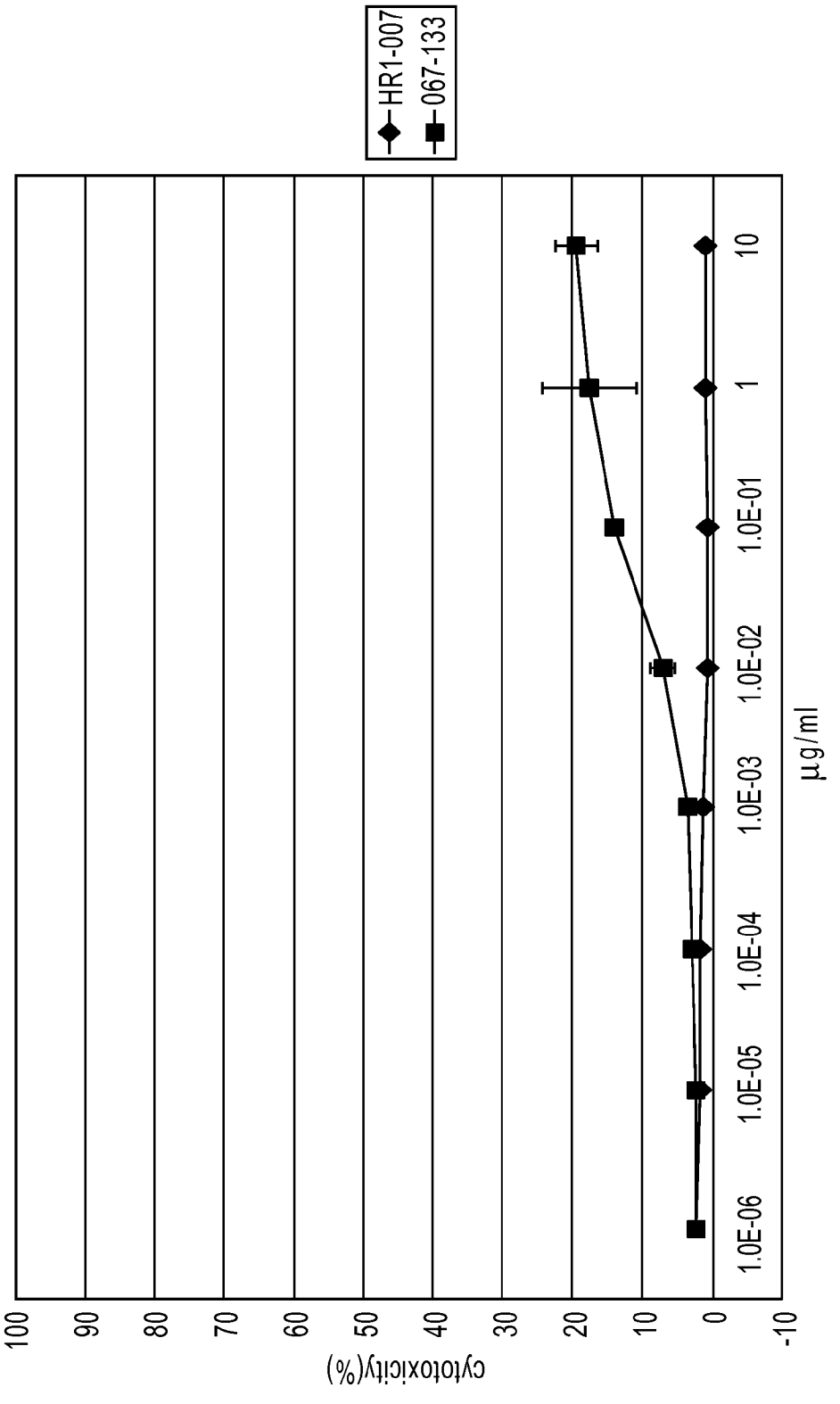

HR1-007
067-133
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1.0E-06
1.0E-05
1.0E-04
1.0E-03
1.0E-02
1.0E-01
1
10
μg/ml

Fig.61

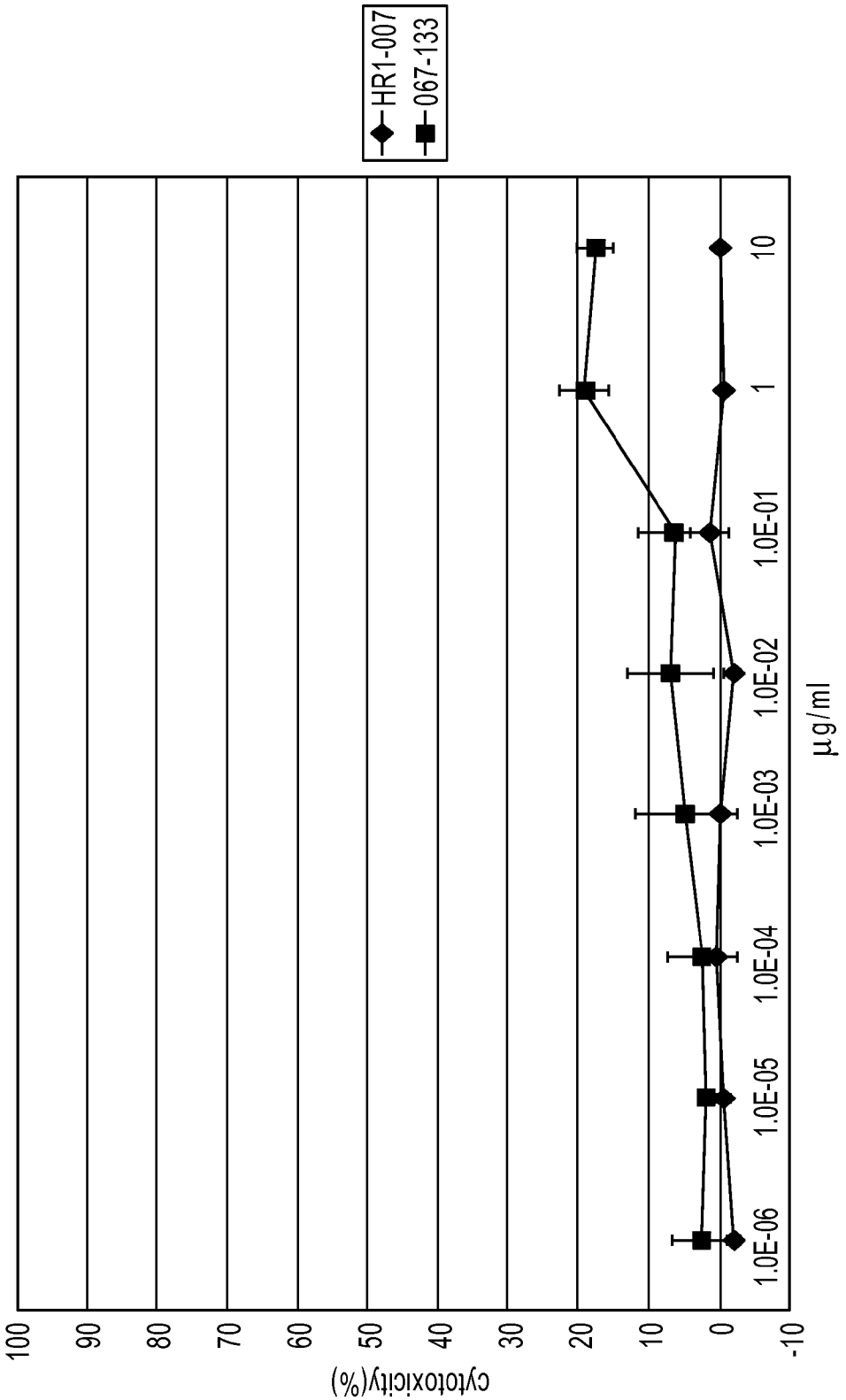

HR1-007
067-133
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1.0E-06
1.0E-05
1.0E-04
1.0E-03
1.0E-02
1.0E-01
1
10
μg/ml

Fig.62

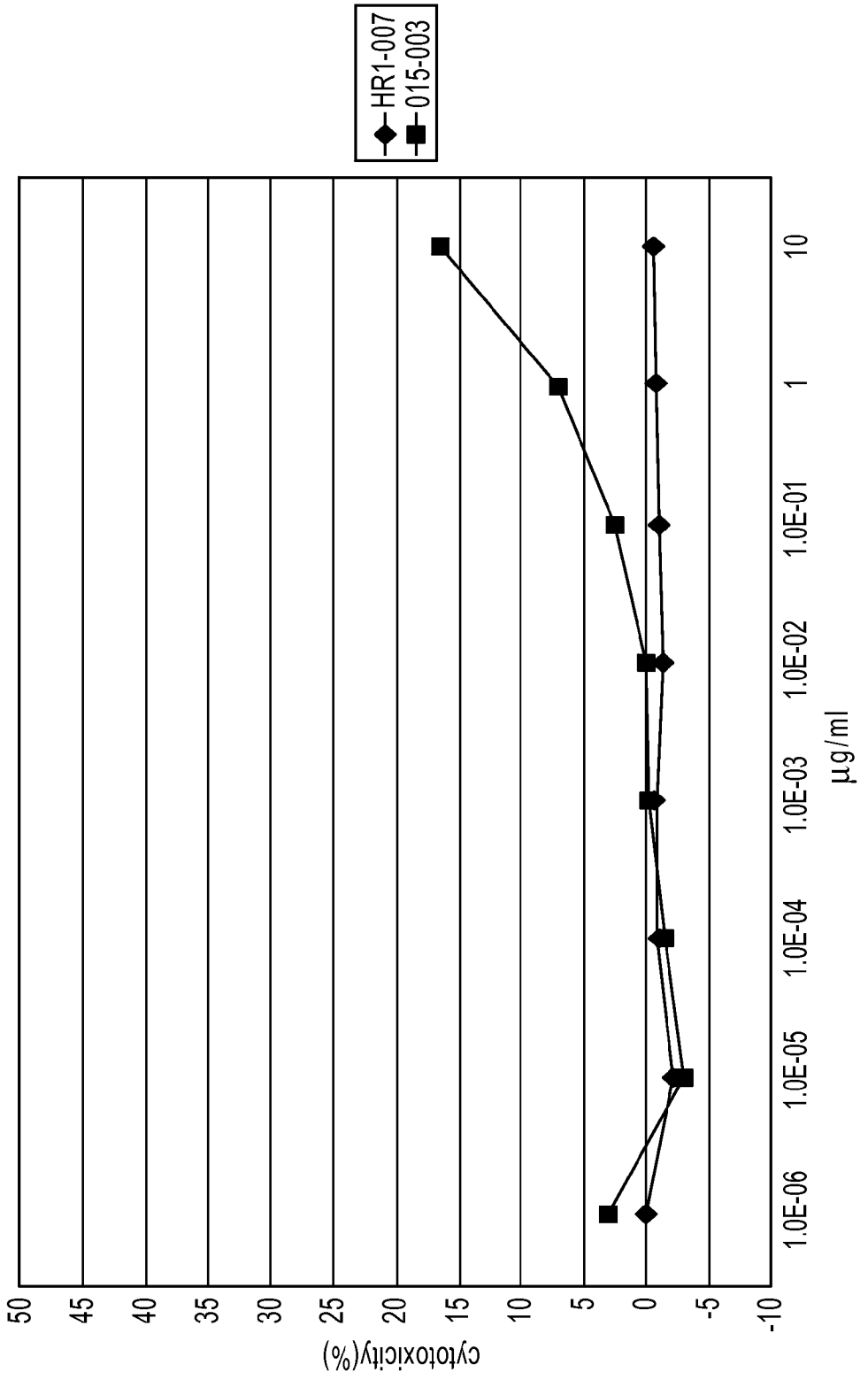

HR1-007
015-003
cytotoxicity(%)
50
45
40
35
30
25
20
15
10
5
0
-5
-10
1.0E-06
1.0E-05
1.0E-04
1.0E-03
1.0E-02
1.0E-01
1
10
μg/ml

Fig.63

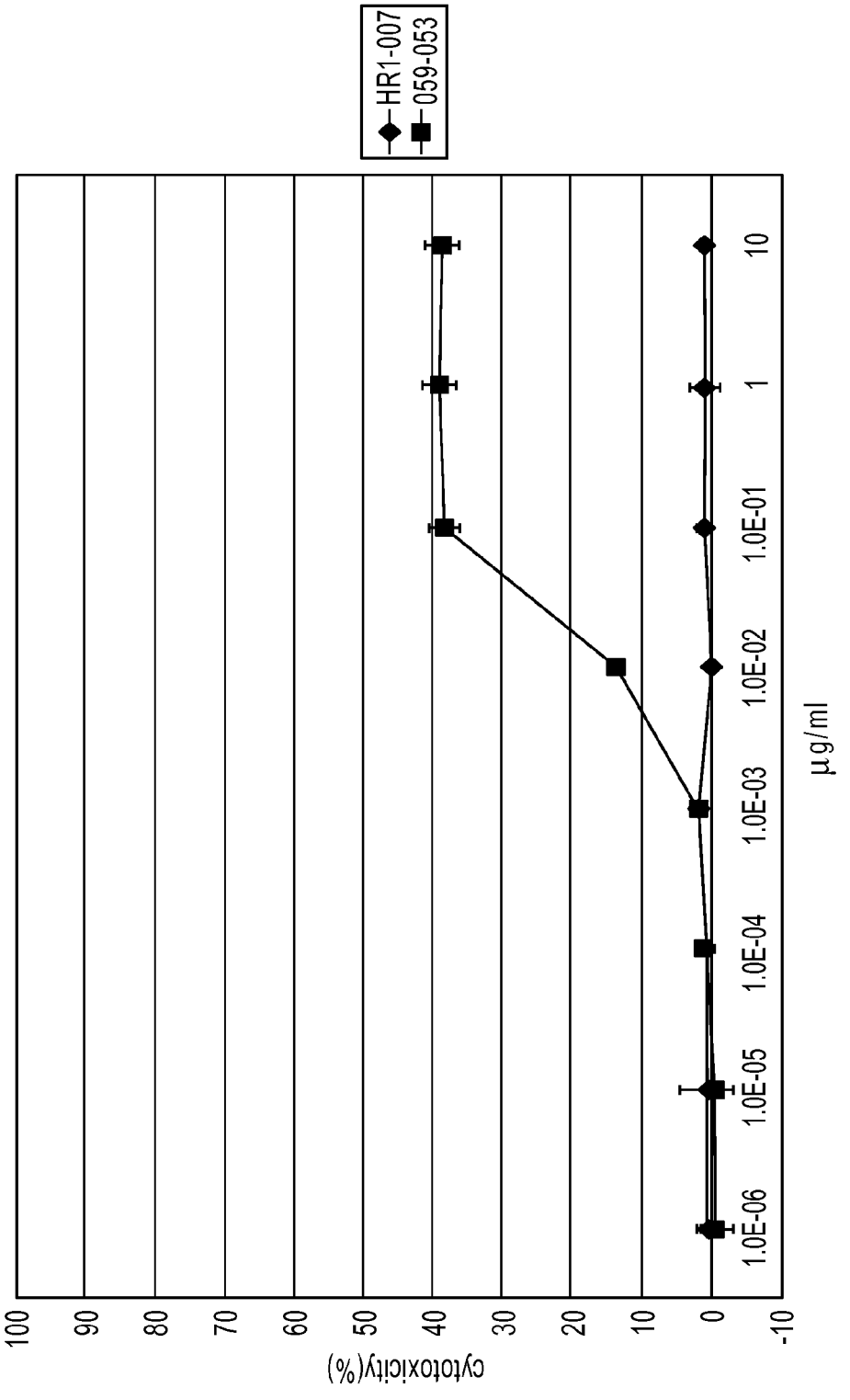

HR1-007
059-053
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1.0E-06
1.0E-05
1.0E-04
1.0E-03
1.0E-02
1.0E-01
1
10
μg/ml

Fig.64

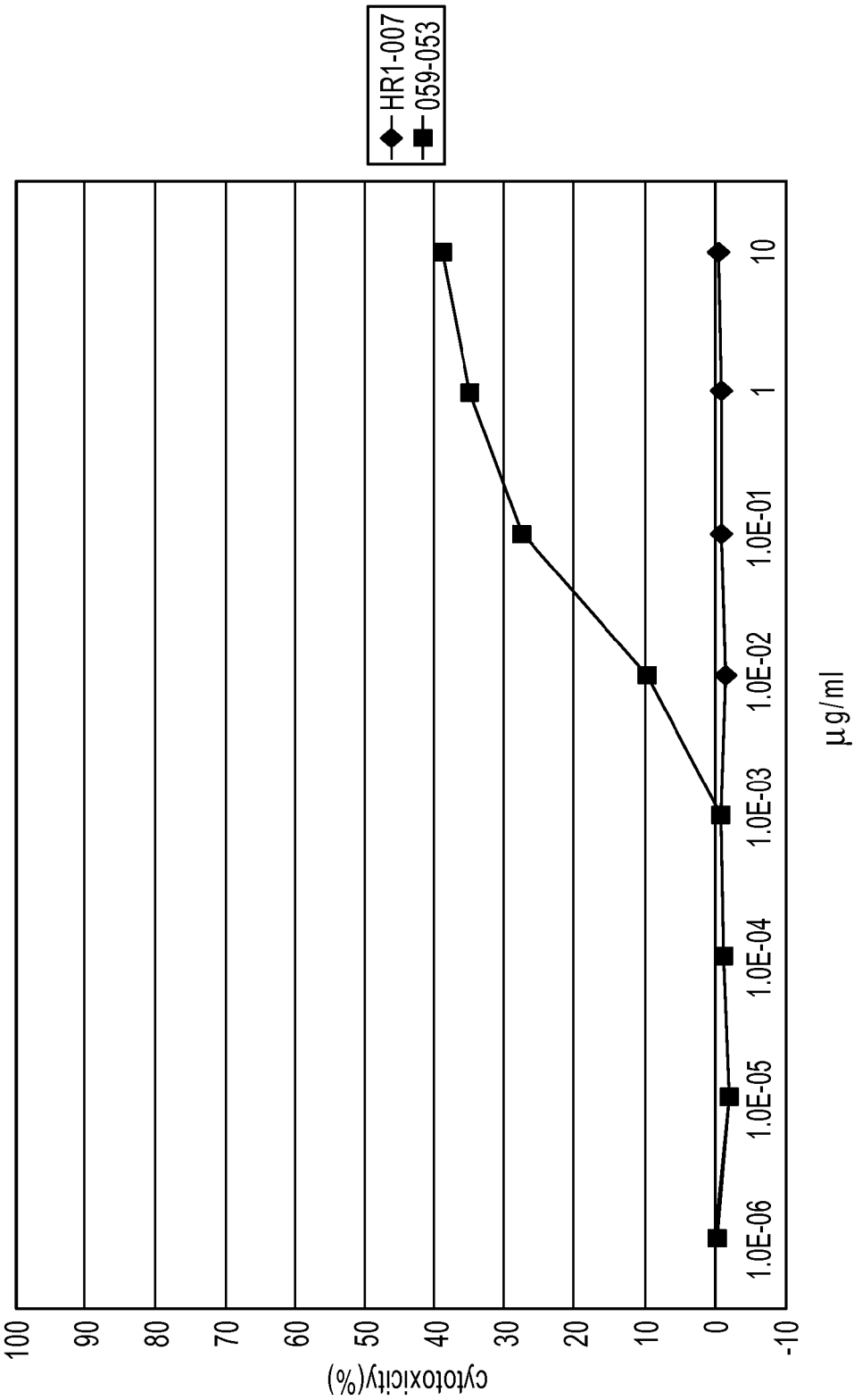
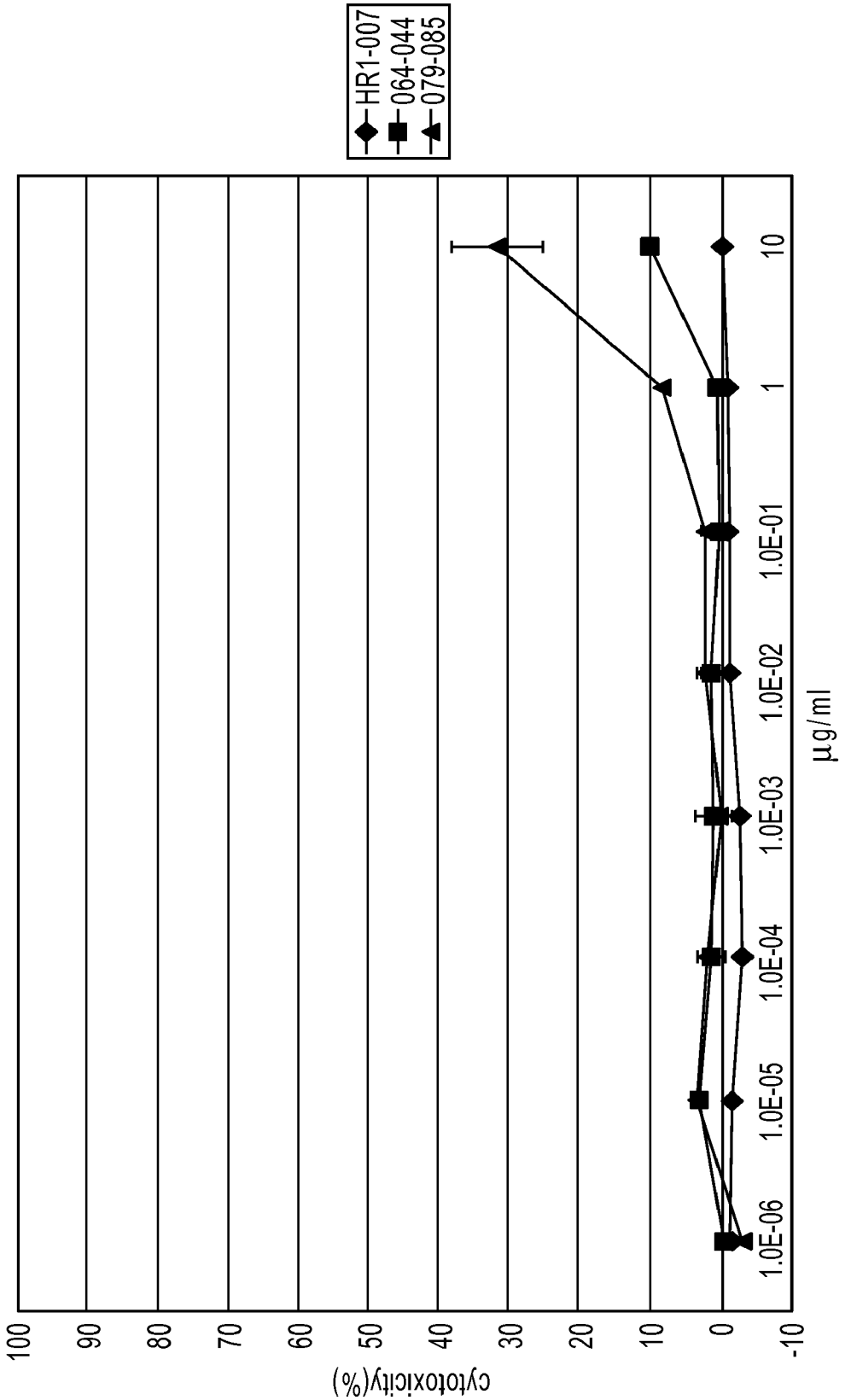

HR1-007
059-053
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1.0E-06
1.0E-05
1.0E-04
1.0E-03
1.0E-02
1.0E-01
1
10
μg/ml

Fig.65


HR1-007
064-044
079-085
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1.0E-06
1.0E-05
1.0E-04
1.0E-03
1.0E-02
1.0E-01
1
10
μg/ml

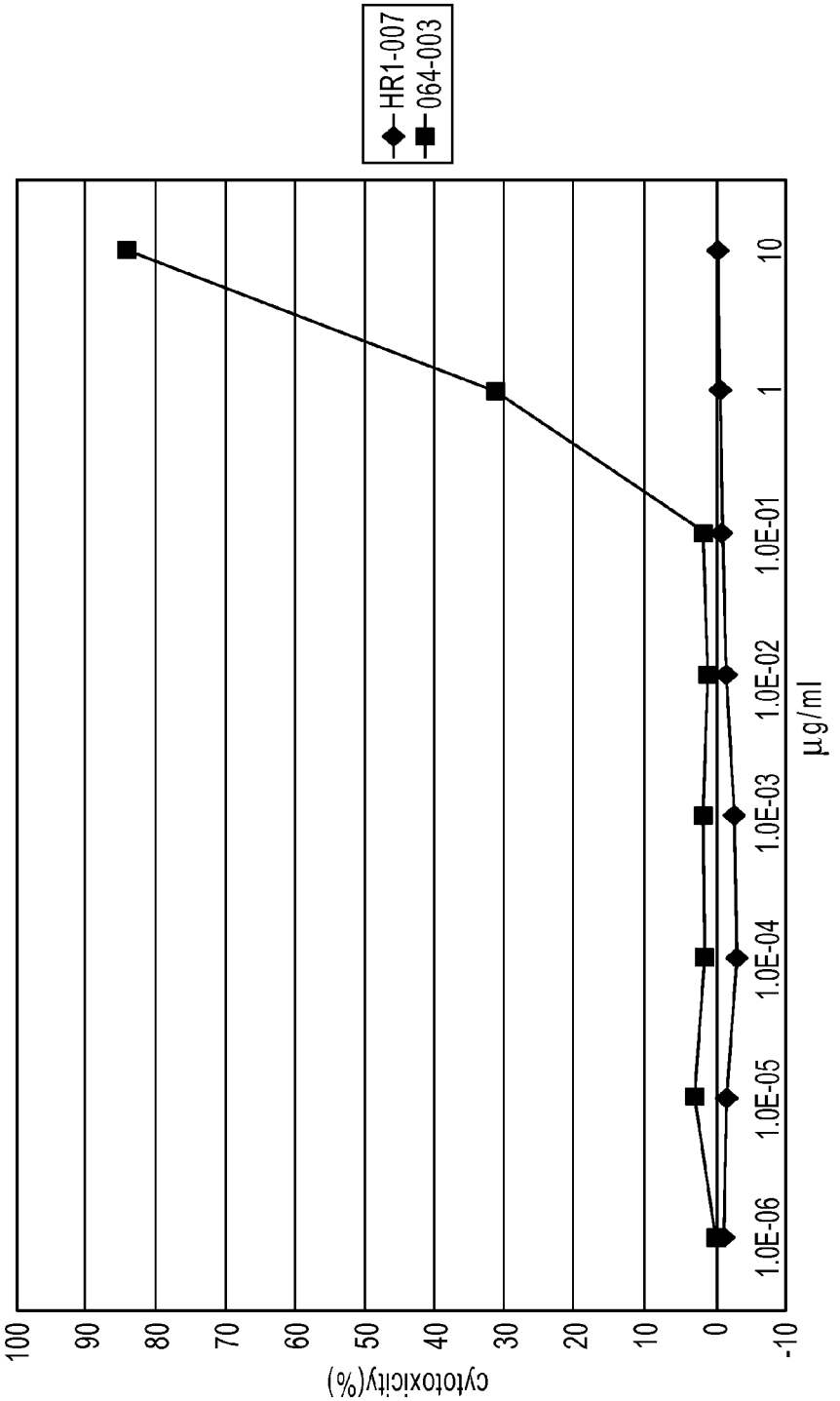

HR1-007
064-003
cytotoxicity(%)
100
90
80
70
60
50
40
30
20
10
0
-10
1.0E-06
1.0E-05
1.0E-04
1.0E-03
1.0E-02
1.0E-01
1
10
μg/ml

Fig. 66

Fig.67

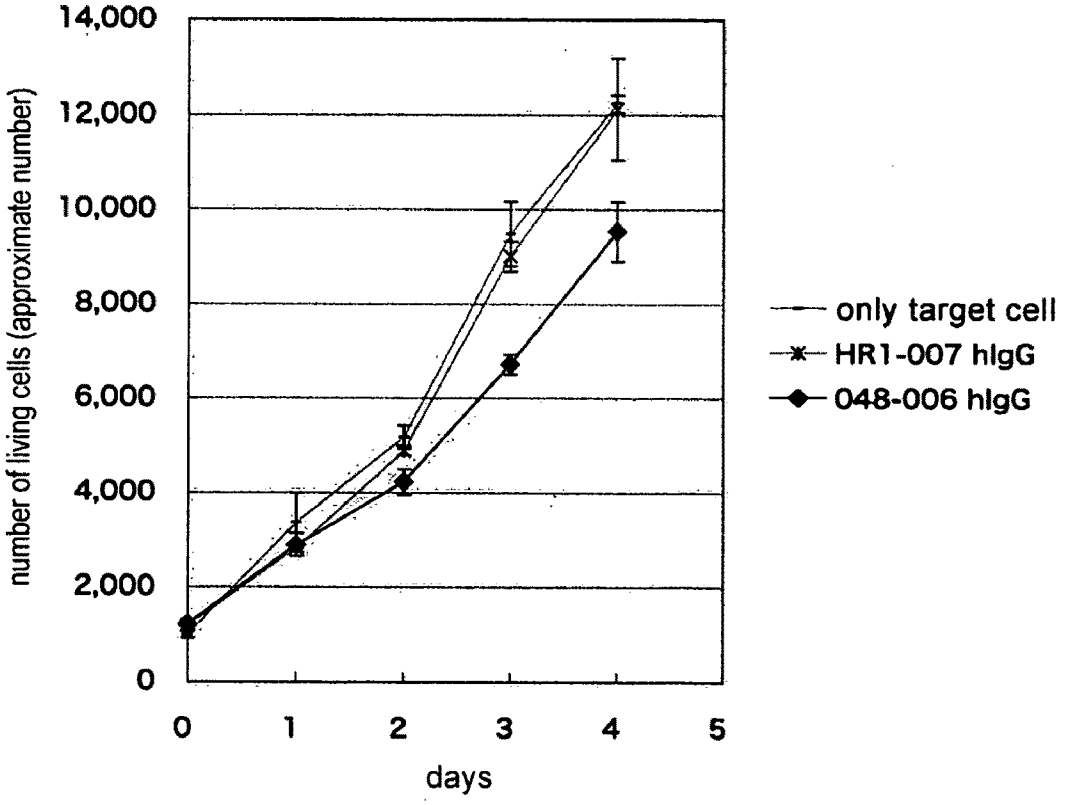

14,000
12,000
10,000
8,000
6,000
4,000
2,000
0
number of living cells (approximate number)
0
1
2
3
4
5
days
only target cell
HR1-007 hIgG
048-006 hIgG

Fig.68

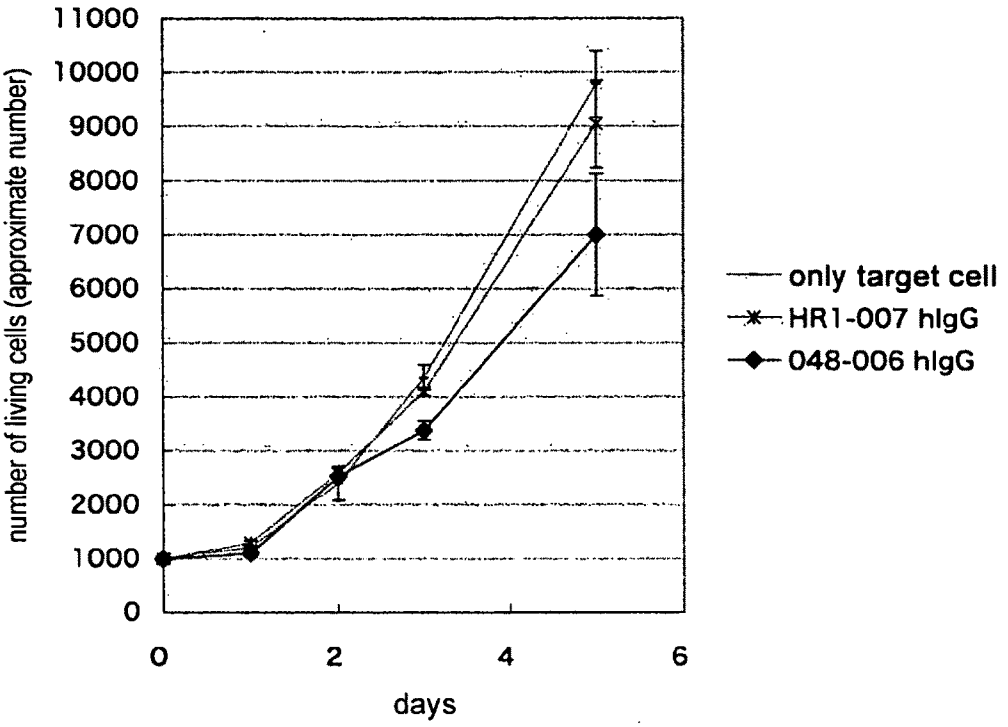

11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
number of living cells (approximate number)
0
2
4
6
days
only target cell
HR1-007 hIgG
048-006 hIgG

Fig.69

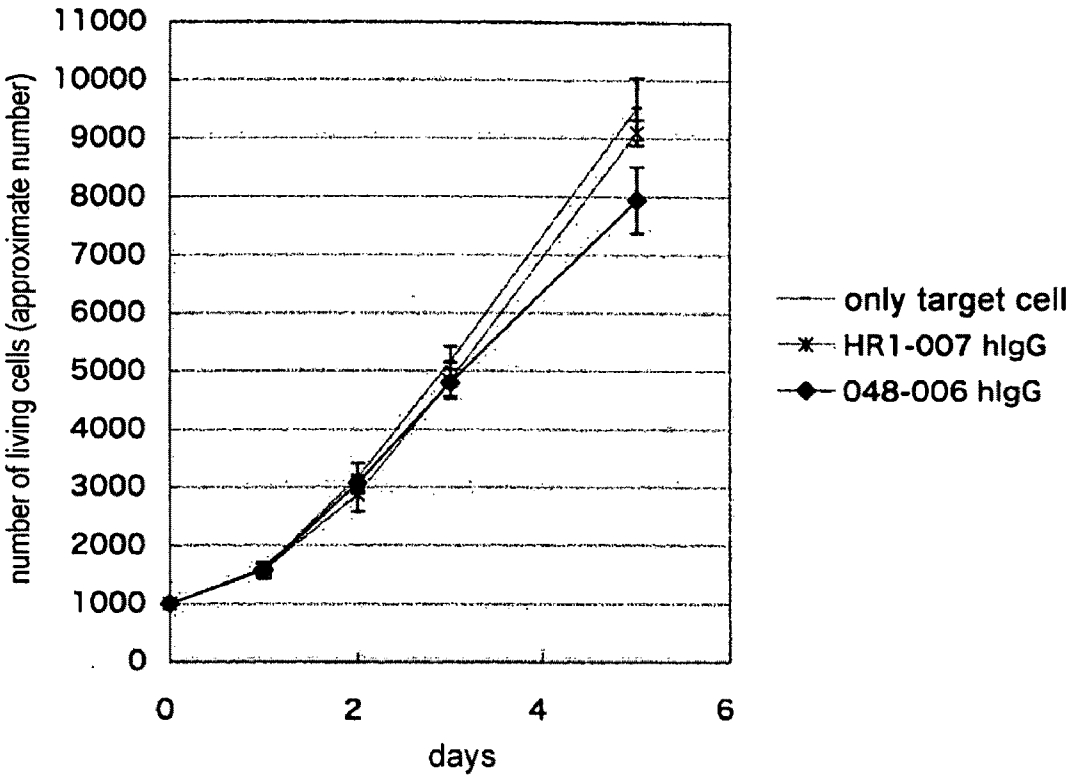

11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
number of living cells (approximate number)
0
2
4
6
days
only target cell
HR1-007 hIgG
048-006 hIgG

Fig.70

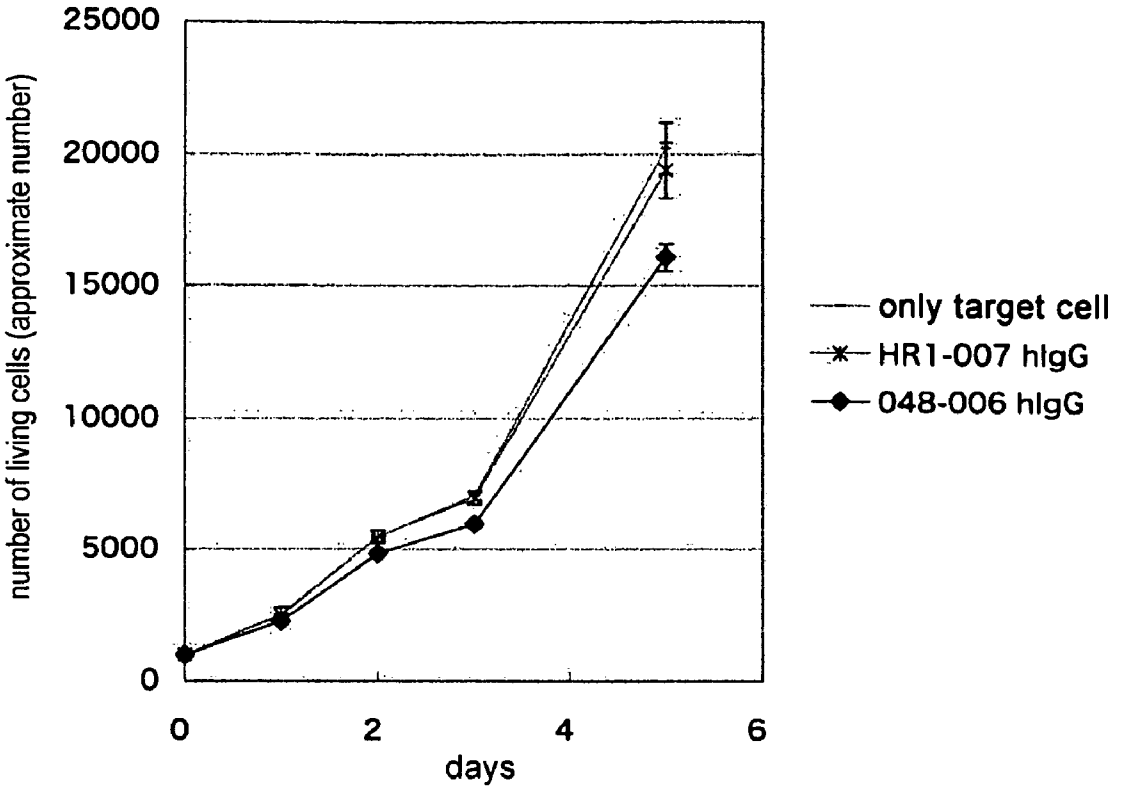

25000
20000
15000
10000
5000
0
number of living cells (approximate number)
0
2
4
6
days
only target cell
HR1-007 hIgG
048-006 hIgG

Fig.71

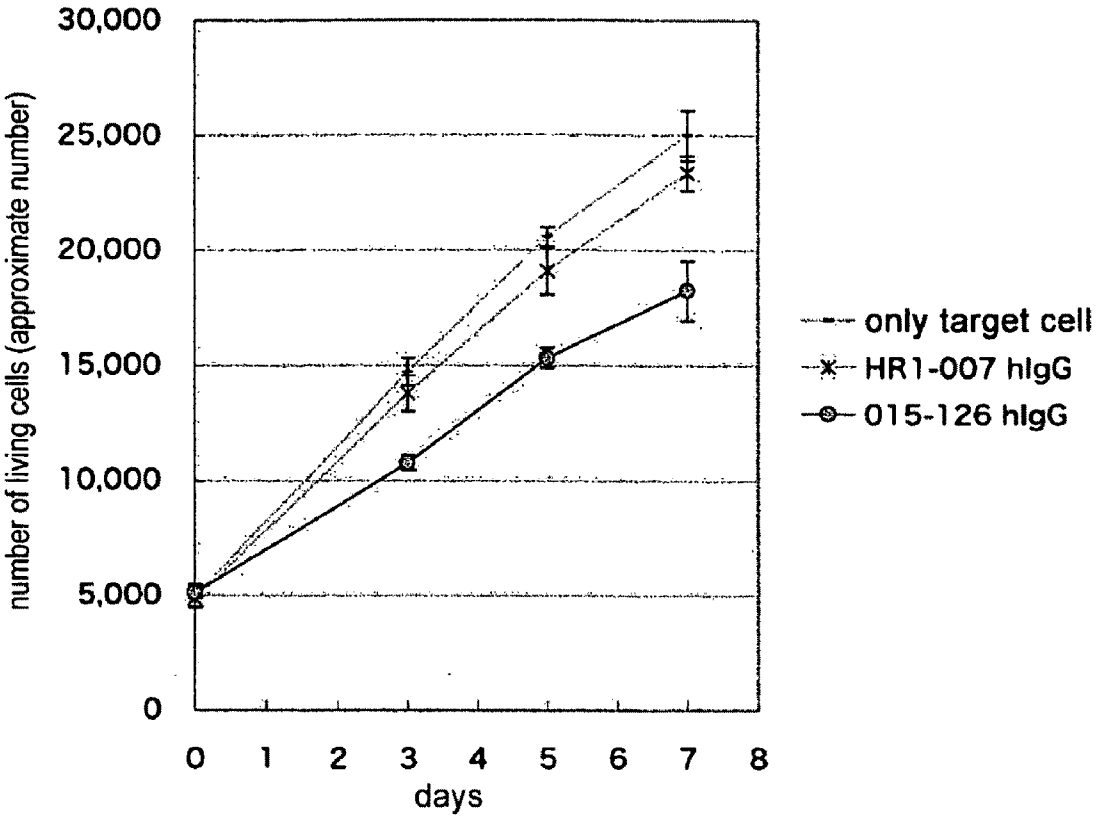

30,000
25,000
20,000
15,000
10,000
5,000
0
number of living cells (approximate number)
0 1 2 3 4 5 6 7 8
days
only target cell
HR1-007 hIgG
015-126 hIgG

Fig.72

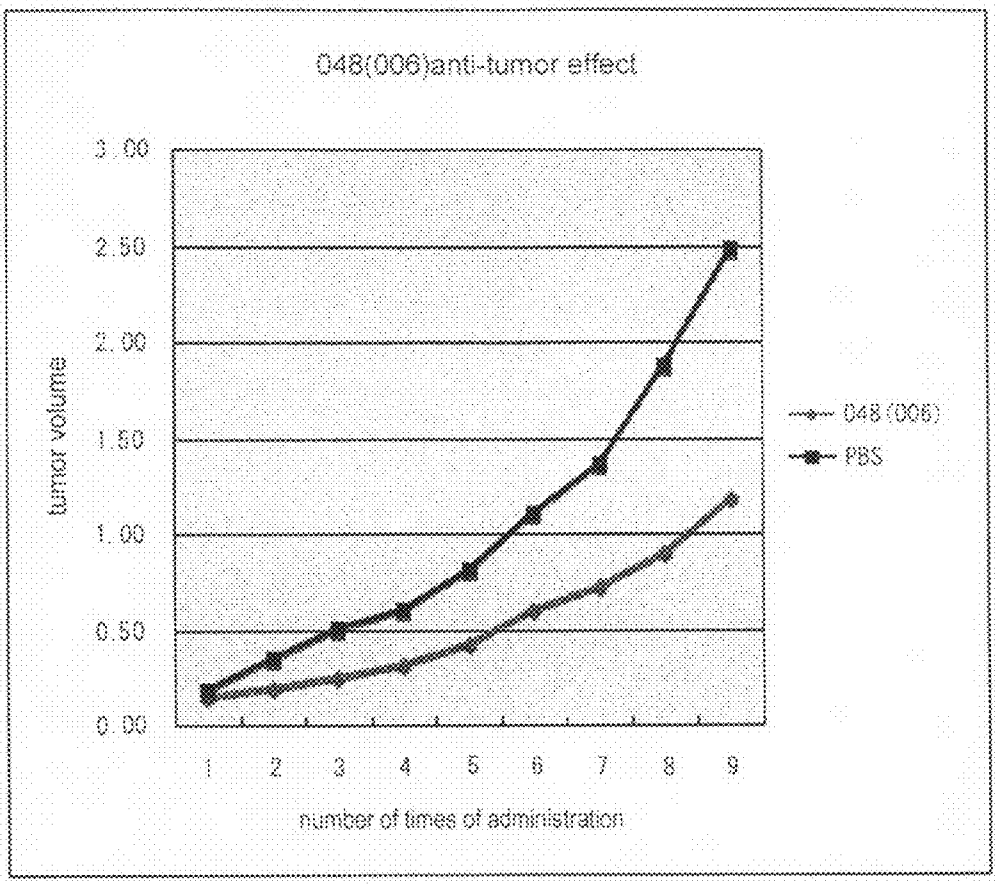

048(006)anti-tumor effect
3.00
2.50
2.00
1.50
1.00
0.50
0.00
tumor volume
1
2
3
4
5
6
7
8
9
number of times of administration
048 (006)
PBS

Fig. 73

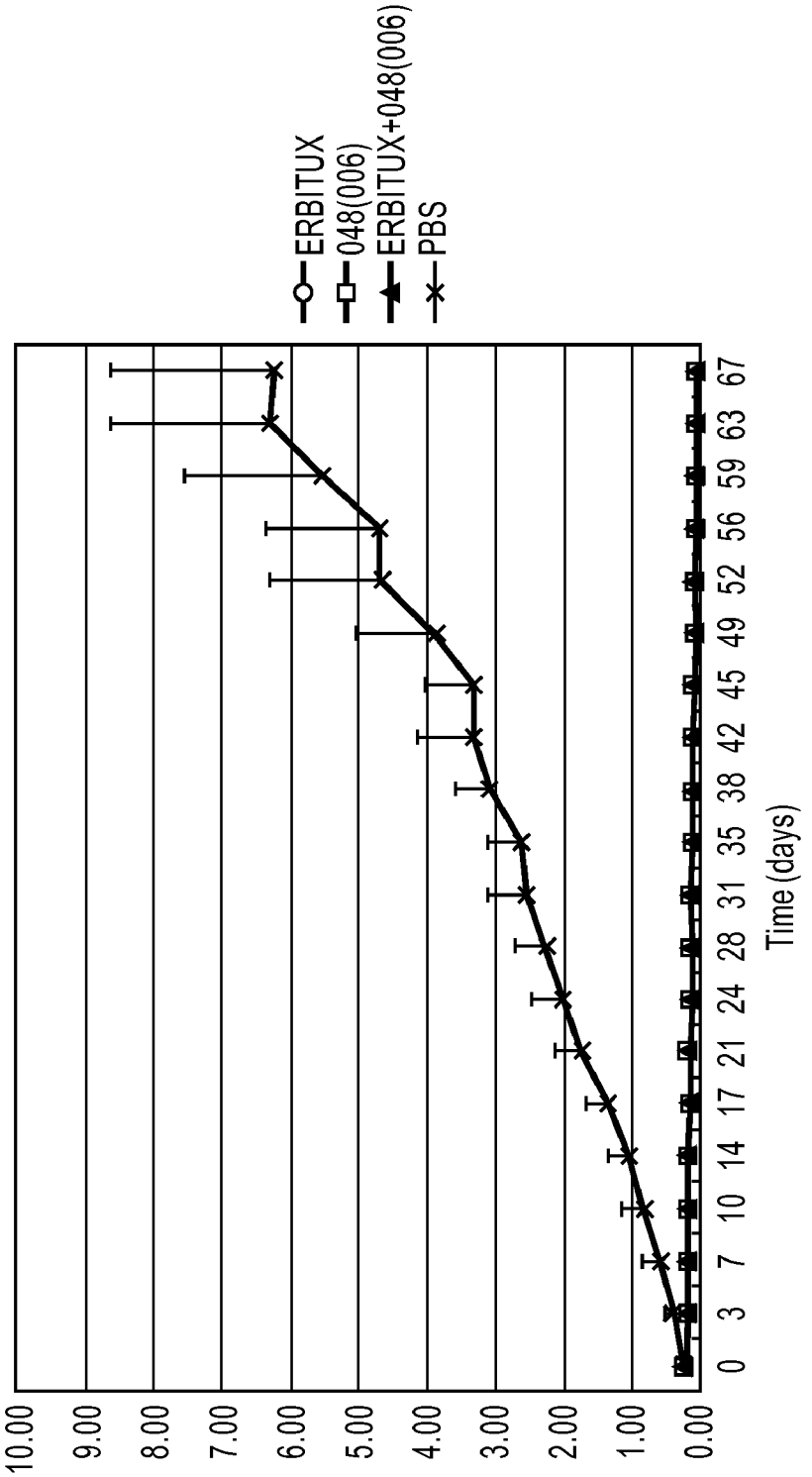
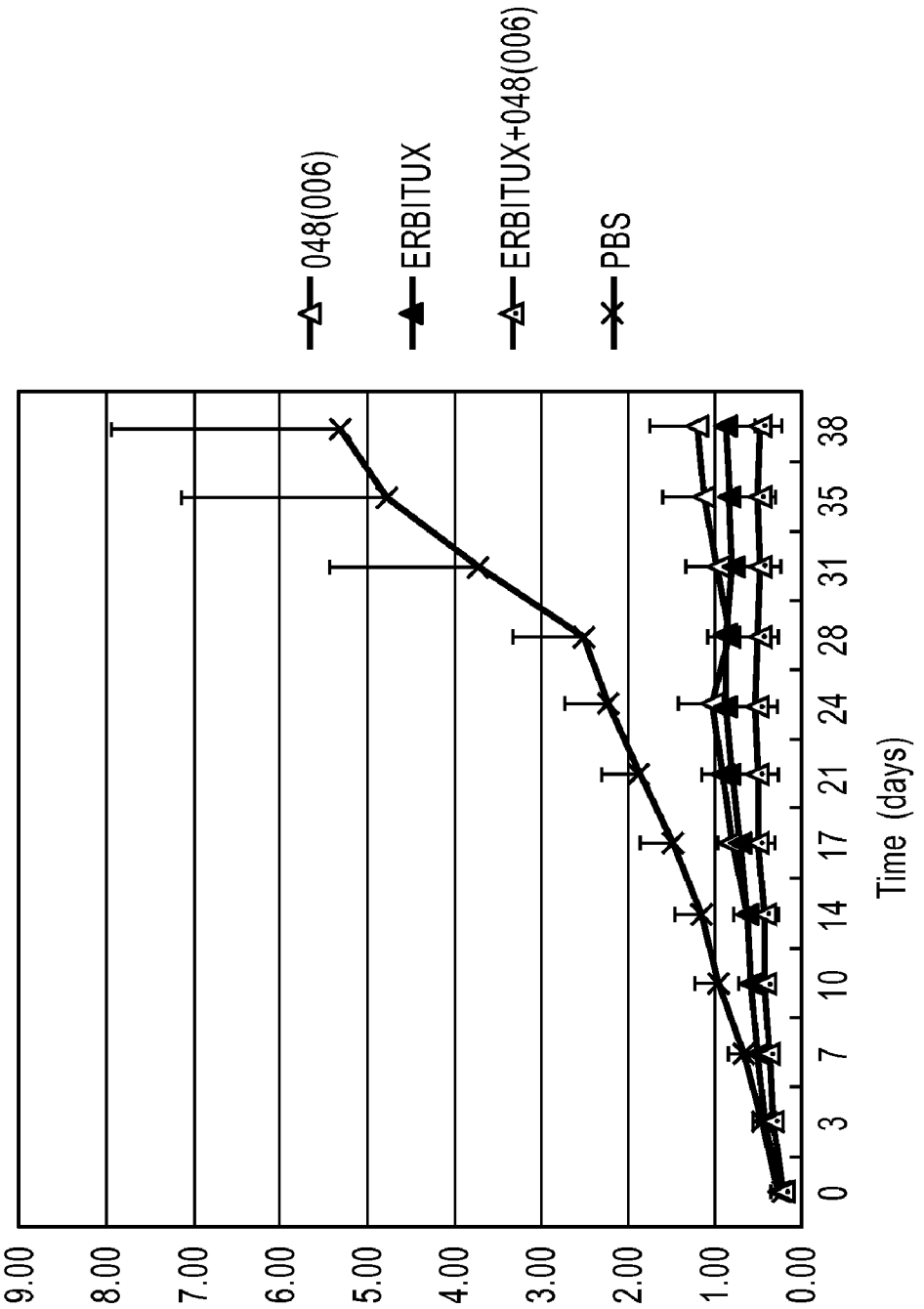

ERBITUX
048(006)
ERBITUX+048(006)
PBS
10.00
9.00
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
0 3 7 10 14 17 21 24 28 31 35 38 42 45 49 52 56 59 63 67
Time (days)

Fig. 74


048(006)
ERBITUX
ERBITUX+048(006)
PBS
9.00
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
0
3
7
10
14
17
21
24
28
31
35
38
Time (days)

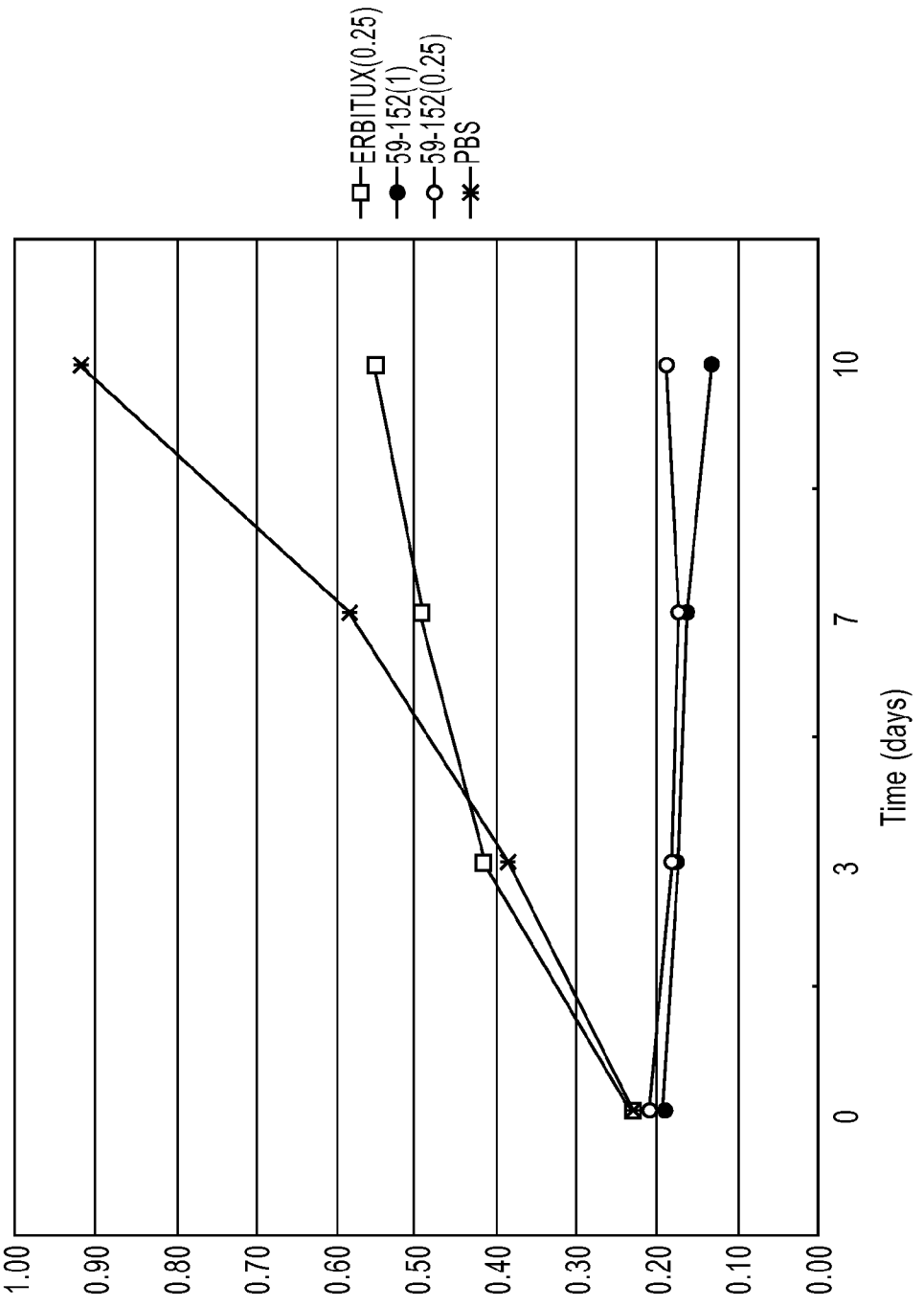

ERBITUX(0.25)
59-152(1)
59-152(0.25)
PBS
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
0
3
7
10
Time (days)

Fig. 75

Fig.76A

Ⓐ

	origin organ	name of cell line	origin
liver	HCV+	HepG2	
		Nuk-1	
		OCTH-16	
	HBV+	HT17	poorly differentiated hepatic cell carcinoma
	HBV+	Hep3B	
	immortalize liver cell	THLE-3	
	intrahepatic bile duct cancer	HLF	hepatic left lobe
		RBE	undifferentiated hepatic cell carcinoma
kidney	clear cell carcinoma	CCF-RC1	
		CCF-RC2	
		Caki-1	
		Caki-2	
	adenocarcinoma	ACHN	
	normal	293	established from abdominal dropsy
		040520IT	
pancreas		MIA-PaCa2	
		PANC-1	
lung cancer	adenocarcinoma	A549	
		PC-14	lung-derived poorly differentiated
		NCI-N441	papillary type adenocarcinoma
		Calu-3	abdominal dropsy
	squamous cell carcinoma line	EBC-1	
		RERF-LC-AI	
stomach cancer	adenocarcinoma	MKN-45	solid-type gastric adenocarcinoma
		SNU-5	poorly differentiated adenocarcinoma
		NCI-N87	from highly differentiated liver metastatic focus
ovarian cancer	adenocarcinoma	SKOv3	abdominal dropsy
		KF28	
	ovarian mesonephroma	RMG-1	
	ovarian mesonephroma	RMG-2	
large bowel	colon adenocarcinoma	CACO-2	
		CW-2	

Ⓐ *Fig.76B*

	medium	subculture method
	DMEM+10%FBS+NEAA or GIT	0.25%Trypsin
	Williams+10%FBS	
	Williams+10%FBS	
	EMEM+2mM L-glutamine+10%FBS (or Williams+1-%FBS)	
	EMEM+2mM L-glutamine+10%FBS (or Williams+1-%FBS)	
	special medium	
	DMEM+10%FBS+100μg/ml Kanamycin	0.2%Trypsin+0.02%EDTA
	RPMI1640+10%FCS	0.25%Trypsin
	RPMI1640	Trypsin-EDTA
	10%FBS	Trypsin-EDTA
	1%Pn-SM	Trypsin-EDTA
	MEM+10%FCS+NEAA	0.25%Trypsin
	DMEM-F12+10%FBS+1%Pn-SM	EDTA solution
	DMEM(including 4mM L-glutamin·1.5g/L sodium bicarbonate ·4.5g/L glucose) +10%FBS+2.5%horse serum	0.25%Trypsin, 0.53 mM EDTA solution
	RPMI1640+10%FCS or Eagle's MEM+10%FBS	0.02%EDTA-PBS
	DMEM+10%FBS	0.25%Trypsin
	RPMI1640+10%FBS	Dilution
	RPMI1640 (2mM L=glutamine·1.5g/L NaHCO3·4.5g/L glucose· 10mM HEPES·1.0mMSodiumPyruvate) +10%FBS	0.25%Trypsin+0.02%EDTA
	EMEM (2mM L-glutamine·1.5g/L NaHC03·4.5g/L glucose· 10mM HEPES·1.0mMSodiumPyravate) +10%FBS	0.25%Trypsin +0.53mM EDTA
	MEM+10% FBS or RPMI1640+10% FBS	0.25%Trypsin
	MEM+10%FBS	0.25%Trypsin
	RPMI1640+10%FBS	0.25%Trypsin+0.02%EDTA
	Iscove's Modified Dulbecco's Medium (with 4mM L-glutamine·1.5g/L NaHCO3)+20%FBS	Dilution after centrifugation
	RPMI1640 (2mM L-glutamine·1.5g/L NaHCO3·4.5g/L glucose· 10mM HEPES·1.0mMSodiumPyruvate) +10%FBS	0.25% Trypsin+0.53mM EDTA
	·1cCoy's 5a medium(with 1.5mM L-glutamine) +10%FBS	0.25%Trypsin+0.53mMEDTA
	Ham'sF12+10%FBS	0.25% Trypsin-0.02% EDTA
	MEM+20%FCS+NEAA	0.05%Trypsin+0.02%EDTA
	RPMI1640+10%FCS	0.25% Trypsin

Fig. 77

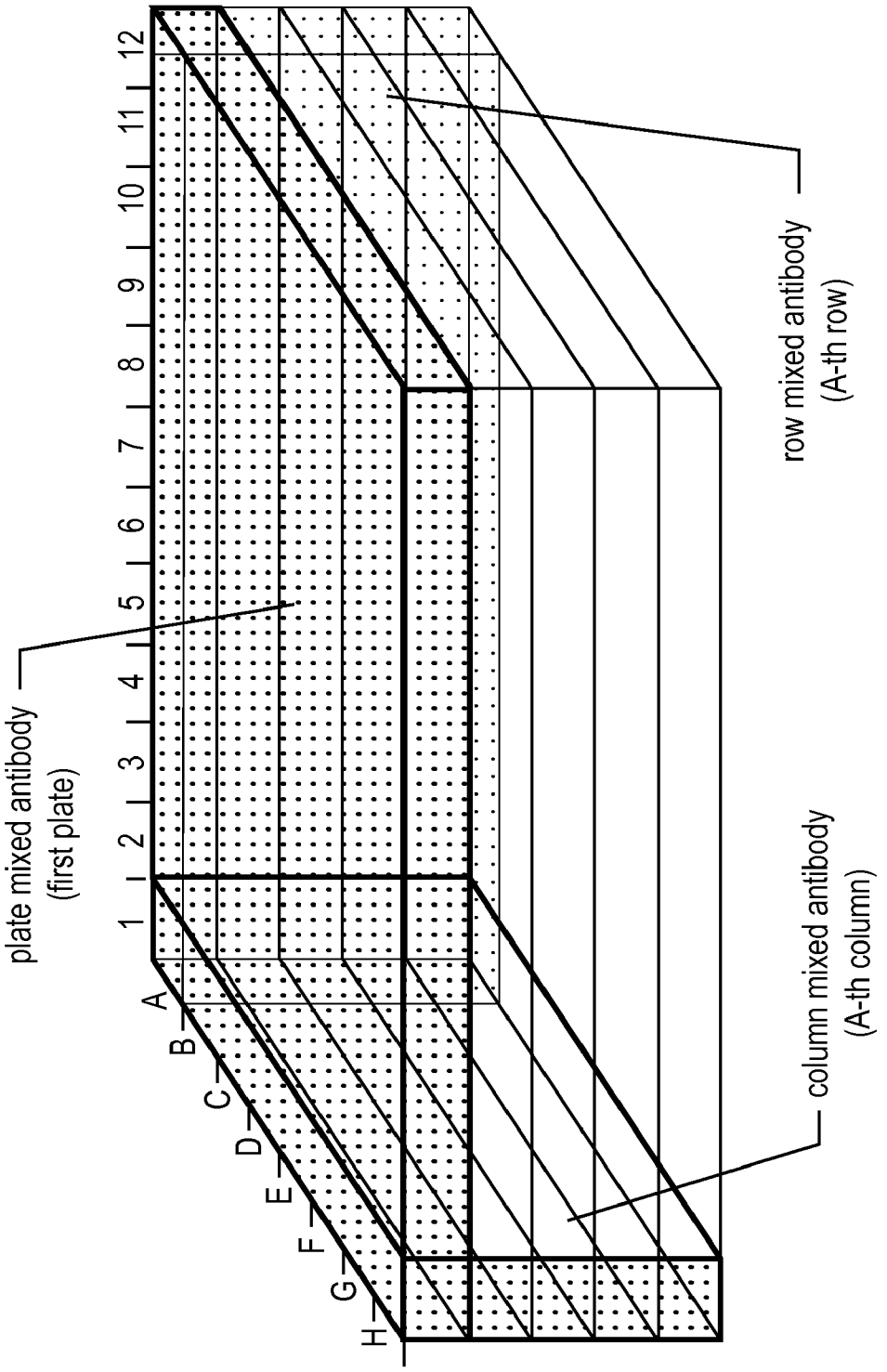


plate mixed antibody
(first plate)
row mixed antibody
(A-th row)
column mixed antibody
(A-th column)
A
B
C
D
E
F
G
H
1
2
3
4
5
6
7
8
9
10
11
12

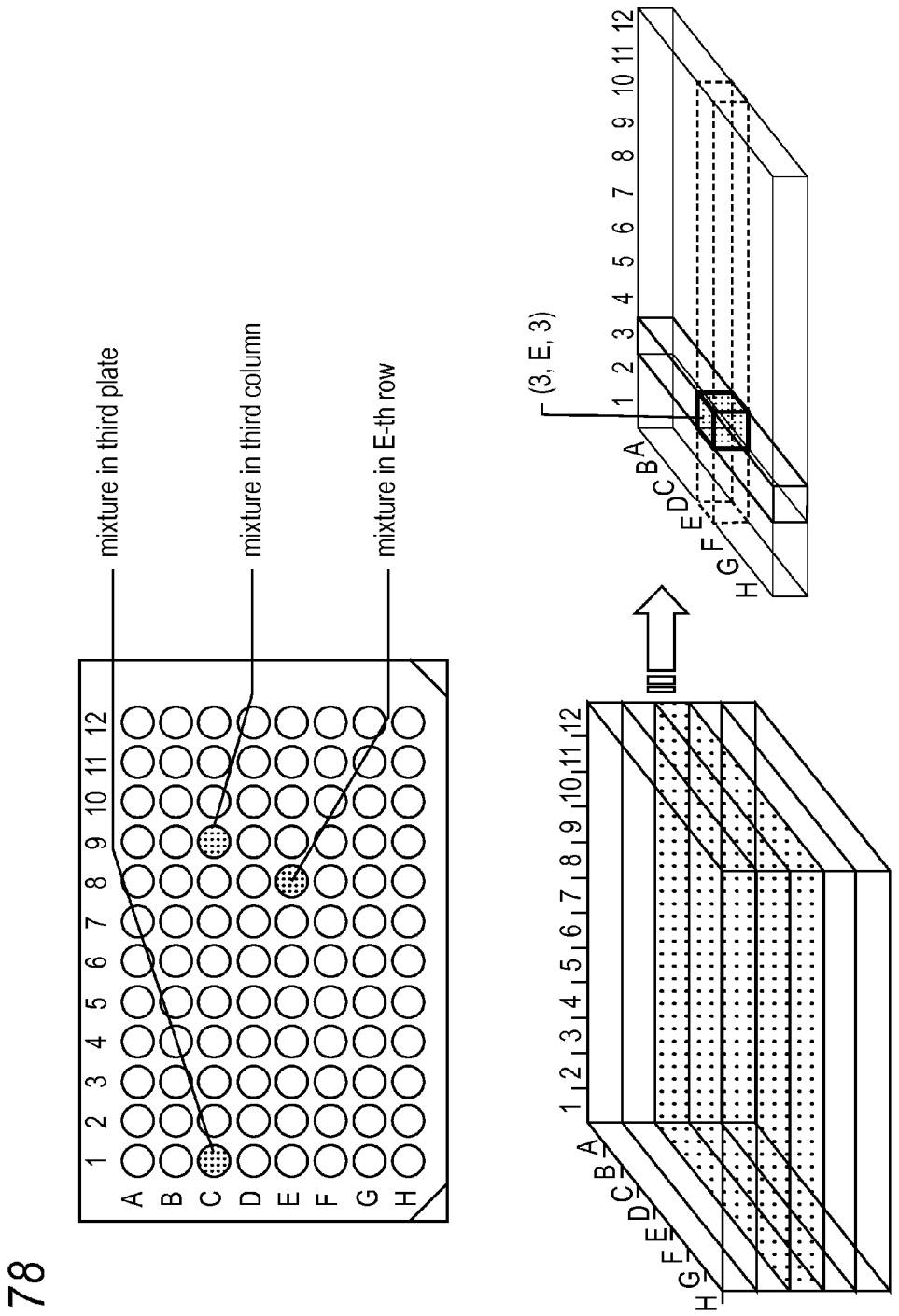

mixture in third plate
mixture in third column
mixture in E-th row
1 2 3 4 5 6 7 8 9 10 11 12
A B C D E F G H
(3, E, 3)

Fig. 78

Fig.79

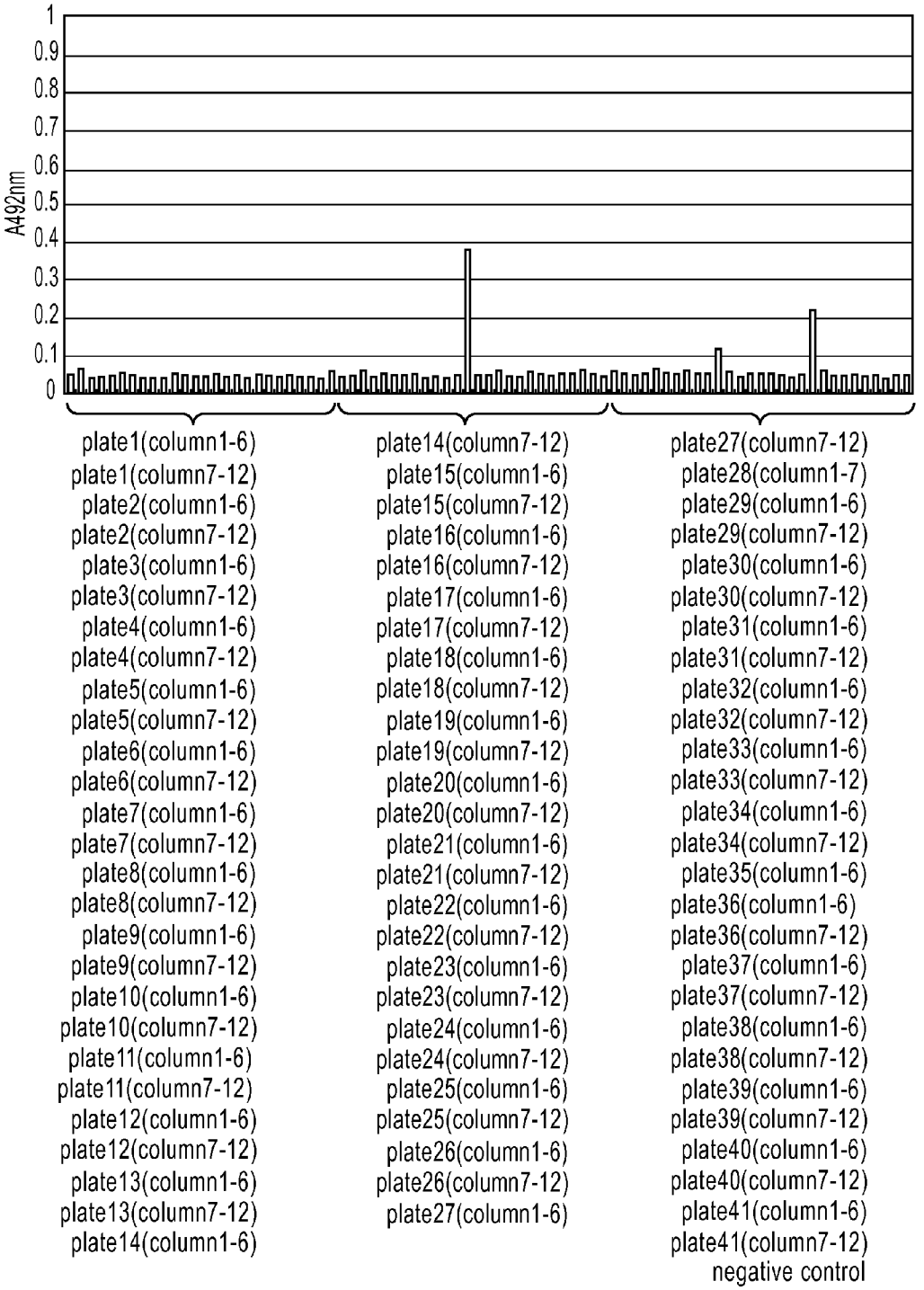
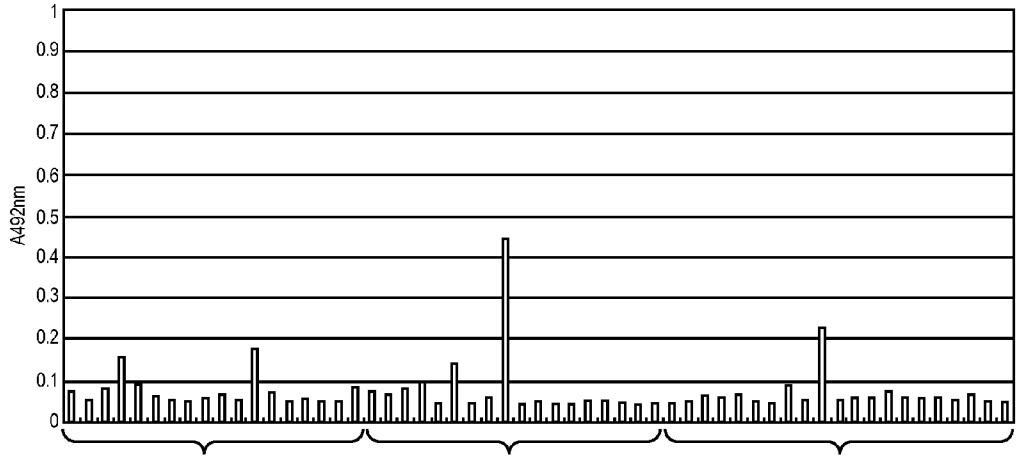

A492nm
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
plate1(column1-6)
plate1(column7-12)
plate2(column1-6)
plate2(column7-12)
plate3(column1-6)
plate3(column7-12)
plate4(column1-6)
plate4(column7-12)
plate5(column1-6)
plate5(column7-12)
plate6(column1-6)
plate6(column7-12)
plate7(column1-6)
plate7(column7-12)
plate8(column1-6)
plate8(column7-12)
plate9(column1-6)
plate9(column7-12)
plate10(column1-6)
plate10(column7-12)
plate11(column1-6)
plate11(column7-12)
plate12(column1-6)
plate12(column7-12)
plate13(column1-6)
plate13(column7-12)
plate14(column1-6)
plate14(column7-12)
plate15(column1-6)
plate15(column7-12)
plate16(column1-6)
plate16(column7-12)
plate17(column1-6)
plate17(column7-12)
plate18(column1-6)
plate18(column7-12)
plate19(column1-6)
plate19(column7-12)
plate20(column1-6)
plate20(column7-12)
plate21(column1-6)
plate21(column7-12)
plate22(column1-6)
plate22(column7-12)
plate23(column1-6)
plate23(column7-12)
plate24(column1-6)
plate24(column7-12)
plate25(column1-6)
plate25(column7-12)
plate26(column1-6)
plate26(column7-12)
plate27(column1-6)
plate27(column7-12)
plate28(column1-7)
plate29(column1-6)
plate29(column7-12)
plate30(column1-6)
plate30(column7-12)
plate31(column1-6)
plate31(column7-12)
plate32(column1-6)
plate32(column7-12)
plate33(column1-6)
plate33(column7-12)
plate34(column1-6)
plate34(column7-12)
plate35(column1-6)
plate36(column1-6)
plate36(column7-12)
plate37(column1-6)
plate37(column7-12)
plate38(column1-6)
plate38(column7-12)
plate39(column1-6)
plate39(column7-12)
plate40(column1-6)
plate40(column7-12)
plate41(column1-6)
plate41(column7-12)
negative control
sample

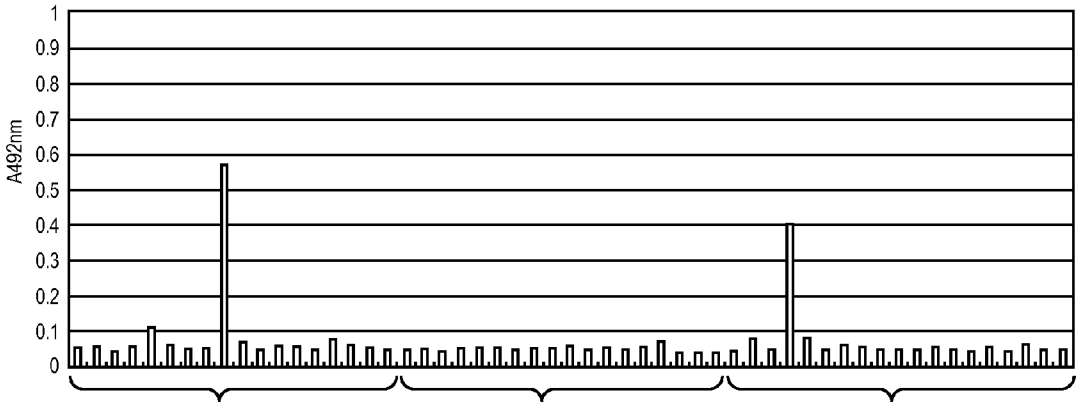
Fig.80



rowA (plate1-6)
rowB (plate1-6)
rowC (plate1-6)
rowD (plate1-6)
rowE (plate1-6)
rowF (plate1-6)
rowG (plate1-6)
rowH (plate1-6)
rowA (plate7-12)
rowB (plate7-12)
rowC (plate7-12)
rowD (plate7-12)
rowE (plate7-12)
rowF (plate7-12)
rowG (plate7-12)
rowH (plate7-12)
rowA (plate13-18)
rowB (plate13-18)
rowC (plate13-18)
rowD (plate13-18)
rowE (plate13-18)
rowF (plate13-18)
rowG (plate13-18)
rowH (plate13-18)
rowA (plate19-24)
rowB (plate19-24)
rowC (plate19-24)
rowD (plate19-24)
rowE (plate19-24)
rowF (plate19-24)
rowG (plate19-24)
rowH (plate19-24)
rowA (plate25-31)
rowB (plate25-31)
rowC (plate25-31)
rowD (plate25-31)
rowE (plate25-31)
rowF (plate25-31)
rowG (plate25-31)
rowH (plate25-31)
rowA (plate32-38)
rowB (plate32-38)
rowC (plate32-38)
rowD (plate32-38)
rowE (plate32-38)
rowF (plate32-38)
rowG (plate32-38)
rowH (plate32-38)
rowA (plate39-41)
rowB (plate39-41)
rowC (plate39-41)
rowD (plate39-41)
rowE (plate39-41)
rowF (plate39-41)
rowG (plate39-41)
rowH (plate39-41)
negative control

sample

Fig.81



column1 (plate 1,5,9,13,21,25,29,33,37)
column2 (plate 1,5,9,13,21,25,29,33,37)
column3 (plate 1,5,9,13,21,25,29,33,37)
column4 (plate 1,5,9,13,21,25,29,33,37)
column5 (plate 1,5,9,13,21,25,29,33,37)
column6 (plate 1,5,9,13,21,25,29,33,37)
column7 (plate 1,5,9,13,21,25,29,33,37)
column8 (plate 1,5,9,13,21,25,29,33,37)
column9 (plate 1,5,9,13,21,25,29,33,37)
column10 (plate 1,5,9,13,21,25,29,33,37)
column11 (plate 1,5,9,13,21,25,29,33,37)
column12 (plate 1,5,9,13,21,25,29,33,37)
column1 (plate 2,6,9,10,14,18,22,26,30,34,38)
column2 (plate 2,6,9,10,14,18,22,26,30,34,38)
column3 (plate 2,6,9,10,14,18,22,26,30,34,38)
column4 (plate 2,6,9,10,14,18,22,26,30,34,38)
column5 (plate 2,6,9,10,14,18,22,26,30,34,38)
column6 (plate 2,6,9,10,14,18,22,26,30,34,38)
column7 (plate 2,6,9,10,14,18,22,26,30,34,38)
column8 (plate 2,6,9,10,14,18,22,26,30,34,38)
column9 (plate 2,6,9,10,14,18,22,26,30,34,38)
column10 (plate 2,6,9,10,14,18,22,26,30,34,38)
column11 (plate 2,6,9,10,14,18,22,26,30,34,38)
column12 (plate 2,6,9,10,14,18,22,26,30,34,38)
column1 (plate 3,7,11,15,19,23,27,31,35)
column2 (plate 3,7,11,15,19,23,27,31,35)
column3 (plate 3,7,11,15,19,23,27,31,35)
column4 (plate 3,7,11,15,19,23,27,31,35)
column5 (plate 3,7,11,15,19,23,27,31,35)
column6 (plate 3,7,11,15,19,23,27,31,35)
column7 (plate 3,7,11,15,19,23,27,31,35)
column8 (plate 3,7,11,15,19,23,27,31,35)
column9 (plate 3,7,11,15,19,23,27,31,35)
column10 (plate 3,7,11,15,19,23,27,31,35)
column11 (plate 3,7,11,15,19,23,27,31,35)
column12 (plate 3,7,11,15,19,23,27,31,35)
column1 (plate 4,8,12,16,20,24,28,32,36)
column2 (plate 4,8,12,16,20,24,28,32,36)
column3 (plate 4,8,12,16,20,24,28,32,36)
column4 (plate 4,8,12,16,20,24,28,32,36)
column5 (plate 4,8,12,16,20,24,28,32,36)
column6 (plate 4,8,12,16,20,24,28,32,36)
column7 (plate 4,8,12,16,20,24,28,32,36)
column8 (plate 4,8,12,16,20,24,28,32,36)
column9 (plate 4,8,12,16,20,24,28,32,36)
column10 (plate 4,8,12,16,20,24,28,32,36)
column11 (plate 4,8,12,16,20,24,28,32,36)
column12 (plate 4,8,12,16,20,24,28,32,36)
column1,2 (plate 39-41)
column3,4 (plate 39-41)
column5,6 (plate 39-41)
column7,8 (plate 39-41)
column9,10 (plate 39-41)
column11,12 (plate 39-41)
negative control

sample

Fig.82

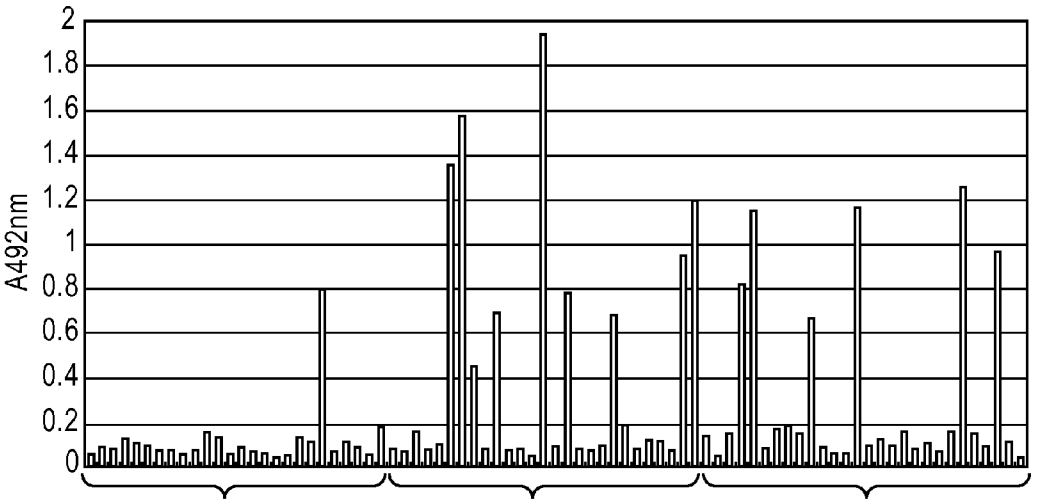


plate1 (column1-6)
plate1 (column7-12)
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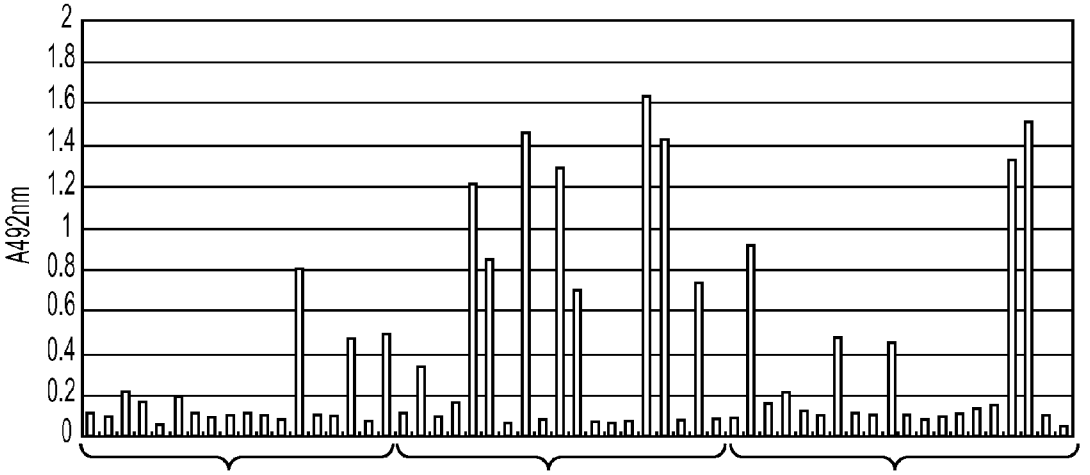
negative control

sample

Fig. 83



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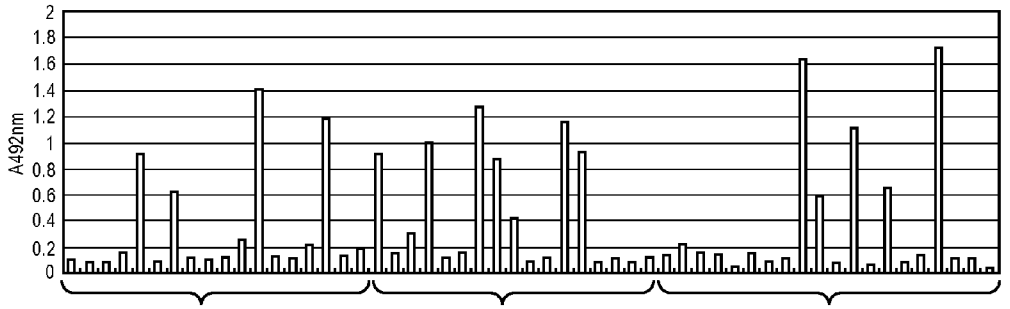
rowH (plate39-41)
negative control

sample

Fig.84



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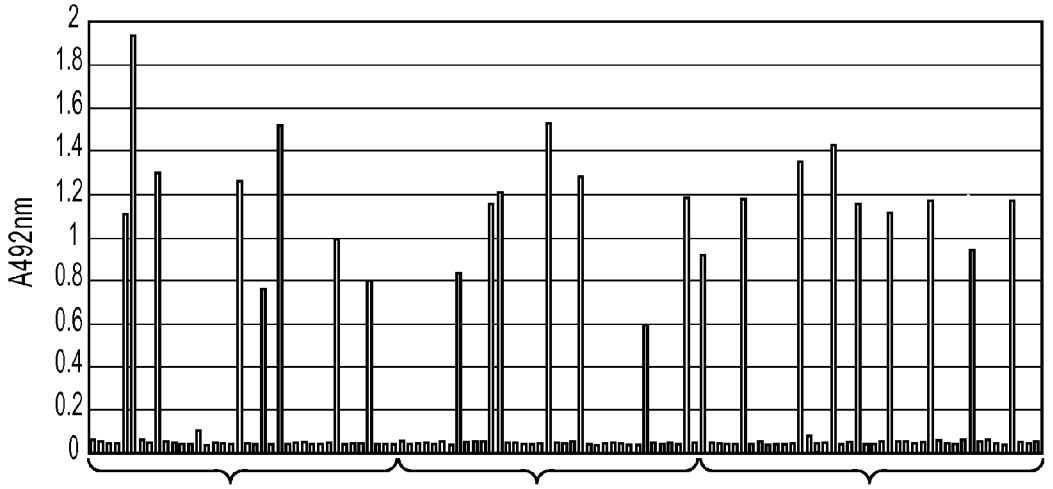
column11,12 (plate 39-41)
negative control

sample

Fig.85



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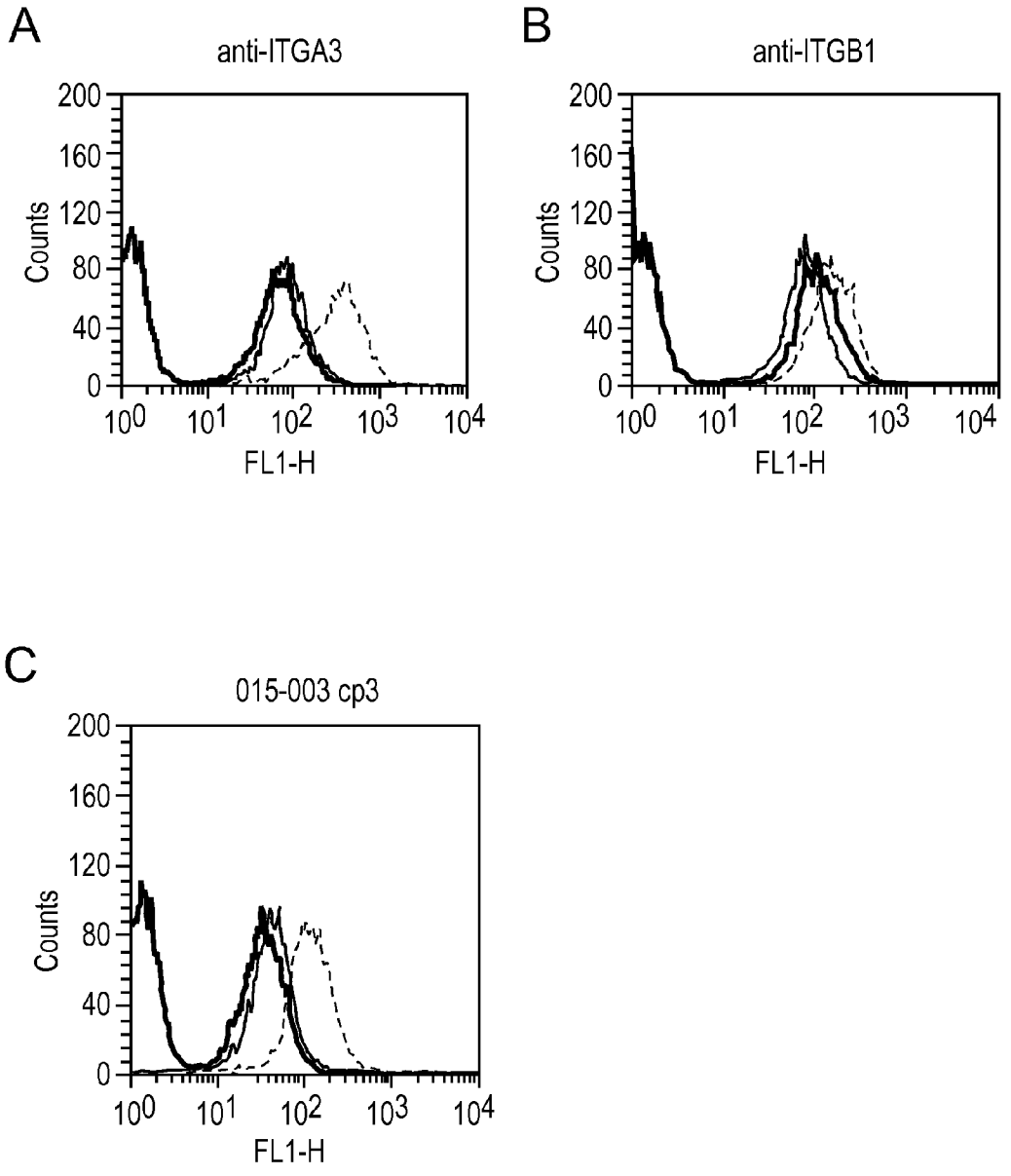
negative control

sample

Fig.86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160
120
80
40
0
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FL1-H
B
anti-ITGB1
Counts
200
160
120
80
40
0
10^0 10^1 10^2 10^3 10^4
FL1-H
C
015-003 cp3
Counts
200
160
120
80
40
0
10^0 10^1 10^2 10^3 10^4
FL1-H

Fig.87

subject antigen	name of clone	cancer tissue (clinical specimen) determined to be specific to cancer by immunostaining
HER1	048-006	kidney, liver, lung, pancreas, stomach
	057-091	kidney
	059-152	kidney
HER2	015-126	lung
HGFR	067-126	lung
	067-133	lung
	067-287	lung
LAR	064-044	kidney, liver, lung
	065-030	lung
	065-358	lung
	066-019	lung
	079-085	kidney, lung
IGSF4	035-029	liver
	035-130	liver
	035-169	liver
	035-212	liver
	035-215	liver
	035-273	liver
	035-283	liver
	040-131	liver
	051-054	liver
	051-181	liver
ALCAM	035-234	kidney, liver, lung, large bowel
	041-118	kidney, liver, lung, stomach, large bowel
	040-107	liver, lung
ICAM1	052-033	liver, lung
	053-042	liver
	053-051	liver, lung
	053-059	liver
	053-085	liver, lung
BCAM	067-024	lung
CD147	059-053	kidney
ITGA3	015-003	liver, lung
	064-002	lung
	064-006	kidney, lung, pancreas
	064-012	kidney, lung, pancreas
	064-014	lung
	064-054	lung
	064-085	lung
	064-093	lung
	064-116	lung
	065-183	lung
	067-142	lung
	068-007	lung
CD44	064-003	lung
EpCAM	067-153	lung, stomach, large bowel
CD46	035-224	liver, lung, stomach, large bowel
	045-011	liver, lung, large bowel
	051-144	kidney liver , lung, stomach
	052-053	liver
	052-073	liver
	053-049	liver
	3172-120	liver, lung, pancreas, stomach
	066-069	lung
CD73	067-213	lung

Fig.88

antigen	antibody clone	squamous carcinoma		adenosquamous carcinoma	alveolar adenocarcinoma	adenocarcinoma									large cell carcinoma	
		050707	050725	051219	050623	060501	060116	050823A	060119	060214	051020	050822	060627	060608	051025	060515	050929	060413
						papillary type	papillary type	papillary type	papillary type	papillary type	papillary type	mixed type			mixed type	mixed type		
		moderately differentiated			highly differentiated	highly differentiated			highly differentiated	highly differentiated	highly differentiated		poorly differentiated	poorly differentiated				
		IA	I A	IB	IA	IA	IB	IB	IB	IB	IB	IB	IIB	IIIA	IIIA	IIIB	IIIA	IIIA
HER1	048-006	+	+	-	-	+	+	+	+	+-	-	-	+	+-	+	+	+	+
HER2	015-126	-	-	+	-	+	-	-	-	-	-	-	+	+	+	+	+	-
HGFR	067-133	-	-	-	-	+	-	-	-	-	-	-	+	-	-	+	-	-
LAR	064-044	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-
IgSF4	076-048	-	-	-	±	+	-	+	+	+	±	±	-	+	-	+	-	+
CD147	059-053	-	-	-	-	+	-	-	-	-	-	-	+	+	-	+	+	-

METHOD OF CLASSIFYING ANTIBODY, METHOD OF IDENTIFYING ANTIGEN, METHOD OF OBTAINING ANTIBODY OR ANTIBODY SET, METHOD OF CONSTRUCTING ANTIBODY PANEL AND ANTIBODY OR ANTIBODY SET AND USE OF THE SAME

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation-in-part of international application No. PCT/JP2007/063689, filed Jul. 9, 2007, which claims priority to Japanese applications No. 2006-189872, filed Jul. 10, 2007 and No. 2007-058458, filed Mar. 8, 2008. The contents of these three applications are hereby incorporated by reference in their entirety.

FIELD OF THE INVENTION

[0002] The present invention relates to a method of classifying a plurality of antibodies, a method of identifying antigen, a panel displaying characteristics of an antibody, and the like, as well as an antibody related to a disease and a use thereof.

BACKGROUND OF THE INVENTION

[0003] Success of Herceptin to breast cancer (see, non-patent document 1) and Rituxan (non-patent document 2) to malignant lymphoma B shows that an antibody is effective as a therapeutic agent to a cancer. Certain antibodies exhibit an ADCC effect (non-patent document 3) and/or a CDC effect (non-patent document 4) by forming a complex with an antigen molecule existing on the cell membrane and the effects kill a target cell (cell expressing an antigen). The ADCC effect or the CDC effect may cause apoptosis. Such an effect of an antibody is specific to an antigen. That is to say, an antibody acts on cells expressing an antigen which the antibody recognizes regardless of whether the cells are cancer cells or normal cells. Therefore, the success in development of antibody therapeutic agents to cancers is dependent on discovery of antigens expressing in a cancer-specific manner and recognized by an antibody so as to cause the ADCC effect or the CDC effect. An antibody against to such an antigen is a promising candidate of a therapeutic agent capable of reliably killing target cancer cells while minimizing the influence (side effect) on normal cells.

[0004] In antibody drug development, it is essential to obtain antibodies that recognize "intact state" target cancer antigens existing on the surface of a cell membrane. However, since the target cancer antigen is membrane protein, it has been difficult to obtain an antibody against even known cancer antigen. In order to solve these problems, present inventors have produced a huge human antibody library including as many as 100 billion independent clones and established a comprehensive acquisition method for antibodies to proteins (cell surface antigens) existing on the surface of the cell membrane of cancer cells and tissues by using the library (patent documents 1 to 3).

[Patent document 1] WO01/062907

[Patent document 2] WO2001/096401

[Patent document 3] Japanese Patent Unexamined Publication No. 2005-185281

[Non-patent document 1] Mass R, et al.: The Concordance Between the Clinical Trials Assay (CTA) and Fluorescence in Situ Hybridization (FISH) in the Herceptin Pivotal Trials.: Proc Am Soci Clin Oncol 19, 75a, 2000

[Non-patent document 2] Berinstein N L, Grillo-Lopez A J, White C A, Bence-Bruckler I, Maloney D, Czuczman M, et al. Association of serum Rituximab (IDEC-C2B8) concentration and anti-tumor response in the treatment of recurrent low-grade or follicular non-Hodgkin's lymphoma. Annals of Oncology 1998, 9:995-1001.

[Non-patent document 3] Bruggemann M., Williams G. T., Bindon C. I., Clark M. R., Walker M. R., Jefferis R., Waldmann H., Neuberger M. S. (1987). Comparison of the effector functions of human immunoglobulins using a matched set of chimeric antibodies. J. Exp. Med., 166, 1351-1361.

[Non-patent document 4] Loos M. (1982). The classical complement pathway: mechanism of activation of the first component by antigen-antibody complexes. Prog. Allergy, 30, 135-192. Mol. Immunol. 1982 May; 19 (5): 651-7.

SUMMARY OF THE INVENTION

[0005] Currently, the present inventors can comprehensively obtain antibodies to cell surface antigens. As the next step, it is necessary to identify an antibody to each antibody and to screen useful antibodies. However, it will take a much labor and time and considerably high cost to individually identify an antigen for the comprehensively obtained antibodies.

[0006] Furthermore, the comprehensively obtained antibodies may include unnecessary antibodies from the viewpoint that they do not have sufficient affinity and reactivity, or they have substantially the same as the other antibodies. Therefore, method for efficiently screening useful antibodies has been demanded.

[0007] On the other hand, the comprehensively obtained antibodies may include antibodies such as candidates of diagnostic agents and therapeutic agents, which are extremely important from the medical viewpoint.

[0008] Under such circumstances, the present invention aims at the effective use of comprehensively obtained antibodies to cell surface antigens in medical fields and research fields, and has an object to provide a useful method therefor. That is to say, the present invention has an object to provide a method of classifying a plurality of antibodies to cell surface antigens rapidly. Also, the present invention has another object to provide a method of rapidly identifying an antigen for the antibody. Furthermore, the present invention has a further object to provide a method of promoting to use useful information obtained by such methods. The present invention has a yet further object to provide an antibody effective for treatment and diagnosis of cancers.

[0009] In view of the above-mentioned objects, the present inventors carry out an analysis of an antibody by the following approach: preparing cell lines that are expected to express cell surface antigens for the obtained antibodies; allowing each antibody to react with the cell lines; and carrying out the flow cytometry analysis.

[0010] The present inventors focus on the histogram of the results of the flow cytometry analysis and classify the antibodies based on the similarity so as to obtain a plurality of antibodies groups. Then, it is confirmed that antigens to antibodies belonging to the same antibody group are common. This fact means that it is possible to determine antigens for all antibodies by selecting the respective antibody in each antibody group and identifying the antigen of the representative antibody. Thus, the present inventors have succeeded in find-

ing a method for identifying antigens comprehensively and rapidly. On the other hand, the present inventors carry out classification of antibodies and identification of an antigen according to the above-mentioned technique and consider the reactivity between each antibody group and clinical samples so as to search for clinically applicable antibodies. As a result, the present inventors have succeeded in finding a novel antibody specific to certain kinds of cancers. Furthermore, they have reached the findings that information obtained by using a clinical sample (relationship between the antibody and disease) is extremely useful for establishing methods for diagnosis and treatment.

[0011] The present invention provides, for example, a method of classifying antibody, and the like, mentioned below based on the above-mentioned results and findings.

<Method of Classifying Antibody>

[0012] [1] A method of classifying antibody including the following steps:

[0013] (1) preparing a plurality of antibodies recognizing cell surface antigen;

[0014] (2) bringing each of the antibodies into contact with cells of the same kinds;

[0015] (3) analyzing each cell after step (2) by flow cytometry so as to obtain data showing reactivity between the antibody and the cell surface; and

[0016] (4) comparing the obtained data and classifying antibodies based on the similarity of the data.

[2] The method of classifying antibody according to [1], wherein the cell surface antigen is an intact cell surface antigen.

[3] The classifying method according to [1] or [2], wherein the cell surface antigen is a cell surface antigen of a cancer cell.

[4] The classifying method according to [1], wherein the plurality of antibodies recognize cell surface antigen are composed of an assembly of antibodies derived from antibody clones selected as being capable of recognizing a cell surface antigen, from an antibody library.

[5] The classifying method according to [4], wherein the antibody library is a phage antibody library.

[6] The classifying method according to [1], wherein the antibody is an antibody to which a label material is bound or fused.

[7] The classifying method according to [1], wherein the antibody does not include a label material and the method includes a step of labeling the antibody bound to the cell after step (2).

[8] The classifying method according to [1], wherein the cell is an established cell line.

[9] The classifying method according to [1], wherein the cell is an established cancer cell line.

[10] The classifying method according to [1], wherein the data are shown in a histogram showing a relationship between a binding amount of antibodies and a number of cells, and the similarity of the data is determined by comparing the shapes of the histograms.

[11] The classifying method according to [1], wherein the data are shown in a histogram showing a relationship between a binding amount of antibodies and a number of cells, and the similarity of the data is determined based on one or more values selected from the group consisting of a median value, a mode, a maximum value, a range, a standard deviation, a kurtosis and a skewness of the histogram.

[12] The classifying method according to [11], wherein the similarity of the data is determined based on the values of the median value, the mode, and the kurtosis and a skewness of the histogram.

[13] The classifying method according to [10] or [11], wherein the binding amount of antibody is shown by a fluorescence intensity.

[14] The classifying method according to [1], wherein in step (4), a plurality of antibodies having the identical or high similar data are classified into one antibody group.

[15] The classifying method according to [1], wherein two or more kinds of cells are prepared and each kind of cell is subjected to steps (2) to (4).

[16] The classifying method according to [15], wherein a plurality of antibodies having the identical or high similar data with respect to two or more kinds of cells in the cells are classified into one antibody group.

[17] The classifying method according to [1], wherein an antibody that has been determined to have a low reactivity with respect to the cell surface antigen during classification or after classification is excluded.

[18] The classifying method according to [1], wherein classification results of antibodies are displayed as a panel.

[19] The classifying method according to any of [α] to [18], wherein after step (4), the following steps are carried out:

[0017] (i) associating the classified antibodies to a combination of n pieces of parameters including a first parameter, a second parameter, . . . , and an n-th parameter (wherein, n represents an integer of 2 or more, each parameter has two or more parameter values and the same parameter value is given to two or more antibodies in each parameter);

[0018] (ii) with respect to each parameter, preparing antibody mixtures of the antibodies having the same parameter value;

[0019] (iii) examining a reactivity of each of the antibody mixtures with a target antigen by an enzyme linked immunosorbent assay (ELISA) so as to specify the antibody mixture which shows reactivity;

[0020] (iv) specifying a combination of a parameter name and a parameter value that are common to the antibody group contained in the specified antibody mixture;

[0021] (v) selecting an antibody corresponding to the combination specified in the step (iv) in terms of all parameters among the antibodies subjected to step (i); and

[0022] (vi) classifying the selected antibodies into one antibody group.

[20] The classifying method according to [19], wherein the steps (i) to (v) are repeated several times under the conditions in which the combination of parameters is different in each trial; an antibody in which results of all trials are not contradictory is selected; and the antibody is subjected to the step (vi).

[21] The classifying method according to [19], further including the following steps between the step (v) and the step (vi);

[0023] (v-1) newly associating the classified antibodies selected in step (v) with a combination of n pieces of parameters in a same manner as in the step (i);

[0024] (v-2) with respect to each parameter, preparing the antibody mixture of antibodies having the same parameter value for each parameter;

[0025] (v-3) examining a reactivity of each of the antibody mixtures with a target antigen by an enzyme linked immunosorbent assay (ELISA) so as to specify the antibody mixture showing the reactivity;

[0026] (v-4) determining a combination of a parameter name and a parameter value that are common to the antibody group contained in the specified antibody mixture; and

[0027] (v-5) selecting an antibody having the combination specified in the step (v-4) in terms of all parameters among the antibodies subjected to the step (v-1).

[22] The classifying method according to [21], wherein the steps (v-1) to (v-4) are repeated twice or more.

[23] The classifying method according to any of [19] to [22], wherein n is 3.

[24] The classifying method according to any of [19] to [23], wherein two or more kinds of target antigens are prepared and the steps (iii) to (vi) are carried out by using each target antigen.

[25] The classifying method according to any of [19] to [24], wherein the target antigen is an antigen selected from the group consisting of HER1, HER2, CD46, ITGA3, ICAM1, ALCAM, CD147, IgSF4, BCAM, C1qR, CD44, CD73, LAR, EpCAM and HGFR.

<Identifying Method of Antigen>

[0028] [26] An identifying method of an antigen including the following steps:

[0029] (1) preparing a plurality of antibodies recognizing cell surface antigen;

[0030] (2) bringing each of the antibodies into contact with cells of the same kind;

[0031] (3) analyzing each cell after step (2) by flow cytometry so as to obtain data showing the reactivity between the antibody and the cell surface;

[0032] (4) comparing the obtained data and classifying antibodies based on the similarity of the data;

[0033] (5) selecting one or several antibodies from each antibody group formed in the step (4) and identifying an antigen thereof; and

[0034] (6) associating the antigens identified in the step (5) with an antibody group, based on the estimation that antigens to antibodies belonging to the same antibody group are identical or have high relationship, and.

[27] The identification method according to [26], wherein in the step (5), one antibody is selected from each antibody group.

[28] The identification method according to [26], wherein in the step (5), from the results of a flow cytometry analysis, an antibody that is determined to have a high reactivity with respect to an antigen is selected.

[29] The identification method according to [26], wherein in the step (5), the identification of an antigen is carried out by one or more methods selected from the group consisting of an immunoprecipitation test, Western blotting, affinity chromatography, proteomics techniques (electrophoresis, mass spectrometry, genome data base retrieve, and analysis by bioinformatics), and an expression analysis of corresponding gene.

[30] The identification method according to [26], further including a step of examining a reactivity between an antigen identified in the step (5) and an antibody belonging to an antibody group with which the antigen is associated in the step (6) so as to confirm that the estimation is correct.

[31] The identification method according to [26], wherein an identification result of antigen is displayed as a panel.

[32] The identification method according to [31], wherein the panel is any of the following (a) to (c):

[0035] (a) a panel displaying a plurality of antibodies showing identical or high similar data in the flow cytometry analysis in the step (3) as one antibody group in which each antibody group is associated with its antigen;

[0036] (b) a panel displaying a plurality of antibodies showing identical or high similar data in the flow cytometry analysis in the step (3) as one antibody group in which each antibody group is associated with a cell expressing a cell surface antigen recognized by the each antibody group; and

[0037] (c) a panel displaying a plurality of antibodies showing identical or high similar data in the flow cytometry analysis in the step (3) as one antibody group in which each antibody group, its antigen and a cell expressing a cell surface antigen recognized by the antibody group are associated with each other.

<Method of Obtaining Antibody or Antibody Set, Antibody or Antibody Set to be Obtained>

[0038] [33] A method of obtaining an antibody having a relationship with respect to a certain disease, the method comprising the following steps:

[0039] (1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to [1];

[0040] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0041] (3) selecting an antibody in the antibody group, to which an antibody having a specific reactivity to any of diseases belongs, as a useful antibody.

[34] A method of obtaining an antibody having a relationship with respect to a certain disease, the method comprising the following steps:

[0042] (1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to [19];

[0043] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0044] (3) selecting an antibody in the antibody group, to which an antibody having a specific reactivity to any of diseases belongs, as a useful antibody.

[35] A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

[0045] (1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to [1];

[0046] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0047] (3') selecting a disease to which two or more antibodies show a specific reactivity, then selecting antibodies from the antibody group, to which the antibody having a specific reactivity to the disease belongs, and combining the selected antibodies.

[36] A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

[0048] (1) selecting two or more antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to [1];

[0049] (2) with respect to two kinds or more diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0050] (3) selecting antibodies from the antibody group, to which the antibody having a specific reactivity to any of disease belongs, and combining the selected antibodies.

[37] A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

[0051] (1) selecting two or more antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to [1];

[0052] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0053] (3) selecting an antibody from the antibody group to which the antibody having a specific reactivity to any of diseases belongs, and an antibody belonging to other antibody group whose antigen is common to that of the antibody group, and combining the selected antibodies.

[38] A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

[0054] (1) selecting two or more antibody groups recognizing the common antigen from the plurality of antibody groups classified by the classifying method according to [1];

[0055] (2) with respect to one kind or two or more kinds of pathologic conditions, examining a reactivity between an antibody in each of the selected antibody groups and a pathologic condition; and

[0056] (3) connecting information about the reactivity and then combining the antibodies in the antibody groups.

[39] A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

[0057] (1) selecting one or two or more antibody groups from the plurality of antibody groups classified by the classifying method according to [19];

[0058] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0059] (3') selecting a disease to which two or more antibodies show a specific reactivity, then selecting antibodies from an antibody group which the antibodies showing a specific reactivity to the disease belong to, and combining the selected antibodies.

[40] A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

[0060] (1) selecting two or more antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to [19];

[0061] (2) with respect to two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease in two or more kinds of diseases; and

[0062] (3) selecting antibodies from the antibody group to which the antibody having a specific reactivity to any of diseases belong, and combining the selected antibodies.

[41] A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

[0063] (1) selecting two or more antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to [19];

[0064] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0065] (3) selecting an antibody from the antibody group to which the antibody having a specific reactivity to any of disease belongs, and an antibody belonging to other antibody group whose antigen is common to that of the antibody group, and combining the selected antibodies.

[42] A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

[0066] (1) selecting two or more antibody groups recognizing the common antigen from the plurality of antibody groups classified by the classifying method according to [19];

[0067] (2) with respect to one kind or two or more kinds of pathologic conditions, examining a reactivity between an antibody in each of the selected antibody groups and a pathologic condition; and

[0068] (3) associating information about the reactivity and then combining the antibodies in the antibody groups.

[43] The obtaining method according any of [33] to [42], wherein the disease is selected from the group consisting of kidney cancer, hepatic cell carcinoma, gallbladder and liver cancer, alveolar cell carcinoma, lung squamous cell cancer, pulmonary adenocarcinoma, pancreas cancer, adenocarcinoma, and ovarian cancer.

[44] The obtaining method according any of [33] to [42], wherein in the step (2), the reactivity is examined by one or more methods selected from the group consisting of an immunostaining procedure, an immunoprecipitation method, a flow cytometry analysis, cell ELISA, an intermolecular interactive analysis between a disease-related molecule (disease causative gene product and the like) and an antibody, and application test to a disease model cell (or animal).

[45] An isolated antibody obtained by the method according to [33] or [34].

[46] An antibody set obtained by the method described in any of [35] to [42].

<Production Method of Panel, Panel, and Combination of Antibody or Antibody Set and Panel>

[0069] [47] A production method of a panel displaying a relationship between an antibody and a disease, the method comprising the following steps:

[0070] (1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to [1];

[0071] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0072] (3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

[48] A production method of a panel displaying a relationship between an antibody and a disease, the method comprising the following steps:

[0073] (1) selecting two or more of antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to [1];

[0074] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0075] (3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

[49] A production method of a panel displaying a relationship between an antibody and a pathologic condition, the method comprising the following steps:

[0076] (1) selecting two or more of antibody groups recognizing a common antigen from the plurality of antibody groups classified by the classifying method according to [1];

[0077] (2) with respect to one kind or two or more kinds of pathologic condition, examining a reactivity between an antibody in each of the selected antibody groups and a certain pathologic condition of disease; and

[0078] (3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

[50] A production method of a panel displaying a relationship between an antibody and a disease, the method comprising the following steps:

[0079] (1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to [19];

[0080] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0081] (3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

[51] A production method of a panel displaying a relationship between an antibody and a disease, the method comprising the following steps:

[0082] (1) selecting two or more of antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to [19];

[0083] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0084] (3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

[52] A production method of a panel displaying a relationship between an antibody and a pathologic condition, the method comprising the following steps:

[0085] (1) selecting two or more of antibody groups recognizing a common antigen from the plurality of antibody groups classified by the classifying method according to [19];

[0086] (2) with respect to one kind or two or more kinds of pathologic condition, examining a reactivity between an antibody in each of the selected antibody groups and a certain pathologic condition of disease; and

[0087] (3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

[53] A panel produced by the method according to any of [47] to [52].

[54] A combination of an antibody or an antibody set and a panel selected from the group consisting of the following (a) to (d);

[0088] (a) a combination of the isolated antibody obtained by the method according to [33] and the panel produced by the method according to [47];

[0089] (b) a combination of the antibody set obtained by the method according to [35] and the panel produced by the method according to [47];

[0090] (c) a combination of the antibody set obtained by the method according to [36] and the panel produced by the method according to [48];

[0091] (d) a combination of the antibody set obtained by the method according to [37] and the panel produced by the method according to [48];

[0092] (e) a combination of the antibody set obtained by the method according to [38] and the panel produced by the method according to [49];

[0093] (f) an isolated antibody obtained by the method according to [34] and the panel produced by the method according to [50];

[0094] (g) a combination of the antibody set obtained by the method according to [39] and the panel produced by the method according to [50];

[0095] (h) a combination of the antibody set obtained by the method according to [40] and the panel produced by the method according to [51];

[0096] (i) a combination of the antibody set obtained by the method according to [41] and the panel produced by the method according to [51]; and

[0097] (j) a combination of the antibody set obtained by the method according to [42] and the panel produced by the method according to [52].

[55] A method of testing a disease in which a cell surface antigen is an indicator, the method comprising the following steps:

[0098] (1) preparing a cell or a tissue separated from a subject;

[0099] (2) examining a reactivity between the cell or the tissue and each antibody displayed on the panel according to [53]; and

[0100] (3) collating the results in the step (2) with the panel.

<Method of Selecting Optimum Treatment Method>

[0101] [56] A method of selecting an optimum treatment method for a certain disease, the method comprising the following steps:

[0102] (1) preparing a cell or a tissue separated from a subject;

[0103] (2) examining a reactivity between the cell or the tissue and each antibody displayed on the panel according to [53];

[0104] (3) collating the results in the step (2) with the panel, and

[0105] (4) selecting an effective antibody according to the results of collating.

[57] The method according to [56], wherein the effective antibody is an antibody showing a specific reactivity in the step (2) or an antibody equivalent thereto.

[58] The method according to [56] or [57], wherein the certain disease is a disease in which a cell surface antigen selected from the group consisting of HER1, HER2, CD46, ITGA3, ICAM1, ALCAM, CD147, IgSF4, BCAM, C1qR, CD44, CD73, LAR, EpCAM and HGFR is an indicator.

[59] The method according to any of [56] to [58], wherein the panel displays two or more antibodies selected from the group consisting of 048-006 antibody, 057-091 antibody, 059-152 antibody, 048-040 antibody, 054-101 antibody, 055-147 antibody, 059-173 antibody, 067-149 antibody, 067-176 antibody, 015-126 antibody, 015-044 antibody, 015-102 antibody, 015-136 antibody, 015-143 antibody, 015-209 antibody, 039-016 antibody, 053-216 antibody, 075-024 antibody, 075-110 antibody, 086-032 antibody, 086-035 anti-

body, 086-036 antibody, 086-061 antibody, 086-138 antibody, 086-182 antibody, 035-224 antibody, 045-011 antibody, 051-144 antibody, 052-053 antibody, 052-073 antibody, 053-049 antibody, 3172-120 antibody, 066-069 antibody, 015-003 antibody, 064-002 antibody, 064-006 antibody, 064-012a antibody, 064-012b antibody, 064-014 antibody, 064-054 antibody, 064-085 antibody, 064-093 antibody, 064-116 antibody, 065-183 antibody, 067-142 antibody, 068-007 antibody, 052-033 antibody, 053-042 antibody, 053-051 antibody, 053-059 antibody, 053-085 antibody, 035-234 antibody, 040-107 antibody, 041-118 antibody, 066-174 antibody, 083-040 antibody, 029-143 antibody, 045-134 antibody, 062-101 antibody, 062-109 antibody, 084-103 antibody, 052-274 antibody, 029-067 antibody, 083-131 antibody, 059-053 antibody, 064-003 antibody, 067-213 antibody, 067-153 antibody, 067-126 antibody, 067-133 antibody, 067-287 antibody, 064-044 antibody, 065-030 antibody, 065-358 antibody, 066-019 antibody, 079-085 antibody, 067-024 antibody and 076-048 antibody.

[60] A method of selecting an optimum treatment method of a certain disease, the method comprising the following steps:

[0106] (1) preparing a panel displaying a reactivity between one or more antibodies selected from the group consisting of 048-006 antibody, 015-126 antibody, 067-133 antibody, 064-044 antibody, 076-048 antibody and 059-053 antibody, and a clinical cancer tissue of one or more diseases selected from the group consisting of squamous carcinoma, adenosquamous carcinoma, alveolar adenocarcinoma, adenocarcinoma, and large cell carcinoma, and a cell or tissue separated from a subject;

[0107] (2) examining a reactivity between the cell or the tissue and each antibody displayed on the panel;

[0108] (3) collating the results in the step (2) with the panel, and

[0109] (4) selecting an effective antibody according to the results of collating.

[61] The method according to [60], wherein the effective antibody is an antibody showing a specific reactivity in the step (2) or an antibody equivalent thereto.

[62] The method according to [60] or [61], wherein the certain disease is a disease selected from the group consisting of squamous carcinoma, adenosquamous carcinoma, alveolar adenocarcinoma, adenocarcinoma, and large cell carcinoma.

<Isolated Antibody>

[0110] [63] An isolated antibody having affinity to HER1, comprising:

[0111] a heavy chain variable region CDR3 and a light chain variable region CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3 and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (1) to (3);

[0112] heavy chain variable regions CDR2 and CDR3 and light chain variable regions CDR2 and CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (4) to (6);

[0113] heavy chain variable regions CDR1 to CDR3 and light chain variable regions CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (7) to (9) and (13) to (18); or

[0114] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) selected from the group consisting of the following (10) to (12) and (19) to (24);

(1) SEQ ID NO: 4 and SEQ ID NO: 8

(2) SEQ ID NO: 12 and SEQ ID NO: 16

(3) SEQ ID NO: 20 and SEQ ID NO: 24

(4) SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 7, and SEQ ID NO: 8

(5) SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 15, and SEQ ID NO: 16

(6) SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 23, and SEQ ID NO: 24

(7) SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 7, and SEQ ID NO: 8

(8) SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 15, and SEQ ID NO: 16

(9) SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 23, and SEQ ID NO: 24

(10) SEQ ID NO: 1, and SEQ ID NO: 5

(11) SEQ ID NO: 9, and SEQ ID NO: 13

(12) SEQ ID NO: 17, and SEQ ID NO: 21

(13) SEQ ID NO: 484 (VH CDR1), SEQ ID NO: 485 (VH CDR2), SEQ ID NO: 486 (VH CDR3), SEQ ID NO: 488 (VL CDR1), SEQ ID NO: 489 (VL CDR2), and SEQ ID NO: 490 (VL CDR3)

(14) SEQ ID NO: 492 (VH CDR1), SEQ ID NO: 493 (VH CDR2), SEQ ID NO: 494 (VH CDR3), SEQ ID NO: 496 (VL CDR1), SEQ ID NO: 497 (VL CDR2), and SEQ ID NO: 498 (VL CDR3)

(15) SEQ ID NO: 500 (VH CDR1), SEQ ID NO: 501 (VH CDR2), SEQ ID NO: 502 (VH CDR3), SEQ ID NO: 504 (VL CDR1), SEQ ID NO: 505 (VL CDR2), and SEQ ID NO: 506 (VL CDR3)

(16) SEQ ID NO: 508 (VH CDR1), SEQ ID NO: 509 (VH CDR2), SEQ ID NO: 510 (VH CDR3), SEQ ID NO: 512 (VL CDR1), SEQ ID NO: 513 (VL CDR2), and SEQ ID NO: 514 (VL CDR3)

(17) SEQ ID NO: 516 (VH CDR1), SEQ ID NO: 517 (VH CDR2), SEQ ID NO: 518 (VH CDR3), SEQ ID NO: 520 (VL CDR1), SEQ ID NO: 521 (VL CDR2), and SEQ ID NO: 522 (VL CDR3)

(18) SEQ ID NO: 524 (VH CDR1), SEQ ID NO: 525 (VH CDR2), SEQ ID NO: 526 (VH CDR3), SEQ ID NO: 528 (VL CDR1), SEQ ID NO: 529 (VL CDR2), and SEQ ID NO: 530 (VL CDR3)

(19) SEQ ID NO: 483 (VH), and SEQ ID NO: 487 (VL)

(20) SEQ ID NO: 491 (VH), and SEQ ID NO: 495 (VL)

(21) SEQ ID NO: 499 (VH), and SEQ ID NO: 503 (VL)

(22) SEQ ID NO: 507 (VH), and SEQ ID NO: 511 (VL)

(23) SEQ ID NO: 515 (VH), and SEQ ID NO: 519 (VL), and

(24) SEQ ID NO: 523 (VH), and SEQ ID NO: 527 (VL)

[0115] [64] An isolated antibody having affinity to HER2, comprising:

[0116] a heavy chain variable region CDR3 and a light chain variable region CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3 and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) shown in the following (1);

[0117] heavy chain variable regions CDR2 and CDR3 and light chain variable regions CDR2 and CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) shown in the following (2);

[0118] heavy chain variable regions CDR1 to CDR3 and light chain variable regions CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (3) and (5) to (19); or

[0119] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) selected from the group consisting of the following (4) and (20) to (34);

(1) SEQ ID NO: 28, and SEQ ID NO: 32

(2) SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 31, and SEQ ID NO: 32

(3) SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 31, and SEQ ID NO:32

(4) SEQ ID NO: 25, and SEQ ID NO: 29

(5) SEQ ID NO: 532 (VH CDR1), SEQ ID NO: 533 (VH CDR2), SEQ ID NO: 534 (VH CDR3), SEQ ID NO: 536 (VL CDR1), SEQ ID NO: 537 (VL CDR2), and SEQ ID NO: 538 (VL CDR3)

(6) SEQ ID NO: 540 (VH CDR1), SEQ ID NO: 541 (VH CDR2), SEQ ID NO: 542 (VH CDR3), SEQ ID NO: 544 (VL CDR1), SEQ ID NO: 545 (VL CDR2), and SEQ ID NO: 546 (VL CDR3)

(7) SEQ ID NO: 548 (VH CDR1), SEQ ID NO: 549 (VH CDR2), SEQ ID NO: 550 (VH CDR3), SEQ ID NO: 552 (VL CDR1), SEQ ID NO: 553 (VL CDR2), and SEQ ID NO: 554 (VL CDR3)

(8) SEQ ID NO: 556 (VH CDR1), SEQ ID NO: 557 (VH CDR2), SEQ ID NO: 558 (VH CDR3), SEQ ID NO: 560 (VL CDR1), SEQ ID NO: 561 (VL CDR2), and SEQ ID NO: 562 (VL CDR3)

(9) SEQ ID NO: 564 (VH CDR1), SEQ ID NO: 565 (VH CDR2), SEQ ID NO: 566 (VH CDR3), SEQ ID NO: 568 (VL CDR1), SEQ ID NO: 569 (VL CDR2), and SEQ ID NO: 570 (VL CDR3)

(10) SEQ ID NO: 572 (VH CDR1), SEQ ID NO: 573 (VH CDR2), SEQ ID NO: 574 (VH CDR3), SEQ ID NO: 576 (VL CDR1), SEQ ID NO: 577 (VL CDR2), and SEQ ID NO: 578 (VL CDR3)

(11) SEQ ID NO: 580 (VH CDR1), SEQ ID NO: 581 (VH CDR2), SEQ ID NO: 582 (VH CDR3), SEQ ID NO: 584 (VL CDR1), SEQ ID NO: 585 (VL CDR2), and SEQ ID NO: 586 (VL CDR3)

(12) SEQ ID NO: 588 (VH CDR1), SEQ ID NO: 589 (VH CDR2), SEQ ID NO: 590 (VH CDR3), SEQ ID NO: 592 (VL CDR1), SEQ ID NO: 593 (VL CDR2), and SEQ ID NO: 594 (VL CDR3)

(13) SEQ ID NO: 596 (VH CDR1), SEQ ID NO: 597 (VH CDR2), SEQ ID NO: 598 (VH CDR3), SEQ ID NO: 600 (VL CDR1), SEQ ID NO: 601 (VL CDR2), and SEQ ID NO: 602 (VL CDR3)

(14) SEQ ID NO: 604 (VH CDR1), SEQ ID NO: 605 (VH CDR2), SEQ ID NO: 606 (VH CDR3), SEQ ID NO:608 (VL CDR1), SEQ ID NO:609 (VL CDR2), and SEQ ID NO: 610 (VL CDR3)

(15) SEQ ID NO: 612 (VH CDR1), SEQ ID NO: 613 (VH CDR2), SEQ ID NO: 614 (VH CDR3), SEQ ID NO: 616 (VL CDR1), SEQ ID NO: 617 (VL CDR2), and SEQ ID NO: 618 (VL CDR3)

(16) SEQ ID NO: 620 (VH CDR1), SEQ ID NO: 621 (VH CDR2), SEQ ID NO: 622 (VH CDR3), SEQ ID NO: 624 (VL CDR1), SEQ ID NO: 625 (VL CDR2), and SEQ ID NO: 626 (VL CDR3)

(17) SEQ ID NO: 628 (VH CDR1), SEQ ID NO: 629 (VH CDR2), SEQ ID NO: 630 (VH CDR3), SEQ ID NO: 632 (VL CDR1), SEQ ID NO: 633 (VL CDR2), and SEQ ID NO: 634 (VL CDR3)

(18) SEQ ID NO: 636 (VH CDR1), SEQ ID NO: 637 (VH CDR2), SEQ ID NO: 638 (VH CDR3), SEQ ID NO: 640 (VL CDR1), SEQ ID NO: 641 (VL CDR2), and SEQ ID NO: 642 (VL CDR3)

(19) SEQ ID NO: 644 (VH CDR1), SEQ ID NO: 645 (VH CDR2), SEQ ID NO: 646 (VH CDR3), SEQ ID NO: 648 (VL CDR1), SEQ ID NO: 649 (VL CDR2), and SEQ ID NO: 650 (VL CDR3)

(20) SEQ ID NO: 531 (VH), and SEQ ID NO: 535 (VL)

(21) SEQ ID NO: 539 (VH), and SEQ ID NO: 543 (VL)

(22) SEQ ID NO: 547 (VH), and SEQ ID NO: 551 (VL)

(23) SEQ ID NO: 555 (VH), and SEQ ID NO: 559 (VL)

(24) SEQ ID NO: 563 (VH), and SEQ ID NO: 567 (VL)

(25) SEQ ID NO: 571 (VH), and SEQ ID NO: 575 (VL)

(26) SEQ ID NO: 579 (VH), and SEQ ID NO: 583 (VL)

(27) SEQ ID NO: 587 (VH), and SEQ ID NO: 591 (VL)

(28) SEQ ID NO: 595 (VH), and SEQ ID NO: 599 (VL)

(29) SEQ ID NO: 603 (VH), and SEQ ID NO: 607 (VL)

(30) SEQ ID NO: 611 (VH), and SEQ ID NO: 615 (VL)

(31) SEQ ID NO: 619 (VH), and SEQ ID NO: 623 (VL)

(32) SEQ ID NO: 627 (VH), and SEQ ID NO: 631 (VL)

(33) SEQ ID NO: 635 (VH), and SEQ ID NO: 639 (VL), and

(34) SEQ ID NO: 643 (VH), and SEQ ID NO: 647 (VL)

[0120] [65] An isolated antibody having affinity to CD46 antigen, comprising:

[0121] a heavy chain variable region CDR3 and a light chain variable region CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3 and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (1) to (7);

[0122] heavy chain variable regions CDR2 and CDR3 and light chain variable regions CDR2 and CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (8) to (14);

[0123] heavy chain variable regions CDR1 to CDR3 and light chain variable regions CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (15) to (22); or

[0124] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) selected from the group consisting of the following (23) to (30);

(1) SEQ ID NO: 36, and SEQ ID NO: 40

(2) SEQ ID NO: 44, and SEQ ID NO: 48

(3) SEQ ID NO: 52, and SEQ ID NO: 56

(4) SEQ ID NO: 60, and SEQ ID NO: 64

(5) SEQ ID NO: 68, and SEQ ID NO: 72

(6) SEQ ID NO: 76, and SEQ ID NO: 80

(7) SEQ ID NO: 84, and SEQ ID NO: 88

(8) SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 39, and SEQ ID NO: 40

(9) SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 47, and SEQ ID NO: 48

(10) SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 55, and SEQ ID NO: 56

(1) SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 63, and SEQ ID NO: 64

(12) SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 71, and SEQ ID NO: 72

(13) SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 79, and SEQ ID NO: 80

(14) SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 87, and SEQ ID NO: 88

(15) SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 39, and SEQ ID NO: 40

(16) SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 47, and SEQ ID NO: 48

(17) SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 55, and SEQ ID NO: 56

(18) SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 62, SEQ ID NO: 63, and SEQ ID NO: 64

(19) SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 70, SEQ ID NO: 71, and SEQ ID NO: 72

(20) SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 78, SEQ ID NO: 79, and SEQ ID NO: 80

(21) SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 86, SEQ ID NO: 87, and SEQ ID NO: 88

(22) SEQ ID NO: 756 (VH CDR1), SEQ ID NO: 757 (VH CDR2), SEQ ID NO: 758 (VH CDR3), SEQ ID NO: 760 (VL CDR1), SEQ ID NO: 761 (VL CDR2), and SEQ ID NO: 762 (VL CDR3)

(23) SEQ ID NO: 33, and SEQ ID NO: 37

(24) SEQ ID NO: 41, and SEQ ID NO: 45

(25) SEQ ID NO: 49, and SEQ ID NO: 53

(26) SEQ ID NO: 57, and SEQ ID NO: 61

(27) SEQ ID NO: 65, and SEQ ID NO: 69

(28) SEQ ID NO: 73, and SEQ ID NO: 77

(29) SEQ ID NO: 81, and SEQ ID NO: 85

(30) SEQ ID NO: 755 (VH), and SEQ ID NO: 759 (VL)

[0125] [66] An isolated antibody having affinity to ITAG3, comprising:

[0126] a heavy chain variable region CDR3 and a light chain variable region CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3 and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) shown in the following (1);

[0127] heavy chain variable regions CDR2 and CDR3 and light chain variable regions CDR2 and CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) shown in the following (2);

[0128] heavy chain variable regions CDR1 to CDR3 and light chain variable regions CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (3) and (5) to (16); or

[0129] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) selected from the group consisting of the following (4) and (17) to (28);

(1) SEQ ID NO: 92, and SEQ ID NO: 96

(2) SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 95, and SEQ ID NO: 96

(3) SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 94, and SEQ ID NO: 95,

(4) SEQ ID NO: 89, and SEQ ID NO: 93

(5) SEQ ID NO: 676 (VH CDR1), SEQ ID NO: 677 (VH CDR2), SEQ ID NO: 678 (VH CDR3), SEQ ID NO: 680 (VL CDR1), SEQ ID NO: 681 (VL CDR2), and SEQ ID NO: 682 (VL CDR3)

(6) SEQ ID NO: 684 (VH CDR1), SEQ ID NO: 685 (VH CDR2), SEQ ID NO: 686 (VH CDR3), SEQ ID NO: 688 (VL CDR1), SEQ ID NO: 689 (VL CDR2), and SEQ ID NO: 690 (VL CDR3)

(7) SEQ ID NO: 692 (VH CDR1), SEQ ID NO: 693 (VH CDR2), SEQ ID NO: 694 (VH CDR3), SEQ ID NO: 696 (VL CDR1), SEQ ID NO: 697 (VL CDR2), and SEQ ID NO: 698 (VL CDR3)

(8) SEQ ID NO: 700 (VH CDR1), SEQ ID NO: 701 (VH CDR2), SEQ ID NO: 702 (VH CDR3), SEQ ID NO: 704 (VL CDR1), SEQ ID NO: 705 (VL CDR2), and SEQ ID NO: 706 (VL CDR3)

(9) SEQ ID NO: 708 (VH CDR1), SEQ ID NO: 709 (VH CDR2), SEQ ID NO: 710 (VH CDR3), SEQ ID NO: 712 (VL CDR1), SEQ ID NO: 713 (VL CDR2), and SEQ ID NO: 714 (VL CDR3)

(10) SEQ ID NO: 716 (VH CDR1), SEQ ID NO: 717 (VH CDR2), SEQ ID NO: 718 (VH CDR3), SEQ ID NO: 720 (VL CDR1), SEQ ID NO: 721 (VL CDR2), and SEQ ID NO: 722 (VL CDR3)

(11) SEQ ID NO: 724 (VH CDR1), SEQ ID NO: 725 (VH CDR2), SEQ ID NO: 726 (VH CDR3), SEQ ID NO: 728 (VL CDR1), SEQ ID NO: 729 (VL CDR2), and SEQ ID NO: 730 (VL CDR3)

(12) SEQ ID NO: 732 (VH CDR1), SEQ ID NO: 733 (VH CDR2), SEQ ID NO: 734 (VH CDR3), SEQ ID NO: 736 (VL CDR1), SEQ ID NO: 737 (VL CDR2), and SEQ ID NO: 738 (VL CDR3)

(13) SEQ ID NO: 740 (VH CDR1), SEQ ID NO: 741 (VH CDR2), SEQ ID NO: 742 (VH CDR3), SEQ ID NO: 744 (VL CDR1), SEQ ID NO: 745 (VL CDR2), and SEQ ID NO: 746 (VL CDR3)

(14) SEQ ID NO: 748 (VH CDR1), SEQ ID NO: 749 (VH CDR2), SEQ ID NO: 750 (VH CDR3), SEQ ID NO: 752 (VL CDR1), SEQ ID NO: 753 (VL CDR2), and SEQ ID NO: 754 (VL CDR3)

(15) SEQ ID NO: 764 (VH CDR1), SEQ ID NO: 765 (VH CDR2), SEQ ID NO: 766 (VH CDR3), SEQ ID NO: 768 (VL CDR1), SEQ ID NO: 769 (VL CDR2), and SEQ ID NO: 770 (VL CDR3)

(16) SEQ ID NO: 772 (VH CDR1), SEQ ID NO: 773 (VH CDR2), SEQ ID NO: 774 (VH CDR3), SEQ ID NO: 776 (VL CDR1), SEQ ID NO: 777 (VL CDR2), and SEQ ID NO: 778 (VL CDR3)

(17) SEQ ID NO: 675 (VH), and SEQ ID NO: 679 (VL)

(18) SEQ ID NO: 683 (VH), and SEQ ID NO: 687 (VL)

(19) SEQ ID NO: 691 (VH), and SEQ ID NO: 695 (VL)

(20) SEQ ID NO: 699 (VH), and SEQ ID NO: 703 (VL)

(21) SEQ ID NO: 707 (VH), and SEQ ID NO: 711 (VL)

(22) SEQ ID NO: 715 (VH), and SEQ ID NO: 719 (VL)

(23) SEQ ID NO: 723 (VH), and SEQ ID NO: 727 (VL)

(24) SEQ ID NO: 731 (VH), and SEQ ID NO: 735 (VL)

(25) SEQ ID NO: 739 (VH), and SEQ ID NO: 743 (VL)

(26) SEQ ID NO: 747 (VH), and SEQ ID NO: 751 (VL)

(27) SEQ ID NO: 763 (VH), and SEQ ID NO: 767 (VL), and

(28) SEQ ID NO: 771 (VH), and SEQ ID NO: 775 (VL)

[0130] [67] An isolated antibody having affinity to ICAM1, comprising:

[0131] a heavy chain variable region CDR3 and a light chain variable region CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3 and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (1) to (5);

[0132] heavy chain variable regions CDR2 and CDR3 and light chain variable regions CDR2 and CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (6) to (10);

[0133] heavy chain variable regions CDR1 to CDR3 and light chain variable regions CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (11) to (15); or

[0134] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) selected from the group consisting of the following (16) to (20);

(1) SEQ ID NO: 100, and SEQ ID NO: 104

(2) SEQ ID NO: 108, and SEQ ID NO: 112

(3) SEQ ID NO: 116, and SEQ ID NO: 120

(4) SEQ ID NO: 124, and SEQ ID NO: 128

(5) SEQ ID NO: 132, and SEQ ID NO: 136

(6) SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 103, and SEQ ID NO: 104

(7) SEQ ID NO: 107, SEQ ID NO: 108, SEQ ID NO: 111, and SEQ ID NO: 112

(8) SEQ ID NO: 115, SEQ ID NO: 116, SEQ ID NO: 119, and SEQ ID NO: 120

(9) SEQ ID NO: 123, SEQ ID NO: 124, SEQ ID NO: 127, and SEQ ID NO: 128

(10) SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 135, SEQ ID NO: 136

(11) SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 102, SEQ ID NO: 103, and SEQ ID NO: 104

(12) SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 111, and SEQ ID NO: 112

(13) SEQ ID NO: 114, SEQ ID NO: 115, SEQ ID NO: 116, SEQ ID NO: 118, SEQ ID NO: 119, and SEQ ID NO: 120

(14) SEQ ID NO: 122, SEQ ID NO: 123, SEQ ID NO: 124, SEQ ID NO: 126, SEQ ID NO: 127, and SEQ ID NO: 128

(15) SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, and SEQ ID NO: 136

(16) SEQ ID NO: 97, and SEQ ID NO: 101

(17) SEQ ID NO: 105, and SEQ ID NO: 109

(18) SEQ ID NO: 113, and SEQ ID NO: 117

(19) SEQ ID NO: 121, and SEQ ID NO: 125

(20) SEQ ID NO: 129, and SEQ ID NO: 133

[0135] [68] An isolated antibody having affinity to ALCAM, comprising:

[0136] a heavy chain variable region CDR3 and a light chain variable region CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3 and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (1) to (5);

[0137] heavy chain variable regions CDR2 and CDR3 and light chain variable regions CDR2 and CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (6) to (10);

[0138] heavy chain variable regions CDR1 to CDR3 and light chain variable regions CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (11) to (15) and (21) to (28); or

[0139] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) selected from the group consisting of the following (16) to (20) and (29) to (36);

(1) SEQ ID NO: 140, and SEQ ID NO: 144

(2) SEQ ID NO: 148, and SEQ ID NO: 152

(3) SEQ ID NO: 156, and SEQ ID NO: 160

(4) SEQ ID NO: 164, and SEQ ID NO: 168

(5) SEQ ID NO: 172, and SEQ ID NO: 176

(6) SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 143, and SEQ ID NO: 144

(7) SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 151, and SEQ ID NO: 152

(8) SEQ ID NO: 155, SEQ ID NO: 156, SEQ ID NO: 159, and SEQ ID NO: 160

(9) SEQ ID NO: 163, SEQ ID NO: 164, SEQ ID NO: 167, and SEQ ID NO: 168

(10) SEQ ID NO: 171, SEQ ID NO: 172, SEQ ID NO: 175, and SEQ ID NO: 176

(1) SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 142, SEQ ID NO: 143, and SEQ ID NO: 144

(12) SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 150, SEQ ID NO: 151, and SEQ ID NO: 152

(13) SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, SEQ ID NO: 158, SEQ ID NO: 159, and SEQ ID NO: 160

(14) SEQ ID NO: 162, SEQ ID NO: 163, SEQ ID NO: 164, SEQ ID NO: 166, SEQ ID NO: 167, and SEQ ID NO: 168

(15) SEQ ID NO: 170, SEQ ID NO: 171, SEQ ID NO: 172, SEQ ID NO: 174, SEQ ID NO: 175, and SEQ ID NO: 176

(16) SEQ ID NO: 137, and SEQ ID NO: 141

(17) SEQ ID NO: 145, and SEQ ID NO: 149

(18) SEQ ID NO: 153, and SEQ ID NO: 157

(19) SEQ ID NO: 161, SEQ ID NO: 165

(20) SEQ ID NO: 169, and SEQ ID NO: 173

(21) SEQ ID NO: 780 (VH CDR1), SEQ ID NO: 781 (VH CDR2), SEQ ID NO 782 (VH CDR3), SEQ ID NO: 784 (VL CDR1), SEQ ID NO: 785 (VL CDR2), and SEQ ID NO: 786 (VL CDR3)

(22) SEQ ID NO: 788 (VH CDR1), SEQ ID NO: 789 (VH CDR2), SEQ ID NO: 790 (VH CDR3), SEQ ID NO: 792 (VL CDR1), SEQ ID NO: 793 (VL CDR2), and SEQ ID NO: 794 (VL CDR3)

(23) SEQ ID NO: 796 (VH CDR1), SEQ ID NO: 797 (VH CDR2), SEQ ID NO: 798 (VH CDR3), SEQ ID NO: 800 (VL CDR1), SEQ ID NO: 801 (VL CDR2), and SEQ ID NO: 802 (VL CDR3)

(24) SEQ ID NO: 804 (VH CDR1), SEQ ID NO: 805 (VH CDR2), SEQ ID NO: 806 (VH CDR3), SEQ ID NO: 808 (VL CDR1), SEQ ID NO: 809 (VL CDR2), and SEQ ID NO: 810 (VL CDR3)

(25) SEQ ID NO: 812 (VH CDR1), SEQ ID NO: 813 (VH CDR2), SEQ ID NO: 814 (VH CDR3), SEQ ID NO: 816 (VL CDR1), SEQ ID NO: 817 (VL CDR2), and SEQ ID NO: 818 (VL CDR3)

(26) SEQ ID NO: 820 (VH CDR1), SEQ ID NO: 821 (VH CDR2), SEQ ID NO: 822 (VH CDR3), SEQ ID NO: 824 (VL CDR1), SEQ ID NO: 825 (VL CDR2), and SEQ ID NO: 826 (VL CDR3)

(27) SEQ ID NO: 828 (VH CDR1), SEQ ID NO: 829 (VH CDR2), SEQ ID NO: 830 (VH CDR3), SEQ ID NO: 832 (VL CDR1), SEQ ID NO: 833 (VL CDR2), and SEQ ID NO: 834 (VL CDR3)

(28) SEQ ID NO: 836 (VH CDR1), SEQ ID NO: 837 (VH CDR2), SEQ ID NO: 838 (VH CDR3), SEQ ID NO: 840 (VL CDR1), SEQ ID NO: 841 (VL CDR2), and SEQ ID NO: 842 (VL CDR3)

(29) SEQ ID NO: 779 (VH), and SEQ ID NO: 783 (VL)

(30) SEQ ID NO: 787 (VH), and SEQ ID NO: 791 (VL)

(31) SEQ ID NO: 795 (VH), and SEQ ID NO: 799 (VL)

(32) SEQ ID NO: 803 (VH), and SEQ ID NO: 807 (VL)

(33) SEQ ID NO: 811 (VH), and SEQ ID NO: 815 (VL)

(34) SEQ ID NO: 819 (VH), and SEQ ID NO: 823 (VL)

(35) SEQ ID NO: 827 (VH), and SEQ ID NO: 831 (VL), and

(36) SEQ ID NO: 835 (VH), and SEQ ID NO: 839 (VL)

[0140] [69] An isolated antibody having affinity to CD147 antigen, comprising:

[0141] a heavy chain variable region CDR3 and a light chain variable region CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3 and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) shown in the following (1);

[0142] heavy chain variable regions CDR2 and CDR3 and light chain variable regions CDR2 and CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) shown in the following (2);

[0143] heavy chain variable regions CDR1 to CDR3 and light chain variable regions

[0144] CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) shown in the following (3); or

[0145] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) shown in the following (4);

(1) SEQ ID NO: 180, and SEQ ID NO: 184

(2) SEQ ID NO: 179, SEQ ID NO: 180, SEQ ID NO: 183, and SEQ ID NO: 184

(3) SEQ ID NO: 178, SEQ ID NO: 179, SEQ ID NO: 180, SEQ ID NO: 182, SEQ ID NO: 183, and SEQ ID NO: 184, and

(4) SEQ ID NO: 177, and SEQ ID NO: 181

[0146] [70] An isolated antibody having affinity to C1qR, comprising:

[0147] heavy chain variable regions CDR1 to CDR3 and light chain variable regions CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) shown in the following (1); or

[0148] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) shown in the following (2);

(1) SEQ ID NO: (VH CDR1) 452, SEQ ID NO: 453 (VH CDR2), SEQ ID NO: 454 (VH CDR3), SEQ ID NO: (VL CDR1) 456, SEQ ID NO: 457 (VL CDR2), and SEQ ID NO: 458 (VL CDR3), and

(2) SEQ ID NO: 451 (VH), and SEQ ID NO: 455 (VL)

[0149] [71] An isolated antibody having affinity to CD44, comprising:

[0150] heavy chain variable regions CDR1 to CDR3 and light chain variable regions CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ. ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) shown in the following (1); or

[0151] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) shown in the following (2);

(1) SEQ ID NO: 460 (VH CDR1), SEQ ID NO: 461 (VH CDR2), SEQ ID NO: 462 (VH CDR3), SEQ ID NO: 464 (VL CDR1), SEQ ID NO: 465 (VL CDR2), and SEQ ID NO: 466 (VL CDR3), and

(2) SEQ ID NO: 459 (VH), and SEQ ID NO: 463 (VL)

[0152] [72] An isolated antibody having affinity to CD73, comprising:

[0153] heavy chain variable regions CDR1 to CDR3 and light chain variable regions CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1; SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) shown in the following (1); or

[0154] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) shown in the following (2);

(1) SEQ ID NO: 468 (VH CDR1), SEQ ID NO: 469 (VH CDR2), SEQ ID NO: 470 (VH CDR3), SEQ ID NO: 472 (VL CDR1), SEQ ID NO: 473 (VL CDR2), and SEQ ID NO: 474 (VL CDR3), and

(2) SEQ ID NO: 467 (VH), and SEQ ID NO: 471 (VL)

[0155] [73] An isolated antibody having affinity to EpCAM, comprising:

[0156] heavy chain variable regions CDR1 to CDR3 and light chain variable regions CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) shown in the following (1); or

[0157] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) shown in the following (2);

(1) SEQ ID NO: 476 (VH CDR1), SEQ ID NO: 477 (VH CDR2), SEQ ID NO: 478 (VH CDR3), SEQ ID NO: 480 (VL CDR1), SEQ ID NO: 481 (VL CDR2), and SEQ ID NO: 482 (VL CDR3), and

(2) SEQ ID NO: 475 (VH), and SEQ ID NO: 479 (VL)

[0158] [74] An isolated antibody having affinity to HGFR, comprising:

[0159] heavy chain variable regions CDR1 to CDR3 and light chain variable regions CDR1 to CDR3 specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR2, SEQ ID NO showing an amino acid sequence of a heavy chain variable region CDR3, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR1, SEQ ID NO showing an amino acid sequence of a light chain variable region CDR2, and SEQ ID NO showing an amino acid sequence of a light chain variable region CDR3) selected from the group consisting of the following (1) to (3); or

[0160] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) selected from the group consisting of the following (4) to (6);

(1) SEQ ID NO: 652 (VH CDR1), SEQ ID NO: 653 (VH CDR2), SEQ ID NO: 654 (VH CDR3), SEQ ID NO: 656 (VL CDR1), SEQ ID NO: 657 (VL CDR2), and SEQ ID NO: 658 (VL CDR3)

(2) SEQ ID NO: 660 (VH CDR1), SEQ ID NO: 661 (VH CDR2), SEQ ID NO: 662 (VH CDR3), SEQ ID NO: 664 (VL CDR1), SEQ ID NO: 665 (VL CDR2), and SEQ ID NO: 666 (VL CDR3)

(3) SEQ ID NO: 668 (VH CDR1), SEQ ID NO: 669 (VH CDR2), SEQ ID NO: 670 (VH CDR3), SEQ ID NO: 672 (VL CDR1), SEQ ID NO: 673 (VL CDR2), and SEQ ID NO: 674 (VL CDR3)

(4) SEQ ID NO: 651 (VH), and SEQ ID NO: 655 (VL)

(5) SEQ ID NO: 659 (VH), and SEQ ID NO: 663 (VL), and

(6) SEQ ID NO: 667 (VH), and SEQ ID NO: 671 (VL)

[0161] [75] An isolated antibody having affinity to LAR, comprising:

[0162] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) selected from the group consisting of the following (1) to (5);

(1) SEQ ID NO: 944 (VH), and SEQ ID NO: 945 (VL)

(2) SEQ ID NO: 946 (VH), and SEQ ID NO: 947 (VL)

(3) SEQ ID NO: 948 (VH), and SEQ ID NO: 949 (VL)

(4) SEQ ID NO: 950 (VH), and SEQ ID NO: 951 (VL), and

(5) SEQ ID NO: 952 (VH), and SEQ ID NO: 953 (VL)

[0163] [76] An isolated antibody having affinity to BCAM, comprising:

[0164] a heavy chain variable region and a light chain variable region specified by a combination of SEQ ID NOs (SEQ ID NO showing an amino acid sequence of a heavy chain variable region and SEQ ID NO showing an amino acid sequence of a light chain variable region) shown in the group consisting of the following (1);

(1) SEQ ID NO: 954 (VH), and SEQ ID NO: 955 (VL)

<Isolated Nucleic Acid Molecule, Vector, and the Like>

[0165] [77] An isolated nucleic acid molecule, which encodes the heavy chain variable region and/or the light chain variable region of the antibody according to any of [63] to [76].

[78] A vector including the nucleic acid molecule according to [77] in a form capable of being expressed.

[79] A transformant into which the nucleic acid molecule according to [77] is introduced.

[80] A cancer therapeutic agent comprising the antibody according to any of [63] to [76] as an effective ingredient.

[81] A reagent for examining or studying cancer comprising the antibody according to any of [63] to [76].

<Examination Method>

[0166] [82] A method for examining gallbladder and liver cancer or pancreas cancer, the method comprising the following steps:

[0167] (1) preparing subject cells or tissues separated from a living body; and

[0168] (2) detecting a CD46 antigen in the subject cells or tissues.

[83] A method for examining gallbladder and liver cancer or pancreas cancer, the method comprising the following steps:

[0169] (1) preparing subject cells or tissues separated from a living body; and

[0170] (2) detecting ITGA3 in the subject cells or tissues.

[84] A method for examining kidney cancer, hepatic cell carcinoma or gallbladder and liver cancer, the method comprising the following steps:

[0171] (1) preparing subject cells or tissues separated from a living body; and

[0172] (2) detecting ALCAM in the subject cells or tissues.

[85] A method for examining kidney cancer, the method comprising the following steps:

[0173] (1) preparing subject cells or tissues separated from a living body; and

[0174] (2) detecting a CD147 antigen in the subject cells or tissues.

BRIEF DESCRIPTION OF THE DRAWINGS

[0175] FIG. **1** shows one example of a method of obtaining an antibody or an antibody set related to a certain disease.

[0176] FIG. **2** shows another example of a method of obtaining an antibody set related to a certain disease.

[0177] FIG. **3** shows a further example of a method of obtaining an antibody set related to a certain disease.

[0178] FIG. **4** shows a yet further example of a method of obtaining an antibody set related to a certain disease.

[0179] FIG. **5** is a schematic view showing a vector used for producing an scFv antibody gene library.

[0180] FIG. **6** is a schematic view showing a structure of pscFvCA9-E8VHdVLd.

[0181] FIG. **7-1** shows a base sequence (SEQ ID NO: 401) of an insert part of pscFvCA9-E8VHdVLd and an amino acid sequence (SEQ ID NO: 402) encoded by the base sequence.

[0182] FIG. **7-2** shows a part continuing to FIG. **7-1**.

[0183] FIG. **8-1** shows a base sequence (SEQ ID NO: 405) of an insert of pscFvCA-E8VHd and a restriction enzyme site and an amino acid sequence (SEQ ID NO: 406).

[0184] FIG. **8-2** shows a part continuing to FIG. **8-1**.

[0185] FIG. **9** shows a process of screening of an antibody clone specific to liver cancer cell.

[0186] FIG. **10** shows an FCM reactivity (representative example) of an antibody clone, showing histogram (right) and cell fluorescence cytology image (left) showing the reactivity between an antibody clones 035-011 and 041-101 and undifferentiated malignant liver cancer cell line HLF.

[0187] FIG. **11** shows an FCM reactivity (representative example) of an antibody clone, showing histogram (right) and cell fluorescence cytology image (left) showing the reactivity between an antibody clones 041-129, 045-134 and 052-042 and undifferentiated malignant liver cancer cell line HLF.

[0188] FIG. **12** shows histograms obtained by FCM of seven kinds of antibodies, which are overwritten onto each other. This shows that each histogram has a unique shape.

[0189] FIG. **13** shows histograms obtained by FCM of seven kinds of antibodies, which are overwritten onto each other. This shows that all the histograms have high similarity to each other.

[0190] FIG. **14** shows histograms obtained by FCM of four kinds of antibodies, which are overwritten onto each other. This shows that all the histograms have high similarity to each other.

[0191] FIG. **15** shows histograms obtained by FCM of two kinds of antibodies, which are overwritten onto each other. This shows that two histograms have high similarity to each other.

[0192] FIG. **16** shows histograms obtained by FCM of three kinds of antibodies in various cells, which are overwritten onto each other. This shows that even when any cells are used, these antibodies provide histograms having a high similarity to each other.

[0193] FIG. **17** shows a method for classifying the antibody group into groups based on the results of the FCM analysis.

[0194] FIG. **18** is a table showing a classification of a plurality of antibody clones based on the results of the FCM analysis. Each reference mark in Table is shown by a shift amount from the histogram (reference histogram) provided

by the negative control antibody. Double circle mark represents that the shift amount is 20 times or more (the peak value of the is 20 times or more of the reference histogram); "o" (circle mark) represents that the shift amount is 10 times or more; "Δ" (triangle mark) represents that the shift amount is 3 times or more; and "x" represents that the shift amount is less than 3, respectively (an oblique line means no data is obtained).

[0195] FIG. **19** shows the results of RNAi in which CD147 is a subject antigen. Gray color (a); cells that have not subjected to RNAi are stained with an anti-influenza antibody YA14 cp3 as a primary antibody; Green color (b); cells that have not subjected to RNAi are stained with 059-053 cp3 as a primary antibody; Red color (c); cells that have subjected to RNAi are stained with 059-053 cp3 as a primary antibody.

[0196] FIG. **20** shows the results of RNAi in which CD166 is a subject antigen. Gray color (a); cells that have not subjected to RNAi are stained with an anti-influenza antibody YA14 cp3 as a primary antibody; Green color (b); cells that have not subjected to RNAi are stained with 035-234 cp3 as a primary antibody; Red color (c); cells that have subjected to RNAi are stained with 035-234 cp3 as a primary antibody.

[0197] FIG. **21** shows the results of RNAi in which HER1 is a subject antigen. Gray color (a); cells that have not subjected to RNAi are stained with an anti-influenza antibody YA14 cp3 as a primary antibody; Green color (b); cells that have not subjected to RNAi are stained with 048-006 cp3 as a primary antibody; Red color (c); cells that have subjected to RNAi are stained with 048-006 cp3 as a primary antibody.

[0198] FIG. **22** shows the results of RNAi in which HER2 is a subject antigen. Gray color (a); cells that have not subjected to RNAi are stained with an anti-influenza antibody YA14 cp3 as a primary antibody; Green color (b); cells that have not subjected to RNAi are stained with 015-126 cp3 as a primary antibody; Red color (c); cells that have subjected to RNAi are stained with 015-126 cp3 as a primary antibody.

[0199] FIG. **23** shows the results of RNAi in which IgSF4 is a subject antigen. Gray color (a); cells that have not subjected to RNAI are stained with an anti-influenza antibody YA14 cp3 as a primary antibody; light blue color (b); cells that have not subjected to RNAi are stained with 035-273 cp3 as a primary antibody; orange color (c); cells that have subjected to RNAi are stained with 035-273 cp3 as a primary antibody.

[0200] FIG. **24** shows A: an EGF binding inhibitory activity (using A431 cells) of 048-006 antibody and 059-152 antibody; B: an EGF binding inhibitory activity of 048-006 antibody (using low concentration range, A431 cells), and C: an EGF binding inhibitory activity of 048-006 antibody (using low concentration range, A431 cells).

[0201] FIG. **25** shows A: HER1 phosphorylation signal inhibitory activity of 048-006 antibody and 059-152 antibody (results of Western blotting). Lane 1; antibody is not added, lane 2; HR1-007 added (10 μg/ml), lane 3; 048-006 antibody added (10 μg/ml), lane 4; 048-006 antibody added (10 μg/ml), lane 5; 059-152 antibody added (10 μg/ml), lane 6; and 059-152 antibody added (10 μg/ml). Upper part shows the results of Western blotting by using anti-phosphorylation tyrosine antibody (mouse monoclonal antibody). Lower part shows the results of Western blotting by using anti-β actin antibody (rabbit polyclonal antibody). B: HER1 phosphorylation signal inhibitory activity of a 048-006 antibody (low concentration range). Lane 1; not treated, lane 2; antibody is not added, lane 3; HR1-007 is added (1 μg/ml), lane 4; 048-006 antibody added (0.5 μg/ml), lane 5; 048-006 antibody added (0.1 μg/ml), lane 6; and 048-006 antibody added (0.05 μg/ml). After incubation with an antibody for 30 minutes, Her1 was added. Upper part shows the results of Western blotting by using anti-phosphorylation tyrosine antibody (mouse monoclonal antibody). Lower part shows the results of Western blotting by using anti-β actin antibody (rabbit polyclonal antibody). C: Comparison of HER1 phosphorylation signal inhibition effects of 048-006 antibody, 059-152 antibody and ERBITUX (using A-431 cells. Lane 1; HR1-007, lane 2; 048-006 antibody, lane 3; 059-152 antibody, lane 4; ERBITUX, lane 5; antibody is not added (EGF (+)), lane 6; antibody is not added (EGF (−)). D: Comparison of HER1 phosphorylation signal inhibition effects of 048-006 antibody, 059-152 antibody and ERBITUX (using CCF-RC1 cells). Lane 1; HR1-007, lane 2; 048-006 antibody, lane 3; 059-152 antibody, lane 4; ERBITUX, lane 5; antibody is not added (EGF (+)), lane 6; antibody is not added (EGF (−)). E: Comparison of HER1 phosphorylation signal inhibition effects of 048-006 antibody and 059-152 antibody clone and ERBITUX (using Caki-1 cells). Lane 1; HR1-007, lane 2; 048-006 antibody, lane 3; 059-152 antibody, lane 4; ERBITUX, lane 5; antibody is not added (EGF (+)), lane 6; antibody is not added (EGF (−)).

[0202] FIG. **26** shows a result of BIACORE experiment. Fixation method: CM5 chip of BIAcore is used and NHS is used so as to fix a partial sequence of HER1 to sensor. 048-006 antibody is allowed to flow at the above-mentioned concentration to observe signals.

[0203] FIG. **27** shows a result of an ADCC activity test. An antibody to be used: anti-ITGA3 antibody, a target culture cell: HLF.

[0204] FIG. **28** shows a result of an ADCC activity test. An antibody to be used: anti-HER1 antibody, a target culture cell: A-431.

[0205] FIG. **29** shows a result of an ADCC activity test. An antibody to be used: anti-HER1 antibody, a target culture cell: A549.

[0206] FIG. **30** shows a result of an ADCC activity test. An antibody to be used: anti-HER1 antibody, a target culture cell: ACHN.

[0207] FIG. **31** shows a result of an ADCC activity test. An antibody to be used: anti-HER1 antibody, a target culture cell: CCF-RC-1.

[0208] FIG. **32** shows a result of an ADCC activity test. An antibody to be used: anti-HER1 antibody, a target culture cell: NCI-H1373.

[0209] FIG. **33** shows a result of an ADCC activity test. An antibody to be used: anti-HER1 antibody, a target culture cell: SK-OV-3.

[0210] FIG. **34** shows a result of an ADCC activity test. An antibody to be used: anti-HER2 antibody, a target culture cell: BT-474.

[0211] FIG. **35** shows a result of an ADCC activity test. (a) An antibody to be used: anti-ALCAM antibody, 066-174 whose, a target culture cell: NCI-H1373. (b) An antibody to be used: anti-ALCAM antibody, 066-174, target culture cell: CW2. (c) An antibody to be used: anti-ALCAM antibody, 066-174, target culture cell: NCI-H441.

[0212] FIG. **36** shows a result of an ADCC activity test. (a) An antibody to be used: anti-ALCAM antibody, 035-234, target culture cell: CW2. (b) An antibody to be used: anti-ALCAM antibody, 035-234, target culture cell: NCI-H441.

[0213] FIG. **37** shows a result of an ADCC activity test. (a) An antibody to be used: anti-ICAM1 antibody, 053-051, tar-

get culture cell: NCI-H441. (b) An antibody to be used: anti-ICAM1 antibody, 053-051, target culture cell: HepG2.

[0214] FIG. **38** shows a result of an ADCC activity test. (a) An antibody to be used: anti-ICAM1 antibody, 053-059, target culture cell: NCI-H441. (b) An antibody to be used: anti-ICAM1 antibody, 053-059, target culture cell: HepG2.

[0215] FIG. **39** shows a result of an ADCC activity test. (a) An antibody to be used: anti-ICAM1 antibody, 053-085, target culture cell: NCI-H441. (b) An antibody to be used: anti-ICAM1 antibody, 053-085, target culture cell: HepG2.

[0216] FIG. **40** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-HER1 antibody, 048-006 antibody or 059-152 antibody,

[0217] target culture cell: CCF-RC-1.

[0218] FIG. **41** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-HER1 antibody, 048-006 antibody or 059-152 antibody, target culture cell: NCI-H1373.

[0219] FIG. **42** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-HER1 antibody, 048-006 antibody or 059-152 antibody,

[0220] target culture cell: A-431.

[0221] FIG. **43** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-ALCAM antibody, 041-118 antibody, target culture cell: NCI-H1373.

[0222] FIG. **44** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-EpCAM antibody, 067-153 antibody, target culture cell: MKN-45.

[0223] FIG. **45** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-EpCAM antibody, 067-153 antibody, target culture cell: HT-29.

[0224] FIG. **46** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-EpCAM antibody, 067-153 antibody, target culture cell: NCI-H1373.

[0225] FIG. **47** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-HGFR antibody, 067-133 antibody, target culture cell: NCI-H1373.

[0226] FIG. **48** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-HER1 antibody, 055-147 antibody or 059-173 antibody, target culture cell: CCF-RC1.

[0227] FIG. **49** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-HER1 antibody. 048-006 antibody, 059-152 antibody, 055-147 antibody or 059-173 antibody, target culture cell: HT-29.

[0228] FIG. **50** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-HER1 antibody, 048-006 antibody, 055-147 antibody or 059-173 antibody, target culture cell: A431.

[0229] FIG. **51** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-HER1 antibody, 048-006 antibody or 059-152 antibody, target culture cell: ACHN.

[0230] FIG. **52** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-ALCAM antibody, 035-234 antibody or 066-174 antibody,

[0231] target culture cell: NCI-H1373.

[0232] FIG. **53** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-ALCAM antibody, 035-234 antibody or 066-174 antibody, target culture cell: SKOv3.

[0233] FIG. **54** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-ALCAM antibody, 035-234 antibody or 066-174 antibody, target culture cell: CW-2.

[0234] FIG. **55** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-ALCAM antibody, 041-118 antibody, target culture cell: EBC-1.

[0235] FIG. **56** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-ALCAM antibody, 080-040 antibody, target culture cell: NCI-H1373.

[0236] FIG. **57** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-ICAM1 antibody, 053-042 antibody, target culture cell: NCI-H1373.

[0237] FIG. **58** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-ICAM1 antibody, 053-051 antibody, 053-059 antibody or 053-085 antibody, target culture cell: NCI-H1373.

[0238] FIG. **59** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-EpCAM antibody, 067-153 antibody, target culture cell: EBC-1.

[0239] FIG. **60** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-HGFR antibody 067-133 antibody, target culture cell: MKN-45.

[0240] FIG. **61** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-HGFR antibody 067-133 antibody, target culture cell: EBC-1.

[0241] FIG. **62** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-ITGA3 antibody, 015-003 antibody, target culture cell: ACHN.

[0242] FIG. **63** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-CD147 antibody, 059-053 antibody, target culture cell: CCF-RC1.

[0243] FIG. **64** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-CD147 antibody, 059-053 antibody, target culture cell: ACHN.

[0244] FIG. **65** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-PTP-LAR antibody, 064-044 antibody or 079-085 antibody, target culture cell: PC-14.

[0245] FIG. **66** shows antibody dosage dependence of the ADCC activity. An antibody to be used: anti-CD44 antibody. 064-003 antibody, target culture cell: PC-14.

[0246] FIG. **67** shows a result of a cell proliferation inhibition test. An antibody to be used: anti-HER1 antibody (048-006), target subjected cultured cell: A-431.

[0247] FIG. **68** shows a result of a cell proliferation inhibition test. An antibody to be used: anti-HER1 antibody (048-006), target subjected cultured cell: ACHN.

[0248] FIG. **69** shows a result of a cell proliferation inhibition test. An antibody to be used: anti-HER1 antibody (048-006), target subjected cultured cell: NCI-H1373.

[0249] FIG. **70** shows a result of a cell proliferation inhibition test. An antibody to be used: anti-HER1 antibody (048-006), target subjected cultured cell: SK-OV-3.

[0250] FIG. **71** shows a result of a cell proliferation inhibition test. An antibody to be used: anti-HER2 antibody (015-126), target subjected cultured cell: BT-474.

[0251] FIG. **72** shows a result of an antitumor experiment using mouse. An antibody to be used: anti-HER1 antibody (048-006), subject transplant cell: human lung cancer cell H1373 cell.

[0252] FIG. **73** shows a result of an antitumor experiment using mouse. An antibody to be used: anti-HER1 antibody (048-006), subject transplant cell: epidermoid tumor A-431.

[0253] FIG. **74** shows a result of an antitumor experiment using mouse. An antibody to be used: anti-HER1 antibody (048-006), subject transplant cell: epidermoid tumor A-431.

[0254] FIG. **75** shows a result of an antitumor experiment using mouse. An antibody to be used: anti-HER1 antibody (059-152), subject transplant cell: epidermoid tumor A-431.

[0255] FIG. **76** is a table showing culture conditions of cell lines to be used in experiments.

[0256] FIG. **77** is a conceptual diagram of three-dimensional ELISA, showing how each mixture antibody is prepared.

[0257] FIG. **78** is a conceptual diagram of three-dimensional ELISA, showing a procedure of specifying an antibody clone.

[0258] FIG. **79** shows a result of ELISA using a plate mixed antibody (antigen is CD147).

[0259] FIG. **80** shows a result of ELISA using a row mixed antibody (antigen is CD147).

[0260] FIG. **81** shows a result of ELISA using a column mixed antibody (antigen is CD147).

[0261] FIG. **82** shows a result of ELISA using a plate mixed antibody (antigen is HER1).

[0262] FIG. **83** shows a result of ELISA using a row mixed antibody (antigen is HER1).

[0263] FIG. **84** shows a result of ELISA using a column mixed antibody (antigen is HER1).

[0264] FIG. **85** shows a result of ELISA using a selected antibody clone (antigen is HER1).

[0265] FIG. **86** shows a RNAi effect on SKOv-3 cells. A: anit-ITGA3 antibody, B: anit-ITGB1 antibody, C: 015-003 cp3 antibody. Broken line: no RNAi, solid line: ITGA3 RNAi, light-colored solid line: ITGB1 RNAi, gray: and no primary antibody.

[0266] FIG. **87** shows a correspondence between a tissue that has been diagnosed to be specific in immunostaining using a clinical cancer specimen and each antibody clone.

[0267] FIG. **88** shows a reactivity of a clinical cancer specimen and each antibody clone. + represents positive to the immunostaining; ± represents weakly positive to the immunostaining; and – represents negative to the immunostaining.

DETAILED DESCRIPTION OF THE INVENTION

Terms

[0268] For convenience, certain terms employed in the specification are collected herein.

[0269] In the specification, the terms "comprise/include" and "comprising/including" are used to include the meaning of "consisting of:" Therefore, for example, "a product (or method) comprising/including a plurality of elements (members)" necessarily includes also the terms "a product (or method) consisting of a plurality of elements (members)"

[0270] The term "disease" herein is used interchangeably with the terms meaning that some function failure occurs, for example, illness and sickness. Furthermore, unless otherwise noted, in this specification, this term is used to encompass the words meaning the condition (state) of disease such as condition, pathologic condition, symptom, and state of health. That is to say, the term "disease" is used interchangeably with the terms such as condition and pathologic condition.

[0271] The term "isolated" used herein means a state in which it is taken out from the original environment (for example, a natural environment in the case of a natural material), that is to say, means a state that is a different state from the original existing state by an artificial manipulation.

[0272] An "isolated antibody" does not include an antibody in a state in which it is natural state and no external manipulation (artificial manipulation) is given. It does not include an antibody produced in the individual body and remaining therein. An isolated antibody is typically present in a state in which other kinds of antibodies are not contaminated, that is, present singly (as an assembly of the same kinds of antibodies). In the case of an "isolated" state of the CDR region, in addition to the state which is present singly, a state which is present together with the other regions of the antibody is included. That is, the term "isolated CDR" includes not only a CDR that is present singly but also a CDR that is present as a part of an isolated antibody is included.

[0273] "HER1" is also referred to as erbB1, c-erbB-1, EGFR (Epidermal Growth Factor Receptor), or v-erbB. Originally, a gene corresponding to a cancer gene erbB found in the retrovirus that infects chicken and causes carcinogenesis (erythroleukemia) on the genome is isolated. And this gene is determined to be a receptor of EGF. By the way, EGF (Epidermal Growth Factor) as a ligand was found as a factor for promoting the cleavage of the eyelids of newly born mouse and development of an incisor in an extracted solution of the mouse submaxillary gland in 1962, and has been studied widely as cell proliferation, differentiation and survival factors. EGF is a peptide composed of 53 amino acids and has a characteristic structure including three disulfide loops formed of six cysteine residues. Thereafter, this structure has been found in a large number of proteins and is referred to as EGF-like domain. The EGF family has one or more EGF-like domains and directly binds to a receptor type tyrosine kinase EGF receptor (EGFR) family (another name: ErbB family) so as to activate this.

[0274] On the other hand, currently, four kinds of receptor ErbB families has been found and they are called EGFR (ErbB-1), ErbB-2, ErbB-3, and ErbB-4. ErbB-1 and ErbB-2 overexpress in various human tumors and are involved in the deterioration of the prognosis or survival rate. Furthermore, stimuli of these receptors are involved in cell proliferation and in turn involved in several processes related to progress, infiltration, and metastasis of tumor. To date, a phosphorylation inhibiting agent specific to EGFR have been approved as a therapeutic agent for lung cancer. They are found to highly express in many cancers. Cetuximab (ERBITUX, which is mouse/human chimeric antibody) has been developed by ImClone Systems and already marketed. ERBITUX inhibits the initial process of activation of the information transmission passage by the phosphorylation of dimerized-EGFR when it binds to a receptor of EGF as a ligand. Note here that the amino acid sequence of HER1 is shown in SEQ ID NO: 369.

[0275] "HER2" is also referred to as erbB-2, c-erbB-2, or neu. HER2 belongs to a receptor type tyrosine kinase family and its over-expression and gene amplification in the breast cancer, ovarian cancer, stomach cancer, and the like, have been reported. HER2 is a molecule that was found in 1985 when DNA containing a region of gene similar to EGFR was amplified (gene amplification) in the brain tumor and breast cancer derived from glia cells was observed. HER2 has low shedding level and is thought to be very effective as a target molecule in treating cancers. In many institutions, the monoclonal antibody (MoAb) showing effects of promoting or suppressing the tumor proliferation has been produced.

MoAb showing a tumor proliferation suppressing effect is used for clinical test as a simple substance of the antibody or in combination with anti-cancer drugs such as cisplatin, and its efficacy has been reported. The EGFR family includes four kinds, but only EGFR (HER1) and HER4 have both the ligand binding sites and tyrosine phosphorylation enzymatic activity sites. HER2 does not have the ligand binding site. Instead using a ligand, HER2 has a structure that is activated from the first in terms of dimer formation ability. Incidentally, HER3 lacks the tyrosine phosphorylation activity. Therefore, HER2-HER3 hetero-dimer is a functional molecule. Genentech isolated 11 kinds of mouse monoclonal antibodies to HER2 in 1989. Among them, 4D5 was made into a humanized antibody and succeeded in developing Trastuzumab (Herceptin). Note here that the amino acid sequence of HER2 is shown in SEQ ID NO: 370.

[0276] "CD46 antigen" is an O-type sugar chain bonded non-disulfide bonded dimer protein having a molecule weight of 56 to 66 kDa, which is also referred to as MCP (Membrane Co-factor Protein), gp45-70, HuLY-m5, measles virus receptor, MIC10, TLX-B antigen, TRA2, trophoblast leucocyte common antigen, and trophoblast-lymphocyte cross-reactive antigen. This molecule binds to C3b or C4b and is known as Membrane Co-factor Protein (MCP) that is a co-factor for promoting the degradation by serine protease or I factor in plasma. It is also a receptor of the surface protein of measles virus agglutinin and *Streptococcus* group A. It has been reported that it is expressed in the thymus gland cells, T lymphocyte, B lymphocyte, monocyte, granulocyte, NK cells, platelet, endothelial cell, epithelium cells and fibroblast but does not express in the erythrocyte. On the assumption that only cells inducing the production of antibody to cancer specific antigen abnormally expressing in carcinogenicity and escaping from the attack of cancer tissue by complement (complement-dependent cytotoxicity, CDC) may actually grow into cancer, the expression of molecule group having an effect of inhibiting the complement has been analyzed in detail. There have been many reports about the abnormal expression of CD46 in cancer cells, however, few evidence showing that the production of antibody against antigen specific to cancer cells are induced. An amino acid sequence of CD46 antigen is shown in SEQ ID NO: 371.

[0277] "ITGA3 (integrin alpha 3)" is also referred to as alpha 3 beta 1 Epiligrin Receptor, alpha 3 beta 1 Integrin, Epiligrin Receptor, CD49c, VLA-3, Gap b3, Galactoprotein b3, or Laminin-5 Receptor in which integrin α3 chain having a molecular weight of 150 kDa and integrin β1 chain (CD29 molecule) having a molecular weight of 130 kDa are bonded to each other non-covalently to form a VLA-3 complex (α3β1 or CD49c/CD29). It is known as a receptor of laminin, collagen, fibronectin, invasion and epiligrin. Integrin is a hetero dimer molecule composed of α chain and β chain. Twenty four types of α chains and nine types of β chain form a variety of molecule groups by various combination and selective splicing. The extracellular domain binds to the extracellular matrix (for example, collagen, fibronectin, laminin). The side of cytoplasm is bonded to actin filament via talin, filanin, and α-actinin. It functions as an adhesive molecule and further functions as an important role as information transmission molecule. Above all, α3β1 molecule is associated with a tetraspanin molecule C151. Note here that the amino acid sequence of ITGA3 is shown in SEQ ID NO: 372.

[0278] The "ICAM1 (Intercellular adhesion molecule-1)" is also referred to Intercellular Adhesion Molecule 1 or CD54 Antigen and is transmembrane glycoprotein having seven binding sites of the N-bonding sugar chain. The molecular weight is 90 kDa. ICAM belongs to Ig-superfamily and is known to be mainly involved with adhesion of leukocyte. It also mediates T lymphocyte adhesion to an antigen presenting cell (APC) and is involved with the interaction between T cell and T cell or between T cell and B cell. It also involved with the adhesion to endothelial cell in which monocyte, lymphocyte, and neutrophil are activated. ICAM is bonded to integrin of LFA-1 (CD11a/CD18) and Mac-1 (CD11b/CD18). Furthermore, it also is a receptor of rhinovirus. It is expressed on various kinds of activated cells in addition to the endothelial cells. For example, it is expressed on the monocyte. On B- and T-lymphocytes, thymus gland cells, dendritic cells, endothelial cells, fibroblast, keratinocyte, chondrocyte and epithelium cells, expression is enhanced. The characteristics required to obtain during the cancerization process of epithelium cells include capability of invading into cells, and furthermore migrating and being fixed in metastasis. Therefore, it is thought that the expression of adhesion factor contributes to carcinogenesis. The adhesion factor is roughly classified into five groups, i.e., selectin (E-, P-, and L-), molecules (Ig-superfamily) having an immunoglobulin-like domain, integrin, Cadherin, and CD44. In cancerization, it is recognized that the expression of E Cadherin is suppressed. Abnormal expression in some cancer cases has been reported. Note here that the amino acid sequence of ICAM1 is shown in SEQ ID NO: 373.

[0279] "ALCAM (Activaed leukocyte cell adhesion molecule)" is transmembrane protein that is also referred to as CD166 antigen, KG-CAM, CD6 Ligand, and Neurolin. ALCAM is an immunoglobulin superfamily molecule including ten N-bonding type sugar chain added sites. ALCAM has a molecular weight of 100 to 105 kDa and is composed of five extracellular Ig-like domains and the intracellular terminus having 32 amino acid, and short transmembrane region. ALCAM is one of the adhesive molecules, is present on the activated leukocyte and is identified as a ligand molecule to CD6 molecule (which functions as a signal receptor in T cells). ALCAM also functions as an adhesion factor in homophylic (ALCAM-ALCAM) or heterophylic (ALCAM-CD6) interaction. It is suggested that ALCAM can form oligomer at intercellular adhesion site via three C2-like domains near the membrane. The distribution of ALCAM is not restricted by cell strains and ALCAM is expressed in various types of cells such as hematopoietic cells, endothelial cells, epithelium cells of the thymic cortex and thymic medulla, mesenchymal cell of the bone marrow, fibroblast, liver cells, and the like. In the peripheral blood, it is weakly expressed in activated T- and B-cells, monocyte, circulated dendritic cells, and granulocyte. Although ALCAM shows wide dispersion of tissues, the expression of ALCAM is generally limited to cell populations involved in proliferation or migration. In the thymus gland, since ALCAM is expressed in CD6+thymus gland cells, and thymus gland epithelium cells, its interaction with CD6 molecule is thought to play a role in the differentiation of T cells. In addition, it is suggested that ALCAM adhesive molecules are involved in the fetal blood formation, differentiation of angioblastic cells, and capillary angiogenesis. The roles of ALCAM in cancerization is variously assumed (e.g., controlling of MMP activation, causing internalization and recycling, functioning as a substrate of ADM17 and ADAM10 (abbreviation of a disintegrin and metalloprotease), protecting from apoptosis and autophasy),

however, no decisive roles have not reported. The interaction of ALCAM-CD6 is thought to be carried out in the both direction. The amino acid sequence of ALCAM is shown in SEQ ID NO: 374.

[0280] "CD147 antigen" is membrane glycoprotein belonging to an immunoglobulin superfamily and is also referred to as BSG, TCSF (Tumor cell-derived collagenase stimulatory factor), 5F7 protein, OK blood group protein, basigin protein, collagenase stimulatory factor protein, EMMPRIN (Extracellular matrix metalloproteinase Inducer), M6 activation antigen, human leukocyte activation antigen M6, or the like. D147 antigen has two aspects. One is observed when it functions on the cell surface, it exhibits the activation of MMP-1, 2, 3 (matrix metalloprotease) and the lectin activity recognizing oligomannose as membrane glycoprotein having two Ig domains. The activation of MMP receives much attention in cancers (which is also known as EMMPRIN in Europe and America). That is to say, CD147 antigen expressing in cancer cells activates MMP expressing in the surrounding fibroblast and contributes to the infiltration of cancers. On the other hand, the activation of oligomannose lectin is especially important in the interaction of nerve cells and indicated to have a relationship with respect to neurite outgrowth. The second aspect is a function in cells. CD147 antigen forms a homo dimer. It is reported that this formation needs N-terminal Ig domain and does not need addition of sugar chain. CD147 has the following interesting reports: integrin $\alpha 3\beta 1$ and CD147 form a complex, and in this case, TM4SF (tetraspanin) molecule does not join the complex. In cancerization, the production of D147 changes anchorage-dependent growth to independent growth, which is promoted by the production of hyaluronic acid (hyaluronam). It is interesting that the receptor of hyaluronic acid includes CD44 and RHAMM. CD147 induces the production of MMP, and a part of CD147 is solubilized due to the effect of the MMP. CD147 acts on integrin so as to change the structure of cells. CD147 affects the angiogenesis. Furthermore, mass expression-cell proliferation of CD147 and Cyclophin A has been found.

[0281] The amino acid sequence of the CD147 antigen is shown in SEQ ID NO: 375.

[0282] "IgSF4" is an abbreviation of immunogloblin superfamily member 4 and is also referred to as BL2, ST17, NECL2, TSLC1, IGSF4A, SYNCAM, and sTSLC-1. IgSF4 has homology of NCAM (neural cell adhesion molecule) and amino acid sequence. IgSF4 is thought to be expressed from human 11-chromosome, 11q23.2. It has been reported that IgSF4 expressed as a suppression gene in a lung cancer specific manner and that IgSF4 is involved in the nerve adhesion in the brain (Biederer T et al. Science. 2002 Aug. 30; 297 (5586): 1525-31). The sequence information of IgSF4 is recorded in a NCBI-PUBMED database (Accession No. NM_01433, Definition: *Homo sapiens* immunoglobulin superfamily, member 4 (IGSF4), mRNA). As to the relationship with respect to the carcinogenesis, as shown by the name TSLC1 (tumor suppressor in lung cancer 1), it receives attention as a tumor suppressor gene. However, IgSF4 shows high expression in 100% adult T cell leukemia (ATL) cells and it is suggested that IgSF4 may work as oncogene. The amino acid sequence of IgSF4 is shown in SEQ ID NO: 376.

[0283] "C1qR" is a complement receptor encoding a type I membrane protein. This protein functions as a receptor for complement protein C1q, mannose binding lictin, and lung surfactant protein A. Two or more polypeptides of 70 kDa are bonded by disulfide bonding so as to form C1qR. Removing an immune complex is an important function of the complement and the C1q receptor is a functional receptor that is bonded to a collagen portion of C1q thereby linking the immune complex to phagocyte. It is suggested that C1qR forms complex with CD43. The amino acid sequence of C1 qR is shown in SEQ ID NO: 446.

[0284] "CD44" is a transmembrane protein belonging to a hyaladherin family, which is cell surface glycoprotein related to cellular interaction, cell adhesion and cell migration. It is a hyaluronic acid receptor. It is thought that a wide variety of the structural and functional isoforms of proteins by the selective splicing or post-translation modification of this molecule may be involved in tumor metastasis. The CD44 molecule is expressed in almost all the cells and tissues. However, in general, it is not expressed in the platelet, liver cell, cardiac muscle, uridiferous tubule epithelium, testis, and skin. The amino acid sequence of CD44 is shown in SEQ ID NO: 447.

[0285] "CD73" is also referred to as 5-prime-ribonucleotide phosphohydrolase and transforms purine 5-prime mononucleotides into nucleosides at the neutral pH. The enzyme mediates glycosylphosphatidyl inositol to the surface of the outside of the plasma membrane and is bonded to the surface of the outside of the plasma membrane. CD73 is a homodimer composed of two 70 kDA subunits. CD73 is used as a marker of the lymphocyte differentiation. It has been known that the deletion of this gene is related to various immune defective diseases. The amino acid sequence of CD73 is shown in SEQ ID NO: 448.

[0286] "EpCAM" has 22 or more names as to only the number of names used and cited several times in research paper. This antigen exists on genome 2p21. This antigen is a protein having a full length of 314aa, and 34920 Da. In the documents in which this molecule is examined at the mRNA level, it is detected in healthy human individuals, 100% in the peripheral blood (PB) level and 40% in the bone marrow (BM) level. It has been reported that it can be detected in large intestine but cannot detected in the liver, prostate, and lung. In cancer cell line, in the relationship with respect to p53, the methylation of EpCAM is lost due to the mutation or deletion of p53 and the amplification is induced. The amino acid sequence of EpCAM is shown in SEQ ID NO: 449.

[0287] The first Met gene discovered as a search product of oncogene using NIH3T3 gene is HGFR (Hepatocyte growth factor receptor). HGF is also referred to as a scatter factor and is utterly independently isolated as a molecule having an extremely different apparent function. Similar to HER1 and PDGF, HGFR is a receptor having a ligand binding domain outside the cells and has a tyrosine phosphorylation enzymatic activity site at the cytoplasm side, however, the function is extremely different. In general, when the cell proliferation factor or a differentiation induction factor is bonded to a receptor so as to cause the phosphorylation of protein, it finally activates the transcription factor and expresses a certain gene set by way of some of the limited information transmission pathway (Ras/MAP kinase pathway, and the like). In this case, the type of the cell response is finally determined by transcription factor. Thus, when the cancerization may activate some of the proliferation factors-receptor, it is thought that changes other than cancerization are not likely to occur in the cells. Currently, as to the cancerization, the phenomenon called epithelial-mesenchymal transition (EMT) receives much attention and the factor plays a core role in the phenomenon. In such examples, since a large

number of molecules cooperatively function, detail analysis is needed. The amino acid sequence of HGFR is shown in SEQ ID NO: 450.

[0288] LAR (Leukocyte common Antigen-Related) belongs to a PTP (protein tyrosine phosphatase) family. The PTPs are known to be molecules to modulate the process in the various aspects of the cancerization, division cycle, differentiation, cell growth, and the like. The structure thereof includes an extracellular region, mono-transmembrane region, and two tandem catalyzing domain in the cytoplasm (homolog of protein tyrosine phosphatase). The extracellular region has a structure similar to nerve cell adhesion factor, which includes three Ig-like domains and nine non-Ig like domains (homolog of NCAM). The function of this molecule is involved in the cell adhesion in the formation adherents junctions in the epithelium. Note here that it is confirmed that this molecule is highly expressed in insulin sensitive mast cells, and insulin resistant cells. Therefore, it is suggested that it is related to insulin. Furthermore, it is reported that anti-LAR antibody has an insulin receptor inhibitory activity of the insulin receptor forced expressing body (Knock-down of LAR protein tyrosine phosphatase induces insulin resistance: Mander A, Hodgkinson C P, Sale G J.: FEBS Lett. 2005 Jun. 6; 579 (14): 3024-8.).

[0289] Furthermore, LAR is expressed on the membrane of all the leukocytes and is referred to as protein tyrosine phosphatase receptor type F (PTPRF) and protein sequence (SEQ ID NO: 941) thereof is registered as TDHULK in Protein sequence database of the Protein Information Resource (PIR).

[0290] BCAM (basal cell adhesion molecule) (Lutheran blood group) is referred to as CD239 antigen and its protein sequence is registered as Q86VC7 (UniProtKB/Swiss-Prot) and 13800 (PIR) (SEQ ID NO: 942). It produces a selective splicing product from a single gene in the chromosome 19q13.2-q13.3. It is a glycoprotein having an immunoglobulin-like domain. It is a mono-transmembrane type and expressed widely. Its expression in the pancreas is high and its expression in the brain is low. The BCAM antigen is modulated excessively in certain cells, thus inducing the malignant alteration of cancers. Also, it is shown that it is overexpressed in the living body with ovarian cancers.

[0291] In the present invention, "liver cancer" is intended to be widely interpreted and it includes liver carcinoma and liver sarcoma. Furthermore, the term "cancer" in the present invention is interchangeably with "tumor." Furthermore, in the stages before the pathological diagnosis is not established, that is, before whether the tumor is benign or malignant has not been determined, the term may include benign tumor, benign-malignant borderline lesion, and malignant tumor collectively.

[0292] Cancers are called under the name of the organs in which the cancers are developed or the name of development body tissue. Main examples include tongue cancer, gingival cancer, pharynx cancer, maxillary cancer, laryngeal cancer, salivary gland cancer, esophageal cancer, stomach cancer, small intestinal cancer, large bowel cancer, rectum cancer, liver cancer, biliary tract cancer, gallbladder cancer, pancreas cancer, lung cancer, breast cancer, thyroid gland cancer, adrenal gland cancer, hypophyseal tumor, pinealoma, uterine cancer, ovarian cancer, vaginal cancer, urinary bladder cancer, kidney cancer, prostate cancer, urethral cancer, retinoblastoma, conjunctival cancer, gliocystoma, glioblastoma, skin cancer, leukemia, malignant lymphoma, testicular tumor, osteosarcoma, rhabdomyoblastoma, leiomyosarcoma, blood vessel sarcoma, liposarcoma, chondrosarcoma, Ewing's sarcoma, and the like. Furthermore, depending upon the characteristics of the sites of the organs of development, cancers are subclassified into, for example, upper, middle, and lower pharynx cancers, upper, middle, and lower esophageal cancers, gastric cardia cancer, gastropyloric cancer, cervical cancer, cancer of uterine body, and the like. These cancers are included in the "cancers" of the present invention but the cancers are not limited to these alone.

[0293] In the specification, if necessary, the following abbreviations (in parentheses) are used according to the practice.

[0294] Heavy chain (H chain), light chain (L chain), heavy chain variable region (VH), light chain variable region (VL), complementarity determining region (CDR), first complementarity determining region (CDR1), second complementarity determining region (CDR2), third complementarity determining region (CDR3), first complementarity determining region of heavy chain (VH CDR1), second complementarity determining region of heavy chain (VH CDR2), third complementarity determining region of heavy chain (VH CDR3), first complementarity determining region of light chain (VL CDR1), second complementarity determining region of light chain (VL CDR2), third complementarity determining region of light chain (VL CDR3)

[0295] The first aspect of the present invention relates to a method of classifying antibody. The classifying method of the present invention includes the following steps.

[0296] (1) preparing a plurality of antibodies recognizing cell surface antigen;

[0297] (2) bringing each of the antibodies into contact with cells of the same kinds;

[0298] (3) analyzing each cell after step (2) by flow cytometry so as to obtain data showing reactivity between the antibody and the cell surface; and

[0299] (4) comparing the obtained data and classifying antibodies based on the similarity of the data.

Step (1)

[0300] In the classifying method of the present invention, firstly, a plurality of antibodies recognizing cell surface antigen are prepared. For convenience of explanation, the antibody classified by the classifying method of the present invention is also referred to as a "sample antibody."

[0301] In the present invention, the "cell surface antigen" is a molecule in which at least a part thereof exists outside the cell and which forms an antigenic determinant on the surface of the cell. For example, protein such as transmembrane type protein having a cell membrane transmembrane domain and an extracellular domain and GPI anchor type protein, which are linked to cell membrane via glycolipid and the like and existing on the surface of the extracellular surface, can form such an antigenic determinant. The cell surface antigen can be formed by a simple protein (basically, constituent includes only amino acids), a conjugated protein (constituent other than amino acid are contained. For example, glycoprotein and lipoprotein), or a modified protein (a protein modified by, for example, phosphorylation, acetylation, and methylation), and the like. Furthermore, two or more same types or different types of molecules may cooperatively form an antigen determinant.

[0302] The "cell surface antigen" of the present invention is not particularly limited to animal cells and may include cell

surface antigens of plant cells, microorganism cells, and the like. Preferably, "cell surface antigen" of the present invention is the cell surface antigen of animal cells. It is known that the animal cells have various cell surface antigens. The "animal cells" herein include mammalian cells and non-mammalian cells, but preferably mammalian cells. Above all, human cells are preferable.

[0303] Preferably, a plurality of antibodies recognizing the intact cell surface antigen are prepared. The "intact state" means that the original state is maintained. It has the same meaning that "not denatured state."

[0304] The "antibody recognizing cell surface antigen" represents an antibody recognizing and binding the cell surface antigen with highly specific recognition mechanism between the antigen and the antibody. The origins, types, classes, forms and the like, of antibodies are not particularly limited. Therefore, the "antibody" in the present invention includes an antibody of non-human animals such as mouse and rat, a chimeric antibody in which a part of the region is substituted with that of other animal (including human), a humanized antibody, and human antibody. Preferably, human antibody or human type antibody (humanized antibody) are used. Antibody fragments such as Fab, Fab', F(ab')2, scFv, and dsFv antibody may be used. An antibody for treatment application includes an antibody in which VH and VL (Fv region) are converted into IgG type is included.

[0305] An antibody recognizing a cell surface antigen can be prepared by, for example, bringing an antibody library into contact with the cell surface antigens and recovering the antibodies bound to the cell surface antigens. One of such preparation methods is a method reported by the present inventors before (Japanese Patent Unexamined Publication No. 2005-185281). This method makes it possible to select an antibody clone recognizing intact cell surface antigen from the phage antibody library. The present invention can preferably use the antibody assembly derived from each antibody clone. The "assembly derived from each antibody clone" herein includes the selected antibody clone itself, or the product prepared by using the gene. The latter example includes an antibody in which genes of the selected antibody clone is transformed by an appropriate host (for example, *E. coli*) and the host is expressed, or an antibody to which further genetic engineering modification is added in the host or by the use of the host and then the modified antibody is expressed.

[0306] The above-mentioned publication discloses as the antibody having a human Fv region, scFv-CL-cp3 antibody (an antibody in which a phage protein cpIII is fused to scFV via the light chain constant region), scFv-CL-pp antibody (an: antibody in which two proteins A are fused to scFV via the light chain constant region), scFv-CL-pp-Avi antibody (an antibody in which avidin is fused to scFv-CL-pp antibody), scFv-CL-Avi antibody (an antibody in which avidin is fused to scFV via the light chain constant region), scFv-CL-pp-Avi or antibody obtained by biotining scFv-CL-Avi antibody (an antibody in which biotin is bonded to an avidin part), and the like. The present invention can preferably use any of these types of antibodies. These antibodies having a human Fv region are very useful in providing an antibody for treatment (production of an antibody for treatment can be proceeded advantageously).

[0307] Note here that the contents disclosed Japanese Patent Unexamined Publication No. 2005-185281 are herein incorporated by reference in its entity.

[0308] A combination of separately prepared antibodies may be used as the "plurality of antibodies recognizing cell surface antigen" in the present invention. In this case, the preparation method of each antibody may be the same as or different from each other.

[0309] An antibody in which a label material has been bound or fused in advance (which is collectively referred to as "labeled sample antibody") may be used. The former example can include an antibody labeled with fluorescence pigment. The latter example can include an antibody in which fluorescence proteins (fluorescence protein fused antibody) such as GFP (Green Fluorescent Protein) and RFP (Red Fluorescent Protein) have been fused. Such fluorescence protein fused antibody can be prepared easily by using genetic engineering technique.

Step (2)

[0310] Next, the sample antibodies are brought into contact with cells of the same kinds, respectively. That is to say, cells to be used are determined, and then the cells are brought into contact with the sample antibody for each sample antibody. The sample antibody recognizing the surface antigen of the cells to be used binds to the cell surface. The binding amount of the sample antibody is dependent upon the expression amount of the cell surface antigen recognized by the antibody.

[0311] Cells that are brought into contact with the sample antibody are not particularly limited and may be arbitrarily selected from animal cells, plant cells, microorganism cells, and the like. For example, in one preferable embodiment, cells derived from a patent having a certain disease (or having a certain pathologic condition) are used. The "certain disease" includes various kinds of cancers, for example. The tissues or organs from which the cells are derived are not particularly limited. An example of the certain disease include kidney cancer, hepatic cell carcinoma, gallbladder and liver cancer, alveolar cell carcinoma, lung squamous cell cancer, pulmonary adenocarcinoma, pancreas cancer, adenocarcinoma, ovarian cancer, and the like.

[0312] Cells forming a highly uniform cell population are preferably used. It is preferable because such cells can provide easier or simpler data, facilitates the comparison of data and provides more reliable comparison results in the below-mentioned flow cytometry analysis. The typical example of such cells is established cell line (cell line). Preferable examples include established cancer cell line such as liver cancer cell line HepG2, undifferentiated liver cancer cell line HLF, liver cancer cell line OCTH, intrahepatic bile duct cancer cell line RBE, pancreatic cancer cell line PANC-1, pancreas cancer cell line MIA-Paca2, kidney cancer cell line CCFRC1, kidney cancer cell line Caki-1, kidney cancer cell line ACHN, kidney cancer cell line 293T, ovarian cancer cell line KF28, ovarian cancer cell line SKOv3, ovarian cancer cell line KF-28, ovarian cancer cell line RMG-1, ovarian cancer cell line RMG-2, breast cancer cell line BT474, vulvar mucosa epithelium cell line A431, stomach cancer cell line SNU-5, stomach cancer cell line MKN45, stomach cancer cell line NCI-N87, cancer cell line RERF-LC-AI, pulmonary adenocarcinoma cell line PCI4, lung cancer cell line NCI-H441, lung squamous cell canceEBC1, pulmonary adenocarcinoma cell line H1373, pulmonary adenocarcinoma cell line A549, pulmonary adenocarcinoma cell line Calu-3, pulmonary adenocarcinoma cell line PC14, large bowel cancer cell line CaCo2, large bowel cancer cell line CW2, hamster ova-

rian cancer cell line CHO, and the like. Note here that cells whose uniformity is improved by culture operation is one of the most preferable cells.

[0313] Each sample antibody is brought into contact with cells in an appropriate solution. At this time, it is preferable that the conditions are set so that the properties of the sample antibody are not affected and cells are not damaged. For example, cells and the sample antibodies are co-existed in the culture solution suitable for the existence and proliferation of the cells, in the phosphoric acid buffer and citric acid buffer, in physiologic saline, or in a solution in which BSA for suppressing non-specific adsorption is added, at room temperature to low temperatures (for example, 0° C. to 25° C., preferably 4° C. to 15° C.), for 20 minutes to 3 hours. During this time, the solution may be stirred.

[0314] The conditions under which each sample antibody and cells are brought into contact with each other are made to be uniform in order to obtain highly reliable data.

[0315] After contacting operation mentioned above, labeling is carried out if necessary (other than the case when a labeled sample antibody is used). The "labeling" herein denotes labeling the sample antibody bound to the surface of the cells. For example, labeling can be carried out by reacting (contacting) an antibody having a specific binding ability to the sample antibody to which a label material has been bound (antibody to be detected) with cells after the contacting operation. Instead of directly binding an antibody to be detected to the sample antibody, other antibodies and the like may be interposed therebetween. Thus, various labeling techniques can be employed and a person skilled in the art can select an appropriate technique. In the flow cytometry analysis, in general, fluorescent dye is used as a label material. Fluorescent dye such as Alexa488, AMCA, Cascade Blue (registered trademark), FITC, PerCPTM, CyTM3, Texas Red (registered trademark), CyTM5, APC, TRITC, and the like, can be used.

Step (3)

[0316] Subsequently, cells after subjecting to the step (2) are analyzed by flow cytometry so as to obtain data showing the reactivity between the antibody and the cell surface. That is to say, cells after subjecting the contacting operation to the sample antibody are subjected to the flow cytometry analysis, and the binding property to the sample antibody is examined. Preferably, as the data showing the "reactivity" herein, histogram showing the relationship between the antibody binding amount and the number of cells is used. That is to say, one-parameter histogram in which the antibody binding amount is used as a parameter is used. The one-parameter histogram is one display method in the flow cytometry. The one-parameter histogram is generally shown in a graph in which X-axis represents one indicator (parameter) and Y-axis represents the number of cells. For the device used for the flow cytometry analysis, for example, devices from BECKMAN COULTER, Japan Becton, Dickinson and Company, and the like can be used in the present invention. The operation may be carried out according to the basic operation and analysis conditions attached to the device. Furthermore, many research paper and documents about the flow cytometry analysis are published. See, for example, Cao T M, et al. Cancer. 2001 Jun. 15; 91 (12): 2205-13., Storek K J, et al. Blood 97: 3380-3389, WEIR'S HANDBOOK OF EXPERIMENTAL IMMUNOLOGY Vol. II <Blackwell Science>, Little MT and R. Storb Nature Reviews Cancer 2002 2: 231-238.

[0317] Typical procedure of the flow cytometry analysis is described below. The sample antibody and cells are reacted with each other, then reacted with antibody to be detected labeled with fluorescent dye, so that cells are labeled with fluorescence. The amount of sample antibody to be bound varies depending upon the amount of antigen existing on the surface of the cells. As a result, the amount of fluorescent label of the cells becomes different. Therefore, by measuring the fluorescence intensity, the affinity between the antigen existing on the surface of the cell and the ample antibody and the amount of antigen can be estimated. In general, prior to the detection of the fluorescence intensity, forward scatter light (FSC) and side scatter light (SSC) are measured and gated, so that the fluorescence intensity of only the target cell population is measured. Specifically, for example, the forward scatter light and the side scatter light are shown in X-axis and Y-axis, respectively. The cell population (when established cell lines or cultured cells are used, the cell population becomes extremely uniform) that are assumed to be living cells from the data obtained by dot plot expansion are gated, and the fluorescence intensity within the gate is measured. The measurement result is shown in a form of, for example, histogram. Note here that the terms related to the histogram obtained in the flow cytometry analysis are mentioned below.

[0318] The "number of samples" denotes number of data and generally represented by n. The "total" denotes a total of data and generally represented by T. "Mean value" denotes an average of data and is calculated by dividing the total by the number of samples. The mean value is susceptible to abnormal data. The "median value" is a value located in the middle when the data are aligned in ascending numeric order. When the number of data is odd number, the average of two middle values is defined as a median value. The median value is less susceptible to abnormal data as compared with the mean value and shows the characteristics of the population more accurately. The "mode" denotes a value whose frequency is maximum in the data. In the case of the flow cytometry analysis, the mode is the same as a peak value. The mode is less susceptible to abnormal data as compared with the mean value. The "maximum value" is a maximum value of data and generally represented by Max.

[0319] The "range value" is difference between the maximum value and the minimum value and generally called range and referred to as R. The "dispersion" is a value showing the degree of variation of data. The larger the dispersion is, the larger the variation is. In general, it is referred to as V. The dispersion is obtained by dividing the sum of squares deviation by the number of samples (in the case of sample survey, divided by (number of samples −1)). The "standard deviation" denotes square root of the dispersion and is generally referred to as u. The "coefficient of variation" is a value obtained by dividing the standard deviation by an average value and is generally referred to as CV. Since the standard deviation does not clearly shows the degree of variation of data, the standard deviation is normalized by dividing it by the average value. In the flow cytometry analysis, it is frequently used as a value showing the resolving power of the device. The "kurtosis" is one of the indicators representing the distribution in the population and generally is referred to as H. The distribution in which the kurtosis is 0 is defined as normal distribution. When the kurtosis is larger than 0, the distribution has sharper apex than the normal distribution. When the kurtosis is smaller than 0, the distribution becomes more

flatness than the normal distribution. The "skewness" denotes a value showing the left-right symmetry of the population and generally is referred to as G. When the skewness is 0, distribution becomes left-right symmetric. When the skewness is larger than 0, the distribution distorts in the right direction. When the skewness is smaller than 0, the distribution distorts in the left direction.

Step (4)

[0320] Next, the obtained data are compared and sample antibodies are classified based on the similarity of the obtained data. Herein, "based on the similarity" means that the similarly of data are used as a criterion of classification. An example of criterion (classification criterion) based on the similarity of data is shown below.

[0321] (a) A plurality of antibodies having the identical or highly similar data are classified into one antibody group. Specifically, for example, plurality of antibodies having extremely similar histogram is defined as one group when the shape of the histogram showing the distribution of cells is determined by the kurtosis, skewness and the like.

[0322] (b) An antibody providing specific data forms one antibody group by itself.

[0323] (c) An antibody having a low reactivity with respect to the antigen is excluded

[0324] (the antibody does not belong to any groups).

[0325] In the present invention, each antibody is classified by one or two or more criteria selected from the above-mentioned classification criteria (a) to (c).

[0326] The similarity of data can be determined based on the parameter specifying the data. However, the specific determination method is dependent upon the types of data. In the case where data are represented by numeric values, it is possible to determine the similarity based on the degree of similarity of numeric values (for example, when 1, 2, and 5 are given as data, it is determined that the similarity between 1 and 2 has high similarity).

[0327] Furthermore, when a histogram is given as data, it is possible to determine the similarity of data based on the shape of the histogram. As a result of the investigation by the present inventors, it is determined that the shape of the histogram in the flow cytometry analysis is highly dependent upon the kinds of the antigen. In other words, when the antigens to be recognized are the same, regardless of the kinds of antibodies, it is determined that the histogram having an identity or high similarity can be obtained. Base on this fact, in one embodiment of the present invention, by comparing the shapes of the histogram showing the results of the flow cytometry analysis, the similarity of data is determined. Specifically, the similarity of data can be determined by comparison by visual observation or by comparison of one or two or more of parameters specifying the histogram. The parameters herein can employ one or more values selected from the group consisting of median value, mode, maximum value, range, standard deviation, kurtosis, and skewness of the histogram. Preferably, determination is carried out in terms of two or more values, furthermore preferably three or more values, and yet furthermore preferably four or more values. By increasing parameters to be used in determination, the determination accuracy can be improved. Among these parameters, it is said to be advantageous that the median value, mode, or kurtosis that are parameters deeply related to the shapes of the histogram are employed for carrying out the determination at high accuracy. Preferably, a combination of two or more of these parameters is used. Specifically, for example, the similarity of the histogram may be determined based on the median value, mode, and kurtosis.

[0328] When two data to be compared have similar values in terms of employed parameters, the similarity between the two data is determined to be high. When the difference between two values ($100\times(A-B)/A$ (%) when the two values are A, B ($A \geqq B$)) is within 10%, preferably within 5%, and furthermore preferably within 3%, the two values are determined to be similar.

[0329] In one embodiment of the present invention, when or after the sample antibodies are classified, sample antibodies having a low reactivity to the cell surface antigen are removed. Thereby, an antibody group including highly useful sample antibodies can be formed. The degree of the reactivity of the antibody can be determined by using the results of the flow cytometry analysis. Specifically, the mode (peak value) of the histogram obtained with respect to the sample antibody to be determined and the mode (that is to say, the maximum mode in the group) of the histogram obtained with respect to the sample antibody having the maximum reactivity in the antibody group to which the sample antibody belongs. As a result, when the former is ½ or less of the latter, preferably ⅕ or less, furthermore preferably 1/10, it is determined that the sample antibody to be determined has low reactivity.

[0330] In one embodiment of the present invention, the reactivity of each sample antibody is examined in two or more kinds of cells and the sample antibodies are classified by using the results. That is to say, two or more kinds of cells are prepared and by using the prepared cells, steps (2) to (4) are carried out.

[0331] The expression amount, distribution, and the like of the cell surface antigens are dependent upon the kinds of cells. Therefore, two antibodies having high similarity in data obtained by using certain cells, that is, two antibodies having the common antigens should provide data having high similarity when the other cells are used. Thus, when the two antibodies to be compared provide data with high similarity with respect to more than two kinds of cells, the probability that the antibodies have the common antigens is extremely high. Furthermore, when such results are obtained, it can be easily determined that the two antibodies have the common antigens. Thus, the use of two kinds or more cells can make it accurate and easy to determine the identity of antigens.

[0332] In one preferable embodiment of the present invention, sample antibodies having identical or highly similar data with respect to at least two kinds of cells are classified into one antibody group.

[0333] Furthermore, by observing the classification results of the case where two or more kinds of cells are used, kinds or amount of antigens to be expressed can be compared between the cells. Therefore, more useful information can be provided in studying the properties of these cells.

[0334] In one embodiment of the present invention, a classification result is displayed as a panel. The "panel" in this specification is a product in which a plurality of elements (for example, antigen, antibody, antibody group, cell, name of disease, name of pathologic condition), are displayed in the form of tables or drawings, in which the elements are associated with each other, on media such as a display and paper. Each element is represented by general name, abbreviation, alias, or symbol or code representing thereof, and the like. The panel of the present invention shows the relationship with respect to two kinds or more of elements.

[0335] The term "associating to" in the present invention means that two or more elements are linked. Therefore, in the tabular format panel showing the association between an antigen and an antibody group, for example, both elements are displayed in adjacent to each other, or both elements are displayed in the same cells, or both elements are linked by a line or something, so that it can be understood that the both elements form a pair.

[0336] In the panel herein, typically, antibody groups are displayed in a way in which they are associated with each other for each antigen (or for each antigen having high association) expressed by the cells that have been subjected to the flow cytometry analysis. Therefore, this panel makes it possible to access antibodies useful for studying surface antigens of the cells. Thus, the panel itself of the present invention has a great value. A panel formed by using two kinds or more of cells makes it possible to understand the presence, expression amount, and the like, of antigens expressing between cells. Such a panel has further higher values.

[0337] In the panel of the present invention, antibodies may be arranged regularly in accordance with the reactivity to antigens. Thus, the difference in the reactivity between antibodies can be made obvious.

[0338] According to the classifying method in the present invention, a plurality of antibodies recognizing the same antigen (or antigens having high association) are associated with each other. In other words, for each antigen (or for each antigen having high association), antibody assembly (antibody group) recognizing the antigen can be obtained. These antibody groups are useful for studying cell surface antigen and have high usability. Furthermore, according to the classifying method of the present invention, a large number of antibodies can be classified rapidly for each antigen (or for each antigen having high association). That is to say, the classifying method of the present invention is useful for classification of a large number of antibodies and allows comprehensive classification of antibodies. The term "highly associated" or "having high association" used for antigen means that two or more antigens have a close association in a living body, for example, the antigens are not the same molecules but exhibit one function cooperatively (for example, two antigens are bound so as to form one complex functionally).

[0339] According to the classifying method of the present invention, typically, plurality of antibodies are associated with each other for each antigen (or for each antigen having high association). Therefore, in studying certain antigens, a plurality of antibodies can be used or suitable antibodies can be selectively used if necessary, which leads to better results or significant findings and means that studying can be proceeded advantageously.

[0340] On the other hand, by executing the classifying method of the present invention, it is possible to understand the expression amount of distribution of cell surface antigens (antigen are unknown) in certain cells (that is, cells that are brought into contact with the sample antibody). Thus, the classifying method of the present invention provides useful information on the properties of the certain cells and is useful for studying the cells (in particular, the surface antigens).

[0341] Note here that when antigens to all the sample antibodies are unknown, antigens to which each antibody group is associated are not identified. On the other hand, when some identified antigens are contained in a part of the sample antibodies, an antigen to which the antibody group containing the antibody becomes an identified antigen. Thus, it is also possible to associate an antibody group with the identified antigen.

[0342] According to the above-mentioned classifying method, antibodies are classified based on the reactivity between the antigens and certain cell surfaces and the antibody groups are formed. Therefore, antibodies belonging to the same antibody group have the same (or highly similar) reactivity to the surface of cells used for classification. However, it is not necessarily ensured that all the antibodies belonging to the same antibody group can recognize the same antigens. Even if the recognizing antigen is the same, the reactivity to cells expressing antigens on the cell surface may be different. Furthermore, the opposite case may occur (even if the recognizing antigen is different, the reactivity to cells expressing antigens on the cell surface may be the same, for example, one of the complex may be recognized).

[0343] Therefore, in order to form an antibody for each recognizing antigen, one embodiment of the present invention carries out the following steps (i) to (vi) after the step (4).

[0344] (i) associating the classified antibodies with a combination of n pieces of parameters including a first parameter, a second parameter, . . . , and an n-th parameter (wherein, n represents an integer of 2 or more, each parameter has two or more parameter values and the same parameter value is given to two or more antibodies in each parameter);

[0345] (ii) with respect to each parameter, preparing an antibody mixture of the antibodies having the same parameter value;

[0346] (iii) examining a reactivity of each of the antibody mixtures with a target antigen by an enzyme linked immunosorbent assay (ELISA) so as to specify the antibody mixture which shows reactivity;

[0347] (iv) specifying a combination of a parameter name and a parameter value that are common to the antibody group contained in the specified antibody mixture;

[0348] (v) selecting an antibody corresponding to the combination specified in the step (iv) in terms of all parameters among the antibodies subjected to step (i); and

[0349] (vi) classifying the selected antibodies into one antibody group.

[0350] According to the classifying method of this embodiment, an antibody group can be formed for each antigen to be recognized. That is to say, antibody groups having various individualities recognizing the same antigen can be obtained. Furthermore, the combination of the plurality of parameters is associated with each antigen and then an antibody mixture is prepared according to a predetermined regulation. Then, based on the results of ELISA (Enzyme-Linked immunosorbent assay) using the antibody mixture, an antibody recognizing a target antigen is determined. By this unique technique, antibodies can be classified rapidly and efficiently. Furthermore, at the same time when the antibodies are classified, as to at least a part of the antibodies, an antigen is identified. That is to say, the classifying method of this embodiment is a method of rapidly and efficiently obtaining an antibody whose antigen has been identified, which dramatically promote the increase in the number of antibodies whose antigens have been identified. On the other hand, the classification results show the presence form or expression from on the cell surface used in flow cytometry analysis, which provides extremely useful information for study and development of the application of antibody (for example, treatment of cancer). Furthermore, when the presence of a

certain antigen is clarified based on the classification results, it is possible to obtain an unknown antigen (for example, complex counterpart) that is thought to be possible to exist in a form of a complex with the antigen. That is to say, the classifying method of this embodiment efficiently functions as determining a novel antigen or novel molecule complex. Hereinafter, each step is described in detail. For convenience of explanation, the classifying method of this embodiment is also referred to as "n dimensional ELISA method."

Step (i)

[0351] In this step, a combination of n pieces of parameters consisting of the first parameter, the second parameter, . . . , and the n-th parameter are associated with antibodies classified by the preceding steps (steps (1) to (4)). Thus, each antibody has n-dimensional address (a parameter value of the first parameter, a parameter value of the second parameter, . . . , and a parameter value of the n-th parameter).

[0352] In general, association is carried out with respect to all the antibodies that have been classified in the preceding steps, although the association is not limited to this. That is to say, the association may be carried out only a part of the antibodies that has been classified in the preceding steps. In this case, a part of antibodies are excluded from the antibodies to be classified.

[0353] Herein, "n" is an integer of two or more. That is to say, to each antibody, two or more combinations of parameters are associated. The number of "n" does not have an upper limit. When the number of "n" is too large, operations in the subsequent steps (for example, preparation of an antibody mixture, specification of an antibody mixture showing the reactivity) may be excessively complicated. Therefore, "n" is preferably three to five.

[0354] On the other hand, each parameter is made to have two or more parameter values and the same parameter values of each parameter are made to be provided to two or more kinds of antibodies. Specifically, parameter values of the first parameter may be 1, 2, 3 and 4, and each parameter value is provided to five kinds of antibodies, respectively. The number of the parameter values is set for each parameter. Furthermore, similar to the number of parameters, the number of the parameter values does not have an upper limit. In order to make the analysis in the following steps (iv) and (v) be efficient and improve the accuracy thereof, it is preferable that the kinds of antibodies contained in each antibody mixture are not excessively large number. Therefore, each parameter value may be set so that the kinds of antibodies contained in each antibody mixture is preferably 200 or less, and furthermore preferably, 100 or less. Specifically, for example, the number of the parameter values can be set to between 2 and 100. Note here that the kind of antibodies contained in each antibody mixture is dependent upon the setting of the parameter, and may not be equal between antibody mixtures.

Step (ii)

[0355] In this step, an antibody mixture, in which antibodies having the same parameter value are mixed, is prepared. The antibody mixture is prepared for each parameter. For example, when the values of the first parameter is 1, 2, 3 and 4, an antibody mixture mixing antibodies to which 1 is given as the first parameter, an antibody mixture mixing antibodies to which 2 is given as the first parameter, an antibody mixture mixing antibodies to which 3 is given as the first parameter, and an antibody mixture mixing antibodies to which 4 is given as the first parameter are prepared. By the same procedure, as to the remaining parameters, antibody mixtures are prepared. Thus, antibody mixtures in the same number as the total number of the number of the first parameter, the number of the second parameter, and the number of the n-th parameter are prepared.

[0356] In general, an antibody mixture, in which all antibodies having the same parameter values are mixed, are prepared although the antibody mixture is not limited to this. An antibody mixture may be prepared by selecting a part of all antibodies having the same parameter values and mixing thereof. Thus, the selection of antibodies may be carried out in this stage.

[0357] It is preferable that an antibody mixture is prepared so that all antibodies are contained in equal amount and the amount of each antibody (that is, concentration for each antibody) is equal between antibody mixtures. Adjusting the amount of antibodies in this way facilitates the specification of the antibody mixture based on the reactivity in the following ELISA.

Step (iii)

[0358] In this step, the reactivity between each of the antibody mixtures and the target antigen is examined by ELISA so as to specify the antibody mixture showing the reactivity. When at least one of the antibodies recognizing the target antigen is contained in the antibody to be used for preparing the antibody mixture, a plurality of antibody mixtures shows the reactivity. On the other hand, when the antibody recognizing the target antigen is not contained, any of the antibody mixtures will not show reactivity. In this case, the operation is terminated without continuing the following operations.

[0359] The target antigen herein nay include HER1, HER2, CD46, ITGA3, ICAM1, ALCAM, CD147, IgSF4, BCAM, CIqR, CD44, CD73, LAR, EpCAM, HGFR, and the like. The target antigen can be arbitrarily selected. The antigen determined by the below-mentioned identification methods (step (5) and (6)) may be used as the target antigen herein.

Step (iv)

[0360] In this step, a combination of a parameter name and a parameter value that are common to the antibody group contained in the specified antibody mixture is specified. In the present invention, the combination specified herein is referred to as "positive combination." Specifically, the positive combination is specified like (first parameter, parameter value a1), (second parameter, parameter value a2), . . . , (the n-th parameter, parameter value an). When a plurality of antibody mixtures having the different degree of reactivity are recognized in the step (iii), similarly, specification may be carried out for each level of the reactivity. For example, the middle level of positive combination may be specified like (first parameter, parameter value a1), (second parameter, parameter value a2), . . . , (the n-th parameter, parameter value an); and the high level of positive combination may be specified like (first parameter, parameter value b1), (second parameter, parameter value b2), . . . , (the n-th parameter, parameter value bn).

Step (v)

[0361] In this step, antibodies corresponding to the combination specified in step (iv) as to all parameters are selected from the antibody subjected to step (i). That is to say, anti-

bodies in which all parameters are positive combination are selected. For example, when (first parameter, parameter value a1), (second parameter, parameter value a2), . . . , (the n-th parameter, parameter value an) are specified as the positive combination, antibodies having (parameter value a1, parameter value a2, . . . , parameter value an) is selected.

Step (vi)

[0362] In this step, the selected antibodies are classified into one antibody group. Thus, an antibody group showing the reactivity to the target antigen can be made into one group. In other words, an antibody group whose antigen is determined can be obtained. Note here that when only one antibody is selected in the step (v), this only one antibody makes one an antibody group.

[0363] When two or more kinds of target antigens are prepared and the above-mentioned steps (iii) to (vi) are carried out by using each target antigen, two or more antibody groups recognizing different antigens can be obtained.

[0364] In one embodiment of the present invention, the steps (i) to (v) are tried a plurality of times under the conditions in which the combination of parameters is changed every trial. For example, in the first trial, analysis is carried out in which four parameter combinations composed of numeric values (for example, antibody 1 (001, 001, 001, 001), antibody 2 (002, 002, 002, 002), . . .) are associated with each antibody. In the second trial, analysis is carried out in which three parameter combinations composed of alphabets (for example, antibody 1 (ααα, ααα, ααα), antibody 2 (βββ, βββ, βββ, βββ), . . .) are associated with each antibody. Note here that each trial is carried out so that the antibody group formed in each trial is not completely identical. The "antibody group is completely identical" means that the numbers of groups are the same and the kinds of antibodies contained in each group are the same over the all groups.

[0365] After a plurality of times of trials, antibodies in which the results in all trials are not contradictory and which show the binding positive reaction to the target antigen are selected. Then, the step (vi) is carried out by using the selected antibody (a plurality of antibodies).

[0366] When trials are carried out at a plurality of times and only an antibody that provides not-contradictory (that is, consistent) results are selected, an antibody having a target antigen reactivity (intended antibody) can be efficiently obtained.

[0367] The number of times of trial in the steps (i) to (v) is not particularly limited. It may be arbitrarily set by considering the number of antibodies to be treated, the number of "positive combinations" that is anticipated at one trial. For example, the number of times of trial can be twice to five times.

[0368] In a further embodiment of the present invention, the following steps are carried out between the step (v) and the step (vi).

[0369] (v-1) newly associating the classified antibodies selected in step (v) with a combination of n pieces of parameters in a same manner as in the step (i);

[0370] (v-2) with respect to each parameter, preparing the antibody mixture of antibodies having the same parameter value;

[0371] (v-3) examining a reactivity of each of the antibody mixtures with a target antigen by an enzyme linked immunosorbent assay (ELISA) so as to specify the antibody mixture showing the reactivity;

[0372] (v-4) determining a combination of a parameter name and a parameter value that are common to the antibody group contained in the specified antibody mixture; and

[0373] (v-5) selecting an antibody having the combination specified in the step (v-4) in terms of all parameters among the antibodies subjected to the step (v-1).

[0374] Note here that the steps (v-1) to (v-4) are repeated twice or more, if necessary. In this embodiment, a combination of parameters is newly associated with antibodies selected in one trial. Then, the selection of antibody is carried out again. By repeating trials, the intended antibody is narrowed. Thus, classification accuracy is improved.

[0375] Herein, with reference to FIGS. **77** and **78**, the principle of the n-dimensional ELISA method is described more particularly. FIGS. **77** and **78** are conceptual diagrams in a case where n is 3 (three dimensional ELISA method). In this example, a general-purposed 96-well microwell plate is used. Firstly, plates in the number necessary to the number of antibody clones are prepared. In this example, the number of antibody clones is made to be 4,800 and 50 plates (4,800 well in total) are prepared.

[0376] Next, the antibody clone is placed in the well sequentially and the antibody clones are arranged in the plate. Thus, each antibody clone is associated with an address consisting of a plate number (first parameter), a plate row name (second parameter), and a plate column number (third parameter). For example, the address of the antibody clone in the first plate, row A and first column in a well becomes (1, A, 1).

[0377] Subsequently, a mixture of antibody clones having the same plate number (referred to as a plate mixed antibody), a mixture of antibody clones having the same plate row name (referred to as a row mixed antibody), and a mixture of antibody clones having the same plate column number (referred to as a column mixed antibody) are prepared, respectively (FIG. **77**). The number of the respective mixed antibodies are 50 (first plate mixed antibody to fifth plate mixed antibody), 8 (row A mixed antibody to row H mixed antibody), and 12 (first column mixed antibody to twelfth column mixed antibody), sequentially.

[0378] The mixed antibodies prepared as mentioned above are placed in wells in a newly prepared 96-well microwell plate sequentially, and the mixed antibodies are aligned in the plate. In this example, in the plate, the first to seventh columns are assigned to the plate mixed antibody, the eighth column is assigned to the row mixed antibody, and the ninth to tenth columns are assigned to the column mixed antibody (upper part of FIG. **78**). The thus obtained plates are used and ELISA method is carried out. Then, by examining the well showing the reactivity, the address of the intended antibody clone (antibody clone showing the reactivity to the target antigen) is specified. In this example, a well in which the plate mixed antibody of the third plate is placed, a well in which the row mixed antibody of the row E is placed, and a well in which the column mixed antibody of the third column show the reactivity, (3, E, 3) is specified as an address of the intended antibody (lower part of FIG. **78**). Finally, antibody clone to which the specified address is associated with is obtained as the intended antibody.

[0379] The second aspect of the present invention provides an identifying method of an antigen to each antibody classified in the classifying method of the present invention. In the identification method of the present invention, following the

above-mentioned steps (1) to (4) in the classifying method of the present invention, the below-mentioned steps are carried out.

[0380] (5) selecting one or several antibodies from each antibody group formed in the step (4) and identifying an antigen thereof, and

[0381] (6) associating the antigens identified in the step (5) with an antibody group, on the estimation that antigens to antibodies belonging to the same antibody group are identical or have high relationship, and

Step (5)

[0382] In this step, antibodies to be identified are selected. The criteria of selection are not particularly limited, and antibodies that are judged to have high reactivity with respect to antigen from the results of the flow cytometry analysis may be selected. This is because when such an antibody is used, the identification operation using the antigen antibody reaction can be carried out advantageously.

[0383] The number of antibody to be selected is typically one, but the number is not necessarily limited to one. If necessary, several antibodies (for example, two or three antibodies) are selected. When a plurality of antibodies are selected from one antibody group, the identification results of antibodies can be compared with each other, and thereby the reliability of the identification results can be improved. On the other hand, when the identification operation is carried out by selecting a more than necessary number of antibodies, excessive workload is applied. As a result, the effect that is originally intended by the present invention is decreased. Then, it is preferable that the number of antibodies to be selected is small. Specifically, the number is preferably five or less, further preferably three or less, and the most preferably two or less. In order to maximize the effect of the present invention, the number of antibody to be selected from each antibody group is one.

[0384] Identification of an antigen to an selected antibody (hereinafter, referred to as "selected antibody") can be carried out by using a method such as mass spectrometry, immunoprecipitation test, Western blotting, affinity chromatography, RNAi, proteomics techniques (analysis by electrophoresis, mass spectrometry, genome data base retrieve, and bioinformatics), and analysis of expression of corresponding gene. Among them, a method by the proteomics technique based on the mass spectrometry is suitable for identification of unknown antigen and preferable for the identification method employed in the present invention. Note here that these methods are not exclusive to each other and two or more of them can be used if necessary.

[0385] The mass spectrometry is a method of determining the mass of samples by separating ions generated from samples such as protein and peptide according to mass/electric charge (m/z), and measuring the intensity thereof. Since soft ionization methods such as an ESI method (Electro Spray Ionization) and an MALDI method (Matrix Assisted Laser Deporption Ionization) are developed, the mass spectrometry is widely used for analyzing living body sample such as protein and peptide.

[0386] A mass spectrometer is generally composed of ion source, mass spectrometer, and detector. According to sample types and analysis purposes, various mass spectrometers are commercially available. For identification of protein or peptide, MS/MS (Mass spectrometry/mass spectrometry) by a tandem mass spectrometry such as ESI Q-TOF MS, MALDI-TOF MS, and the like are used. A measurement method combining liquid chromatography and mass spectrometer (LC-MAS (liquid chromatography/Electro Spray Ionization mass spectrometer), LC-MS/MS, etc.), and the like, can be also used.

[0387] In the tandem mass spectrometer, two mass spectrometers are linked in series in which ions generated in the ion source are separated in the first mass spectrometer (MS 1) and allowed to pass through only a single ion peak. Then, inactive gas particles are allowed to collide with the ions so as to be degraded into product ions. This product ion is analyzed by the second mass spectrometer (MS 2). According to the combination of the first mass spectrometer (MS 1) and the second mass spectrometer (MS 2), tandem mass spectrometers such as Q-TOF, TOF-TOF, Q-Q, and Q-IT (Iontrap) are present. Like Q-TOF (a tandem mass spectrometer in which Quadrupole mass spectrometer: Q-MS and TOF mass spectrometer (Time-of-flight mass spectrometer: TOF-MS are linked in series), hybrid type tandem mass spectrometer composed of two different kinds of mass spectrometers is excellent in MS/MS measurement ability and suitable for identifying the amino acid sequence of protein and peptide.

[0388] In order to identify the amino acid sequence from the results of the mass spectrometer, a PMF method (peptide mass fingerprinting method) of carrying out genome data search by using experiment results, MS/MS ion search method and the like, are used. Furthermore, de novo sequencing method of determining the amino acid sequence by mathematical operation from the MS/MS spectrum without carrying out genome data search may be used.

[0389] On the other hand, an immunoprecipitation test, Western blotting technique, affinity chromatography, RNAi, and the like, are effective method when a selected antibody is anticipated to recognize the known antigen. These methods can examine the reactivity between the selected antibody and well-known antigen. That is to say, in the immunoprecipitation test, it is examined whether or not the selected antibody and certain known antigen form an immunoprecipitate. When an immunoprecipitate is formed, the known antigen is determined to be the antigen of the selected antibody. On the other hand, in the Western blotting technique, it is examined whether or not the selected antibody can recognize an antigen protein transferred to a PVDF membrane etc. Furthermore, in the affinity chromatography, the adsorption property of the selective antibody to a column supporting a certain known antigen is examined. The presence or the degree of adsorption property is determined. Herein, as the known antigen, commercially available antigens, or antigens expressed from a gene and purified can be used. Furthermore, operations of the immunoprecipitation test, Western blotting technique, affinity chromatography, and the like, can be carried out in the usual manner. In the investigation in RNAi, RNAi of the known antigen is allowed to act on forcedly expressed cells or cells to which an antibody is reacted. It is determined that the subject antibody recognizes the subject antigen when the staining property FCM or the degree of cell immunostaining is reduced.

Step (6)

[0390] In the identification method of the present invention, following the step (5), it is assumed that antigens to each antigen belonging to the same antibody group are identical or have high association. According to the assumption, the antigens identified in the step (5) are associated with an antibody

group. Thus, all antibodies belonging to the same antibody group are associated with one antigen.

[0391] In one embodiment of the present invention, the above assumption (estimation as to the association of antigen) is verified. That is to say, in this embodiment, the reactivity between the antigen identified in the step (5) and the antibody belonging to the antibody group with which the antigen is associated in the step (6) is examined so as to confirm that the above assumption is correct. Specifically, firstly, antibodies are selected from the antibody group that needs verification. Preferably, all the antibodies are selected, and the reactivity thereof is verified. Next, the reactivity of each antibody to the identified antigen (hereinafter, referred to as "identified antigen") is examined by using the immunoprecipitation test or ELISA (including cell ELISA), and RNAi. For example, in the immunoprecipitation test, by reacting the antibody to an solution or an extracted solution of cells that express the identified antigen, then, proteins recovered as the immunoprecipitates are detected by, for example, electrophoresis. Thereby, the reactivity of each antibody to the identified antigen can be confirmed. On the other hand, in ELISA, for example, by a series of operations including preparation of well in which an identified antigen is fixed, addition of antibody, addition of labeled antibody, and measurement amount of labeled antibodies, the reactivity of each antibody with respect to the identified antigen can be confirmed. Furthermore, also by examining the binding property to cells forcedly expressing the identified antigen, the reactivity of each antigen to the identified antigen can be confirmed. In the verification by RNAi, by allowing the known RNAi to act on cells forcedly expression the identified antigen or subjected cells showing the antibody reaction. When, the staining property of the subjected antibody in FCM and cell immunostaining is reduced, it is recognized that the subjected antigen is recognized.

[0392] Furthermore, when disease-related molecules (disease causative gene products, etc.) can be obtained in same forms such as purified protein or recombinant protein, the intermolecular interaction between such molecules and the antibodies can be examined in vitro (classical methods using fluorescence spectroscopy, gel filtration, and ultracentrifugation; a method using surface plasmon resonance phenomenon; a method using quartz-crystal resonator microbalance, and the like) or in vivo (monomolecular tracing method, fluorescence resonance energy metastasis (fluorescence resonance energy transfer: FRET) observation method, and the like).

[0393] When specific reactivity is observed between the identified antigen and each antibody, it is judged that the above assumption is correct.

[0394] In one embodiment of the present invention, identification results are displayed on a panel. Specifically, the panel is any of the following (a) to (c).

[0395] (a) a panel displaying as one antibody group a plurality of antibodies providing data identical to or similar to each other in the flow cytometry analysis in the step (3) in which each antibody group is associated with its antigen;

[0396] (b) a panel displaying as one antibody group a plurality of antibodies providing data identical to or similar to each other in the flow cytometry analysis in the step (3) in which each antibody in the antibody group is associated with a cell expressing a cell surface antigen recognized by the each antibody group; and

[0397] (c) a panel displaying as one antibody group a plurality of antibodies providing histogramidentical to or similar to each other in the flow cytometry analysis in the step (3) in which each antibody group, its antigen and a cell expressing a cell surface antigen recognized by the antibody are associated with each other.

[0398] The above-mentioned panels are useful for studying identified antigens, and for studying or classifying certain cells displayed on the panel.

[0399] The panel (a) displays the relationship between each antigen to the antibody group. Therefore, it is useful in searching an antibody to a certain antigen. The panel (a) can be formed by displaying by the use of diagrams or tabular formats the association between each antibody group and the antigen by using identification results by steps (5) and (6) of the present invention in which a plurality of antibodies providing identical or highly similar data in the flow cytometry analysis in the step (3) of the present invention are defined as one group.

[0400] The panel (b) shows the association between the antibody group and cells. Therefore, it is useful in searching an antibody to a certain cell surface antigen. Furthermore, when the panel displays the association between the antibody group and a plurality of cells, useful information on the distribution of cell surface antigen can be provided. The panel (b) can be formed by displaying by the use of diagrams or tabular formats the association between each antibody group and cells expression the cell surface antigen recognized thereby by using identification results by steps (5) and (6) of the present invention in which a plurality of antibodies providing identical or highly similar data in the flow cytometry analysis in the step (3) of the present invention are defined as one group.

[0401] The panel (c) combines the panel (a) and the panel (b). This panel shows that the kinds or distribution state of a cell surface antigen expressed by certain cells and allows easy and rapid search of antibodies to the antigens of interest. The panel (c) can be formed by displaying by the use of diagrams or tabular formats the association between each antibody group and cells expression the cell surface antigen recognized by the antigen and each antibody group by using identification results by steps (5) and (6) of the present invention in which a plurality of antibodies providing identical or highly similar histogram in the flow cytometry analysis in the step (3) of the present invention are defined as one group.

[0402] In the identification method of the present invention, identification of antigen with respect to only a part of the antibodies in the antibody group, and as to the other antibodies, antigens are determined by estimation. Therefore, as compared with the case where identification operation is carried out for each antibody, necessary labor and time can be radically reduced. In other words, according to the identification method of the present invention, antigen of each antibody can be determined rapidly and easily. Note here that as shown in the below-mentioned Examples, as far as the present inventors have investigated, error in estimation has not been confirmed. The reliability of this method has been confirmed.

[0403] On the other hand, according to the identification method of the present invention, it is possible to understand the kinds of surface antigens expressed by certain cells. Furthermore, information on the expression amount can be obtained. When the classification of antibodies is carried out by using two kinds or more cells, information on the distribution state of the cell surface antigens can be obtained. Thus,

the identification method of the present invention brings useful information as to the cell surface antigen.

[0404] As a result, according to the identification method of the present invention, it is possible to obtain an assembly of antibodies capable of recognizing antigens for each identified antigen (or for each of the plurality of antigens having high association). These antibody groups are useful for study of the cell surface antigens, classification and diagnosis of diseases, and the like. These antibody groups are expected to be applied to the field of treatment.

[0405] The present invention further provides an application of information obtained by the classifying method or the identification method of the present invention. As one of the applications, the third aspect of the present invention relates to a method of obtaining an antibody or an antibody set having a association with respect to a certain disease. The method of obtaining the antibody of the present invention (the first embodiment of the third aspect) includes the following steps.

[0406] (1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to the present invention;

[0407] (2) with respect to one kind or two or more kinds of diseases examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0408] (3) selecting an antibody in the antibody group, to which an antibody having a specific reactivity to any of diseases belongs, as a useful antibody.

[0409] On the other hand, a method of obtaining an antibody set of the present invention (the second embodiment of the third aspect) includes the step (3') instead of the step (3):

[0410] (3') selecting diseases to which two or more antibodies show a specific reactivity, then selecting antibodies from the antibody group, to which the antibody having a specific reactivity to the disease belongs, and combining the selected antibodies.

[0411] Hereinafter, the detail of each step is described with reference to FIG. **1**. For convenience of explanation, in FIG. **1**, it is assumed that the antibody groups 1 to 5 are obtained by the classifying method of the present invention and three antibodies belong to each antibody group. Furthermore, in this example, it is assumed that antigens to each antibody group have been already identified.

[0412] Firstly, in the step (1), focused antibody group (antibody groups 1, 3, and 5) are selected (FIG. **1**, (**1**)). As in this example, two or more antibody groups may be selected.

[0413] Next, in the step (2), the reactivity between an antibody to each of the selected antibody groups and a certain disease is examined. Specifically, a sample (cells or tissues) derived from a patient having a certain disease is prepared, and then, the reactivity of each antibody to the sample is examined (FIG. **1**, (**2**)). Two or more antibodies from each of the selected antibody groups are selected, and thereby the reactivity of them may be examined. The "certain disease" herein is not particularly limited but it may include various kinds of cancers, for example, kidney cancer, hepatic cell carcinoma, gallbladder and liver cancer, alveolar cell carcinoma, lung squamous cell cancer, pulmonary adenocarcinoma, pancreas cancer, adenocarcinoma, or ovarian cancer. In the example shown in FIG. **1**, the reactivity with respect to two kinds or more of diseases are examined simultaneously. However, the examination is not limited to this alone. The reactivity to one disease may be examined. Furthermore, the reactivity with respect to a certain pathologic condition in the certain disease may be examined.

[0414] The reactivity with respect to the samples derived from a patient can be detected and evaluated by using an immunohistochemical staining technique, an immunoprecipitation method, flow cytometry analysis, cell ELISA and the like. These methods are not exclusive to each other and therefore two or more of these methods can be used if necessary. Among them, it is preferable to employ the immunohistochemical staining technique. The immunohistochemical staining technique permits rapid and sensitive detection. Furthermore, its operation is relatively simple.

[0415] In the immunohistochemical staining technique, tissues collected from a patient and an antibody are brought into contact with each other, and then, specifically bonded antibodies are detected. Concretely, the method of the present invention can be carried out according to the following immunohistochemical staining technique.

[0416] The immunohistochemical staining of living tissue is generally carried out by the following procedures (a) to 0). Note here that the immunohistochemical staining of living tissue can be referred to as various documents and publications (for example, "Enzyme-labeled Antibody Method" 3rd revised edition, K. Watanabe and K. Nakane (ed), Gakusai Kikaku).

(a) Immobilization—Paraffin Embedding Method Tissue surgically collected from a living body is immobilized in formalin, paraformaldehyde, absolute ethyl alcohol, and the like, and then embedded in paraffin. In general, it is dehydrated with alcohol, treated with xylene and embedded in paraffin. The paraffin embedded specimen is cut into a desired thickness (for example, 3 to 5 μm thick) and extended on a slide glass. Instead of the paraffin embedding specimen, an alcohol immobilized specimen, a dry sealed specimen, a frozen specimen, and the like may be used.

(b) Deparaffinization

[0417] In general, treatment is carried out with xylene, alcohol, and purified water sequentially in this order.

(c) Pretreatment (Antigen Activation)

[0418] If necessary, for antigen activation, for example, enzyme treatment, heat treatment and/or pressurization treatment are carried out.

(d) Removal of Endogeneous Peroxidase

[0419] When peroxidase is used as a labeling material for staining, endogeneous peroxidase activation is removed by carrying out with hydrogen peroxide solution.

(e) Non-Specific Reaction Inhibition

[0420] Non-specific reaction is inhibited by treating a section with bovine serum albumin solution (for example, 1% solution) for several minutes to several tens of minutes. Note here that this process may be omitted when the following primary antibody reaction is carried out by using an antibody solution impregnated with bovine serum albumin.

(f) Primary Antibody Reaction

[0421] An antibody diluted to an appropriate concentration is dropped on the slide glass and allowed to react for ten

minutes to several hours. After reaction, the reacted produce is washed with an appropriate buffer solution such as phosphate buffer.

(g) Addition of Labeling Reagent

[0422] As the label material, peroxidase is frequently used. Secondary antibody bonded to peroxidase is dropped on the section and then allowed to react for ten minutes to several hours. After reaction, the reacted product is washed with an appropriate buffer solution such as phosphate buffer.

(h) Color Reaction

[0423] DAB (3,3'-diaminobenzidine) is dissolved in Tris buffer. Then, hydrogen peroxide solution is added. The thus prepared coloring solution is impregnated into a section for several minutes (for example, five minutes) so as to color the section. After coloring, the section is sufficiently washed with tapped water so as to remove DAB.

(i) Nuclear Staining

[0424] The section is subjected to nuclear staining by reacting it with Mayer hematoxylin for several seconds to several tens seconds. It was washed with flowing water for saddening (in general, for several minutes).

(j) Dehydration, Clearing, Encapsulation

[0425] The section is dehydrated with alcohol, clearing treated with xylene, and finally encapsulated with synthesized resin, glycerine, rubber syrup, and the like.

[0426] An antibody that is recognized to have specific reactivity to any of diseases can detect a cell surface antigen characterizing the disease with high sensitivity. Such an antibody is expected to be used as a diagnosis or treatment antibody of the disease. Then, in the step (3), an antibody of the antibody group including such an antibody is selected (FIG. **1** (**3**)). As a result, in this example, as to disease A, an antibody (antibody 1-1, 1-2 or 1-3) of the antibody group 1 and an antibody of the antibody group 3 (antibody 3-1, 3-2 or 3-3) are selected. As to disease B, an antibody (antibody 5-1, 5-2 or 5-3) of the antibody group 5 is selected. In this way, a specific antibody for a certain diseases can be obtained.

[0427] In the step (3'), a disease in which two or more antibodies show the specific reactivity is selected, and then, each antibody is selected from the antibody group to which the antibody showing the specific reactivity to the disease belongs, is selected, and the selective antibodies are combined (FIG. **1**, (**3'**)). That is to say, in this example, the disease A is selected and the antibodies of antibody groups 1 and 3, which are antibody groups to which the antibody showing the specific reactivity to the disease A belongs, are combined. Thus, the antibody set showing specific to a certain disease is obtained.

[0428] Herein, by comparing the specificities (cross reactivity) of the antibodies in the antibody group, an antibody having the most excellent property may be selected (in this example, antibody 1-2, antibody 3-3, and antibody 5-3 are selected. See, FIG. **1**, (**4**)). By adding this step, more useful antibody or antibody set can be obtained.

[0429] Furthermore, an antibody set may be structured by combining an arbitrary antibody that does not have reactivity to the diseases with the antibodies selected as the antibodies showing the reactivity to a certain disease (in this example, for example, the antibody 4-1 is combined to an antibody of the antibody group 1 and antibody of antibody group 3). By using such an antibody set, detail characterization of the disease can be possible.

[0430] According to the obtaining method of the present invention, an antibody (or antibody set) to a disease-specific antigen can be obtained. The antibody (or antibody set), which are as it is or to which necessary modification is added, is useful for study, classifying, diagnosing and treating the disease or the pathologic condition. Thus, this method provides an extremely useful tool in the field of medicine.

[0431] The third embodiment of this aspect provides the obtaining method of antibody set including the following steps.

[0432] (1) selecting two or more antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to the present invention;

[0433] (2) with respect to two kinds or more of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0434] (3) selecting antibodies from the antibody group, to which the antibody having a specific reactivity to any of disease belongs, and combining the selected antibodies.

[0435] Hereinafter, the detail of each step is described with reference to FIG. **2**. For convenience of explanation, in FIG. **2**, it is assumed that the antibody groups 1 to 6 are obtained by the classifying method of the present invention and three antibodies belong to each antibody group. The antigens (antigen A) in the antibody groups 1 to 3 are common. Similarly, the antigens (antigen B) in the antibody groups 4 and 5 are also common.

[0436] In the step (1) of this embodiment, two or more antibody groups recognizing different antigens (antibody groups 1, 4, and 6) are selected (see, FIG. **2** (1)). In the following step (2), the reactivity between the antibodies (antibodies 1-1, 4-1, and 6-1) in each of the selected antibody groups and certain diseases (diseases A to D) are examined (FIG. **2**, (**2**)). In the step (3), antibodies in the antibody groups to which the antibody belong showing specific reactivity to any of diseases are combined. That is to say, in this example, an antibody of antibody group 1 to which an antibody 1-1 showing specific reactivity to disease A and an antibody of antibody group 4 to which an antibody 4-1 showing specific reactivity to disease B are combined to form an antibody set (FIG. **2**, (**3**)). Thus, an antibody set (the antibody 1-1 and the antibody 4-1) including an antibody specific to disease A and an antibody specific to disease B is obtained. This antibody set is useful for detecting, for example, disease A or disease B and this antibody is a reagent effective to the discrimination of the diseases A and B.

[0437] Note here that by comparing the specificity (cross reactivity) and the like between the antibodies in the antibody group, an antibody having the most excellent property may be selected (In this example, the antibody 1-2 and the antibody 4-3 are selected. FIG. **2**, (**4**)). By adding this step, it is possible to obtain a more useful antibody set.

[0438] As a result of carrying out the classifying method and the identification method of the present invention, assuming that a plurality of antibodies groups recognizing the same antigen are obtained, the fourth embodiment of this aspect provides a obtaining method of an antibody set including the following steps.

[0439] (1) selecting two or more antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to the present invention;

[0440] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0441] (3) selecting an antibody from the antibody group to which the antibody having a specific reactivity to any of disease belongs, and an antibody belonging to other antibody group whose antigen is common to that of the antibody group, and combining the selected antibodies.

[0442] Hereinafter, the detail of each step is described with reference to FIG. **3**. For convenience of explanation, in FIG. **3**, it is assumed that the antibody groups 1 to 6 are obtained by the classifying method of the present invention and three antibodies belong to each antibody group. The antigens (antigen A) in the antibody groups 1 to 3 are common. Similarly, the antigens (antigen B) in the antibody groups 4 and 5 are also common.

[0443] In the step (1) of this embodiment, two or more antibody groups recognizing different antigens (antibody groups 1, 4, and 6) are selected (see, FIG. **3** (**1**)). In the following step (2), the reactivity between the antibodies (antibodies 1-1, 4-1, and 6-1) in each of the selected antibody groups- and certain diseases (diseases A to D) are examined (FIG. **3**, (**2**)). In the step (3), an antibody of the antibody group to which an antibody showing the specific reactivity to any of diseases and an antibody belonging to other antibody group whose antigen is common to the group are selected, respectively. The selected antibodies are combined so as to form an antibody set (FIG. **3**, (**3**)). That is to say, in this example, an antibody in antibody group 1 to which antibody 1-1 belongs showing specific reactivity to disease A and an antibody of the antibody groups 2 and 3 whose antigens are common are combined. Thus, an antibody set specific to the disease A is obtained. Similarly, an antibody in antibody group 4 to which antibody 4-1 belongs showing specific reactivity to disease B and an antibody of the antibody group 5 whose antigen is common to that of antibody group 4. Thus, an antibody set specific to the disease B is obtained. As shown in this example, "another antibody group" herein is not particularly one but a plurality antibody groups may be present.

[0444] Herein, even in the case of cancers of the same organ, depending upon patients, the pathologic condition (grade of malignancy) may be largely different. The difference in such pathologic conditions is thought to be involved to the expression forms of the specific antigens. On the other hand, the antibody sets obtained in this embodiment are not different in the level recognized by an antigen but include antibodies that are different in the level of epitope. That is to say, this is an antibody set including a plurality of antibodies that are different in the epitope to be recognized. Such an antibody set permits multilateral detection or evaluation of expression forms of antigen. For example, such an antibody set is useful for detection of certain pathologic conditions in, for example, cancers, or a determination of the grade of malignancy.

[0445] Note here that by comparing the specificity (cross reactivity) and the like in the antibodies in the antibody group, an antibody having the most excellent property may be finally selected (FIG. **3**, (**4**)). By adding this step, it is possible to obtain a more useful antibody set.

[0446] As a result of carrying out the classifying method and the identification method of the present invention, assuming that a plurality of antibodies groups recognizing the same antigen are obtained, the fifth embodiment of this aspect provides a obtaining method of an antibody set including the following steps.

[0447] (1) selecting two or more antibody groups recognizing the same antigen from the plurality of antibody groups classified by the classifying method according to the present invention;

[0448] (2) with respect to one kind or two or more kinds of pathologic conditions, examining a reactivity between an antibody in each of the selected antibody groups and a pathologic condition; and

[0449] (3) associating information about the reactivity and then combining the antibodies in the antibody groups.

[0450] Hereinafter, the detail of each step is described with reference to FIG. **4**. For convenience of explanation, in FIG. **4**, it is assumed that the antibody groups 1 to 6 are obtained by the classifying method of the present invention and three antibodies belong to each antibody group. The antigens (antigen A) in the antibody groups 1 to 3 are common. Similarly, the antigens (antigen B) in the antibody groups 4 and 5 are also common.

[0451] In the step (1) of this embodiment, two or more antibody groups recognizing common antigen (antibody groups 1 to 3) are selected (see, FIG. **4** (**1**)). In the following step (2), the reactivity between the antibodies (antibodies 1-1, 2-1, and 3-1) in each of the selected antibody groups and certain various diseases are examined (FIG. **4**, (**2**)). Specifically, as to various pathologic conditions of certain disease, samples (cells or tissue) derived from a patient are prepared, and the reactivity between the samples and each antibody is examined. In the step (3), the obtained reactivity is associated with each other (FIG. **4**, (**2**), right column), and then antibodies of each of the selected antibody groups (antibody groups 1 to 3) are combined so as to form an antibody set (FIG. **4**, (**3**)). Thus, antibody sets specific to the certain pathologic condition of certain disease is obtained (in this example, an antibody set specific to pathologic condition of disease A including antibodies of the antibody groups 1 to 3 is obtained). The antibody set obtained in this embodiment is typically not different in the level of an antigen but include antibodies that are different in the level of epitope. Therefore, similar to the antibody set according to the above-mentioned embodiment, for example, the antibody set is useful detecting the certain pathologic condition in, for example, cancer, or a determination of the grade of malignancy. Note here that it is preferable that an antibody set is constructed by excluding antibodies showing no specific reactivity with respect to any pathologic conditions.

[0452] By comparing the specificity (cross reactivity) and the like in the antibodies in the antibody group, an antibody having the most excellent property may be finally selected (in this example, antibodies 1-2, 2-1 and 3-3 are selected, FIG. **4**, (**4**)). By adding this step, it is possible to obtain a more useful antibody set.

[0453] A further aspect of the present invention provides a production method of a panel displaying a association between an antibody and a disease (or pathologic condition). In the first embodiment of this aspect, the following steps are carried out.

[0454] (1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to the present invention;

[0455] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0456] (3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

[0457] When one antibody group is selected in the step (1), as to one antibody or a plurality of antibodies whose antigen is common, a panel displaying the association with respect to a certain disease can be obtained. In the latter case, as to a plurality of antibodies whose antigen is common antigen, from the viewpoint of the association with respect to the disease, difference or points of difference (one caused by the cross reactivity and the like) can be read out. That is to say, the panel gives an important suggestion as to the property of the antibody. On the other hand, when two or more antibody groups are selected in the step (1), as to a plurality of antibodies whose antigen is different (however, when several antibodies from each antibody group in the step (1), antibodies whose antigen is common is contaminated), a panel displaying the association with respect to the certain disease is obtained. This panel gives information on the antibody group useful for study, classification and diagnosis. The panel itself has a great value. Form this panel, the association between a plurality of antigen and disease can be read out. That is to say, the panel gives an important suggestion as to the association between each antigen and disease.

[0458] Herein, in the step (2), it is preferable to examine the reactivity of the antibody as to two or more diseases. Thus, a panel displaying the association (linkage) between each antibody and two or more diseases can be obtained. The panel displays more pieces of information and further displays the association between diseases. Suggestion that is useful and important for study, classification and diagnosis of the diseases can be obtained.

[0459] In the second embodiment of this aspect, the following steps are carried out.

[0460] (1) selecting two or more of antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to the present invention;

[0461] (2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

[0462] (3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

[0463] In this embodiment, a panel displaying the association between a plurality of antibodies whose antigen is different and a certain disease can be obtained. This panel gives information on an antibody group useful for study, classification and diagnosis for a disease and the panel itself has a great value. Form this panel, the association (linkage) between a plurality of antigens and disease can be read out. That is to say, the panel gives important suggestions as to the association between each antigen and disease as well as the association between antigens.

[0464] Herein, in the step (2), it is preferable to examine the reactivity of the antibody as to two or more diseases. Thus, a panel displaying the association between each antibody and two or more diseases can be obtained. The panel displays more pieces of information and further displays the association between diseases. Suggestion that is useful and important for study, classification and diagnosis of the diseases can be obtained.

[0465] In the third embodiment of this aspect, the following steps are carried out.

[0466] (1) selecting two or more of antibody groups recognizing a common antigen from the plurality of antibody groups classified by the classifying method according to the present invention;

[0467] (2) with respect to one kind or two or more kinds of pathologic condition, examining a reactivity between an antibody in each of the selected antibody groups and a certain pathologic condition of disease; and

[0468] (3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

[0469] In this embodiment, as to a plurality of antibodies whose antigen is common, a panel displaying the association with respect to a pathologic condition of a certain disease can be obtained. This panel gives information on antibody group that is useful for study of each pathologic condition, study of difference between pathologic conditions, classification of pathologic conditions, or diagnosis on the level of the pathologic condition. The panel itself has a great value.

[0470] Herein, in the step (2), it is preferable to examine the reactivity of the antibody as to two or more pathologic conditions. Thus, a panel displaying the association between each antibody and two or more pathologic conditions can be obtained. This panel displays not only more pieces of information but also the association between the pathologic conditions. Suggestion that is useful and important to study, classification and diagnosis of each pathologic condition can be obtained.

[0471] Note here that the first embodiment of this aspect corresponds to the first and second embodiments of the third aspect. Similarly, the third aspect of the second embodiment corresponds to the third and fourth embodiments of the third aspect, respectively. Therefore, as to the matters that are not specifically noted in this aspect, the explanation of the corresponding third aspect is employed. In the panel of the present invention, the term "association between antibody and disease (or pathologic condition)" is displayed by characters showing subject diseases (or pathologic conditions) are positive or negative to the antibody (for example, "to positive," "to negative," "positive," and "negative") or marks (for example, "o," "x," "P," and "N") etc. The display is not limited to two-stage display and, display may be carried out in four stages, for example, strongly positive, moderate positive, weak positive, and negative.

[0472] The number of antibodies displayed in one panel is not particularly limited. For example, the number is 1 to 1000, preferably 2 to 100, and further preferably 5 to 59.

[0473] Furthermore, in addition to the association between an antibody and a certain disease (or pathologic condition), an antigen to each antibody may be shown. The combination of the panel of this aspect and the antibody (or antibody set) obtained in the above-mentioned obtaining method of the present invention becomes an effective tool for study, classification and diagnosis of diseases, pathologic conditions, or the like. That is to say, according to the combination, both information, i.e., an antibody (or an antibody set) specific to a disease or a pathologic condition and the association

between the antibody (or the antibody set) and the disease or the pathologic condition can be obtained simultaneously.

[0474] The present invention further relates to a method of testing a disease in which a cell surface antigen is an indicator, the method comprising the following steps.

[0475] (1) preparing a cell or a tissue separated from a subject;

[0476] (2) examining a reactivity between the cell or the tissue and each antibody displayed on the panel (panel displaying the association between an antibody and a disease (or a pathologic condition)) according to the present invention; and

[0477] (3) collating the results in the step (2) with the panel.

[0478] According to the testing method of the present invention, as to a disease or a pathologic condition to be tested (hereinafter, referred to as "diseased to be tested"), information about the presence of contraction of a subject, contraction risk, pathologic conditions, and the like, can be obtained. That is to say, the testing method of the present invention is effective means for diagnosing the subjected disease. Furthermore, when the testing method of the present invention is carried out along with the treatment, the therapeutic effect can be evaluated based on the testing results. Thus, the testing method of the present invention may be used for monitoring the therapeutic effect.

[0479] In the step (1), cells or tissue separated from a subject (that is, a living body) (hereinafter, referred to as "subject cell, and the like") are prepared. The term "separated from a subject" means a state in which a part of cells or tissue of a subject is extracted and completely isolated form a subject as a living body. A person who needs information about a disease to be tested is a subject. A subject may be a patient of a disease to be tested or may be an apparent healthy person. The "apparent healthy person" means a person who has not recognized to be a patient of a disease to be tested prior to the application of the testing method of the present invention.

[0480] In the step (2), the reactivity between the subject cells and the like and each antibody displayed on the panel of the present invention is examined. That is to say, by using an immunologic procedure (for example, immunohistochemical staining technique), whether or not the tested cells express an antigen recognized by each antibody is examined. According to the immunologic procedure, in general, information on the expression amount of antigens can be obtained. Therefore, in addition to the presence of expression antigen, the expression amount may be also examined. An example of the immunologic procedure includes ELISA method, radioimmunoassay, flow cytometry analysis, immunoprecipitation method, immune-blotting, and the like.

[0481] In the step (3), the results of the step (2) (reactivity of each antibody) is collated with the panel of the present invention. The panel of the present invention displays the association between each antibody and a disease or a pathologic condition. Therefore, this step clarifies the association between the tested cells etc. and the disease via the reactivity with respect to each antibody.

[0482] A further application of the above-mentioned panel also includes the following method of the present invention, that is, the optimum method of treating certain diseases, which includes the following steps.

[0483] (1) preparing a cell or a tissue separated from a subject;

[0484] (2) examining a reactivity between the cell or the tissue and each antibody displayed on the panel (a panel displaying the association between the antibody and disease (or pathologic condition)) according to the present invention;

[0485] (3) collating the results in the step (2) with the panel, and

[0486] (4) selecting an effective antibody according to the results of collating.

[0487] In the selection method of the present invention, similar to the above-mentioned testing method, after the steps (1) to (3) are carried out, according to the collation results, an effective antibody is selected (the step (4)). As the effective antibody, typically, an antibody showing a specific reactivity in the step (2) is selected. An antibody equivalent to the antibody showing a specific reactivity in the step (2) may be also selected. The "equivalent antibody" means an antibody having equivalent properties (reactivity or activity) to the reference antibody. An example of the equivalent antibody may be an antibody in which the sequence of the heavy chain variable region and the sequence of the light chain variable region are not substantially different from that of the reference antibody (completely identical, or slightly different so that the reactivity or activity is not affected). Another example of the equivalent antibody may be an antibody in which no difference is observed in all of the sequence of each CDR constituting heavy chain variable region and the sequence of each CDR constituting light chain variable region when it is compared with the reference antibody.

[0488] Diseases to which the selection method of the present invention is applied is a disease in which cell surface antigen selected from the group consisting of HER1, HER2, CD46, ITGA3, ICAM1, ALCAM, CD147, IgSF4, BCAM, C1qR, CD44, CD73, LAR, EpCAM and HGFR is an indicator. That is to say, for selecting optimum treatment methods suitable for various diseases characterized by the expression of the cell surface antigen, the present invention can be used. According to the present invention, optimum treatment method suitable for each patient can be selected. Thus, tailor-made medicine can be realized.

[0489] It is preferable that the panel used in the selection method of the present invention displays two or more antibodies selected from the group consisting of 048-006 antibody, 057-091 antibody, 059-152 antibody, 048-040 antibody, 054-101 antibody, 055-147 antibody, 059-173 antibody, 067-149 antibody, 067-176 antibody, 015-126 antibody, 015-044 antibody, 015-102 antibody, 015-136 antibody, 015-143 antibody, 015-209 antibody, 039-016 antibody, 053-216 antibody, 075-024 antibody, 075-110 antibody, 086-032 antibody, 086-035 antibody, 086-036 antibody, 086-061 antibody, 086-138 antibody, 086-182 antibody, 035-224 antibody, 045-011 antibody, 051-144 antibody, 052-053 antibody, 052-073 antibody, 053-049 antibody, 3172-120 antibody, 066-069 antibody, 015-003 antibody, 064-002 antibody, 064-006 antibody, 064-012a antibody, 064-012b antibody, 064-014 antibody, 064-054 antibody, 064-085 antibody, 064-093 antibody, 064-116 antibody, 065-183 antibody, 067-142 antibody, 068-007 antibody, 052-033 antibody, 053-042 antibody, 053-051 antibody, 053-059 antibody, 053-085 antibody, 035-234 antibody, 040-107 antibody, 041-118 antibody, 066-174 antibody, 083-040 antibody, 029-143 antibody, 045-134 antibody, 062-101 antibody, 062-109 antibody, 084-103 antibody, 052-274 antibody, 029-067 antibody, 083-131 antibody, 059-053 antibody, 064-003 antibody, 067-213 antibody, 067-153 antibody, 067-126 antibody, 067-133 antibody, 067-287 antibody, 064-044 antibody, 065-030 anti-

body, 065-358 antibody, 066-019 antibody, 079-085 antibody, 067-024 antibody, and 076-048 antibody.

[0490] In one embodiment of the selecting method of the present invention, the following steps are carried out.

[0491] (1) preparing a panel displaying a reactivity between one or more antibodies selected from the group consisting of 048-006 antibody, 015-126 antibody, 067-133 antibody, 064-044 antibody, 076-048 antibody and 059-053 antibody, and a clinical cancer tissue of one or more diseases selected from the group consisting of squamous carcinoma, adenosquamous carcinoma, alveolar adenocarcinoma, adenocarcinoma, and large cell carcinoma, and a cell or tissue separated from a subject;

[0492] (2) examining reactivity between the cell or the tissue and each antibody displayed on the panel;

[0493] (3) collating the results in the step (2) with the panel, and

[0494] (4) selecting an effective antibody according to the results of collating. In the step (1) of this embodiment, a panel displaying the reactivity between an antibody successfully obtained by the present inventor and clinical cancer tissue of a certain disease is prepared. In addition, cells or tissue separated from a subject are prepared. The step (2) or later are carried out similar to the above-mentioned embodiments. Note here that, a specific example of the panel to be used in this embodiment is a panel shown in FIG. **69**.

[0495] Also in this embodiment, an antibody showing the specific reactivity in the step (2) or the equivalent antibody thereto is selected as an effective antibody. The selection method of this embodiment is preferred for selecting the suitable treatment method of squamous carcinoma, adenosquamous carcinoma, alveolar adenocarcinoma, adenocarcinoma, or large cell carcinoma.

[0496] As a further aspect of the present invention provides an isolated antibody (or an antibody set) obtained in the above-mentioned obtaining method of an antibody (or an obtaining method of an antibody set). As shown in the below-mentioned Examples, the present inventors have succeeded in actually obtaining by the method of the present invention, an antibody relevant to HER1, an antibody relevant to HER2, an antibody relevant to CD46, an antibody relevant to ITGA3, an antibody relevant to ICAM1, an antibody relevant to ALCAM, an antibody relevant to CD147, an antibody relevant to C1qR, an antibody relevant to CD44, an antibody relevant to CD73, an antibody relevant to EpCAM, an antibody relevant to HGFR, an antibody relevant to LAR, and an antibody relevant to BCAM. Furthermore, in the current testing method, it is possible to obtain an antibody capable of recognizing two clinical specimen s that are determined to have the same disease (pathologic condition). With this antibody, a certain disease can be newly classified based on the expression state of an antigen and further such a disease can be examined.

[0497] A further aspect of the present invention provides an antibody successfully obtained by the present inventors and the application thereof. As shown in the below-mentioned Examples, the present inventors succeeded in obtaining nine kinds of antibodies to HER1 (048-006 antibody, 057-091 antibody, 059-152 antibody, 048-040 antibody, 054-101 antibody, 055-147 antibody, 059-173 antibody, 067-149 antibody, and 067-176 antibody), 16 kinds of antibodies to HER2 (015-126 antibody, 015-044 antibody, 015-102 antibody, 015-136 antibody, 015-143 antibody, 015-209 antibody, 039-016 antibody, 053-216 antibody, 075-024 antibody, 075-110 antibody, 086-032 antibody, 086-035 antibody, 086-036 antibody, 086-061 antibody, 086-138 antibody, and 086-182 antibody), eight kinds of antibodies to CD46 (035-224 antibody, 045-011 antibody, 051-144 antibody, 052-053 antibody, 052-073 antibody, 053-049 antibody, 3172-120 antibody, and 066-069 antibody), 13 kinds of antibodies to ITGA3 (015-003 antibody, 064-002 antibody, 064-006 antibody, 064-012a antibody, 064-012b antibody, 064-014 antibody, 064-054 antibody, 064-085 antibody, 064-093 antibody, 064-116 antibody, 065-183 antibody, 067-142 antibody, and 068-007 antibody), five kinds of antibodies to ICAM1 (052-033 antibody, 053-042 antibody, 053-051 antibody, 053-059 antibody, and 053-085 antibody), 13 kinds of antibodies to ALCAM (035-234 antibody, 040-107 antibody, 041-118 antibody, 066-174 antibody, 083-040 antibody, 029-143 antibody, 045-134 antibody, 062-101 antibody, 062-109 antibody, 084-103 antibody, 052-274 antibody, 029-067 antibody, and 083-131 antibody), one kind of antibody to CD147 antibody (059-053 antibody), one kind of antibody to C1qR (070-016 antibody), one kind of antibody to CD44 (064-003 antibody), one kind of antibody to CD73 (067-213 antibody), one kind of antibody to EpCAM (067-153 antibody), three kinds of antibodies to HGFR (067-126 antibody, 067-133 antibody, and 067-287 antibody), five kinds of antibodies to LAR (064-044 antibody, 065-030 antibody, 065-358 antibody, 066-019 antibody, and 079-085 antibody), and one kind of antibody to BCAM (067-024 antibody). Since these antibodies are recognize an extracellular domain of antigen in a state in which it is expressed on the surface of the cell membrane, they are useful for staining cells and tissues, and the like. As a result of analysis of sequences of each antibody, the following sequence information is obtained. Note here that, following to the antibody name, the amino acid sequence of the heavy chain variable region; the amino acid sequence of the heavy chain CDR1; the amino acid sequence of the heavy chain CDR2; the amino acid sequence of the heavy chain CDR3; the amino acid sequence of the light chain variable region; the amino acid sequence of the light chain CDR1; the amino acid sequence of the light chain CDR2; and the amino acid sequence of the light chain CDR3 are described sequentially in this order.

1. Antibody to HER1

[0498] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. As to the below-mentioned nine kinds of antibody clones, the sequences are analyzed.

[0499] 048-006 antibody: SEQ ID NO: 1 (VH); SEQ ID NO: 2 (VH CDR1); SEQ ID NO: 3 (VH CDR2); SEQ ID NO: 4 (VH CDR3); SEQ ID NO: 5 (VL); SEQ ID NO: 6 (VL CDR1); SEQ ID NO: 7 (VL CDR2); SEQ ID NO: 8 (VL CDR3)

[0500] 057-091 antibody: SEQ ID NO: 9 (VH); SEQ ID NO: 10 (VH CDR1); SEQ ID NO: 11 (VH CDR2); SEQ ID NO: 12 (VH CDR3); SEQ ID NO: 13 (VL); SEQ ID NO: 14 (VL CDR1); SEQ ID NO: 15 (VL CDR2); SEQ ID NO: 16 (VL CDR3)

[0501] 059-152 antibody: SEQ ID NO: 17 (VH); SEQ ID NO: 18 (VH CDR1); SEQ ID NO: 19 (VH CDR2); SEQ ID NO: 20 (VH CDR3); SEQ ID NO: 21 (VL); SEQ ID NO: 22 (VL CDR1); SEQ ID NO: 23 (VL CDR2); SEQ ID NO: 24 (VL CDR3)

[0502] 048-040 antibody: SEQ ID NO: 483 (VH); SEQ ID NO: 484 (VH CDR1); SEQ ID NO: 485 (VH CDR2); SEQ ID

NO: 486 (VH CDR3); SEQ ID NO: 487 (VL); SEQ ID NO: 488 (VL CDR1); SEQ ID NO: 489 (VL CDR2); SEQ ID NO: 490 (VL CDR3)

[0503] 054-101 antibody: SEQ ID NO: 491 (VH); SEQ ID NO: 492 (VH CDR1); SEQ ID NO: 493 (VH CDR2); SEQ ID NO: 494 (VH CDR3); SEQ ID NO: 495 (VL); SEQ ID NO: 496 (VL CDR1); SEQ ID NO: 497 (VL CDR2); SEQ ID NO: 498 (VL CDR3)

[0504] 055-147 antibody: SEQ ID NO: 499 (VH); SEQ ID NO: 500 (VH CDR1); SEQ ID NO: 501 (VH CDR2); SEQ ID NO: 502 (VH CDR3); SEQ ID NO: 503 (VL); SEQ ID NO: 504 (VL CDR1); SEQ ID NO: 505 (VL CDR2); SEQ ID NO: 506 (VL CDR3)

[0505] 059-173 antibody: SEQ ID NO: 507 (VH); SEQ ID NO: 508 (VH CDR1); SEQ ID NO: 509 (VH CDR2); SEQ ID NO: 510 (VH CDR3); SEQ ID NO: 511 (VL); SEQ ID NO: 512 (VL CDR1); SEQ ID NO: 513 (VL CDR2); SEQ ID NO: 514 (VL CDR3)

[0506] 067-149 antibody: SEQ ID NO: 515 (VH); SEQ ID NO: 516 (VH CDR1); SEQ ID NO: 517 (VH CDR2); SEQ ID NO: 518 (VH CDR3); SEQ ID NO: 519 (VL); SEQ ID NO: 520 (VL CDR1); SEQ ID NO: 521 (VL CDR2); SEQ ID NO: 522 (VL CDR3)

[0507] 067-176 antibody: SEQ ID NO: 523 (VH); SEQ ID NO: 524 (VH CDR1); SEQ ID NO: 525 (VH CDR2); SEQ ID NO: 526 (VH CDR3); SEQ ID NO: 527 (VL); SEQ ID NO: 528 (VL CDR1); SEQ ID NO: 529 (VL CDR2); SEQ ID NO: 530 (VL CDR3)

[0508] As mentioned in the below-mentioned Examples, the relationships between these antibodies and pancreatic cancer cell line PANC-1, kidney cancer cell line CCFRC1, kidney cancer cell line Caki-1, ovarian cancer cell line KF28, stomach cancer cell line SNU-5, lung squamous cell carcinoma line RERF-LC-AI, ovarian cancer cell line RMG-1, undifferentiated hepatic cell carcinoma cancer cell line HLF, ovarian cancer cell line SKOv3, pulmonary adenocarcinoma cell line PC14, kidney cancer cell line ACHN, lung squamous cell carcinoma line EBC1, vulva mucosal epithelial cell line A431, pulmonary adenocarcinoma cell line H1373, hepatic cell carcinoma cell line HepG2, and kidney cancer clinical specimen established cell line (as to the above mention, based on the results of the cell line staining), as well as the relationships between these antibodies and kidney cancer, hepatic cell carcinoma, gallbladder and liver cancer, lung squamous cell cancer, pulmonary adenocarcinoma, and pancreas cancer (as to the above mention, based on the results of the tissue staining) are experimentally confirmed.

2. Antibody to HER2

[0509] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. As to the below-mentioned 16 kinds of antibody clones, the sequences are analyzed.

[0510] 015-126 antibody SEQ ID NO: 25 (VH); SEQ ID NO: 26 (VH CDR1); SEQ ID NO: 27 (VH CDR2); SEQ ID NO: 28 (VH CDR3); SEQ ID NO: 29 (VL); SEQ ID NO: 30 (VL CDR1); SEQ ID NO: 31 (VL CDR2); SEQ ID NO: 32 (VL CDR3)

[0511] 015-044 antibody SEQ ID NO: 531 (VH); SEQ ID NO: 532 (VH CDR1); SEQ ID NO: 533 (VH CDR2); SEQ ID NO: 534 (VH CDR3); SEQ ID NO: 535 (VL); SEQ ID NO: 536 (VL CDR1); SEQ ID NO: 537 (VL CDR2); SEQ ID NO: 538 (VL CDR3)

[0512] 015-102 antibody SEQ ID NO: 539 (VH); SEQ ID NO: 540 (VH CDR1); SEQ ID NO: 541 (VH CDR2); SEQ ID NO: 542 (VH CDR3); SEQ ID NO: 543 (VL); SEQ ID NO: 544 (VL CDR1); SEQ ID NO: 545 (VL CDR2); SEQ ID NO: 546 (VL CDR3)

[0513] 015-136 antibody SEQ ID NO: 547 (VH); SEQ ID NO: 548 (VH CDR1); SEQ ID NO: 549 (VH CDR2); SEQ ID NO: 550 (VH CDR3); SEQ ID NO: 551 (VL); SEQ ID NO: 552 (VL CDR1); SEQ ID NO: 553 (VL CDR2); SEQ ID NO: 554 (VL CDR3)

[0514] 015-143 antibody SEQ ID NO: 555 (VH); SEQ ID NO: 556 (VH CDR1); SEQ ID NO: 557 (VH CDR2); SEQ ID NO: 558 (VH CDR3); SEQ ID NO: 559 (VL); SEQ ID NO: 560 (VL CDR1); SEQ ID NO: 561 (VL CDR2); SEQ ID NO: 562 (VL CDR3)

[0515] 015-209 antibody SEQ ID NO: 563 (VH); SEQ ID NO: 564 (VH CDR1); SEQ ID NO: 565 (VH CDR2); SEQ ID NO: 566 (VH CDR3); SEQ ID NO: 567 (VL); SEQ ID NO: 568 (VL CDR1); SEQ ID NO: 569 (VL CDR2); SEQ ID NO: 570 (VL CDR3)

[0516] 039-016 antibody SEQ ID NO: 571 (VH); SEQ ID NO: 572 (VH CDR1); SEQ ID NO: 573 (VH CDR2); SEQ ID NO: 574 (VH CDR3); SEQ ID NO: 575 (VL); SEQ ID NO: 576 (VL CDR1); SEQ ID NO: 577 (VL CDR2); SEQ ID NO: 578 (VL CDR3)

[0517] 053-216 antibody SEQ ID NO: 579 (VH); SEQ ID NO: 580 (VH CDR1); SEQ ID NO: 581 (VH CDR2); SEQ ID NO: 582 (VH CDR3); SEQ ID NO: 583 (VL); SEQ ID NO: 584 (VL CDR1); SEQ ID NO: 585 (VL CDR2); SEQ ID NO: 586 (VL CDR3)

[0518] 075-024 antibody SEQ ID NO: 587 (VH); SEQ ID NO: 588 (VH CDR1); SEQ ID NO: 589 (VH CDR2); SEQ ID NO: 590 (VH CDR3); SEQ ID NO: 591 (VL); SEQ ID NO: 592 (VL CDR1); SEQ ID NO: 593 (VL CDR2); SEQ ID NO: 594 (VL CDR3)

[0519] 075-110 antibody SEQ ID NO: 595 (VH); SEQ ID NO: 596 (VH CDR1); SEQ ID NO: 597 (VH CDR2); SEQ ID NO: 598 (VH CDR3); SEQ ID NO: 599 (VL); SEQ ID NO: 600 (VL CDR1); SEQ ID NO: 601 (VL CDR2); SEQ ID NO: 602 (VL CDR3)

[0520] 086-032 antibody SEQ ID NO: 603 (VH); SEQ ID NO: 604 (VH CDR1); SEQ ID NO: 605 (VH CDR2); SEQ ID NO: 606 (VH CDR3); SEQ ID NO: 607 (VL); SEQ ID NO: 608 (VL CDR1); SEQ ID NO: 609 (VL CDR2); SEQ ID NO: 610 (VL CDR3)

[0521] 086-035 antibody SEQ ID NO: 611 (VH); SEQ ID NO: 612 (VH CDR1); SEQ ID NO: 613 (VH CDR2); SEQ ID NO: 614 (VH CDR3); SEQ ID NO: 615 (VL); SEQ ID NO: 616 (VL CDR1); SEQ ID NO: 617 (VL CDR2); SEQ ID NO: 618 (VL CDR3)

[0522] 086-036 antibody SEQ ID NO: 619 (VH); SEQ ID NO: 620 (VH CDR1); SEQ ID NO: 621 (VH CDR2); SEQ ID NO: 622 (VH CDR3); SEQ ID NO: 623 (VL); SEQ ID NO: 624 (VL CDR1); SEQ ID NO: 625 (VL CDR2); SEQ ID NO: 626 (VL CDR3)

[0523] 086-061 antibody SEQ ID NO: 627 (VH); SEQ ID NO: 628 (VH CDR1); SEQ ID NO: 629 (VH CDR2); SEQ ID NO: 630 (VH CDR3); SEQ ID NO: 631 (VL); SEQ ID NO: 632 (VL CDR1); SEQ ID NO: 633 (VL CDR2); SEQ ID NO: 634 (VL CDR3)

[0524] 086-138 antibody SEQ ID NO: 635 (VH); SEQ ID NO: 636 (VH CDR1); SEQ ID NO: 637 (VH CDR2); SEQ ID

NO: 638 (VH CDR3); SEQ ID NO: 639 (VL); SEQ ID NO: 640 (VL CDR1); SEQ ID NO: 641 (VL CDR2); SEQ ID NO: 642 (VL CDR3)

[0525] 086-182 antibody SEQ ID NO: 643 (VH); SEQ ID NO: 644 (VH CDR1); SEQ ID NO: 645 (VH CDR2); SEQ ID NO: 646 (VH CDR3); SEQ ID NO: 647 (VL); SEQ ID NO: 648 (VL CDR1); SEQ ID NO: 649 (VL CDR2); SEQ ID NO: 650 (VL CDR3)

[0526] As mentioned in the below-mentioned Examples, the relationships between these antibodies and pulmonary adenocarcinoma cell line Calu-3, ovarian cancer cell line SKOv3, and breast cancer cell line BT474 (based on the results of the cell line staining) are experimentally confirmed.

3. Antibody to CD46

[0527] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. Finally 87 kinds of antibody clones are identified. As to the below-mentioned eight kinds of antibody clones, the sequences are analyzed.

[0528] 035-224 antibody SEQ ID NO: 33 (VH); SEQ ID NO: 34 (VH CDR1); SEQ ID NO: 35 (VH CDR2); SEQ ID NO: 36 (VH CDR3); SEQ ID NO: 37 (VL); SEQ ID NO: 38 (VL CDR1); SEQ ID NO: 39 (VL CDR2); SEQ ID NO: 40 (VL CDR3)

[0529] 045-011 antibody SEQ ID NO: 41 (VH); SEQ ID NO: 42 (VH CDR1); SEQ ID NO: 43 (VH CDR2); SEQ ID NO: 44 (VH CDR3); SEQ ID NO: 45 (VL); SEQ ID NO: 46 (VL CDR1); SEQ ID NO: 47 (VL CDR2); SEQ ID NO: 48 (VL CDR3)

[0530] 051-144 antibody SEQ ID NO: 49 (VH); SEQ ID NO: 50 (VH CDR1); SEQ ID NO: 51 (VH CDR2); SEQ ID NO: 52 (VH CDR3); SEQ ID NO: 53 (VL); SEQ ID NO: 54 (VL CDR1); SEQ ID NO: 55 (VL CDR2); SEQ ID NO: 56 (VL CDR3)

[0531] 052-053 antibody SEQ ID NO: 57 (VH); SEQ ID NO: 58 (VH CDR1); SEQ ID NO: 59 (VH CDR2); SEQ ID NO: 60 (VH CDR3); SEQ ID NO: 61 (VL); SEQ ID NO: 62 (VL CDR1); SEQ ID NO: 63 (VL CDR2); SEQ ID NO: 64 (VL CDR3)

[0532] 052-073 antibody SEQ ID NO: 65 (VH); SEQ ID NO: 66 (VH CDR1); SEQ ID NO: 67 (VH CDR2); SEQ ID NO: 68 (VH CDR3); SEQ ID NO: 69 (VL); SEQ ID NO: 70 (VL CDR1); SEQ ID NO: 71 (VL CDR2); SEQ ID NO: 72 (VL CDR3)

[0533] 053-049 antibody SEQ ID NO: 73 (VH); SEQ ID NO: 74 (VH CDR1); SEQ ID NO: 75 (VH CDR2); SEQ ID NO: 76 (VH CDR3); SEQ ID NO: 77 (VL); SEQ ID NO: 78 (VL CDR1); SEQ ID NO: 79 (VL CDR2); SEQ ID NO: 80 (VL CDR3)

[0534] 3172-120 antibody SEQ ID NO: 81 (VH); SEQ ID NO: 82 (VH CDR1); SEQ ID NO: 83 (VH CDR2); SEQ ID NO: 84 (VH CDR3); SEQ ID NO: 85 (VL); SEQ ID NO: 86 (VL CDR1); SEQ ID NO: 87 (VL CDR2); SEQ ID NO: 88 (VL CDR3)

[0535] 066-069 antibody SEQ ID NO: 755 (VH); SEQ ID NO: 756 (VH CDR1); SEQ ID NO: 757 (VH CDR2); SEQ ID NO: 758 (VH CDR3); SEQ ID NO: 759 (VL); SEQ ID NO: 760 (VL CDR1); SEQ ID NO: 761 (VL CDR2); SEQ ID NO: 762 (VL CDR3)

[0536] As mentioned in the below-mentioned Examples, the relationships between these antibodies and large bowel cancer cell line CaCo2, stomach cancer cell line MKN45, undifferentiated hepatic cell carcinoma cell line HLF, liver cancer cell line HepG2, intrahepatic bile duct cell cancer cell line RBE, pancreas cancer cell line PANC1, kidney cancer cell line CCFRC1, kidney cancer cell line Caki-1, lung cancer cell line NCI-H441, lung squamous cell cancer EBC1, stomach cancer cell line NCI-N87, stomach cancer cell line SNU-5, lung squamous cell carcinoma line RERF-LC-AI, hepatic cell carcinoma clinical specimen s, breast cancer cell line BT474, kidney cancer cell line 293T, pulmonary adenocarcinoma cell line PC14, kidney cancer cell line ACHN, and pulmonary adenocarcinoma cell line H1373 (as to the above mention, based on the results of the cell line staining), as well as the relationships between these kidney cancer, hepatic cell carcinoma, gallbladder and liver cancer, pulmonary adenocarcinoma, and pancreas cancer (as to the above mention, based on the results of the tissue staining) are experimentally confirmed.

4. Antibody to ITGA3

[0537] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. As to the below-mentioned 13 kinds of antibody clones, the sequences are analyzed.

[0538] 015-003 antibody SEQ ID NO: 89 (VH); SEQ ID NO: 90 (VH CDR1); SEQ ID NO: 91 (VH CDR2); SEQ ID NO: 92 (VH CDR3); SEQ ID NO: 93 (VL); SEQ ID NO: 94 (VL CDR1); SEQ ID NO: 95 (VL CDR2); SEQ ID NO: 96 (VL CDR3)

[0539] 064-002 antibody SEQ ID NO: 675 (VH); SEQ ID NO: 676 (VH CDR1); SEQ ID NO: 677 (VH CDR2); SEQ ID NO: 678 (VH CDR3); SEQ ID NO: 679 (VL); SEQ ID NO: 680 (VL CDR1); SEQ ID NO: 681 (VL CDR2); SEQ ID NO: 682 (VL CDR3)

[0540] 064-006 antibody SEQ ID NO: 683 (VH); SEQ ID NO: 684 (VH CDR1); SEQ ID NO: 685 (VH CDR2); SEQ ID NO: 686 (VH CDR3); SEQ ID NO: 687 (VL); SEQ ID NO: 688 (VL CDR1); SEQ ID NO: 689 (VL CDR2); SEQ ID NO: 690 (VL CDR3)

[0541] 064-012a antibody SEQ ID NO: 691 (VH); SEQ ID NO: 692 (VH CDR1); SEQ ID NO: 693 (VH CDR2); SEQ ID NO: 694 (VH CDR3); SEQ ID NO: 695 (VL); SEQ ID NO: 696 (VL CDR1); SEQ ID NO: 697 (VL CDR2); SEQ ID NO: 698 (VL CDR3)

[0542] 064-012b antibody SEQ ID NO: 699 (VH); SEQ ID NO: 700 (VH CDR1); SEQ ID NO: 701 (VH CDR2); SEQ ID NO: 702 (VH CDR3); SEQ ID NO: 703 (VL); SEQ ID NO: 704 (VL CDR1); SEQ ID NO: 705 (VL CDR2); SEQ ID NO: 706 (VL CDR3)

[0543] 064-014 antibody SEQ ID NO: 707 (VH); SEQ ID NO: 708 (VH CDR1); SEQ ID NO: 709 (VH CDR2); SEQ ID NO: 710 (VH CDR3); SEQ ID NO: 711 (VL); SEQ ID NO: 712 (VL CDR1); SEQ ID NO: 713 (VL CDR2); SEQ ID NO: 714 (VL CDR3)

[0544] 064-054 antibody SEQ ID NO: 715 (VH); SEQ ID NO: 716 (VH CDR1); SEQ ID NO: 717 (VH CDR2); SEQ ID NO: 718 (VH CDR3); SEQ ID NO: 719 (VL); SEQ ID NO: 720 (VL CDR1); SEQ ID NO: 721 (VL CDR2); SEQ ID NO: 722 (VL CDR3)

[0545] 064-085 antibody SEQ ID NO: 723 (VH); SEQ ID NO: 724 (VH CDR1); SEQ ID NO: 725 (VH CDR2); SEQ ID NO: 726 (VH CDR3); SEQ ID NO: 727 (VL); SEQ ID NO: 728 (VL CDR1); SEQ ID NO: 729 (VL CDR2); SEQ ID NO: 730 (VL CDR3)

[0546] 064-093 antibody SEQ ID NO: 731 (VH); SEQ ID NO: 732 (VH CDR1); SEQ ID NO: 733 (VH CDR2); SEQ ID

NO: 734 (VH CDR3); SEQ ID NO: 735 (VL); SEQ ID NO: 736 (VL CDR1); SEQ ID NO: 737 (VL CDR2); SEQ ID NO: 738 (VL CDR3)

[0547] 064-116 antibody SEQ ID NO: 739 (VH); SEQ ID NO: 740 (VH CDR1); SEQ ID NO: 741 (VH CDR2); SEQ ID NO: 742 (VH CDR3); SEQ ID NO: 743 (VL); SEQ ID NO: 744 (VL CDR1); SEQ ID NO: 745 (VL CDR2); SEQ ID NO: 746 (VL CDR3)

[0548] 065-183 antibody SEQ ID NO: 747 (VH); SEQ ID NO: 748 (VH CDR1); SEQ ID NO: 749 (VH CDR2); SEQ ID NO: 750 (VH CDR3); SEQ ID NO: 751 (VL); SEQ ID NO: 752 (VL CDR1); SEQ ID NO: 753 (VL CDR2); SEQ ID NO: 754 (VL CDR3)

[0549] 067-142 antibody SEQ ID NO: 763 (VH); SEQ ID NO: 764 (VH CDR1); SEQ ID NO: 765 (VH CDR2); SEQ ID NO: 766 (VH CDR3); SEQ ID NO: 767 (VL); SEQ ID NO: 768 (VL CDR1); SEQ ID NO: 769 (VL CDR2); SEQ ID NO: 770 (VL CDR3)

[0550] 068-007 antibody SEQ ID NO: 771 (VH); SEQ ID NO: 772 (VH CDR1); SEQ ID NO: 773 (VH CDR2); SEQ ID NO: 774 (VH CDR3); SEQ ID NO: 775 (VL); SEQ ID NO: 776 (VL CDR1); SEQ ID NO: 777 (VL CDR2); SEQ ID NO: 778 (VL CDR3)

[0551] As mentioned in the below-mentioned Examples, the relationships between these antibodies and undifferentiated hepatic cell carcinoma cell line HLF, ovarian cancer cell line SKOv3, kidney cancer cell line ACHN, kidney cancer cell line Caki-1, pulmonary adenocarcinoma cell line H1373, lung squamous cell cancer EBC1, vulva mucosal epithelial cell line A431, breast cancer cell line BT474, pulmonary adenocarcinoma cell line PC14, kidney cancer cell line CCFRC1, hepatic cell carcinoma cell line OCTH, intrahepatic bile duct cell cancer RBE, pancreas cancer cell line PANC-1, pancreas cancer cell line MIA-Paca2, pulmonary adenocarcinoma cell line A549, pulmonary adenocarcinoma cell line NCI-N441, lung squamous cell carcinoma line Calu-3, lung squamous cell carcinoma line RERF-LC-AI, stomach cancer cell line SNU5, stomach cancer cell line MKN45, stomach cancer cell line NCI-N87, large bowel cancer cell line CW2, ovarian cancer cell line SKOv3, ovarian cancer cell line KF-28, ovarian cancer cell line RMG-1, and ovarian cancer cell line RMG-2 (as to the above mention, based on the results of the cell line staining), as well as the relationships between these antibodies and gallbladder and liver cancer and pancreas cancer (as to the above mention, based on the results of the tissue staining) are experimentally confirmed.

5. Antibody to ICAM1

[0552] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. Finally, 22 kinds of antibody clones are identified. As to the below-mentioned five kinds of antibody clones, the sequences are analyzed.

[0553] 052-033 antibody SEQ ID NO: 97 (VH); SEQ ID NO: 98 (VH CDR1); SEQ ID NO: 99 (VH CDR2); SEQ ID NO: 100 (VH CDR3); SEQ ID NO: 101 (VL); SEQ ID NO: 102 (VL CDR1); SEQ ID NO: 103 (VL CDR2); SEQ ID NO: 104 (VL CDR3)

[0554] 053-042 antibody SEQ ID NO: 105 (VH); SEQ ID NO: 106 (VH CDR1); SEQ ID NO: 107 (VH CDR2); SEQ ID NO: 108 (VH CDR3); SEQ ID NO: 109 (VL); SEQ ID NO: 110 (VL CDR1); SEQ ID NO: 111 (VL CDR2); SEQ ID NO: 112 (VL CDR3)

[0555] 053-051 antibody SEQ ID NO: 113 (VH); SEQ ID NO: 114 (VH CDR1); SEQ ID NO: 115 (VH CDR2); SEQ ID NO: 116 (VH CDR3); SEQ ID NO: 117 (VL); SEQ ID NO: 118 (VL CDR1); SEQ ID NO: 119 (VL CDR2); SEQ ID NO: 120 (VL CDR3)

[0556] 053-059 antibody SEQ ID NO: 121 (VH); SEQ ID NO: 122 (VH CDR1); SEQ ID NO: 123 (VH CDR2); SEQ ID NO: 124 (VH CDR3); SEQ ID NO: 125 (VL); SEQ ID NO: 126 (VL CDR1); SEQ ID NO: 127 (VL CDR2); SEQ ID NO: 128 (VL CDR3)

[0557] 053-085 antibody SEQ ID NO: 129 (VH); SEQ ID NO: 130 (VH CDR1); SEQ ID NO: 131 (VH CDR2); SEQ ID NO: 132 (VH CDR3); SEQ ID NO: 133 (VL); SEQ ID NO: 134 (VL CDR1); SEQ ID NO: 135 (VL CDR2); SEQ ID NO: 136 (VL CDR3)

[0558] As mentioned in the below-mentioned Examples, the relationships between these antibodies and liver cancer cell line HepG2, pulmonary adenocarcinoma cell line PC14, and cell line established from kidney clinical specimen (as to the above mention, based on the results of the cell line staining), as well as the relationships between these antibodies and hepatic cell carcinoma (as to the above mention, based on the results of the tissue staining) are experimentally confirmed.

6. Antibody to ALCAM

[0559] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. As to the below-mentioned 13 kinds of antibody clones, the sequences are analyzed.

[0560] 035-234 antibody SEQ ID NO: 137 (VH); SEQ ID NO: 138 (VH CDR1); SEQ ID NO: 139 (VH CDR2); SEQ ID NO: 140 (VH CDR3); SEQ ID NO: 141 (VL); SEQ ID NO: 142 (VL CDR1); SEQ ID NO: 143 (VL CDR2); SEQ ID NO: 144 (VL CDR3)

[0561] 040-107 antibody SEQ ID NO: 145 (VH); SEQ ID NO: 146 (VH CDR1); SEQ ID NO: 147 (VH CDR2); SEQ ID NO: 148 (VH CDR3); SEQ ID NO: 149 (VL); SEQ ID NO: 150 (VL CDR1); SEQ ID NO: 151 (VL CDR2); SEQ ID NO: 152 (VL CDR3)

[0562] 041-118 antibody SEQ ID NO: 153 (VH); SEQ ID NO: 154 (VH CDR1); SEQ ID NO: 155 (VH CDR2); SEQ ID NO: 156 (VH CDR3); SEQ ID NO: 157 (VL); SEQ ID NO: 158 (VL CDR1); SEQ ID NO: 159 (VL CDR2); SEQ ID NO: 160 (VL CDR3)

[0563] 066-174 antibody SEQ ID NO: 161 (VH); SEQ ID NO: 162 (VH CDR1); SEQ ID NO: 163 (VH CDR2); SEQ ID NO: 164 (VH CDR3); SEQ ID NO: 165 (VL); SEQ ID NO: 166 (VL CDR1); SEQ ID NO: 167 (VL CDR2); SEQ ID NO: 168 (VL CDR3)

[0564] 083-040 antibody SEQ ID NO: 169 (VH); SEQ ID NO: 170 (VH CDR1); SEQ ID NO: 171 (VH CDR2); SEQ ID NO: 172 (VH CDR3); SEQ ID NO: 173 (VL); SEQ ID NO: 174 (VL CDR1); SEQ ID NO: 175 (VL CDR2); SEQ ID NO: 176 (VL CDR3)

[0565] 029-143 antibody SEQ ID NO: 779 (VH); SEQ ID NO: 780 (VH CDR1); SEQ ID NO: 781 (VH CDR2); SEQ ID NO 782 (VH CDR3); SEQ ID NO: 783 (VL); SEQ ID NO: 784 (VL CDR1); SEQ ID NO: 785 (VL CDR2); SEQ ID NO: 786 (VL CDR3)

[0566] 045-134 antibody SEQ ID NO: 787 (VH); SEQ ID NO: 788 (VH CDR1); SEQ ID NO: 789 (VH CDR2); SEQ ID NO: 790 (VH CDR3); SEQ ID NO: 791 (VL); SEQ ID NO: 792 (VL CDR1); SEQ ID NO: 793 (VL CDR2); SEQ ID NO: 794 (VL CDR3)

[0567] 062-101 antibody SEQ ID NO: 795 (VH); SEQ ID NO: 796 (VH CDR1); SEQ ID NO: 797 (VH CDR2); SEQ ID NO: 798 (VH CDR3); SEQ ID NO: 799 (VL); SEQ ID NO: 800 (VL CDR1); SEQ ID NO: 801 (VL CDR2); SEQ ID NO: 802 (VL CDR3)

[0568] 062-109 antibody SEQ ID NO: 803 (VH); SEQ ID NO: 804 (VH CDR1); SEQ ID NO: 805 (VH CDR2); SEQ ID NO: 806 (VH CDR3); SEQ ID NO: 807 (VL); SEQ ID NO: 808 (VL CDR1); SEQ ID NO: 809 (VL CDR2); SEQ ID NO: 810 (VL CDR3)

[0569] 084-103 antibody SEQ ID NO: 811 (VH); SEQ ID NO: 812 (VH CDR1); SEQ ID NO: 813 (VH CDR2); SEQ ID NO: 814 (VH CDR3); SEQ ID NO: 815 (VL); SEQ ID NO: 816 (VL CDR1); SEQ ID NO: 817 (VL CDR2); SEQ ID NO: 818 (VL CDR3)

[0570] 052-274 antibody SEQ ID NO: 819 (VH); SEQ ID NO: 820 (VH CDR1); SEQ ID NO: 821 (VH CDR2); SEQ ID NO: 822 (VH CDR3); SEQ ID NO: 823 (VL); SEQ ID NO: 824 (VL CDR1); SEQ ID NO: 825 (VL CDR2); SEQ ID NO: 826 (VL CDR3)

[0571] 029-067 antibody SEQ ID NO: 827 (VH); SEQ ID NO: 828 (VH CDR1); SEQ ID NO: 829 (VH CDR2); SEQ ID NO: 830 (VH CDR3); SEQ ID NO: 831 (VL); SEQ ID NO: 832 (VL CDR1); SEQ ID NO: 833 (VL CDR2); SEQ ID NO: 834 (VL CDR3)

[0572] 083-131 antibody SEQ ID NO: 835 (VH); SEQ ID NO: 836 (VH CDR1); SEQ ID NO: 837 (VH CDR2); SEQ ID NO: 838 (VH CDR3); SEQ ID NO: 839 (VL); SEQ ID NO: 840 (VL CDR1); SEQ ID NO: 841 (VL CDR2); SEQ ID NO: 842 (VL CDR3)

[0573] As mentioned in the below-mentioned Examples, the relationships between these antibodies and liver cancer cell line (HepG2, OCTH, Hep3B, and HLF), kidney cancer cell line (Caki-1, CCFRC1, ACHN, 293T, and cell line established from the clinical specimen), lung cancer cell line (PC14, NCI-H441, EB. C-1, RERF-LC-AI, A549, and H1373), ovarian cancer cell line (SKOv3, KF-28, RMG1, and RMG2), stomach cancer cell line (NCI-N87), large bowel cancer cell line (CW2), breast cancer cell line (BT474), acute myelocytic leukemia AML clinical specimen, and hamster ovarian cancer cell line CHO (as to the above mention, based on the results of the cell line staining), as well as the relationships between these antibodies and kidney cancer, hepatic cell carcinoma, gallbladder and liver cancer, lung squamous cell cancer, alveolar cell carcinoma, and adenocarcinoma (as to the above mention, based on the results of the tissue staining) are experimentally confirmed.

7. Antibody to CD147

[0574] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. As to the below-mentioned one kind of antibody clone, the sequence is analyzed.

[0575] 059-053 antibody SEQ ID NO: 177 (VH); SEQ ID NO: 178 (VH CDR1); SEQ ID NO: 179 (VH CDR2); SEQ ID NO: 180 (VH CDR3); SEQ ID NO: 181 (VL); SEQ ID NO: 182 (VL CDR1); SEQ ID NO: 183 (VL CDR2); SEQ ID NO: 184 (VL CDR3)

[0576] As mentioned in the below-mentioned Examples, the relationships between this antibody the and liver cancer cell line HepG2, kidney cancer cell line CCFRC1, kidney cancer cell line ACHN, kidney cancer cell line Caki-1, pulmonary adenocarcinoma PC14, and cell line established from kidney cancer clinical specimen (as to the above mention, based on the results of the cell line staining), as well as the relationships between these antibodies and kidney cancer (as to the above mention, based on the results of the tissue staining) are experimentally confirmed.

8. Antibody to C1qR

[0577] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. As to the below-mentioned one kind of antibody clone, the sequence is analyzed.

[0578] 070-016 antibody SEQ ID NO: 451 (VH); SEQ ID NO: (VH CDR1) 452; SEQ ID NO: 453 (VH CDR2); SEQ ID NO: 454 (yH CDR3); SEQ ID NO: 455 (VL); SEQ ID NO: (VL CDR1) 456; SEQ ID NO: 457 (VL CDR2); SEQ ID NO: 458 (VL CDR3)

[0579] The relationship between this antibody and leukemia is experimentally confirmed. That is to say, in cell line staining using this antibody, leukemia AML cell line Nohno 1 and leukemia AML clinical specimen shows a strong positive property (MFI=20 or more). Furthermore, in the process of growing the leukemia cell line, this antibody is added to the growing temperature, rapid aggregation of cancer cells can be confirmed. Moreover, the antibody amount necessary to cause these phenomena is relatively low concentration.

9. Antibody to CD44

[0580] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. As to the below-mentioned one kind of antibody clone, the sequence is analyzed.

[0581] 064-003 antibody SEQ ID NO: 459 (VH); SEQ ID NO: 460 (VH CDR1); SEQ ID NO: 461 (VH CDR2); SEQ ID NO: 462 (VH CDR3); SEQ ID NO: 463 (VL); SEQ ID NO: 464 (VL CDR1); SEQ ID NO: 465 (VL CDR2); SEQ ID NO: 466 (VL CDR3)

[0582] The relationships between this antibody and liver cancer, lung cancer, ovarian cancer, and stomach cancer are experimentally confirmed. That is to say, in the cell staining using this antibody, hepatic cell carcinoma HLF, pulmonary adenocarcinoma cell line PC14, pulmonary adenocarcinoma cell line NCI-H1373, and ovary adenocarcinoma cell line SKOv3 show the strong positive property (MFI=20 or more), and epidermoid cancer cell line A431 and lung squamous cell cancer EBC1 show the weak positive property (MFI=3 or more). Furthermore, in immunostaining using this antibody, a case in which a pulmonary adenocarcinoma clinical specimen shows cancer specific stained image is observed, and cancer portions of alveolar cell carcinoma and lung squamous cell cancer show the weak positive property.

10. Antibody to CD73

[0583] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. As to the below-mentioned one kind of antibody clone, the sequence is analyzed.

[0584] 067-213 antibody SEQ ID NO: 467 (VH); SEQ ID NO: 468 (VH CDR1); SEQ ID NO: 469 (VH CDR2); SEQ ID NO: 470 (VH CDR3); SEQ ID NO: 471 (VL); SEQ ID NO: 472 (VL CDR1); SEQ ID NO: 473 (VL CDR2); SEQ ID NO: 474 (VL CDR3)

[0585] The relationships between this antibody and liver cancer, lung cancer, and ovarian cancer are experimentally confirmed. That is to say, in the cell staining using this anti-

body, pulmonary adenocarcinoma cell line NCI-H1373, and lung squamous cell cancer EBC1 show the strong positive property (MFI=20 or more), and liver cancer cell line HLF, ovary adenocarcinoma cell line SKOv3, and pulmonary adenocarcinoma cell line PC14 show the weak positive property (MFI=3 or more). Furthermore, in immunostaining using this antibody, a cancer-specific stained image is obtained in a pulmonary adenocarcinoma clinical specimen and a stained image showing the weak positive property to a cancer portion is obtained in lung squamous cell cancer.

11. Antibody to EpCAM

[0586] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. As to the below-mentioned one kind of antibody clone, the sequence is analyzed.

[0587] 067-153 antibody SEQ ID NO: 475 (VH); SEQ ID NO: 476 (VH CDR1); SEQ ID NO: 477 (VH CDR2); SEQ ID NO: 478 (VH CDR3); SEQ ID NO: 479 (VL); SEQ ID NO: 480 (VL CDR1); SEQ ID NO: 481 (VL CDR2); SEQ ID NO: 482 (VL CDR3)

[0588] The relationships between this antibody and liver cancer, lung cancer, ovarian cancer, stomach cancer, and large bowel cancer are experimentally confirmed. That is to say, in the cell staining using this antibody, pulmonary adenocarcinoma cell line NCI-H1373 and lung squamous cell carcinoma line LK-2 show the strong positive property (MFI=20 or more); lung squamous cell cancer EBC1 and pulmonary adenocarcinoma cell line PCI4 show the positive property (MFI=10 or more); and ovary adenocarcinoma cell line SKOv3 shows the weak positive property (MFI=3 or more). Furthermore, in immunostaining using this antibody, an extremely excellent cancer-specific stained image is obtained in each clinical specimen of large bowel cancer, pulmonary adenocarcinoma, lung squamous cell cancer, stomach cancer. A stained image having a weak cancer specific positive property is obtained in a part of hepatic cell carcinoma clinical specimens.

12. Antibody to HGFR

[0589] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. Finally 87 kinds of antibody clones are identified. As to the below-mentioned three kinds of antibody clones, the sequences are analyzed.

[0590] 067-126 antibody SEQ ID NO: 651 (VH); SEQ ID NO: 652 (VH CDR1); SEQ ID NO: 653 (VH CDR2); SEQ ID NO: 654 (VH CDR3); SEQ ID NO: 655 (VL); SEQ ID NO: 656 (VL CDR1); SEQ ID NO: 657 (VL CDR2); SEQ ID NO: 658 (VL CDR3)

[0591] 067-133 antibody SEQ ID NO: 659 (VH); SEQ ID NO: 660 (VH CDR1); SEQ ID NO: 661 (VH CDR2); SEQ ID NO: 662 (VH CDR3); SEQ ID NO: 663 (VL); SEQ ID NO: 664 (VL CDR1); SEQ ID NO: 665 (VL CDR2); SEQ ID NO: 666 (VL CDR3)

[0592] 067-287 antibody SEQ ID NO: 667 (VH); SEQ ID NO: 668 (VH CDR1); SEQ ID NO: 669 (VH CDR2); SEQ ID NO: 670 (VH CDR3); SEQ ID NO: 671 (VL); SEQ ID NO: 672 (VL CDR1); SEQ ID NO: 673 (VL CDR2); SEQ ID NO: 674 (VL CDR3)

[0593] The relationships between this antibody and lung cancer, liver cancer, ovarian cancer, large bowel cancer, and stomach cancer are experimentally confirmed. That is to say, in cell line staining using this antibody, lung squamous cell cancer EBC1 shows a strong positive property (MFI=20 or more); alveolar adenocarcinoma NCI-H1373 shows the positive property (MFI=10 or more); and epidermoid cancer cell line A431, ovary adenocarcinoma cell line SKOv3, pulmonary adenocarcinoma cell line PC14, and hepatic cell carcinoma HLF show the weak positive property (MFI=3 or more). Furthermore, in immunostaining using this antibody, a weak positive property to cancer portion in a part of lung squamous cell cancer clinical specimen is obtained.

13. Antibody to LAR

[0594] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. As to the below-mentioned five kinds of antibody clones, the sequence is analyzed.

[0595] 064-044 antibody SEQ ID NO: 944 (VH); and SEQ ID NO: 945 (VL) 065-030 antibody SEQ ID NO: 946 (VH); and SEQ ID NO: 947 (VL)

[0596] 065-358 antibody SEQ ID NO: 948 (VH); and SEQ ID NO: 949 (VL)

[0597] 066-019 antibody SEQ ID NO: 950 (VH); and SEQ ID NO: 951 (VL)

[0598] 079-085 antibody SEQ ID NO: 952 (VH); and SEQ ID NO: 953 (VL)

[0599] In the immunostaining using these antibodies, a positive property is observed in a cancer portion in a part of the lung cancer clinical specimens.

14. Antibody to BCAM

[0600] A plurality of antibodies clones are obtained. Among them, antibodies having the same amino acid sequence are included. As to the below-mentioned one kind of antibody clone, the sequence is analyzed.

[0601] 067-024 antibody SEQ ID NO: 954 (VH); and SEQ ID NO: 955 (VL)

[0602] In the immunostaining using these antibodies, a positive property is observed in a cancer portion in a part of the clinical specimens of lung cancer, liver cancer, and kidney cancer.

[0603] The first embodiment of this aspect provides an isolated antibody having a specific binding property to HER1. The antibody of this form includes the heavy chain variable region CDR3 and the light chain variable region CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the group consisting of the following (1) to (3). Preferably, it includes the heavy chain variable regions CDR2 and CDR3 and the light chain variable regions CDR2 and CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the group consisting of the following (4) to (6). Furthermore, preferably, it includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable

region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2; and SEQ ID NO showing the amino acid sequence of the light chain variable region. CDR3) selected from the group consisting of the following (7) to (9) and (13) to (18). The most preferably, it includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable region and SEQ ID NO showing the light chain variable region) selected from the group consisting of the following (10) to (12) and (19) to (24).

(Combination of CDR3)

(1) SEQ ID NO: 4, SEQ ID NO: 8

(2) SEQ ID NO: 12, SEQ ID NO: 16

(3) SEQ ID NO: 20, SEQ ID NO: 24

(Combination of CDR2 and CDR3)

(4) SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 7, SEQ ID NO: 8

(5) SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 16

(6) SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24

(Combination of CDR1 to CDR3)

(7) SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 6 SEQ ID NO: 7, SEQ ID NO: 8

(8) SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16

(9) SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24

(13) SEQ ID NO: 484 (VH CDR1), SEQ ID NO: 485 (VH CDR2), SEQ ID NO: 486 (VH CDR3), SEQ ID NO: 488 (VL CDR1), SEQ ID NO: 489 (VL CDR2), SEQ ID NO: 490 (VL CDR3)

(14) SEQ ID NO: 492 (VH CDR1), SEQ ID NO: 493 (VH CDR2), SEQ ID NO: 494 (VH CDR3), SEQ ID NO: 496 (VL CDR1), SEQ ID NO: 497 (VL CDR2), SEQ ID NO: 498 (VL CDR3)

(15), SEQ ID NO: 500 (VH CDR1), SEQ ID NO: 501 (VH CDR2), SEQ ID NO: 502 (VH CDR3), SEQ ID NO: 504 (VL CDR1), SEQ ID NO: 505 (VL CDR2), SEQ ID NO: 506 (VL CDR3)

(16) SEQ ID NO: 508 (VH CDR1), SEQ ID NO: 509 (VH CDR2), SEQ ID NO: 510 (VH CDR3), SEQ ID NO: 512 (VL CDR1), SEQ ID NO: 513 (VL CDR2), SEQ ID NO: 514 (VL CDR3)

(17) SEQ ID NO: 516 (VH CDR1), SEQ ID NO: 517 (VH CDR2), SEQ ID NO: 518 (VH CDR3), SEQ ID NO: 520 (VL CDR1), SEQ ID NO: 521 (VL CDR2), SEQ ID NO: 522 (VL CDR3)

(18) SEQ ID NO: 524 (VH CDR1), SEQ ID NO: 525 (VH CDR2), SEQ ID NO: 526 (VH CDR3), SEQ ID NO: 528 (VL CDR1), SEQ ID NO: 529 (VL CDR2), SEQ ID NO: 530 (VL CDR3)

(Combination of Heavy Chain Variable Region and Light Chain Variable Region)

(10) SEQ ID NO: 1, SEQ ID NO: 5

(11) SEQ ID NO: 9, SEQ ID NO: 13

(12) SEQ ID NO: 17, SEQ ID NO: 21

(19) SEQ ID NO: 483 (VH), SEQ ID NO: 487 (VL)

(20) SEQ ID NO: 491 (VH), SEQ ID NO: 495 (VL)

(21) SEQ ID NO: 499 (VH), SEQ ID NO: 503 (VL)

(22) SEQ ID NO: 507 (VH), SEQ ID NO: 511 (VL)

(23) SEQ ID NO: 515 (VH), SEQ ID NO: 519 (VL)

(24) SEQ ID NO: 523 (VH), SEQ ID NO: 527 (VL)

[0604] Note here that (1), (4), (7), and (10) correspond to 048-006 antibody; (2), (5), (8), and (11) correspond to 057-091 antibody; (3), (6), (9), and (12) correspond to 059-152 antibody; (13) and (19) correspond to 048-040 antibody; (14) and (20) correspond to 054-101 antibody; (15) and (21) correspond to 055-147 antibody; (16) and (22) correspond to 059-173 antibody; (17) and (23) correspond to 067-149 antibody; as well as (18) and (24) correspond to 067-176 antibody. Therefore, the antibody of the present invention is expected to have high specificity to HER1.

[0605] The second embodiment of this aspect provides an isolated antibody having a specific binding property to HER2. The antibody of this form includes the heavy chain variable region CDR3 and the light chain variable region CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) shown in the following (1). Preferably, it includes the heavy chain variable regions CDR2 and CDR3 and the light chain variable regions CDR2 and CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the following (2). Furthermore, preferably, it includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the group consisting of the following (3) and (5) to (19). The most preferably, it includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable

region and SEQ ID NO showing the light chain variable region) selected from the group consisting of the following (4) and (20) to (34).

(Combination of CDR3)

(1) SEQ ID NO: 28, SEQ ID NO: 32

(Combination of CDR2 and CDR3)

(2) SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 31, SEQ ID NO: 32

(Combination of CDR1 to CDR3)

(3) SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32

(5) SEQ ID NO: 532 (VH CDR1), SEQ ID NO: 533 (VH CDR2), SEQ ID NO: 534 (VH CDR3), SEQ ID NO: 536 (VL CDR1), SEQ ID NO: 537 (VL CDR2), SEQ ID NO: 538 (VL CDR3)

(6) SEQ ID NO: 540 (VH CDR1), SEQ ID NO: 541 (VH CDR2), SEQ ID NO: 542 (VH CDR3), SEQ ID NO: 544 (VL CDR1), SEQ ID NO: 545 (VL CDR2), SEQ ID NO: 546 (VL CDR3)

(7) SEQ ID NO: 548 (VH CDR1), SEQ ID NO: 549 (VH CDR2), SEQ ID NO: 550 (VH CDR3), SEQ ID NO: 552 (VL CDR1), SEQ ID NO: 553 (VL CDR2), SEQ ID NO: 554 (VL CDR3)

(8) SEQ ID NO: 556 (VH CDR1), SEQ ID NO: 557 (VH CDR2), SEQ ID NO: 558 (VH CDR3), SEQ ID NO: 560 (VL CDR1), SEQ ID NO: 561 (VL CDR2), SEQ ID NO: 562 (VL CDR3)

(9) SEQ ID NO: 564 (VH CDR1), SEQ ID NO: 565 (VH CDR2), SEQ ID NO: 566 (VH CDR3), SEQ ID NO: 568 (VL CDR1), SEQ ID NO: 569 (VL CDR2), SEQ ID NO: 570 (VL CDR3)

(10) SEQ ID NO: 572 (VH CDR1), SEQ ID NO: 573 (VH CDR1), SEQ ID NO: 574 (VH CDR3), SEQ ID NO: 576 (VL CDR1), SEQ ID NO: 577 (VL CDR2), SEQ ID NO: 578 (VL CDR3)

(11) SEQ ID NO: 580 (VH CDR1), SEQ ID NO: 581 (VH CDR2), SEQ ID NO: 582 (VH CDR3), SEQ ID NO: 584 (VL CDR1), SEQ ID NO: 585 (VL CDR2), SEQ ID NO: 586 (VL CDR3)

(12) SEQ ID NO: 588 (VH CDR1), SEQ ID NO: 589 (VH CDR2), SEQ ID NO: 590 (VH CDR3), SEQ ID NO: 592 (VL CDR1), SEQ ID NO: 593 (VL CDR2), SEQ ID NO: 594 (VL CDR3)

(13) SEQ ID NO; 596 (VH CDR1), SEQ ID NO: 597 (VH CDR2), SEQ ID NO: 598 (VH CDR3), SEQ ID NO: 600 (VL CDR1), SEQ ID NO: 601 (VL CDR2), SEQ ID NO: 602 (VL CDR3)

(14) SEQ ID NO: 604 (VH CDR1), SEQ ID NO: 605 (VH CDR2), SEQ ID NO: 606 (VH CDR3), SEQ ID NO: 608 (VL CDR1), SEQ ID NO: 609 (VL CDR2), SEQ ID NO: 610 (VL CDR3)

(15) SEQ ID NO: 612 (VH CDR1), SEQ ID NO: 613 (VH CDR2), SEQ ID NO: 614 (VH CDR3), SEQ ID NO: 616 (VL CDR1), SEQ ID NO: 617 (VL CDR2), SEQ ID NO: 618 (VL CDR3)

(16) SEQ ID NO: 620 (VH CDR1), SEQ ID NO: 621 (VH CDR2), SEQ ID NO: 622 (VH CDR3), SEQ ID NO: 624 (VL CDR1), SEQ ID NO: 625 (VL CDR2), SEQ ID NO: 626 (VL CDR3)

(17) SEQ ID NO: 628 (VH CDR1), SEQ ID NO: 629 (VH CDR2), SEQ ID NO: 630 (VH CDR3), SEQ ID NO: 632 (VL CDR1), SEQ ID NO: 633 (VL CDR2), SEQ ID NO: 634 (VL CDR3)

(18) SEQ ID NO: 636 (VH CDR1), SEQ ID NO: 637 (VH CDR2), SEQ ID NO: 638 (VH CDR3), SEQ ID NO: 640 (VL CDR1), SEQ ID NO: 641 (VL CDR2), SEQ ID NO: 642 (VL CDR3)

(19) SEQ ID NO: 644 (VH CDR1), SEQ ID NO: 645 (VH CDR2), SEQ ID NO: 646 (VH CDR3), SEQ ID NO: 648 (VL CDR1), SEQ ID NO: 649 (VL CDR2), SEQ ID NO: 650 (VL CDR3)

(Combination of Heavy Chain Variable Region and Light Chain Variable Region)

(4) SEQ ID NO: 25, SEQ ID NO: 29

(20) SEQ ID NO: 531 (VH), SEQ ID NO: 535 (VL)

(21) SEQ ID NO: 539 (VH), SEQ ID NO: 543 (VL)

(22) SEQ ID NO: 547 (VH), SEQ ID NO: 551 (VL)

(23) SEQ ID NO: 555 (VH), SEQ ID NO: 559 (VL)

(24) SEQ ID NO: 563 (VH), SEQ ID NO: 567 (VL)

(25) SEQ ID NO: 571 (VH), SEQ ID NO: 575 (VL)

(26) SEQ ID NO: 579 (VH), SEQ ID NO: 583 (VL)

(27) SEQ ID NO: 587 (VH), SEQ ID NO: 591 (VL)

(28) SEQ ID NO: 595 (VH), SEQ ID NO: 599 (VL)

(29) SEQ ID NO: 603 (VH), SEQ ID NO: 607 (VL)

(30) SEQ ID NO: 611 (VH), SEQ ID NO: 615 (VL)

(31) SEQ ID NO: 619 (VH), SEQ ID NO: 623 (VL)

(32) SEQ ID NO: 627 (VH), SEQ ID NO: 631 (VL)

(33) SEQ ID NO: 635 (VH), SEQ ID NO: 639 (VL)

(34) SEQ ID NO: 643 (VH), SEQ ID NO: 647 (VL)

[0606] Note here that (1) to (4) correspond to 015-126 antibody; (5) and (20) correspond to 015-044 antibody; (6) and (21) correspond to 015-102 antibody; (7) and (22) correspond to 015-136 antibody; (8) and (23) correspond to 015-143 antibody; (9) and (24) correspond to 015-209 antibody; (10) and (25) correspond to 039-016 antibody; (11) and (26) correspond to 053-216 antibody; (12) and (27) correspond to 075-024 antibody; (13) and (28) correspond to 075-110 antibody; (14), (29) correspond to 086-032 antibody; (15) and (30) correspond to 086-035 antibody; (16) and (31) correspond to 086-036 antibody; (17) and (32) correspond to 086-061 antibody; (18) and (33) correspond to 086-138 antibody; as well as (19) and (34) correspond to 086-182 antibody. Therefore, the antibody of the present invention is expected to have high specificity to HER2.

[0607] The third embodiment of this aspect provides an isolated antibody having a specific binding property to CD46 antigen. The antibody of this form includes the heavy chain variable region CDR3 and the light chain variable region CDR3 specified by the combination of SEQ ID NOs (SEQ ID

NO showing the amino acid sequence of the heavy chain variable region CDR3, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the following the group consisting of (1) to (7). Preferably, it includes the heavy chain variable regions CDR2 and CDR3 and the light chain variable regions CDR2 and CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the following the group consisting of (8) to (14). Furthermore preferably, it includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR 1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the following the group consisting of (15) to (21). The most preferably, it includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region and SEQ ID NO showing the amino acid sequence of the light chain variable region) selected from the following the group consisting of (22) to (28).

(Combination of CDR3)

(1) SEQ ID NO: 36, SEQ ID NO: 40

(2) SEQ ID NO: 44, SEQ ID NO: 48

(3) SEQ ID NO: 52, SEQ ID NO: 56

(4) SEQ ID NO: 60, SEQ ID NO: 64

(5) SEQ ID NO: 68, SEQ ID NO: 72

(6) SEQ ID NO: 76, SEQ ID NO: 80

(7) SEQ ID NO: 84, SEQ ID NO: 88

(Combination of CDR2 and CDR3)

(8) SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 39, SEQ ID NO: 40

(9) SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 47, SEQ ID NO: 48

(10) SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 55, SEQ ID NO: 56

(11) SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 63, SEQ ID NO: 64

(12) SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 71, SEQ ID NO: 72

(13) SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 79, SEQ ID NO: 80

(14) SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 87, SEQ ID NO: 88

(Combination of CDR1 to CDR3)

(15) SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40

(16) SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48

(17) SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56

(18) SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64

(19) SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72

(20) SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 80

(21) SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 88

(22) SEQ ID NO: 756 (VH CDR1), SEQ ID NO: 757 (VH CDR2), SEQ ID NO: 758 (VH CDR3), SEQ ID NO: 760 (VL CDR1), SEQ ID NO: 761 (VL CDR2), SEQ ID NO: 762 (VL CDR3)

(Combination of Heavy Chain Variable Region and Light Chain Variable Region)

(23) SEQ ID NO: 33, SEQ ID NO: 37

(24) SEQ ID NO: 41, SEQ ID NO: 45

(25) SEQ ID NO: 49, SEQ ID NO: 53

(26) SEQ ID NO: 57, SEQ ID NO: 61

(27) SEQ ID NO: 65, SEQ ID NO: 69

(28) SEQ ID NO: 73, SEQ ID NO: 77

(29) SEQ ID NO: 81, SEQ ID NO: 85

(30) SEQ ID NO: 755 (VH), SEQ ID NO: 759 (VL)

[0608] Note here that (1), (8), (15) and (23) correspond to 035-224 antibody; (2), (9), (16), and (24) correspond to 045-011 antibody; (3), (10), (17), and (25) correspond to 051-144 antibody; (4), (11), (18), and (26) correspond to 052-053 antibody; (5), (12), (19), and (27) correspond to 052-073 antibody; (6), (13), (20), and (28) correspond to 053-049 antibody; (7), (14), (21), and (29) correspond to 3172-120 antibody; as well as (22) and (30) correspond to 066-069 antibody. Therefore, the antibody of the present invention is expected to have high specificity to a CD46 antigen.

[0609] The fourth embodiment of this aspect provides an isolated antibody having a specific binding property to ITGA3. The antibody of this form includes the heavy chain variable region CDR3 and the light chain variable region CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) shown in the following (1). Preferably, it includes the heavy chain variable regions CDR2 and CDR3 and the light chain variable regions CDR2 and CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable

region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) shown in the following (2). Furthermore, preferably, it includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the group consisting of the following (3) and (5) to (17). The most preferably, it includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable region and SEQ ID NO showing the light chain variable region) selected from the group consisting of the following (4) and (18) to (30).

(Combination of CDR3)

(1) SEQ ID NO: 92, SEQ ID NO: 96

(Combination of CDR2 and CDR3)

(2) SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 95, SEQ ID NO: 96

(Combination of CDR 1 to CDR3)

(3) SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 94, SEQ ID NO: 95, SEQ ID NO: 96

(5) SEQ ID NO: 676 (VH CDR1), SEQ ID NO: 677 (VH CDR2), SEQ ID NO: 678 (VH CDR3), SEQ ID NO: 680 (VL CDR1), SEQ ID NO: 681 (VL CDR2), SEQ ID NO: 682 (VL CDR3)

(6) SEQ ID NO: 684 (VH CDR1), SEQ ID NO: 685 (VH CDR2), SEQ ID NO: 686 (VH CDR3), SEQ ID NO: 688 (VL CDR1), SEQ ID NO: 689 (VL CDR2), SEQ ID NO: 690 (VL CDR3)

(7) SEQ ID NO: 692 (VH CDR1), SEQ ID NO: 693 (VH CDR2), SEQ ID NO: 694 (VH CDR3), SEQ ID NO: 696 (VL CDR1), SEQ ID NO: 697 (VL CDR2), SEQ ID NO: 698 (VL CDR3)

(8) SEQ ID NO: 700 (VH CDR1), SEQ ID NO: 701 (VH CDR2), SEQ ID NO: 702 (VH CDR3), SEQ ID NO: 704 (VL CDR1), SEQ ID NO: 705 (VL CDR2), SEQ ID NO: 706 (VL CDR3)

(9) SEQ ID NO: 708 (VH CDR1), SEQ ID NO: 709 (VH CDR2), SEQ ID NO: 710 (VH CDR3), SEQ ID NO: 712 (VL CDR1), SEQ ID NO: 713 (VL CDR2), SEQ ID NO: 714 (VL CDR3)

(10) SEQ ID NO: 716 (VH CDR1), SEQ ID NO: 717 (VH CDR2), SEQ ID NO: 718 (VH CDR3), SEQ ID NO: 720 (VL CDR1), SEQ ID NO: 721 (VL CDR2), SEQ ID NO: 722 (VL CDR3)

(11) SEQ ID NO: 724 (VH CDR1), SEQ ID NO: 725 (VH CDR2), SEQ ID NO: 726 (VH CDR3), SEQ ID NO: 728 (VL CDR1), SEQ ID NO: 729 (VL CDR2), SEQ ID NO: 730 (VL CDR3)

(12) SEQ ID NO: 732 (VH CDR1), SEQ ID NO: 733 (VH CDR2), SEQ ID NO: 734 (VH CDR3), SEQ ID NO: 736 (VL CDR1), SEQ ID NO: 737 (VL CDR2), SEQ ID NO: 738 (VL CDR3)

(13) SEQ ID NO: 740 (VH CDR1), SEQ ID NO: 741 (VH CDR2), SEQ ID NO: 742 (VH CDR3), SEQ ID NO: 744 (VL CDR1), SEQ ID NO: 745 (VL CDR2), SEQ ID NO: 746 (VL CDR3)

(14) SEQ ID NO: 748 (VH CDR1), SEQ ID NO: 749 (VH CDR2), SEQ ID NO: 750 (VH CDR3), SEQ ID NO: 752 (VL CDR1), SEQ ID NO: 753 (VL CDR2), SEQ ID NO: 754 (VL CDR3)

(15) SEQ ID NO: 764 (VH CDR1), SEQ ID NO: 765 (VH CDR2), SEQ ID NO: 766 (VH CDR3), SEQ ID NO: 768 (VL CDR1), SEQ ID NO: 769 (VL CDR2), SEQ ID NO: 770 (VL CDR3)

(16) SEQ ID NO: 772 (VH CDR1), SEQ ID NO: 773 (VH CDR2), SEQ ID NO: 774 (VH CDR3), SEQ ID NO: 776 (VL CDR1), SEQ ID NO: 777 (VL CDR2), SEQ ID NO: 778 (VL CDR3)

(Combination of Heavy Chain Variable Region and Light Chain Variable Region)

(4) SEQ ID NO: 89, SEQ ID NO: 93

(17) SEQ ID NO: 675 (VH), SEQ ID NO: 679 (VL)

(18) SEQ ID NO: 683 (VH), SEQ ID NO: 687 (VL)

(19) SEQ ID NO: 691 (VH), SEQ ID NO: 695 (VL)

(20) SEQ ID NO: 699 (VH), SEQ ID NO: 703 (VL)

(21) SEQ ID NO: 707 (VH), SEQ ID NO: 711 (VL)

(22) SEQ ID NO: 715 (VH), SEQ ID NO: 719 (VL)

(23) SEQ ID NO: 723 (VH), SEQ ID NO: 727 (VL)

(24) SEQ ID NO: 731 (VH), SEQ ID NO: 735 (VL)

(25) SEQ ID NO: 739 (VH), SEQ ID NO: 743 (VL)

(26) SEQ ID NO: 747 (VH), SEQ ID NO: 751 (VL)

(27) SEQ ID NO: 763 (VH), SEQ ID NO: 767 (VL)

(28) SEQ ID NO: 771 (VH), SEQ ID NO. 775 (VL)

[0610] Note here that (1) to (4) correspond to 015-003 antibody; (5) and (17) correspond to 064-002 antibody; (6) and (18) correspond to 064-006 antibody; (7) and (19) correspond to 064-012a antibody; (8) and (20) correspond to 064-012b antibody; (9) and (21) correspond to 064-014 antibody; (10) and (22) correspond to 064-054 antibody; (11) and (23) correspond to 064-085 antibody; (12) and (24) correspond to 064-093 antibody; (13) and (25) correspond to 064-116 antibody; (14) and (26) correspond to 065-183 antibody; (15) and (27) correspond to 067-142 antibody; as well as (16) and (28) correspond to 068-007 antibody. Therefore, the antibody of the present invention is expected to have high specificity to ITGA3.

[0611] The fifth embodiment of this aspect provides an isolated antibody having a specific binding property to

ICAM1. The antibody of this form includes the heavy chain variable region CDR3 and the light chain variable region CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the following the group consisting of (1) to (5). Preferably, it includes the heavy chain variable regions CDR2 and CDR3 and the light chain variable regions CDR2 and CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the following the group consisting of (6) to (10). Furthermore preferably, it includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the following the group consisting of (11) to (15). The most preferably, it includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region and SEQ ID NO showing the amino acid sequence of the light chain variable region) selected from the following the group consisting of (16) to (20).

(Combination of CDR3)

(1) SEQ ID NO: 100, SEQ ID NO: 104

(2) SEQ ID NO: 108, SEQ ID NO: 112

(3) SEQ ID NO: 116, SEQ ID NO: 120

(4) SEQ ID NO: 124, SEQ ID NO: 128

(5) SEQ ID NO: 132, SEQ ID NO: 136

(Combination of CDR2 and CDR3)

(6) SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 103, SEQ ID NO: 104

(7) SEQ ID NO: 107, SEQ ID NO: 108, SEQ ID NO: 111, SEQ ID NO: 112

(8) SEQ ID NO: 115, SEQ ID NO: 116, SEQ ID NO: 119, SEQ ID NO: 120

(9) SEQ ID NO: 123, SEQ ID NO: 124, SEQ ID NO: 127, SEQ ID NO: 128

(10) SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 135, SEQ ID NO: 136

(Combination of CDR1 to CDR3)

(11) SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 102, SEQ ID NO: 103, SEQ ID NO: 104

(12) SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 111, SEQ ID NO: 112

(13) SEQ ID NO: 114, SEQ ID NO: 115, SEQ ID NO: 116, SEQ ID NO: 118, SEQ ID NO: 119, SEQ ID NO: 120

(14) SEQ ID NO: 122, SEQ ID NO: 123, SEQ ID NO: 124, SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128

(15) SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136

[0612] (Combination of heavy chain variable region and light chain variable region)

(16) SEQ ID NO: 97, SEQ ID NO: 101

(17) SEQ ID NO: 105, SEQ ID NO: 109

(18) SEQ ID NO: 113, SEQ ID NO: 117

(19) SEQ ID NO: 121, SEQ ID NO: 125

(20) SEQ ID NO: 129, SEQ ID NO: 133

[0613] Note here that (1), (6), (11) and (16) correspond to 052-033 antibody; (2), (7), (12), and (17) correspond to 053-042 antibody; (3), (8), (13), and (18) correspond to 053-051 antibody; (4), (9), (14), and (19) correspond to 053-059 antibody; as well as (5), (10), (15), and (20) correspond to 053-085 antibody. Therefore, the antibody of the present invention is expected to have high specificity to ICAM1.

[0614] The sixth embodiment of this aspect provides an isolated antibody having a specific binding property to ALCAM. The antibody of this form includes the heavy chain variable region CDR3 and the light chain variable region CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the group consisting of the following (1) to (5). Preferably, it includes the heavy chain variable regions CDR2 and CDR3 and the light chain variable regions CDR2 and CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the group consisting of the following (6) to (10). Furthermore, preferably, it includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the group consisting of the following (11) to (15) and (21) to (28). The most preferably, it includes the heavy chain

variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable region and SEQ ID NO showing the light chain variable region) selected from the group consisting of the following (16) to (20) and (29) to (36).

(Combination of CDR3)

(1) SEQ ID NO: 140, SEQ ID NO: 144

(2) SEQ ID NO: 148, SEQ ID NO: 152

(3) SEQ ID NO: 156, SEQ ID NO: 160

(4) SEQ ID NO: 164, SEQ ID NO: 168

(5) SEQ ID NO: 172, SEQ ID NO: 176

(Combination of CDR2 and CDR3)

(6) SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 143, SEQ ID NO: 144

(7) SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 151, SEQ ID NO: 152

(8) SEQ ID NO: 155, SEQ ID NO: 156, SEQ ID NO: 159, SEQ ID NO: 160

(9) SEQ ID NO: 163, SEQ ID NO: 164, SEQ ID NO: 167, SEQ ID NO: 168

(10) SEQ ID NO: 171, SEQ ID NO: 172, SEQ ID NO: 175, SEQ ID NO: 176

(Combination of CDR1 to CDR3)

(11) SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144

(12) SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152

(13) SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, SEQ ID NO: 158, SEQ ID NO: 159, SEQ ID NO: 160

(14) SEQ ID NO: 162, SEQ ID NO: 163, SEQ ID NO: 164, SEQ ID NO: 166, SEQ ID NO: 167, SEQ ID NO: 168

(15) SEQ ID NO: 170, SEQ ID NO: 171, SEQ ID NO: 172, SEQ ID NO: 174, SEQ ID NO: 175, SEQ ID NO: 176

(21) SEQ ID NO: 780 (VH CDR1), SEQ ID NO: 781 (VH CDR2), SEQ ID NO 782 (VH CDR3), SEQ ID NO: 784 (VL CDR1), SEQ ID NO: 785 (VL CDR2), SEQ ID NO: 786 (VL CDR3)

(22) SEQ ID NO: 788 (VH CDR1), SEQ ID NO: 789 (VH CDR2), SEQ ID NO: 790 (VH CDR3), SEQ ID NO: 792 (VL CDR1), SEQ ID NO: 793 (yL CDR2), SEQ ID NO: 794 (VL CDR3)

(23) SEQ ID NO: 796 (VH CDR1), SEQ ID NO: 797 (VH CDR2), SEQ ID NO: 798 (VH CDR3), SEQ ID NO: 800 (VL CDR1), SEQ ID NO: 801 (VL CDR2), SEQ ID NO: 802 (VL CDR3)

(24) SEQ ID NO: 804 (VH CDR1), SEQ ID NO: 805 (VH CDR2), SEQ ID NO: 806 (VH CDR3), SEQ ID NO: 808 (VL CDR1), SEQ ID NO: 809 (VL CDR2), SEQ ID NO: 810 (VL CDR3)

(25) SEQ ID NO: 812 (VH CDR1), SEQ ID NO: 813 (VH CDR2), SEQ ID NO: 814 (VH CDR3), SEQ ID NO: 816 (VL CDR1), SEQ ID NO: 817 (VL CDR2), SEQ ID NO: 818 (VL CDR3)

(26) SEQ ID NO: 820 (VH CDR1), SEQ ID NO: 821 (VH CDR2), SEQ ID NO: 822 (VH CDR3), SEQ ID NO: 824 (VL CDR1), SEQ ID NO: 825 (VL CDR2), SEQ ID NO: 826 (VL CDR3)

(27) SEQ ID NO: 828 (VH CDR1), SEQ ID NO: 829 (VH CDR2), SEQ ID NO: 830 (VH CDR3), SEQ ID NO: 832 (VL CDR1), SEQ ID NO: 833 (VL CDR2), SEQ ID NO: 834 (VL CDR3)

(28) SEQ ID NO: 836 (VH CDR1), SEQ ID NO: 837 (VH CDR2), SEQ ID NO: 838 (VH CDR3), SEQ ID NO: 840 (VL CDR1), SEQ ID NO: 841 (VL CDR2), SEQ ID NO: 842 (VL CDR3)

(Combination of Heavy Chain Variable Region and Light Chain Variable Region)

(16) SEQ ID NO: 137, SEQ ID NO: 141

(17) SEQ ID NO: 145, SEQ ID NO: 149

(18) SEQ ID NO: 153, SEQ ID NO: 157

(19) SEQ ID NO: 161, SEQ ID NO: 165

(20) SEQ ID NO: 169, SEQ ID NO: 173

(29) SEQ ID NO: 779 (VH), SEQ ID NO: 783 (VL)

(30) SEQ ID NO: 787 (VH), SEQ ID NO: 791 (VL)

(31) SEQ ID NO: 795 (VH), SEQ ID NO: 799 (VL)

(32) SEQ ID NO: 803 (VH), SEQ ID NO: 807 (VL)

(33) SEQ ID NO: 811 (VH), SEQ ID NO: 815 (VL)

(34) SEQ ID NO: 819 (VH), SEQ ID NO: 823 (VL)

(35) SEQ ID NO: 827 (VH), SEQ ID NO: 831 (VL)

(36) SEQ ID NO: 835 (VH), SEQ ID NO: 839 (VL)

[0615] Note here that (1), (6), (11), and (16) correspond to 035-234 antibody; (2), (7), (12), and (17) correspond to 040-107 antibody; (3), (8), (13), and (18) correspond to 041-118 antibody; (4), (9), (14), and (19) correspond to 066-174 antibody; (5), (10), (15), and (20) correspond to 083-040 antibody; (21) and (29) correspond to 029-143 antibody; (22) and (30) correspond to 045-134 antibody; (23) and (31) correspond to 062-101 antibody; (24) and (32) correspond to 062-109 antibody; (25) and (33) correspond to 084-103 antibody; (26) and (34) correspond to 052-274 antibody; (27) and (35) correspond to 029-067 antibody; as well as (28) and (36) correspond to 083-131 antibody. Therefore, the antibody of the present invention is expected to have high specificity to ALCAM.

[0616] The seventh embodiment of this aspect provides an isolated antibody having a specific binding property to a CD147 antigen. The antibody of this form includes the heavy chain variable region CDR3 and the light chain variable region CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) shown in the following (1). Preferably, it includes the heavy chain variable regions CDR2 and CDR3 and the light chain

variable regions CDR2 and CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the following (2). Furthermore, preferably, it includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2, and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) shown in the following (3). The most preferably, it includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable region and SEQ ID NO showing the light chain variable region) shown in the following (4).

(Combination of CDR3)

(1) SEQ ID NO: 180, SEQ ID NO: 184

(Combination of CDR2 and CDR3)

(2) SEQ ID NO: 179, SEQ ID NO: 180, SEQ ID NO: 183, SEQ ID NO: 184

(Combination of CDR1 to CDR3)

(3) SEQ ID NO: 178, SEQ ID NO: 179, SEQ ID NO: 180, SEQ ID NO: 182, SEQ ID NO: 183, SEQ ID NO: 184

[0617] (Combination of heavy chain variable region and light chain variable region)

(4) SEQ ID NO: 177, SEQ ID NO: 181

[0618] Note here that (1) to (4) correspond to 059-053 antibody. Therefore, the antibody of the present invention is expected to have high specificity to a CD147 antigen.

[0619] The eighth embodiment of this aspect provides an isolated antibody having a specific binding property to C1qR. The antibody of this form includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2 and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) shown in the following (1). Preferably, it includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable region and SEQ ID NO showing the light chain variable region) shown in the following (2).

(Combination of CDR3)

(1) SEQ ID NO: (VH CDR1) 452, SEQ ID NO: 453 (VH CDR2), SEQ ID NO: 454 (VH CDR3), SEQ ID NO: (VL CDR1) 456, SEQ ID NO: 457 (VL CDR2), SEQ ID NO: 458 (VL CDR3)

(Combination of Heavy Chain Variable Region and Light Chain Variable Region)

(2) SEQ ID NO: 451 (VH), SEQ ID NO: 455 (VL)

[0620] Note here that (1) and (2) correspond to 070-016 antibody. Therefore, the antibody of the present invention is expected to have high specificity to C1qR.

[0621] The ninth embodiment of this aspect provides an isolated antibody having a specific binding property to CD44. The antibody of this form includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2 and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) shown in the following (1). Preferably, it includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable region and SEQ ID NO showing the light chain variable region) shown in the following (2).

(Combination of CDR1 to CDR3)

(1) SEQ ID NO: 460 (VH CDR1), SEQ ID NO: 461 (VH CDR2), SEQ ID NO: 462 (VH CDR3), SEQ ID NO: 464 (VL CDR1), SEQ ID NO: 465 (VL CDR2), SEQ ID NO: 466 (VL CDR3)

(Combination of Heavy Chain Variable Region and Light Chain Variable Region)

(2) SEQ ID NO: 459 (VH), SEQ ID NO: 463 (VL)

[0622] Note here that (1) and (2) correspond to 064-003 antibody. Therefore, the antibody of the present invention is expected to have high specificity to CD44.

[0623] The tenth embodiment of this aspect provides an isolated antibody having a specific binding property to CD73. The antibody of this form includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2 and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) shown in the following (1). Preferably, it includes the heavy chain

variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable region and SEQ ID NO showing the light chain variable region) shown in the following (2).

(Combination of CDR1 to CDR3)

(1) SEQ ID NO: 468 (VH CDR1), SEQ ID NO: 469 (VH CDR2), SEQ ID NO: 470 (VH CDR3), SEQ ID NO: 472 (VL CDR1), SEQ ID NO: 473 (VL CDR2), SEQ ID NO: 474 (VL CDR3)

(Combination of Heavy Chain Variable Region and Light Chain Variable Region)

(2) SEQ ID NO: 467 (VH), SEQ ID NO: 471 (VL)

[0624] Note here that (1) and (2) correspond to 067-213 antibody. Therefore, the antibody of the present invention is expected to have high specificity to CD73.

[0625] The eleventh embodiment of this aspect provides an isolated antibody having a specific binding property to EpCAM. The antibody of this form includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2 and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) shown in the following (1). Preferably, it includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable region and SEQ ID NO showing the light chain variable region) shown in the following (2).

(Combination of CDR1 to CDR3)

(1) SEQ ID NO: 476 (VH CDR1), SEQ ID NO: 477 (VH CDR2), SEQ ID NO: 478 (VH CDR3), SEQ ID NO: 480 (VL CDR1), SEQ ID NO: 481 (VL CDR2), SEQ ID NO: 482 (VL CDR3)

(Combination of Heavy Chain Variable Region and Light Chain Variable Region)

(2) SEQ ID NO: 475 (VH), SEQ ID NO: 479 (VL)

[0626] Note here that (1) and (2) correspond to 067-153 antibody. Therefore, the antibody of the present invention is expected to have high specificity to EpCAM.

[0627] The twelfth embodiment of this aspect provides an isolated antibody having a specific binding property to HGFR. The antibody of this form includes the heavy chain variable regions CDR1 to CDR3 and the light chain variable regions CDR1 to CDR3 specified by the combination of SEQ ID NOs (SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR2, SEQ ID NO showing the amino acid sequence of the heavy chain variable region CDR3, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR1, SEQ ID NO showing the amino acid sequence of the light chain variable region CDR2 and SEQ ID NO showing the amino acid sequence of the light chain variable region CDR3) selected from the group consisting of the following (1) to (3). Preferably, it includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable region and SEQ ID NO showing the light chain variable region) selected from the group consisting of the following (4) to (6).

(Combination of CDR1 to CDR3)

(1) SEQ ID NO: 652 (VH CDR1), SEQ ID NO: 653 (VH CDR2), SEQ ID NO: 654 (VH CDR3), SEQ ID NO: 656 (VL CDR1), SEQ ID NO: 657 (VL CDR2), SEQ ID NO: 658 (VL CDR3)

(2) SEQ ID NO: 660 (VH CDR1), SEQ ID NO: 661 (VH CDR2), SEQ ID NO: 662 (VH CDR3), SEQ ID NO: 664 (VL CDR1), SEQ ID NO: 665 (VL CDR2), SEQ ID NO: 666 (VL CDR3)

(3) SEQ ID NO: 668 (VH CDR1), SEQ ID NO: 669 (VH CDR2), SEQ ID NO: 670 (VH CDR3), SEQ ID NO: 672 (VL CDR1), SEQ ID NO: 673 (VL CDR2), SEQ ID NO: 674 (VL CDR3)

[0628] (Combination of heavy chain variable region and light chain variable region)

(4) SEQ ID NO: 651 (VH), SEQ ID NO: 655 (VL)

(5) SEQ ID NO: 659 (VH), SEQ ID NO: 663 (VL)

(6) SEQ ID NO: 667 (VH), SEQ ID NO: 671 (VL)

[0629] Note here that (1) and (4) correspond to 067-126 antibody; (2) and (5) correspond to 067-133 antibody; and (3) and (6) correspond to 067-287 antibody. Therefore, the antibody of the present invention is expected to have high specificity to HGFR.

[0630] The 13rd embodiment of this aspect provides an isolated antibody having a specific binding property to LAR. The antibody of this form includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable region and SEQ ID NO showing the light chain variable region) selected from the group consisting of the following (1) to (5).

(Combination of heavy chain variable region and light chain variable region)

(1) SEQ ID NO: 944 (VH), SEQ ID NO: 945 (VL)

(2) SEQ ID NO: 946 (VH), SEQ ID NO: 947 (VL)

(3) SEQ ID NO: 948 (VH), SEQ ID NO: 949 (VL)

(4) SEQ ID NO: 950 (VH), SEQ ID NO: 951 (VL)

(5) SEQ ID NO: 952 (VH), SEQ ID NO: 953 (VL)

[0631] Note here that (1) corresponds to 064-044 antibody; (2) corresponds to 065-030 antibody; (3) corresponds to 065-358 antibody; (4) corresponds to 066-019 antibody; and (5) corresponds to 079-085 antibody. Therefore, the antibody of the present invention is expected to have high specificity to LAR.

[0632] The 14th embodiment of this aspect provides an isolated antibody having a specific binding property to

BCAM. The antibody of this form includes the heavy chain variable region and the light chain variable region specified by the combination of SEQ ID NOs (SEQ ID NO showing the heavy chain variable region and SEQ ID NO showing the light chain variable region) shown in the following (1).
(Combination of heavy chain variable region and light chain variable region)

(1) SEQ ID NO: 954 (VH), SEQ ID NO: 955 (VL)

[0633] Note here that (1) corresponds to 067-024 antibody. Therefore, the antibody of the present invention is expected to have high specificity to BCAM.

[0634] In the variable region of the antibody of the present invention, the sequence of the framework region (FR region) is not particularly limited as long as it does not substantially affect the specific binding property with respect to corresponding antigen. For example, when the antibody of the present invention is constructed as a humanized antibody, the FR region of a known human antibody can be used. Furthermore, when the antibody of the present invention is constructed as an antibody used as a reagent for detection or used for application to non-human animal species, in some cases, an effect can be expected even if the human antibody FR region is not used, or the use of the human antibody FR region may not appropriate. In such cases, the FR region from non-human animal species (for example, mouse or rat) can be used.

[0635] In one embodiment of the antibody of the present invention, a constant region (for example, in the case of an IgG type antibody) is included in addition to the variable region. The sequence of the constant region in this embodiment is not particularly limited. For example, as mentioned below, when the antibody of the present invention is constructed as a humanized antibody, the constant region of a known human antibody can be used. Furthermore, similar to the above-mentioned FR region, a constant region from non-human animal species (for example, mouse or rat) can be used.

[0636] One embodiment of the antibody of the present invention relates to a humanized antibody. The "humanized antibody" herein denotes an antibody that is allowed to resemble the structure of the human antibody. It includes a humanized chimeric antibody in which only a constant region is replaced by that of human antibody, and a humanized CDR-grafted antibody in which a part other than the CDR (complementarity determining region) existing in the constant region and the variable region is replaced by that of human antibody (P. T. Johons et al., Nature 321, 522 (1986)). In order to improve the antigen binding activity of the humanized CDR-grafted antibody, improved techniques of a method of selecting a human antibody FR that is highly homologous to a mouse antibody, a method of producing a humanized antibody having high homology, and a method of transplanting a human antibody to a mouse CDR and then replacing amino acid in the FR region have been already developed (see, for example, U.S. Pat. Nos. 5,585,089, 5,693,761, 5,693,762, and 6180370, European Patent Nos. 451216 and 682040, and U.S. Pat. No. 2,828,340) and such techniques can be used for producing the humanized antibody of the present invention.

[0637] The humanized chimeric antibody can be produced by, for example, replacing the constant region of an antibody having the above-mentioned structure of H chain variable region and/or structure of L chain variable region by the constant region of a human antibody. As the constant region of the human antibody, known region can be employed. Hereinafter, one example of the method of producing the humanized chimeric antibody is described.

[0638] Firstly, mRNA is extracted from the hybridoma producing a mouse antibody to certain antigens (for example, antigens expressing certain cancers, which have been determined this time, HER1, HER2, CD46, ITGA3, ICAM1, ALCAM, CD147, or the like), and cDNA is synthesized according to the usual procedure. The synthesized cDNA is inserted into a vector so as to construct a cDNA library. From this cDNA library, an H chain gene fragment and an L chain gene fragment are used as a probe, a vector containing an H chain gene and an L chain gene is selected. By sequencing the insertion sequence of the selected vector, the sequences of the gene in the H chain variable region and the L chain variable region can be determined. Based on the thus obtained sequence data, DNA encoding H chain variable region is produced by a chemical synthesis, biochemical cleavage/recombination and the like. DNA encoding the obtained H chain variable region is ligated with DNA encoding a human H chain constant region so as to incorporate it into an expression vector. Thereby, H chain expression vector is produced. As the expression vector, for example, an SV40 virus based vector, an EB virus based vector, and a BPV (papilloma virus) based vector can be used but not limited to these vectors alone. On the other hand, by the similar method, an L chain expression vector is produced. With such H chain expression vector and L chain expression vector, host cells are co-transformed. As the host cell, CHO cell (Chinese hamster ovary cell) (A. Wright & S. L. Morrison, J. Immunol. 160, 3393-3402 (1998)), SP2/0 cell (myeloma) (K. Motmans et al., Eur. J. Cancer Prev. 5, 512-519 (1996), R. P. Junghans et al., Cancer Res. 50, 1495-1502 (1990)), and the like can be suitably used. Furthermore, for transformation, a Lipofectin method (R. W. Malone et al., Proc. Natl. Acad. Sci. USA 86, 6077 (1989), P. L. Felgner et al., Proc. Natl. Acad. Sci. USA 84, 7413 (1987), an electroporation method, a calcium phosphate method (F. L. Graham & A. J. van der Eb, Virology 52, 456-467 (1973)), a DEAE-Dextran method, and the like, are suitably used.

[0639] After the transformant is cultured, a humanized chimeric antibody is separated from the cells of transformant or the culture solution. For separation and purification, methods such as centrifugation, ammonium sulfate fractionation, salting out, ultrafiltration, affinity chromatography, ion-exchange chromatography, and gel filtration chromatography can be appropriately combined and used.

[0640] On the other hand, the humanized CDR-grafted antibody can be produced by, for example, the following method. Firstly, by the method described in the production method of chimeric antibody, the amino acid sequences of the H chain variable region and L chain variable region of the antibody to the certain antigen and the base sequences encoding the amino acid sequences are determined. In addition, the amino acid sequence and the base sequence of each CDR region are determined.

[0641] As the base sequence of the specific CDRs, any of the following combinations are used. Note here that they are shown by SEQ ID NO showing the base sequence of the heavy chain variable region CDR1, SEQ ID NO showing the base sequence of the heavy chain variable region CDR2, SEQ ID NO showing the base sequence of the heavy chain variable region CDR3, SEQ ID NO showing the base sequence of the

light chain variable region CDR1, SEQ ID NO showing the base sequence of the light chain variable region CDR2, and SEQ ID NO showing the base sequence of the light chain variable region CDR3, in this order.

(1) SEQ ID NO 186, SEQ ID NO 187, SEQ ID NO 188, SEQ ID NO 190, SEQ ID NO 191, SEQ ID NO 192

(2) SEQ ID NO 194, SEQ ID NO 195, SEQ ID NO 196, SEQ ID NO 198, SEQ ID NO 199, SEQ ID NO 200

(3) SEQ ID NO: 202, SEQ ID NO: 203, SEQ ID NO: 204, SEQ ID NO: 206, SEQ ID NO: 207, SEQ ID NO: 208

(4) SEQ ID NO: 210, SEQ ID NO: 211, SEQ ID NO: 212, SEQ ID NO: 214, SEQ ID NO: 215, SEQ ID NO: 126

(5) SEQ ID NO: 218, SEQ ID NO: 219, SEQ ID NO: 220, SEQ ID NO: 222, SEQ ID NO: 223, SEQ ID NO: 224

(6) SEQ ID NO: 226, SEQ ID NO: 227, SEQ ID NO: 228, SEQ ID NO: 230, SEQ ID NO: 231, SEQ ID NO: 232

(7) SEQ ID NO: 234, SEQ ID NO: 235, SEQ ID NO: 236, SEQ ID NO: 238, SEQ ID NO: 239, SEQ ID NO: 240

(8) SEQ ID NO: 242, SEQ ID NO: 243, SEQ ID NO: 244, SEQ ID NO: 246, SEQ ID NO: 247, SEQ ID NO: 248

(9) SEQ ID NO: 250, SEQ ID NO: 251, SEQ ID NO: 252, SEQ ID NO: 254, SEQ ID NO: 255, SEQ ID NO: 256

(10) SEQ ID NO: 258, SEQ ID NO: 259, SEQ ID NO: 260, SEQ ID NO: 262, SEQ ID NO: 263, SEQ ID NO: 264

(11) SEQ ID NO: 266, SEQ ID NO: 267, SEQ ID NO: 268, SEQ ID NO: 270, SEQ ID NO: 271, SEQ ID NO: 272

(12) SEQ ID NO: 274, SEQ ID NO: 275, SEQ ID NO: 276, SEQ ID NO: 278, SEQ ID NO: 279, SEQ ID NO: 280

(13) SEQ ID NO: 282, SEQ ID NO: 283, SEQ ID NO: 284, SEQ ID NO: 286, SEQ ID NO: 287, SEQ ID NO: 288

(14) SEQ ID NO: 290, SEQ ID NO: 291, SEQ ID NO: 292, SEQ ID NO: 294, SEQ ID NO: 295, SEQ ID NO: 296

(15) SEQ ID NO: 298, SEQ ID NO: 299, SEQ ID NO: 300, SEQ ID NO: 302, SEQ ID NO: 303, SEQ ID NO: 304

(16) SEQ ID NO: 306, SEQ ID NO: 307, SEQ ID NO: 308, SEQ ID NO: 310, SEQ ID NO: 311, SEQ ID NO: 312

(17) SEQ ID NO: 314, SEQ ID NO: 315, SEQ ID NO: 316, SEQ ID NO: 318, SEQ ID NO: 319, SEQ ID NO: 320

(18) SEQ ID NO: 322, SEQ ID NO: 323, SEQ ID NO: 324, SEQ ID NO: 326, SEQ ID NO: 327, SEQ ID NO: 328

(19) SEQ ID NO: 330, SEQ ID NO: 331, SEQ ID NO: 332, SEQ ID NO: 334, SEQ ID NO: 335, SEQ ID NO: 336

(20) SEQ ID NO: 338, SEQ ID NO: 339, SEQ ID NO: 340, SEQ ID NO: 342, SEQ ID NO: 343, SEQ ID NO: 344

(21) SEQ ID NO: 346, SEQ ID NO: 347, SEQ ID NO: 348, SEQ ID NO: 350, SEQ ID NO: 351, SEQ ID NO: 352

(22) SEQ ID NO: 354, SEQ ID NO: 355, SEQ ID NO: 356, SEQ ID NO: 358, SEQ ID NO: 359, SEQ ID NO: 360

(23) SEQ ID NO: 362, SEQ ID NO: 363, SEQ ID NO: 364, SEQ ID NO: 366, SEQ ID NO: 367, SEQ ID NO: 368

[0642] Note here that these combinations correspond to the combination in CDR1 to CDR3 in 048-006 antibody, 057-091 antibody, and 059-152 antibody (which are antibodies to HER1), 015-126 antibody (which is antibody to HER2), 035-224 antibody, 045-011 antibody, 051-144 antibody, 052-053 antibody, 052-073 antibody, 053-049 antibody, and 3172-120 antibody (which are antibodies to CD46), 015-003 antibody (which is antibody to ITGA3), 052-033 antibody, 053-042 antibody, 053-051 antibody, 053-059 antibody, and 053-085 antibody (which are antibodies to ICAM1), 035-234 antibody, 040-107 antibody, 041-118 antibody, 066-174 antibody, and 083-040 antibody (which are antibodies to ALCAM), 059-053 antibody (which is antibody to CD147).

[0643] Next, FRs (framework regions) sandwiching the CDR region are selected. For selecting the FR, approximately three methods can be employed. The first method is a method using a human antibody frame whose three dimensional structure has been already identified, for example, NEWM, REI, and the like (Riechmann L. et al., Nature 332, 323-3Z7 (1988); Tempst, P R. et al., Protein Engineering 7, 1501-1507 (1994); Ellis J H. et al., J. Immunol. 155, 925-937 (1995)). The second method includes selecting a variable region of a human antibody having the highest homology to a variable region of the intended mouse antibody from database, and using the FR thereof (Queen C. et al., Proc Natl Acad Sci USA 86, 10029-10033 (1989); Rozak M J. et al., J Biol Chem 271, 22611-22618 (1996); Shearman C W. et al., J. Immunol. 147, 4366-4373 (1991)). The third method is a method of selecting amino acid most commonly used in the FR of the human antibody (Sato K. et al., Mol Immunol 31, 371-381 (1994); Kobinger F. et al., Protein Engineering 6, 971-980 (1993); Kettleborough C A. et al., Protein Engineering 4, 773-783 (1991)). The present invention can use any of these methods.

[0644] Even if the amino acid sequence is an amino acid sequence obtained by modifying the amino acid sequence of the selected human FR, it can be used as an amino acid sequence of the FR as long as a finally obtained humanized CDR-grafted antibody has a specific binding property to the corresponding antigens (HER1, HER2, CD46, ITGA3, ICAM1, ALCAM, CD147, and the like). In particular, a part of the amino acid of the selected human FR is changed to the amino acid of the FR of the antibody of the origin of CDR, the property of the antibody may be maintained. The number of the amino acid to be modified is preferably 30% or less relative to the entire FR, further preferably 20% or less relative to the entire FR, and yet further preferably 10% or less relative to the entire FR.

[0645] Next, by combining the FR selected by any of these methods and the above-mentioned CDR, DAN encoding the H chain variable region and L chain variable region is designed. Based on this design, DNA encoding H chain variable region and DNA encoding L chain variable region are produced by the chemical synthesis, biochemical cleavage/recombination, and the like, respectively. Then, DAN encoding the H chain variable region together with the DNA encoding H chain constant region of a human immunoglobulin is incorporated into an expression vector so as to construct an H chain expression vector. Similarly, DAN encoding the L chain variable region together with the DNA encoding L chain constant region of a human immunoglobulin is incorporated into an expression vector so as to construct an L chain expression vector. As the expression vector, for example, an SV40 virus based vector, an EB virus based vector, a BPV (papilloma virus) based vector, and the like can be used but not necessarily limited to these vectors.

[0646] With the H chain expression vector and L chain expression vector that are produced by the above-mentioned method, host cells are co-transformed. As the host cell, CHO cell (Chinese hamster ovary cell) (A. Wright & S. L. Morrison, J. Immunol. 160, 3393-3402 (1998)), SP2/0 cell (myeloma) (K. Motmans et al., Eur. J. Cancer Prev. 5, 512-519 (1996), R. P. Junghans et al., Cancer Res. 50, 1495-1502 (1990)), and the like can be suitably used. Furthermore, for transformation, a Lipofectin method (R. W. Malone et al., Proc. Natl. Acad. Sci. USA 86, 6077 (1989), P. L. Feigner et al., Proc. Natl. Acad. Sci. USA 84, 7413 (1987), an electroporation method, a calcium phosphate method (F. L. Graham & A. J. van der Eb, Virology 52, 456-467 (1973)), a DEAE-Dextran method, and the like, are suitably used.

[0647] After the transformant is cultured, a humanized CDR-grafted antibody is separated from the cells of transformant or the culture solution. For separation and purification, methods such as centrifugation, ammonium sulfate fractionation, salting out, ultrafiltration, affinity chromatography, ion-exchange chromatography, and gel filtration chromatography can be appropriately combined and used.

[0648] Based on the antibody of the present invention or based on the sequence information on the genes encoding the antibody of the present invention, an antibody fragment can be produced. The antibody fragment can include Fab, Fab', $F(ab')_2$, scFv, and dsFv antibodies.

[0649] Fab is a fragment that is obtained by digesting IgG with papain in the presence of cysteine; includes L chain and H chain variable regions as well as an H chain fragment consisting of a C_H1 domain and a part of hinge portion; and has a molecular weight of about 50000. In the present invention, it can be obtained by digesting the antibody with papain. Furthermore, DNA encoding a part of the H chain of the above-mentioned antibody and L chain is incorporated into an appropriate vector, and the vector is used for transforming so as to obtain a transformant. From this transformant, Fab can be prepared.

[0650] Fab' is a fragment having a molecular weight of about 50000, which can be obtained by cleaving the disulfide bond between H chains of $F(ab')_2$ mentioned below. In the present invention, it can be obtained by digesting the above-mentioned antibody with pepsin and cleaving the disulfide bond by the use of a reducing agent. Furthermore, similar to Fab, it can also be prepared by gene engineering with the use of DNA encoding Fab'.

[0651] $F(ab')_2$ is a fragment that is obtained by digesting IgG with pepsin; a fragment (Fab') is linked by disulfide bond including L chain and H chain variable regions as well as an H chain fragment consisting of a C_H1 domain and a part of hinge portion; and has a molecular weight of about 100000. In the present invention, it can be obtained by digesting the antibody with pepsin. Furthermore, similar to Fab, it can also be prepared by gene engineering with the use of DNA encoding $F(ab')_2$.

[0652] scFv is an antibody fragment obtained by linking Fv including an H chain variable region and an L chain variable region to C terminal of one of the chains and N terminal of the other of the chains by using an appropriate peptide linker so as to produce a single chain antibody fragment. As the peptide linker, for example, highly flexible $(GGGGS)_3$ can be used. For example, DNA encoding an scFv antibody is constructed by using DNA encoding H chain variable region and L chain variable region of the above-mentioned antibody and DNA encoding the peptide linker is constructed. This is incorporated into an appropriate vector and this vector is used to obtain a transformant. From this transformant, scFv can be prepared.

[0653] dsFv is an Fv fragment obtained by introducing a Cys residue into an appropriate positions of the H chain variable region and L chain variable region and stabilizing the H chain variable region and chain variable region by disulfide bond. The position in which the Cys residue is introduced in each chain can be determined based on the three dimensional structure anticipated by molecule modeling. In the present invention, for example, the three dimensional structure is anticipated from the amino acid sequence of the H chain variable region and the L chain variable region of the above-mentioned antibody. DNA encoding the H chain variable region and L chain variable region into which difference based on such anticipation is constructed and the constructed DNA is incorporated into the appropriate vector. The vector is used to obtain a transformant. From this transformant, dsFv can be prepared.

[0654] Note here that an antibody fragment can be multimerized by linking an scFv antibody and a dcFv antibody and the like with the use of an appropriate linker, or by allowing streptavidin to be fused.

[0655] By fusing or linking a low molecule compound, protein, a label material, and the like to the antibody of the present invention (including an antibody fragment), a fused antibody or labeled antibody can be formed. An example of the label material may include radioactive material such as ^{125}I, peroxidase, β-D-galactosidase, micro peroxidase, horseradish peroxidase (HRP), fluorescein isothiocyanate (FITC), rhodamine isothiocyanate (RITC), alkaline phosphatase, biotin, and the like.

[0656] The antibody of the present invention (including an antibody fragment) specifically binds to a cancer cell that specifically expresses the antigen by the specific binding property to the corresponding antigen. The use of this property makes it possible to label and detect a cancer cell (or cancer tissue). By gene recombination technology, VH and VL having such a specific binding capacity can be fused to a constant region (Fc region) of IgG so as to transform into an IgG type antibody. The thus obtained IgG type antibody is expected to exhibit a cytotoxic effect via Fc receptor on NK cells. The IgG constant region has subclass. As to the binding of Fc receptor of each IgG subclass of human, IgG1 and IgG3 have the strongest binding, IgG4 has moderate binding and IgG2 has weak binding. In transforming into IgG type antibodies, it is preferable to select a constant region in consideration of this point. Note here that the present inventors have proposed an assay of cytotoxic effect via the secondary antibody instead of IgG type antibody in the previous applications (Japanese Patent Unexamined Publication No. 2005-185281 and PCT/JP2006/303195).

[0657] Actually, as shown in the below-mentioned Examples, since 015-003 antibody as anti-ITGA3 antibody, 048-006 antibody as anti-HER1 antibody, and 015-126 antibody as anti-HER2 antibody are recognized to have an ADCC activity, they themselves can be used for damaging (killing) cancer cells. Herein, when the antibody of the present invention that has transformed into human or human IgG antibody is used, it is less attacked and excluded by the immune system, thus enabling the expected effect to be well exhibited and serious side effects to be avoided.

[0658] Furthermore, the antibody of the present invention can be used as a medium (carrier) for delivering a drug, and

the like, to a specific cancer. That is to say, an anticipated application of use of the antibody of the present invention includes DDS (Drug delivery system) targeting a specific cancer cell.

[0659] Note here that each application of the antibody of the present invention is described in detail below.

(Diagnosis Application)

[0660] Another aspect of the present invention relates to a use as a diagnosis marker of based on the findings of the expression (distribution) of CD46 antigen, ITGA3, ALCAM and CD147 antigen. Specifically, one embodiment of this aspect provides a testing method of gallbladder and liver cancer or pancreas cancer based on the findings that a CD46 antigen is expressed in the gallbladder and liver cancer and the pancreas cancer. The method includes the following steps.

[0661] Step (1): preparing subject cells or tissues separated from a living body.

[0662] Step (2): detecting a CD46 antigen in the subject cells or tissues.

[0663] Information obtained by the testing method of the present invention is useful for diagnosis of gallbladder and liver cancer or pancreas cancer. For example, information obtained by subjecting the above-mentioned method to patients with gallbladder and liver cancer can be used for evaluating or grasping the pathologic condition of patients and for evaluating the therapeutic effect. For example, when the present invention is carried out concurrently with the treatment of gallbladder and liver cancer, based on the resultant information, the therapeutic effect can be evaluated. Specifically, when the method of the present invention is carried out after administering drugs, the change in the expression amount of CD46 antigen in the liver cells is examined and the therapeutic effect can be determined from the increase and decrease of the expression amount. Thus, the method of the present invention may be used for monitoring the therapeutic effect.

[0664] On the other hand, information obtained when the subjects are persons other than the patient, that is, persons that have not recognized to have gallbladder and liver cancer can be used for determination of the presence or absence of contraction of gallbladder and liver cancer, evaluation of contraction risk, and the like. Since the method of the present invention permits diagnosis of liver cancer based on the amount of expression amount of genes, i.e., an objective indicator, its value is extremely high.

[0665] Hereinafter, the steps constituting the present invention are respectively described in detail.

1. Step (1)

[0666] In the step (1), cells or tissues separated from a subject (a subject person, a living body) are prepared. The subjects herein may include not only patients (gallbladder and liver cancer patients or pancreas cancer patients) but also healthy persons (including persons having a risk of contracting gallbladder and liver cancer or pancreas cancer). For example, a part of tissues collected from a subject by biopsy can be used as subject cells or tissues in the method of the present invention.

[0667] The "subject cells or tissues" in the present invention are cells or tissues that are samples (subjects) in the detection in the method of the present invention. The subject cells or tissues are separated from a living body. That is to say, the present invention is applied to the subject cells or tissues in the state in which it is separated from the living body. The term "separated from a living body" means a state in which a part of the living tissue in which subject cells or tissues exist is extracted, thereby the subject cells or tissues are completed separated from the origin living body. In the step (2), when an immunological detection method is employed, the subject cells are generally prepared in a state in which they are present in a living body, that is, in a state in which they are linked to the surrounding cells (as tissue), and used for the method of the present invention. Note here that the subject cells may be used for the method of the present invention after they are separated (isolated) from the surrounding cells.

2. Step (2)

[0668] In the step (2), a CD46 antigen is detected in the prepared subject cells or tissues as subjects. The term "CD46 antigen is detected" means examining whether or not the CD46 antigen is expressed (presence or absence of expression), or figuring out the expression amount of the CD46 antigen as an absolute value or a relative value. The reference of the relative amount herein can be, for example, an amount of CD46 antigen of the reference samples prepared according to the grade of malignancy. In general, the presence of expression of CD46 antigen and the amount if expressed are examined. In detecting the CD46 antigen, it is not essential to determine the amount of CD46 antigens strictly.

[0669] In one embodiment of the present invention, a detection method targeting mRNA that is a transcriptional product of the CD46 antigen is carried out. For the detection (measurement) of mRNA, routine procedures such as an RT-PCR method and various hybridization methods using specific probes (for example, northern hybridization, in situ hybridization) can be employed. In another embodiment of the present invention, a detection method targeting the expression product of the CD46 antigen (protein) is carried out.

[0670] It is preferable that CD46 antigen is detected by immunologic procedures (for example, immunohistochemical staining technique). In the immunologic procedure, anti-CD46 antigen antibody is used, CD46 antigen protein is detected by using the bonding property (binding amount) of the antibodies as an indicator. The immunological detection method permits rapid and sensitive detection. Also, the operation is simple. An example of the detection methods may include ELISA method, radioimmunoassay, FCM, an immunoprecipitation method, immunoblotting, and the like.

[0671] The immunohistochemical staining technique permits rapid and sensitive detection of CD46 antigens. Also, the operation is simple. Therefore, burdens to a subject person (patient) accompanying the detection of CD46 antigen is reduced. In the immunohistochemical staining technique, in general, firstly, a step of bringing the subject cells into contact with the anti-CD46 antibody is carried out. Then, the binding amount of the anti-CD46 antibody is examined. Specifically, according to the above-mentioned immunohistochemical staining technique, the method of the present invention can be carried out.

[0672] The kind or origin of the anti-CD46 antibody to be used in immunostaining procedure is not particularly limited as long as it has a specific binding property to the CD46 antigen. The anti-CD46 antibody may be any of a polyclonal antibody, an oligoclonal antibody (a mixture of several kinds to several tens of antibodies) and a monoclonal antibody. As the polyclonal antibody or the oligoclonal antibody, affinity

purification antibody by antigen can be used besides an IgG fraction derived from anti-serum obtained by immunizing an animal so as to obtain. The anti-CD46 antibody may be antibody fragments such as Fab, Fab', $F(ab')_2$, scFv, and dsFv antibodies.

[0673] The anti-CD46 antibody can be prepared by using an immunologic procedure, phage display technique, ribosome display method, and the like.

[0674] The preparation of a polyclonal antibody by the immunologic procedure can be prepared by the following procedures. An antigen (CD46 or a part thereof) is prepared. An animal such as a rabbit is immunized with this antigen. As this antigen, not only human CD46 but also non-human CD46 such as mouse CD46 can be used. Such CD46 can be obtained by purifying a living body sample. Furthermore, recombinant CD46 may be used. The recombinant human CD46 can be prepared by, for example, introducing a gene encoding CD46 (which may include a part of gene) in an appropriate host by using a vector and expressing the gene within the obtained recombinant cells.

[0675] In order to strengthen the immunity inducing effect, an antigen to which a carrier protein is attached may be used. As the carrier protein, KLH (Keyhole Limpet Hemocyanin), BSA (Bovine Serum Albumin), OVA (Ovalbumin), and the like are used. For binding of the carrier protein, a carbodiimide method, a glutaraldehyde method, a diazo condensation method, an MBS (maleimidobenzoyl oxy succinimide) method, and the like, can be used. On the other hand, an antigen expressing CD46 (or a part thereof) as fusion protein with GST, β galactosidase, maltose bonded protein, or histidine (His) tag, and the like, can be used. Such a fusion protein can be purified by a general method in a simple manner.

[0676] If necessary, immunization is repeated. When the antibody titer is sufficiently increased, blood is collected and subjected to centrifugation so as to obtain serum. The obtained anti-serum is subjected to affinity purification. Thus, a polyclonal antibody is obtained.

[0677] On the other hand, a monoclonal antibody can be prepared by the following procedures. Firstly, an immunization operation is carried out by the similar method to the above-mentioned procedures. If necessary, immunization is repeated. When the antibody titer is sufficiently increased, antibody-producing cells are extracted from an immunized animal. Next, the obtained antibody-producing cells and myeloma cells are fused to each other so as to obtain a hybridoma. Subsequently, this hybridoma is made to be monoclonal. Then, a clone producing antibody showing high specificity to the target protein is selected. A culture solution of the selected clone is purified, thereby the target antibody can be obtained. On the other hand, hybridoma is proliferated into a predetermined number of more, then, transplanted in the abdominal cavity of an animal (for example, mouse), proliferated in the abdominal dropsy. By purifying the abdominal dropsy, the target antibody can be obtained. For purification of the above-mentioned culture solution or purification of the abdominal dropsy, affinity chromatography using protein G, protein A, and the like, is preferably used. Furthermore, affinity chromatography in which an antigen is made into a solid phase can be used. Furthermore, methods such as ion-exchange chromatography, gel filtration chromatography, ammonium sulfate fractionation, and centrifugation can be used. These methods are used singly or in arbitrary combination thereof.

[0678] On the conditions that the specific binding property to CD46 antigen is maintained, the obtained antibody may be subjected to various modifications. In the present invention, such a modified antibody may be used.

[0679] When a labeled antibody is used as an anti-CD46 antibody, the amount of bound antibody can be directly detected by using the labeled amount as an indicator. Therefore, the method is more simplified. On the contrary, it is necessary to prepare an anti-CD46 antibody to which a label material is bound and furthermore, and furthermore, the detection sensitivity is generally reduced. Therefore, it is preferable that indirect methods such as a method using a secondary antibody to which a label material is linked, a method using a polymer to which a secondary antibody and a label material are linked are used. The secondary antibody herein is an antibody having a specific binding property to the anti-CD46 antibody. For example, when an anti-CD46 antibody is prepared as a rabbit antibody, an anti-rabbit IgG antibody can be used. Label secondary antibodies that can be used for various species such as rabbit, goat, and mouse are commercially available (for example, Funakoshi Corporation, COSMO BIO Co., Ltd., etc.). Proper antibodies can be appropriately selected depending upon the anti-CD46 antibody used in the present invention.

[0680] For the label material, the label material arbitrarily selected from the group consisting of peroxidase, β-D-galactosidase, micro peroxidase, horseradish peroxidase (HRP), fluorescein isothiocyanate (FITC), rhodamine isothiocyanate (RITC), alkaline phosphatase, biotin, and radioactive material is preferably used. In particular, a method of using biotin as the label material and reacting avidin peroxidase permits highly sensitive detection.

[0681] The above-mentioned antibody of the present invention may be used as the anti-CD46 antibody. Specifically, for example, antibodies (035-224 antibody, 045-011 antibody, 051-144 antibody, 052-053 antibody, 052-073 antibody, 053-049 antibody, or 3172-120 antibody), which the present inventors have succeeded in obtaining, can be used.

[0682] Another embodiment of this aspect provides a testing method of gallbladder and liver cancer or pancreas cancer based on the findings that ITGA3 is expressed in gallbladder and liver cancer and pancreas cancer. The method includes the following steps.

[0683] Step (1): preparing subject cells or tissues separated from a living body

[0684] Step (2): detecting ITGA3 in the subject cells or tissues

[0685] Information obtained by the testing method of the present invention is useful for diagnosis of gallbladder and liver cancer or diagnosis of pancreas cancer. Since the using method and details of each step are the same as in the case of the CD46 antigen, the description thereof is not mentioned here.

[0686] A further embodiment of this aspect provides an obtaining method of information for diagnosis of kidney cancer, hepatic cell carcinoma or gallbladder and liver cancer based on the findings that ALCAM is expressed in kidney cancer, hepatic cell carcinoma and gallbladder and liver cancer. The method includes the following steps.

[0687] Step (1): preparing subject cells or tissues separated from a living body

[0688] Step (2): detecting ALCAM in the subject cells or tissues

[0689] Information obtained by the testing method of the present invention is useful for diagnosis of kidney cancer, diagnosis of hepatic cell carcinoma, or diagnosis of gallbladder and liver cancer. Since the using method and details of each step are the same as in the case of the CD46 antigen, the description thereof is not mentioned here.

[0690] A yet further embodiment of this aspect provides a testing method of kidney cancer based on the findings that CD147 antigen is expressed in kidney cancer. The method includes the following steps.

[0691] Step (1): preparing subject cells or tissues separated from a living body

[0692] Step (2): detecting a CD147 antigen in the subject cells or tissues

[0693] Information obtained by the testing method of the present invention is useful for diagnosis of kidney cancer. Since the using method and details of each step are the same as in the case of the CD46 antigen, the description thereof is not mentioned here.

(Treatment Application)

[0694] As mentioned in the below-mentioned Examples, the present inventor have succeeded in obtaining antibodies exhibiting Antibody-Dependent Cell-mediated Cytotoxicity (hereinafter, abbreviated as "ADCC") activity to certain antibodies. Furthermore, the present inventors have transformed these antibodies into IgG type and investigated the probability of application to an antibody therapeutic agent. Any antibodies show excellent anti-tumor effect. Based on these findings, the further aspect of the present invention relates to an application of the antibodies successfully obtained by the present inventors in treatment of cancer.

[0695] This aspect firstly provides a drug (cancer therapeutic agent) capable of affecting and damaging in a cancer cell-specific manner using by using ITGA3, HER1, HER2, ALCAM, EpCAM or HGFR as a target, and the treatment method using the same. One embodiment of the drug of the present invention contains anti-ITGA3 antibody as an active ingredient. One preferable embodiment of the drug of the present invention contains an anti-ITGA3 antibody having an ADCC activity as an active ingredient. The drugs of this embodiment can obtain the therapeutic effect by the cytotoxicity using the ADCC activity. As anti-ITGA3 antibody having the ADCC activity, 015-003 antibody (the specific binding property to ITGA3 and it may be partially modified as long as the ADCC activity is maintained) shown in the below-mentioned Examples or different types of antibodies constructed based on the 015-003 antibody (for example, IgG type antibody) can be used. This antibody has both the specific binding property to ITGA3 and the ADCC activity. Therefore, it specifically binds to the cancer cells expressing ITGA3 and then expresses the ADCC activity. Thus, it can damage a cancer cell. The target cancer cell of the drug of this embodiment is not particularly limited, but can target, for example, gallbladder and liver cancer cells and pancreas cancer cells.

[0696] In another embodiment of the present invention, an anti-HER1 antibody is contained as an active ingredient. In the drug of one preferable embodiment of the present invention, anti-HER1 antibody having an ADCC activity is contained as an active ingredient. In the drug of this embodiment, the therapeutic effect can be obtained by the cytotoxicity using the ADCC activity. In the drug of the further preferable embodiment, in addition to the cytotoxicity using the ADCC activity, since inhibition of binding of EGF as a ligand to HER1 and/or inhibition of phosphorylation signal by HER1 are provided, higher therapeutic effect can be obtained. As anti-HER1 antibody having such an ADCC activity, 048-006 antibody, 059-152 antibody, 055-147 antibody or 059-173 antibody shown in the below-mentioned Example (which may be partially modified as long as the specific binding property to HER1 and the ADCC activity are maintained) or different types of antibodies constructed based on them (for example, IgG type) can be used. These antibodies have the specific binding property to HER1, inhibition of binding of EGF to HER1, inhibition of phosphorylation signal of HER1 and ADCC activity. Therefore, they can specifically bind to a cancer cell expressing HER1 and inhibit HER1 activity by inhibition of binding of EGF to HER1 and/or inhibition of phosphorylation signal of HER1, thereafter, exhibit the ADCC activity so as to damage a cancer cell. Furthermore, it is confirmed that the antibody exhibits suppression effect to cancer cells and an anti-tumor effect in animal model, so that the antibody is greatly expected to be used in antibody medicine. The target cancer cell by the drug of this embodiment is not particularly limited, but it can target, for example, cells of kidney cancer, hepatic cell carcinoma, gallbladder and liver cancer, lung squamous cell carcinoma, pulmonary adenocarcinoma, and pancreas cancer.

[0697] In a further embodiment of the present invention, an anti-HER2 antibody is contained as an active ingredient. In the drug of one preferable embodiment of the present invention, anti-HER2 antibody having an ADCC activity is contained as an active ingredient. In the drug of this embodiment, the therapeutic effect can be obtained by the cytotoxicity using the ADCC activity. As anti-HER2 antibody having such an ADCC activity, 015-126 antibody shown in the below-mentioned Example (which may be partially modified as long as the specific binding property to HER2 and the ADCC activity are maintained) or different types of antibodies constructed based on them (for example, IgG type) can be used. This antibody has the specific binding property to HER2 and ADCC activity. Therefore, they can specifically bind to a cancer cell expressing HER2 then exhibits the ADCC activity so as to damage a cancer cell. Furthermore, it is confirmed that the antibody exhibits suppression effect to cancer cells, so that the antibody is greatly expected to be used in antibody medicine. The target cancer cell by the drug of this embodiment is not particularly limited, but it can target, for example, cells of kidney cancer, liver cancer, and pulmonary adenocarcinoma.

[0698] In a further embodiment of the present invention, an anti-ALCAM antibody is contained as an active ingredient. In the drug of one preferable embodiment of the present invention, anti-ALCAM antibody having an ADCC activity is contained as an active ingredient. As anti-ALCAM antibody having such an ADCC activity, 041-118 antibody or 066-174 antibody shown in the below-mentioned Example (which may be partially modified as long as the specific binding property to ALCAM and the ADCC activity are maintained) or different types of antibodies constructed based on them (for example, IgG type) can be used. This antibody has the specific binding property to ALCAM and ADCC activity. Therefore, they can specifically bind to a cancer cell expressing ALCAM then exhibits the ADCC activity so as to damage a cancer cell. The target cancer cell by the drug of this

embodiment is not particularly limited, but it can target, for example, cells of pulmonary adenocarcinoma, ovarian cancer, and large bowel cancer.

[0699] In a yet further embodiment of the present invention, an anti-EpCAM antibody is contained as an active ingredient. In the drug of one preferable embodiment of the present invention, anti-EpCAM antibody having an ADCC activity is contained as an active ingredient. As anti-EpCAM antibody having such an ADCC activity, 067-153 antibody shown in the below-mentioned Example (which may be partially modified as long as the specific binding property to EpCAM and the ADCC activity are maintained) or different types of antibodies constructed based on them (for example, IgG type) can be used. This antibody has the specific binding property to EpCAM and ADCC activity. Therefore, they can specifically bind to a cancer cell expressing EpCAM then exhibits the ADCC activity so as to damage a cancer cell. The target cancer cell by the drug of this embodiment is not particularly limited, but it can target, for example, cells of gastric solid-type adenocarcinoma, colon adenocarcinoma, and pulmonary adenocarcinoma cell.

[0700] In a yet further embodiment of the present invention, an anti-CD147 antibody is contained as an active ingredient. In the drug of one preferable embodiment of the present invention, anti-CD147 antibody having an ADCC activity is contained as an active ingredient. As anti-CD147 antibody having such an ADCC activity, 059-053 antibody shown in the below-mentioned Example (which may be partially modified as long as the specific binding property to CD147 and the ADCC activity are maintained) or different types of antibodies constructed based on them (for example, IgG type) can be used. This antibody has the specific binding property to CD147 and ADCC activity. Therefore, they can specifically bind to a cancer cell expressing CD147 then exhibits the ADCC activity so as to damage a cancer cell. The target cancer cell by the drug of this embodiment is not particularly limited, but it can target, for example, kidney cancer cells.

[0701] In a yet further embodiment of the present invention, an anti-CD44 antibody is contained as an active ingredient. In the drug of one preferable embodiment of the present invention, anti-CD44 antibody having an ADCC activity is contained as an active ingredient. As anti-CD44 antibody having such an ADCC activity, 064-003 antibody shown in the below-mentioned Example (which may be partially modified as long as the specific binding property to CD44 and the ADCC activity are maintained) or different types of antibodies constructed based on them (for example, IgG type) can be used. This antibody has the specific binding property to CD44 and ADCC activity. Therefore, they can specifically bind to a cancer cell expressing CD44 then exhibits the ADCC activity so as to damage a cancer cell. The target cancer cell by the drug of this embodiment is not particularly limited, but it can target, for example, pulmonary adenocarcinoma cells.

[0702] In a yet further embodiment of the present invention, an anti-HGFR antibody is contained as an active ingredient. In the drug of one preferable embodiment of the present invention, anti-HGFR antibody having an ADCC activity is contained as an active ingredient. As anti-HGFR antibody having such an ADCC activity, 067-133 antibody shown in the below-mentioned Example (which may be partially modified as long as the specific binding property to HGFR and the ADCC activity are maintained) or different types of antibodies constructed based on them (for example, IgG type) can be used. This antibody has the specific binding property to HGFR and ADCC activity. Therefore, they can specifically bind to a cancer cell expressing HGFR then exhibits the ADCC activity so as to damage a cancer cell. The target cancer cell by the drug of this embodiment is not particularly limited, but it can target, for example, pulmonary adenocarcinoma cells.

[0703] The present invention furthermore provides a method of reducing the grade of malignancy of a target cell or promoting the normalization by damaging or suppressing the expression of HER1, HER2, CD46, ITGA3, ICAM1, ALCAM, or CD147 in the target cell.

[0704] Herein, the present inventors have investigated and recognized specific expression of CD46 in gallbladder and liver cancer and pancreas cancer, which had not been particularly reported about the relationship with respect to CD46 (see the below-mentioned Example). Similarly, the relationship between gallbladder and liver cancer and pancreas cancer and the expression of ITGA3; the relationship between kidney cancer, hepatic cell carcinoma and gallbladder and liver cancer and ALCAM; as well as the relationship between kidney cancer and CD147 have been clarified (see the below-mentioned Example). Based on the findings, a novel and effective target cell of CD46 is a gallbladder and liver cancer cell and a pancreas cancer cell; a novel and effective target cell of ITGA3 is a gallbladder and liver cancer cell and a pancreas cancer cell; and a novel and effective target cell of CD147 is a kidney cancer cell.

[0705] Note here that the inhibition or suppression of each antigen can be carried out by using an antisense method or RNA interference, or by using ribozyme.

[0706] In the case where expression inhibition by the antisense method is carried out, for example, when transcription is carried out in the target cell, an antisense-construct for generating RNA that is complementary to a portion specific to mRNA encoding this protein is used. Such an antisense-construct is introduced into the target cells, for example, in a form of an expression plasmid. On the other hand, when it is introduced in to the target cells as the antisense-construct, it is possible to employ an oligonucleotide-probe that is hybridized with mRNA or genome DNA sequence encoding this protein and inhibits the expression thereof. As such an oligonucleotide-probe, one having a low resistance to endogenous nuclease such as exonuclease and/or endonuclease is preferably used.

[0707] When DNA molecule is used as an antisense nucleic acid, it is preferable that oligodeoxyribonucleotide derived from a region (for example, a region from −10 to +10) including a translation initiation site of mRNA encoding this protein is used.

[0708] It is preferable that the complementation between the antisense nucleic acid and the target nucleic acid is strict. However, some mismatch may be accepted. The hybridization performance of the antisense nucleic acid with respect to the target nucleic acid is generally dependent upon both the degree of complementation of both nucleic acids and the length thereof. In general, as the antisense nucleic acid to be used is longer, even if the number of mismatch is increased, stable two heavy chains (or three heavy chains) can be formed between the antisense nucleic acid and the target nucleic acid. Persons skilled in the art can confirm the degree of permissible degree of the mismatch by using a standard technique.

[0709] The antisense nucleic acid may be DNA, RNA or a chimera mixture thereof, or derivative or modified type thereof. Furthermore, it may be single stranded or double

stranded. By modifying a base portion, a sugar portion or a skeleton portion of phosphoric acid, the stability and hybridization performance and the like of the antisense nucleic acid can be improved. Furthermore, to the antisense nucleic acid, materials for urging the cell membrane transportation (for example, see Letsinger et al., 1989, Proc. Natl. Acad. Sci. U.S.A. 86:6553-6556; Lemaitre et al., 1987, Proc. Natl. Acad. Sci. 84:648-652; PCT Publication No. WO88/09810, published Dec. 15, 1988) or materials capable of enhancing the affinity with respect to certain cells may be added.

[0710] The antisense nucleic acid can be synthesized by a conventional method, for example, by using commercially available automated DNA synthesizer (for example, Applied Biosystems, and the like). For producing the modulated product or derivative of nucleic acid, you can see, for example, Stein et al. (1988), Nucl. Acids Res. 16:3209, or Sarin et al., (1988), Proc. Natl. Acad. Sci. U.S.A. 85:7448-7451.

[0711] In order to enhance the effect of antisense nucleic acid in the target cells, a strong promoter such as pol II and pol III can be used. That is to say, if a construct including antisense nucleic acid disposed under control of such promoters is introduced into the target cells, it is possible to secure the transcription of sufficient amount of antisense nucleic acid by the effect of the promoter.

[0712] The antisense nucleic acid can be expressed by using any promoters (derivative promoters or constitutive promoters) known to function in the mammalian cells (preferably, human cells). For example, promoters such as a SV40 initial promoter region (Bernoist and Chambon, 1981, Nature 290:304-310), a promoter derived from the 3'-terminal region of Rous sarcoma virus (Yamamoto et al., 1980, Cell 22:787-797), a Herpetic Thymidine Kinase promoter (Wagner et al., 1981, Proc. Natl. Acad. Sci. U.S.A. 78: 1441-1445), and the like, can be used.

[0713] In one embodiment of the present invention, the expression of the protein is inhibited by RNA interference (RNAi). RNAi is a process of a sequence specific post-transcriptional gene suppression that can be caused in the eukaryote. In the RNA interference, double stranded RNA (dsRNA) having a sequence corresponding to the sequence of the target mRNA is used. It is known that mammalian cells have two routes (a sequence specific route and a sequence nonspecific route) affected by dsRNA. In the sequence specific route, relatively long dsRNA is divided into short interference RNAs (siRNAs). Each of the siRNAs has sense and antisense chains of about 21 nucleotides that form siRNA of about 19 nucleotides having protruding portions at the 3' terminal portion. On the other hand, it is thought that a sequence nonspecific route can be caused by arbitrary dsRNA regardless of the sequence as long as it has a predetermined length or longer. In this route, dsRNA, two enzymes, that is, PKR, which becomes an active from and stops whole synthesis of proteins by phosphorylating the translation initiation factor eIF2, and 2', 5' oligoadenylate synthetase, which is involved in the synthesis of an RNAase L activated molecule are activated. In the method of the present invention, in order to minimize the progress of this nonspecific route, it is preferable to use dsRNA including about 30 base pairs or less (see, for example, Hunter et al. (1975) J Biol Chem 250: 409-17; Manche et al. (1992) Mol Cell Biol 12: 5239-48; Minks et al. (1979) J Biol Chem 254: 10180-3; and Elbashir et al. (2001) Nature 411: 494-8).

[0714] Note here that it is confirmed that RNAi is an effective means for reducing the gene expression in various cells (for example, a HeLa cell, a NIH/3T3 cell, a COS cell, a 293 cell, and the like). Furthermore, in general, it can inhibit expression more effectively than by the antisense method.

[0715] The dsRNA used in RNAi can be prepared in vitro or in vivo by chemical synthesis or by using an appropriate expression vector. In the latter method, it is particularly effective to prepare a relatively long dsRNA. For designing dsRNA, in general, sequence peculiar to the target nucleic acid (continuous sequence) is used. Note here that a program and algorithm for selecting an appropriate target sequence have been developed.

[0716] In another embodiment of the present invention, the expression of ITGA3 is carried out by using ribozyme. By using ribozyme for cleave mRNA at the site specific recognition sequence, it is possible to destroy mRNA encoding the protein. However, preferably, a hammerhead ribozyme is used. A method for constructing the hammerhead ribozyme can be seen in, for example, Haseloff and Gerlach, 1988, Nature, 334: 585-591.

[0717] Similar to the antisense method, for example, for the purpose of the stability and target performance, by using a modified oligonucleotide, ribozyme may be constructed. In order to produce an effective amount of ribozyme in the target cells, for example, under the control of a strong promoter (for example, pol II and pol III), it is preferable that the nucleic acid construct in which DNA encoding ribozyme is disposed is used.

[0718] Drugs used for the treatment method (including a method of urging to reducing or normalizing the grade of malignancy of cancer cells, and the like) of the present invention can be formulated according to the conventional method. In formulation, other ingredients acceptable for formulation (for example, carrier, vehicle, disintegrating agents, buffer agent, emulsifying agent, suspending agent, soothing agent, stabilizer, preservative, preservative, physiological saline, and the like) can be contained. An example of the vehicle may include lactose, starch, sorbitol, D-mannitol, and sucrose. An example of the disintegrating agents may include starch, carboxymethyl cellulose, calcium carbonate, and the like. An example of the buffer agent may include phosphate, citrate, acetate, and the like. An example of the emulsifying agent may include gum Arabic, alginate sodium, tragacanth, and the like. An example of the suspending agent may include glyceryl monostearate, aluminum monostearate, methylcellulose, carboxymethyl cellulose, hydroxymethyl cellulose, sodium lauryl sulfate, and the like. An example of the soothing agent may include benzyl alcohol, chlorobutanol, sorbitol, and the like. An example of the stabilizer may include propylene glycol, diethylene sulfite, ascorbic acid, and the like. An example of the preservative may include phenol, benzalkonium chloride, benzyl alcohol, chlorobutanol, methylparaben, and the like. An example of the preservative may include benzalkonium chloride, parahydroxybenzoate, chlorobutanol, and the like.

[0719] The dosage form in the formulation is not particularly limited. An example of the dosage form may include tablet, powdered drug, fine subtilae, granule, capsules, syrup, injectable drug, external preparation, and suppository.

[0720] In the treatment using the drug of the present invention, the drug of the present invention is administered to a subject (patient) with a cancer cell or adult T cell leukemia. The drug of the present invention can be administered to a subject (patient) by oral administration or parenteral administration (intravenous, intra-arterial, subcutaneous, intramus-

cular, intraperitoneal injection, direct introduction to the target cell, and the like) depending upon the dosage form.

[0721] The dosage amount of the drug of the present invention will vary depending on the symptoms, age, sex, body weight, and the like, of the patient, but the person skilled in the art can set an appropriate dosage amount. For example, the dosage amount can be set so that the dosage amount of effective ingredient for adult (body weight: about 60 kg) per day is about 0.001 mg to about 100 mg. The administration schedule can include, for example, once to several times a day, once per two days, or once per three days. For setting the administration schedule, conditions of a patient, efficacy duration time of the drug, and the like, can be considered.

[0722] In another embodiment, the drug of the present invention uses anti-HER1 antibody, anti-HER2 antibody, anti-CD46 antibody, anti-ITGA3 antibody, anti-ICAM1 antibody, anti-ALCAM antibody, anti-CD147 antibody as a carrier for DDS. That is to say, this embodiment provides an immunocomplex obtained by combining a drug (cytotoxin and the like), radioactive isotope, or the like (these are also referred to as "active ingredient" together) to anti-HER1 antibody, and others. The immunocomplex containing a drug (cytotoxin) having a cell-killing activity or a cytotoxic activity is generally referred to as immunotoxin. An example of the cytotoxin may include Taxol, cytochalasin. B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicines, doxorubicin, daunorubicin, dihydroxy-anthracene-dione, mitoxantrone, methramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoid, procaine, tetracaine, lidocaine, propranolol, and puromycin as well as analogue or homologue thereof.

[0723] As the active ingredient contained in the immunocomplex of the present invention, protein or peptide having a desirable biological activity may be used. An example of the candidate for protein and the like that can be used for such a purpose may include abrin, ricin A, *Pseudomonas*-exotoxin, diphteria toxin, tumor necrosis factor, interferon-γ, interleukin I (IL-1), interleukin 2 (IL-2), interleukin 6 (IL-6), a granulocyte macrophage colony stimulating factor (GM-CSF), a granulocyte colony stimulating factor (G-CSF) lymphokine.

[0724] A technology for combining an active component to an antibody is well known and you can see in, for example, Monoclonal Antibodies And Cancer Therapy, Reisfeld et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985), Controlled Drug Delivery (2nd edition.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987), Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), Thorpe et al., "The Preparation And Cytotoxic Properties Of antibody-Toxin Conjugates", Immunol. Rev., 62:119-58 (1982).

(Kit Used in the Present Invention)

[0725] Each method of the present invention (a method for obtaining information for diagnosis, and the like) may be carried out by using a kit of reagent and the like. Another aspect of the present invention provides a kit used for such a purpose. For example, nucleic acid (probe and primer), reaction reagent, dilution, a reactor vessel, and the like, that are used for the method of the present invention can be contained in the kit. Note here that the kit of the present invention is generally includes instruction.

[0726] The user of a kit makes it possible to allow the method of the present invention to be carried out in a simple way and for a short time.

Example

1. Production of Vector for Producing ScFv Antibody Gene Library

[0727] 1-1 Production of Vector for Producing scFV Antibody Gene Library

[0728] As conceptually shown in FIG. **5**, pelB (signal sequence) of M13 phage, His6 tag sequence, cp3 protein of M13 phage (Δcp3 (198aa-406aa) N-terminal deleted capsid protein 3) sequence, protein A protein sequence were incorporated in an appropriate restriction enzyme site of a pTZ19R phagemid vector (Pharmacia) so as to from a vector pAAL-Fab (see Iba Y. et al., Gene 194: 35-46, 1997.). A vector pFCAH9-E8d for incorporation was produced from this pAALFab.

[0729] Genes of a heavy chain and a light chain are inserted into the predetermined position of this vector, thereby completing an actual antibody protein expression vector. The shape of the antibody expressed by the completed vector is a scFv and a light chain constant region CL gene is bonded to the aforementioned cp3 gene. As a result, expression protein has a shape of scFv-CL-cp3. Specifically, the below-mentioned operation is carried out.

Used primer:

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527 Reverse (SEQ ID NO: 377):
5'-CAGGAAACAGCTATGAC-3'

599 E8VHf-PstR: (SEQ ID NO: 378)
3'-CGGCTCCAAGTCGACGTCGTCA-5'

544 E8VHf-PstF: (SEQ ID NO: 379)
5'-CAGCTGCAGCAGTCTGGGGCAGAGCTTGTGAAGCCAGGGGCCTCAGT

CAAGTTGTCCTGCACAGCTTCTGGCTTCAACATTAA-3'

545 E8VHf-XbaR: (SEQ ID NO: 380)
3'-AGACCGAAGTTGTAATTTCTGTGGATATACGTGACCCACTTCGTCTC

CGGACTTTTCCCAGATCTCACCTAACCTTCCTAA-5'

546 E8VHf-XbaF: (SEQ ID NO: 381)
5'-AAGGGTCTAGAGTGGATTGGAAGGATTGATCCTGCGAGTGGTAATAC

TAAATATGACCCGAAGGACAAGGCCACTATAACAGCA-3'

547 E8VHf-EcoR (SEQ ID NO: 382)
3'-TTCCTGTTCCGGTGATATTGTCGTCTGTGTAGGAGGTTGTGTCGGAT

GGATGTCGACTTAAGGGAC-5'

548 E8VHf-EcoF (SEQ ID NO: 383)
5'-CAGCTGAATTCCCTGACATCTGAGGACACTGCCGTCTATTACTGTGC

TGGT-3'

549 E8VHf-BstR (SEQ ID NO: 384):
3'-CAGATAATGACACGACCAATACTAATGCCGTTGAAACTGATGACCCC

GGTTCCGTGGTGCCAGTGGCACAAGG-5'

590 His6-SmaR (SEQ ID NO: 385):
3'-GGTTCTCTAACAGTAGTGGTAGTAGTGGTAATTATTCTCGATAGGGC

CCTCGAA-5'

542 E8VLf-SacF (SEQ ID NO: 386):
5'-GACATCGAGCTCACCCAGTCTCCAGCCTCCCTTTCTGCGTCTGTGGG

AGAAACTGTCACCATCACATGT-3'
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-continued

539 E8VLf-KpnR (SEQ ID NO: 387):
3'-TGACAGTGGTAGTGTACAGCTCGTTCACCCTTATAAGTGTTAATAAA

TCGTACCATGGTCGTC-5'

542 E8VLf-KpnF (SEQ ID NO: 388):
5'-GCATGGTACCAGCAGAAACCAGGGAAATCTCCTCAGCTCCTGGTCTA

T-3'

543 E8VLf-BamR (SEQ ID NO: 389):
3'-GGAGTCGAGGACCAGATATTACGTTTTTGGAATCGTCTACCACACGG

TAGTTCCAAGTCACCGTCACCTAGGCCTTGTGTT-5'

562 E8VLf-XhoR (SEQ ID NO: 390):
3'-TCATGAGGCACCTGCAAGCCACCTCCGTGGTTCGAGCTCTAGTT

T-5'

563 E8VLf-XhoF (SEQ ID NO: 391):
5'-AGTACTCCGTGGACGTTCGGTGGAGGCACCAAGCTCGAGATCAA

A-3'

613 NheR (SEQ ID NO: 392):
3'-ATCGACAGCT-5'

600 E8VLKpnXhoR (SEQ ID NO: 393):
3'-AAGCCACCTCCATGGTTCGAGCTCTAGTTT-5'

LCP3ASC (SEQ ID NO: 394):
3'-TCGAAGTTGTCCTTACTCACAAGCCGCGCGGTCAGCTGAGGTAA-5'

hCH1Bst (SEQ ID NO: 395):
5'-ACCCTGGTCACCGTCTCCTCAGCCTCCACCAAGGGCCCATCGGTCTT

CCCCCTGG-3'

hCH1midAS (SEQ ID NO: 396):
3'-GGGAGTCGTCGCAGCACTGGCACGGGAGGTCGTCGAA-5'

hCH1midS (SEQ ID NO: 397):
5'-GGACTCTACTCCCTCAGCAGCGTCGTGACCGTGCCC-3'

hCH1H6 (SEQ ID NO: 398):
3'-GGGTCGTTGTGGTTCCACCTGTTCTTTCAACTCGGGTTTAGAACAGT

AGTGGTAGTAGTGGTA-5'

hCH1H6Sma (SEQ ID NO: 399):
3'-GGGTTTAGAACAGTAGTGGTAGTAGTGGTAATTATTCTCGATAGGGC

CCTCGAACG-5'

702 BstXhoF (SEQ ID NO: 400):
5'-GGCACCACGGTCACCGTCTCGAGCGCCTCCACC-3'

<Production of pFCAH3-E8T H Chain Part>

1) By using pAALFab as a template, PCR using 527-599 and PCR using 547-590 were carried out so as to produce a DNA fragment.

2) PCR using 544-545, 546-547, and 548-549 was carried out so as to produce a DNA fragment.

3) 1) and 2) were mixed and PCR by 527,590 was carried out, which was cloned to a HindIII-SmaI site of pAALFab.

<pFCAH3-E8T L Chain Part>

4) PCR using 542-562 and 561-613 was carried out so as to produce a DNA fragment.

5) PCR using 538-539 and 542-543 was carried out so as to produce a DNA fragment.

6) 4) and 5) were mixed and PCR by 538, 562 was carried out, which was cloned to a SacI-NheI site of pAALFab.

<pFCAH9-E8d>

7) Production of VH Stuffer Part

[0730] pFCAH3-E8T was digested with XbaI and EcoRI and a klenow fragment was acted thereon so as to be blunted. Thereafter, the self ligation was carried out so as to produce a stuffer of the VH part.

8) Production of VL Stuffer Part

[0731] By using pFCAH3-E8T as a template, PCR with 527-600 was carried out, which was cloned to the HindIII-XhoI site in 7).

9) This was digested with KpnI and subjected to self ligation so as to produce a stuffer of a VL part.

10) Introduction of SfiI, NcoI, SpeI Sites

[0732] By using pFCAH3-E8T as a template, PCR with 527-663 was carried out, which was cloned to the HindIII-SacI site in 1).

11) Introduction of AscI Site

[0733] By using pFCAH3-E8T as a template, PCR with 527-LCP3ASC was carried out, which was cloned to 2) which was completely digested with SacI and partially digested with SalI.

12) Transform of GammaCH1 Part into Human Gene

[0734] Since human gamma CH1 part has BstPI site, cloning was carried out so as to design this site. By using tonsil cDNA as a template, PCR with hCH1Bst-hCH1midS, hCH1midAS-hCH1H6 was carried out and then mixed. PCR with hCH1Bst-hCH16Sma was carried out and the DNA fragment was cloned to the BstPI-Sma site in 3).

13) Introduction of Xho Site

[0735] By using 12) as a template, PCR with 702-663 was carried out and this was cloned to the BstPI-SacI site in 12).

<Production of pscFvCA9-E8VHdVLd>

[0736] pFCAH9-E8d 3 μg (3 μL) (see FIG. **5**D) was mixed with BstPI (3 U/μL) (3 μL), 10×H buffer (5 μL), DW (39 μL) and subjected to restriction enzyme treatment at 37° C. for two hours. After treatment, precipitates obtained by ethanol precipitation were dissolved in 10 μL of TE buffer. To this solution, SacI (10 U/μL) (1 μL), 10×L buffer (5 μL) and DW (34 μL) were mixed. Then, this mixture was subjected to restriction enzyme treatment at 37° C. for two hours and to agarose gel electrophoresis. Thus, 4.7 kb fragment was recovered. The recovered products were subjected to ethanol precipitation to give 10 μL (pFCAH9-E8d BstPI-SacI fragment).

[0737] On the other hand, a primer linF (100 pmol/μL) (5 μL) and a primer linR (100 pmol/μL) (5 μL) were mixed and heated at 94° C. for 5 minutes, and then annealed at 80° C. for 5 minutes, at 70° C. for 5 minutes, and at room temperature for 30 minutes. Two μL of which was mixed with the above-obtained pFCAH9-E8d BstPI-SacI fragment (1 μL), 10× ligation buffer (1.5 μL), DW (9.5 μL), and T4DNA ligase (I μL) and reacted at 16° C. for 16 hours. After reaction, the reacted product was subjected to ethanol precipitation to concentrate to 3 μL. 1.5 μL of them was used to transform *E. coli* DH12S competent cells (20 μL) by electroporation. The obtained plasmid clone was extracted and the base sequence thereof was confirmed. This was named pscFvCA9-E8VHdVLd. FIG. **6** schematically shows a structure of pscFvCA9-

E8VHdVLd. Furthermore, FIGS. **7-1** to **7-2** show the base sequence (SEQ ID NO: 401) of the insert part of pscFvCA9-E8VHdVLd and the amino acid sequence (SEQ ID NO: 402) encoded thereby, respectively.

primer linF (SEQ ID NO: 403)
GTCACCGTCTCGAGAGGCGGTGGCGGATCAGGTGGCGGTGGAAGTGGCGG

TGGTGGGTCCATGGCCGACATCGAGCT

primer linR (SEQ ID NO: 404)
CGATGTCGGCCATGGACCCACCACCGCCACTTCCACCGCCACCTGATCCG

CCACCGCCTCTCGAGACG

1-2 Production of Vector for Temporarily Cloning Heavy Chain Variable Region (VH)

[0738] According to the well-known technique (see Iba Y. et al., Gene 194:35-46, 1997.), firstly, a pAALFab vector (FIG. **5**A) was produced. A portion between XbaI and EcoRI was deleted from the pAALFab vector, and the restriction enzyme cut sites Kpn I, Sfi I, Nco I, and Spe I were newly added. Through pFCAH3-E8T (FIG. **5**B), a vector pscFvCA-E8VHd (FIG. **5**C) capable of cloning VH (heavy chain variable region) was produced. Thus, a vector for temporarily cloning the heavy chain variable region (VH) was obtained. FIGS. **8-1** to **8-2** show the base sequence (SEQ ID NO: 405) of the insert of pscFvCA-E8VHd, the restriction enzyme site and the amino acid sequence (SEQ ID NO: 406) encoded by the base sequence.

[0739] Specifically, the primer 610 and the primer 611 were annealed and annealed produced was cloned to a BstPI-SacI site of pFCAH3-E8T. Thus, a single chain was produced. Furthermore, PCR with the primer 527 and the primer 619 was carried out and this was further cloned to a HindIII-PstI site. Thus, introduction of SfiI, NcoI site was carried out. Hereinafter, primer sequences used for producing the vector are shown.

610 scBstSpeSacF (SEQ ID NO: 407):
5'-CACCACGGTCACCGTCTCCTCAGGCGGTGGCGGATCAGGTGGCGGTG

GAAGTGGCGGTGGTGGGTCTACTAGTGACATCGAGCTCACCCAG-3'

611 scBstSpeSacR (SEQ ID NO: 408):
3'-GTGGTGCCAGTGGCAGAGGAGTCCGCCACCGCCTAGTCCACCGCCAC

CTTCACCGCCACCACCCAGATGATCACTGTAGCTCGAGTGGGTC-5'

527 Reverse (SEQ ID NO: 409):
5'-CAGGAAACAGCTATGAC-3'

619 E8VHf-SftNcoPstR (SEQ ID NO: 410):
3'-GACGCCGGGTCGGCCGGTACCGGCTCCAAGTCGACGTCGTCA-5'

2. Production of Immunoglobulin Light Chain Library

2-1 Isolation of Immunoglobulin Light Chain Gene by Using PCR

[0740] From bone marrow cells (sample No. 59) 4×10^7 cells, and lymphocytes of cord blood and peripheral blood, by using a commercially available kit (Pharmacia Biotech, QuickPrep Micro mRNA Purification Kit), 2.6 μg of mRNA was obtained. From this mRNA, cDNA was produced. The cDNA was produced by using SuperScriptPreamplification System (GibcoBRL). As a primer, oligo dT was used. PCR using the obtained cDNA as a template was carried out by using 5' primer (κ1-κ6, λ1-λ6) and 3' primer (hCKASC primer or hCLASC primer) for obtaining light chain genes. The PCR product was treated with phenol, subjected to ethanol precipitation and suspended in 10 μL of TE buffer. The base sequence of primer and conditions of PCR are shown below. In the base sequence of a primer for obtaining light chain genes, underline part represents NcoI site and AscI site.

5' primer κ1-κ6
hVK1a (SEQ ID NO: 411):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCCGACATCCAGATGACCCA

GTCTCC

hVK2a (SEQ ID NO: 412):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC GATGTTGTGATGACTC

AGTCTCC

hVK3a (SEQ ID NO: 413):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC GAAATTGTGTTGACGC

AGTCTCC

hVK4a (SEQ ID NO: 414):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC GACATCGTGATGACCC

AGTCTCC

hVK5a (SEQ ID NO: 415):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC GAAACGACACTCACGC

AGTCTCC

hVK6a (SEQ ID NO: 416):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC GAAATTGTGCTGACTC

AGTCTCC

5' primer λ1-λ6
hVL1 (SEQ ID NO: 417):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CAGTCTGTGTTGACGC

AGCCGCC

hVL2 (SEQ ID NO: 418):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CAGTCTGCCCTGACTC

AGCCTGC

hVK3a (SEQ ID NO: 419):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC TCCTATGTGCTGACTC

AGCCACC

hVL3b (SEQ ID NO: 420):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC TCTTCTGAGCTGACTC

AGGACCC

hVL4 (SEQ ID NO: 421):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CACGTTATACTGACTC

AACCGCC

hVL5 (SEQ ID NO: 422):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CAGGCTGTGCTCACTC

AGCCGCC

-continued

hVL6 (SEQ ID NO: 423):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC AATTTTATGCTGACTC

AGCCCCA

3'-primer hCKASC (SEQ ID NO: 424):
TCGACTGGCGCGCCGAACACTCTCCCCTGTTGAAGCTCTTTGTG

3'-primer HCLASC (SEQ ID NO: 425):
TCGACTGGCGCGCCGAACATTCTGTAGGGGCCACTGTCTTCTC

Conditions of PCR

[0741]

cDNA	2 μL
10 × buffer # 1 (attached to KOD)	10 μL
dNTP mix (2.0 mM)	10 μL
25 mM MgCl2	4 μL
5' side primer (100 pmol/μL)	1 μL
3' side primer (100 pmol/μL)	1 μL
sterilized MilliQ	71 μL

[0742] KOD DNA polymerase (TYOBO CO LTD., 2.5 U/mL) 1 μL

[0743] 35 cycles, each cycle includes 94° C. for one minute, 55° C. for two minutes and 74° C. for one minute

2-2-1 Incorporation of Light Chain Gene into Phagemid

[0744] The PCR product obtained in 1 was treated with a restriction enzyme in the following conditions.

PCR product	10 μL
10 × NEB4 (attached to AscI)	5 μL
Sterilized MilliQ	33 μL
AscI (NEB, 10 U/μL)	1 μL
NcoI (TAKARA SHUZO, 10 U/μL)	1 μL

[0745] After the reaction at 37° C. for one hour and at 50° C. for one hour, 10 μL of the reacted product was subjected to agarose gel electrophoresis and 600 bp band was cut out to be purified by using geneclean II kit (Funakoshi Corporation). Similar to the PCR product, restriction enzyme-treated pscFvCA9-E8VHdVLd was purified by using geneclean II kit and reacted with the restriction enzyme-treated PCR product at 16° C. for four hours to overnight in the following conditions, thereby carrying out ligation.

restriction enzyme-treated pscFvCA9-E8VHdVLd	2 μL
restriction enzyme-treated PCR product	1 μL
10 × ligation buffer (attached to T4 DNA ligase)	1.5 μL
10 mM ATP	1.5 μL
sterilized MilliQ	8 μL
T4 DNA Iigase (TAKARA SHUZO 10 U/μL)	1 μL

2-2-2 Introduction of Phagemid into *E. coli*

[0746] The obtained ligated DNA was used so as to transform *E. coli* DH12S as follows. That is to say, ligated DNA was subjected to ethanol precipitation once, and dissolved in 3 μL of ⅕ TE (TE that was 5-fold diluted with sterilized MilliQ). 1.5 μL of them was suspended in 20 μL of competent cell DH12S (GIBCO BRL), which was subjected to electroporation in the following conditions.

Electroporator Cell-Porator (Cat. series 1600), product of BRL	
Setting conditions; voltage booster	4 kΩ
capacitance	330 μF
DC volts	LowΩ
charge rate	Fast

[0747] The above-mentioned transformed *E. coli* was planted on a transformation medium (SOB) (2 mL) and shaking cultured at 37° C. for one hour. Then, a part of the cultured product was planted on agar medium (Amp plate) and a remaining part was cultured in a 2×TY medium containing 0.1% glucose and 100 μg/mL ampicillin to form glycerine stock. The agar medium was incubated at 30° C. and growing colony was separated by picking by a picker. A plasmid was prepared, respectively. Then, the light chain gene and the base sequence were examined.

[0748] SOB medium: to 950 mL of purified water, the following components were added and shaken so as to be dissolved completely. Thereafter, 250 mM KCl solution (10 mL) was added so as to adjust to pH 7.0 with 5N NaOH. Purified water was added to adjust to 1000 mL, then sterilized for 20 minutes in the autoclave. Immediately before the use, 5 mL of 2M sterilized $MgCl_2$ was added.

bacto-tryptone	20 g
bacto-yeast extract	5 g
NaCl	0.5 g

[0749] 2×YT medium: to 900 mL of purified water, the following components were added and shaken so as to be dissolved completely. Thereafter, 5 N NaOH was added so as to adjust to pH 7.0 with 5N NaOH. Purified water was added to adjust to 1000 mL, then sterilized for 20 minutes in the autoclave and used.

bacto-tryptone	16 g
bacto-yeast extract	10 g
NaCl	5 g

[0750] The other reagents were purchased form the following suppliers.
(Manufacture/Product name are described in this order)
SIGMA/ampicillin sodium

Wako Pure Chemical/phenol

SIGMA/BSA

[0751] DIFCO/2×YT medium
Wako Pure Chemical/kanamycin sulfate
nacalai tesque/polyethylene glycol 6000
nacalai tesque/Tween 20

KATAYAMA CHEMICAL/NaCl

Wako Pure Chemical/IPTG

[0752] Wako Pure Chemical/skim milk
Wako Pure Chemical/sodium azide

Wako Pure Chemical/triethylamine

[0753] Wako Pure Chemical/hydrogen peroxide
Wako Pure Chemical/OPD tablet

Wako Pure Chemical/ethanol

[0754] The above-mentioned operation is carried out with respect to all of κ1, κ2, κ3, κ4, κ5, and κ6, as well as λ1, λ2, λ3a, λ3b, λ4, λ5, λ6, λ7, λ8, λ9, and λ10 are operated so as to confirm whether or not the intended clones are obtained.

Then, for example, κ1 and κ2, clones in each group, were mixed so that the ratio becomes near the frequency of use. The rate of expression of each group of these light chains in an actual living body is already known. These gene clones amplified by PCR method and incorporated into a vector are mixed so that the ratio becomes near the frequency of use. Thus, VL library was obtained. Constituent ratio in each family in VL library is shown below.

[Table I]

[0755]

TABLE 1

	Vκ		
family	Usage frequency in vivo (%)*	Constitutive ratio in VL library (%)	Constitutive ratio in KL200 (%)
Vκ1	39	37	30.7
Vκ2	12	12	19.8
Vκ3	36	35	33.7
Vκ4	12	12	10.9
Vκ5	1	2	5.0
Vκ6	—**	2***	0.0

*Griffith AD et al. EMBO J. (1994) 13, 3245-60.
**Published data is not shown
***equal amount of cDNA produced with primer VK6-2 and cDNA produced with primer VK6-3 were mixed.

[Table 2]

[0756]

TABLE 2

	Vλ		
family	Usage frequency in vivo (%)*	Constitutive ratio in VL library (%)	Constitutive ratio in KL200 (%)
Vλ1	43	41	34.1
Vλ2	15	15*[3]	15.2
Vλ3	34	32*[4]	25.3
Vλ4	0	1.6*[5]	0.0
Vλ5	0	1.0*[6]	11.1
Vλ6	0	1.0	14.1
Vλ7	6	6	0.0
Vλ8	1	1	0.0
Vλ9	1	1	0.0
Vλ10	—*[2]	1	0.0

*Griffith AD et al. EMBO J. (1994) 13, 3245-60.
*[2]Published data is not shown
*[3]cDNA produced with primer VL2 (5%) and cDNA produced with primer VL2-2 (10%) were mixed.
*[4]cDNA produced with primer VL3a-2 (17%) and cDNA produced with primer VL3b (15%)
*[5]cDNA produced with primer VL4a (0.5%), cDNA produced with primer VL4b (0.5%) and cDNA produced with primer VL4c (0.5%) were mixed.
*[6]cDNA produced with primer VLSabde (0.5%) and cDNA produced with cDNA (0.5%) were mixed.

3. Production of Combinatorial Library of Light Chain Gene Library and Heavy Chain Gene Library (scFv Antibody Gene Library)

3-1-1 Isolation of Immunoglobulin Heavy Chain Gene Using PCR

[0757] By the procedure similar to 2-1, cDNA was prepared by using cord blood, bone marrow fluid, and lymphocyte of peripheral blood as well as a human μ primer (below-mentioned primer, 634) from the tonsil or random hexamer. By using this cDNA as a template, a mixture of equal amount of 5' primer (VH1 to VH7) and 3' primer (four kinds of human JH primers are mixed in equal amount, below-mentioned primers 697 to 700) for obtaining a human antibody heavy chain gene, or human u primer (below-mentioned primer 634) were subjected to PCR. In Table, underlined parts show the SfiI site. Since hVH2a did not correspond to a germ line VH2 family, VH2a-2 was newly designed. Furthermore, since hhVH4a did not correspond to the entire VH4 family, hVH4a-2 was newly designed. Also, VH5a did not correspond to a germ line VH5 subfamily, VH5a-2 was newly designed. Furthermore, as a primer corresponding to VH7, hVH7 was designed. These were also subjected to gene amplification and incorporated into pscFvCA-E8VHd. Then, as to the obtained genes, the base sequence was determined. Since the sequence of hVH5a-2 is extremely similar to that of hVH1a and it is expected that the gene product similar to that amplified with hVH1a, this was not used. The PCR products were subjected to phenol treatment and then ethanol precipitation, and thereafter suspended in 10 μL of TE buffer.

634 hum μ CH1R (SEQ ID NO: 426):
ATGGAGTCGGGAAGGAAGTC

Primers used for amplification of each VH family
Human VH primer, SfiI site is underlined.
628 hVH1a (SEQ ID NO: 427):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CAGGTGCAGCTGGTGC

AGTCTGG

629 hVH2a (SEQ ID NO: 428):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CAGGTCAACTTAAGGG

AGTCTGG

630 hVH3a (SEQ ID NO: 429):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC GAGGTGCAGCTGGTGG

AGTCTGG

631 hVH4a (SEQ ID NO: 430):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CAGGTGCAGCTGCAGG

AGTCGGG

632 hVH5a (SEQ ID NO: 431):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CAGGTGCAGCTGTTGC

AGTCTGC

633 hVH6a (SEQ ID NO: 432):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CAGGTACAGCTGCAGC

AGTCAGG

629-2 hVH2a-2 (SEQ ID NO: 433):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CAGRTCACCTTGAAGG

AGTCTGGTCC

631-2 hVH4a-2 (SEQ ID NO: 434):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CAGGTGCAGCTACAGC

AGTGGGG

632-2 hVH5a-2 (SEQ ID NO: 435):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC GAGGTGCAGCTGGTGC

AGTCTGG

-continued

712 hVH7 (SEQ ID NO: 436):
GTCCTCGCAACTGCGGCCCAGCCGGCCATGGCC CAGGTGCAGCTGGTGC

AATCTGGGTCTGAGT

Human JH primer, BstPI and XhoI sites underlined.
697 hJH1-2 (SEQ ID NO: 437):
GGTGGAGGCACTCGAGACGGTGACCAGGGTGC

698 hJH3 (SEQ ID NO: 438):
GGTGGAGGCACTCGAGACGGTGACCATTGTCC

699 hJH4-5 (SEQ ID NO: 439):
GGTGGAGGCACTCGAGACGGTGACCAGGGTTC

700 hJH6 (SEQ ID NO: 440):
GGTGGAGGCACTCGAGACGGTGACCGTGGTCC

cDNA	2 μL
10 × buffer # 1 (attached to KOD)	10 μL
dNTP mix (2.0 mM)	10 μL
25 mM MgCl2	4 μL
5' primer (100 pmol/(μL)	1 μL
3' primer (100 pmol/μL)	1 μL
sterilized MilliQ	71 μL
KOD DNA polymerase (TYOBO CO LTD., 2.5 U/μL)	1 μL

[0758] PCR conditions: 35 cycles, each cycle includes 94° C. for one minute, 55° C. for two minutes and 74° C. for one minute

3-1-2 Production of Heavy Chain Gene Library

[0759] The PCR product obtained in 3-1-1 was treated with a restriction enzyme in the following conditions.

PCR product	10 μL
10 × K buffer NEB4 (TAKARA SHUZO)	5 μL
Sterilized MilliQ	33 μL
SfiI (NEB, 10 U/μL)	1 μL
XhoI (TAKARA SHUZO, 12 U/μL)	1 μL

[0760] After the reaction at 37° C. for two hours, 10 μL of the reacted product was subjected to agarose electrophoresis and 400 bp band was cut out to be purified by using geneclean II kit (Funakoshi Corporation). Similar to the PCR product, restriction enzyme-treated pscFvCA-E8VHd was purified by using geneclean II kit and reacted with the restriction enzyme-treated PCR product at 16° C. for four hours to overnight in the following conditions, thereby carrying out ligation.

restriction enzyme-treated pscFvCA-E8VHd	2 μL
restriction enzyme-treated PCR product	1 μL
10 × ligation buffer (attached to T4 DNA ligase)	1.5 μL
10 mM ATP	1.5 μL
sterilized MilliQ	8 μL
T4 DNA ligase (TAKARA SHUZO 10 U/μL)	1 μL

3-1-3 Introduction of Phagemid into *E. coli*

[0761] The obtained DNA was transformed into *E. coli* DH12S. Specifically, DNA was subjected to ethanol precipitation once, and dissolved in 3 μL of ⅕ TE (TE that was 5-fold diluted with sterilized MilliQ). 1.5 μL of them was suspended in 20 μL of competent cell DH12S (GIBCO BRL), which was subjected to electroporation.

Electroporator Cell-Porator (Cat. series 1600), product of BRL	
Setting conditions; voltage booster	4 kΩ
capacitance	330 μF
DC volts	LowΩ
charge rate	Fast

[0762] The above-mentioned transformed *E. coli* was planted on a transformation medium (SOB) (2 mL) and shaking cultured at 37° C. for one hour. Then, a part of the cultured product was planted on agar medium (Amp plate) and a remaining part was cultured in a 2×YT medium containing 0.1% glucose and 100 μg/mL ampicillin to form glycerine stock. The agar medium was incubated at 30° C. and growing colony was separated by picking by a picker. A plasmid was prepared, respectively. Then, the heavy chain gene and the base sequence were examined. All of the VH1 to VH7 were treated in the same way to confirm whether or not the target clone was obtained. These clones of each group (family) were mixed so that the ratio was near the use frequency in vivo. Thus, VH library was produced. The constitution ratio of each family in the VH library is shown below.

[Table 3]

[0763]

TABLE 3

family	Usage frequency in vivo (%)*	Constitutive ratio in VH library (%)
VH1	25	29**
VH2	6.6	7
VH3	40	40
VH4	19	19***
VH5	5	—**
VH6	3.8	4
VH7	1.2	2

*Griffith AD et al. EMBO J. (1994) 13, 3245-60.
**Actually, since VH1 and VH5 are amplified with the same primer, they cannot be counted separately.
***cDNA produced with VH4 primer and cDNA produced with VH4-2 primer were mixed in this ratio.

3-2 Production of Combinatorial Gene Library

[0764] VH library (200 μg) was digested with HindIII and XhoI under the following conditions and heavy chain gene is cut out and purified by using geneclean II kit.

VH library 200 μg	100 μL
10 × K buffer (TAKARA SHUZO)	40 μL
sterilized MilliQ	205 μL
HindIII (TAKARA SHUZO40 U/μL)	30 μL
XhoI (TAKARA SHUZO50 U/μL)	25 μL

[0765] A vector pscFvCA9-E8VHdVLd in which a VL library had been inserted was was digested with HindIII and XhoI under the following conditions, and a fragment containing a light chain gene was purified by using geneclean II kit.

pscFvCA9-E8VHdVLd in which a VL library had been inserted	100 μg, 100 μL
10 × K buffer (TAKARA SHUZO)	40 μL
sterilized Milli-Q	230 μL
HindIII (TAKARA SHUZO 40 U/μL)	15 μL
XhoI (TAKARA SHUZO 50 U/μL)	15 μL

[0766] Next, a VH gene library fragment and a pscFvCA9-E8VHdVLd vector into which a light chain gene has been inserted were reacted at 16° C. overnight in the following conditions so as to be ligated.

restriction enzyme-treated VH library fragment	10 μg 50 μL
pscFvCA9-E8VHdVLd containing restriction enzyme-treated VL library fragment	40 μg 50 μL
10 × ligation buffer (attached to T4 DNA ligase)	100 μL
10 mM ATP	100 μL
Sterilized MilliQ	670 μL
T4 DNA ligase (TAKARA SHUZO 10 U/μL)	30 μL

[0767] The DNA in which the reaction had been completed was used to transform *E. coli* DH12S. Specifically, DNA was subjected to ethanol precipitation once, and dissolved in 30 μL of ⅕ TE (TE 5-fold diluted with sterilized MilliQ). This was suspended in 500 μL of competent cell DH12S (GIBCO BRL), and electroporation was carried out.

Electroporator Cell-Porator (Cat. series 1600), product of BRL	
Setting conditions; voltage booster	4 kΩ
capacitance	330 μF
DC volts	LowΩ
charge rate	Fast

[0768] The above-mentioned transformed *E. coli* was planted on a transformation medium (SOB) (12 mL) and shaking cultured at 37° C. for one hour. Then, a part of the cultured product was planted on agar medium (Amp plate) and a remaining part was cultured in a 2×YT medium (500 mL) containing 0.1% glucose and 100 μg/mL ampicillin to form glycerine stock. The agar medium was incubated at 30° C. and the number of clones were estimated from the number of growing colonies. 8.5×10^{10} clones were obtained.

4. Production of scFv-CL Antibody Phage Library from scFv-CL Antibody Gene Library

[0769] To 16 of 5-liter flasks containing 300 mL of 2×YT medium to which 1% glucose and 100 μg/mL ampicillin had been added, 2.5 mL of AIMS-5 suspension was added and shaking cultured at 37° C. Every one hour, the absorbance at the wavelength of 600 nm was measured and the culture solution was proliferated until the absorbance became 1.0. To the culture solution, 12 mL each of helper phage solution (M13KO7) was added for each flask so as to infect the helper phage, culture at 37° C. for two hours. Thus, phage infected DH12S was obtained.

[0770] To 24 of 5-L flasks, 2×YT medium (600 mL), 100 μg/mL ampicillin (0.6 mL), 50 μg/m 38 L kanamycin (0.8 mL), and helper phage infected DH12S (200 mL) were added and shaking cultured at 37° C. for 20 hours.

[0771] The bacterial cells were centrifuged at 8000 rpm at 4° C. for 10 minutes, and supernatant was recovered. 4 L of 20% polyethylene glycol/2.5M NaCl was added to the supernatant, after it was quietly stirred for about 20 minutes, centrifuged at 8000 rpm at 4° C. for 20 minutes. The precipitate was dissolved in 1 L of PBS, 200 mL of 20% polyethylene glycol/2.5M NaCl was added thereto, after it was quietly stirred for about 20 minutes, and centrifuged at 8000 rpm at 4° C. for 20 minutes. The supernatant was discarded and further, centrifuged at 8000 rpm at 4° C. for 3 minutes, and the precipitate was recovered. The precipitate was dissolved in PBS to which 0.05% NaN_3 was added, after it was centrifuged at 1000 rpm at 4° C. for 15 minutes and the supernatant was recovered, further, centrifuged at 8000 rpm at 4° C. for 3 minutes and the supernatant was recovered.

[0772] The titer of the recovered phage solution was checked as followings: the phage solution was diluted with PBS in 10^6, 10^7 and 10^8-fold, out of these, 10 μL was infected with 990 μL of DH12S, cultured at 37° C. for one hour. 100 μL of them was plated on LBGA plate and cultured at 30° C. for 18 hours. The titer of the stock solution before dilution was calculated by counting the number of colonies. The stock solution of the phage solution was suspended in PBS containing 0.05% NaN_3 so as to be 2×10^{14}/mL.

5. Obtaining of Antibody Clone Specific to Cancer Cell

5-1 Phage Antibody Screening Using Cancer Cell Line

[0773] Phage antibodies of various cancer cell lines or clinical specimens were isolated by the following procedure. Kinds of used cell lines are described below. The culture conditions of the cell line are show in Table of FIG. **38**.

[0774] pancreatic cancer cell lines PANC-1, MIA-Paca2

[0775] kidney cancer cell lines CCFRC1, Caki-1, CCFRC1, Caki-1, ACHN

[0776] ovarian cancer cell lines KF28, RMG-1, RMG-2, SKOv3

[0777] stomach cancer cell lines SNU-5, MKN45, NCI-N87

[0778] lung squamous cell carcinoma lines RERF-LC-AI, EBC1

[0779] pulmonary adenocarcinoma cell lines Calu-3, NCI-H441, A549, PC14

[0780] hepatic cell carcinoma cell lines HepG2, OCTH, Hep3B

[0781] hepatic cell carcinoma clinical specimen (HCV positive),

[0782] intrahepatic bile duct cell carcinoma cell line RBE

[0783] stomach cancer cell lines SNU5, MKN45, NCI-N87

[0784] large bowel cancer cell lines CW2, CaCo2

[0785] acute myelocytic leukemia, AML clinical specimen

[0786] An adherent cell line group in 6 well plate (Falcon 3516) and a suspended cell line such as ATL-derived cell line in suspended culture flask (70 ml (slant neck)), which had been cultured in a medium (RPMI-1640: Sigma-Aldrich, 10% fetal calf serum, 1% penicillin-streptomycin solution) in a CO_2 incubator at 37° C., were used.

[0787] The adherent cell line was dissociated from culture dish with 2 mg/ml collagenase I (Gibco BRL)/cell dissocia-

tion buffer (Gibco BRL), and then recovered with 10% FBS/DMEM. On the other hand, the suspended cells were, as they were, centrifuged (400×g, 4° C., two minutes) to remove the medium once.

[0788] After such operation, each cell was washed with 1% BSA, 0.05% NaN_3/PBS (BSA solution) and centrifuged (400×g, 4° C., two minutes) to remove the supernatant.

[0789] Cells from the clinical specimen derived from clinical tissue material prepared in 6 well plate (Falcon 3516), which had been cultured in a medium (RPMI-1640: Sigma-Aldrich, 10% fetal calf serum, 1% penicillin-streptomycin solution) in a CO_2 incubator at 37° C., were used.

[0790] Cells were washed with cooled PBS and 4×10^7 of cells were used for screening. This was mixed with 1×10^{13} cfu of human antibody phage library, so that the final concentration of the reaction solution was made to be 1% BSA-0.1% NaN_3/MEM and the volume was made to be 1.6 ml. The reaction was carried out while rotating slowly at 4° C. for four hours. After the reaction was completed, the reaction solution was divided into two parts and each part was stratified on 0.6 ml of organic solution (dibutyl phtalate cycloheximide 9:1) and subjected to centrifugation at centrifugal force of 3000 rpm by using a micro-centrifugal machine for two minutes, so that cells were allowed to precipitate at the bottom of the tube. From each tube, the solution was discarded and cells were suspended in 0.7 ml of 1% BSA/MEM, stratified on 0.7 ml of organic solvent and subjected to centrifugation. This operation was repeated again. Then the solution was discarded and cells were suspended in 0.3 ml PBS, frozen with liquid nitrogen and melted at 37° C.

[0791] This was infected with 20 ml of *E. coli* DH12S (OD 0.5) for one hour, the part of it was plated on an Ampicillin plate and the titer of the collected phage was calculated. Phage infected *E. coli* was cultured over night in 600 ml of 2×YTGA culture medium (2×YT, 200 μg/ml ampicillin sulfate, 1% glucose) at 30° C. overnight. The cultured product (10 ml) that had been cultured over night was mixed with 200 ml of 2×YTA culture medium (2×YT, 200 μg/ml ampicillin sulfate) and cultured at 37° C. for 1 hour. Thereafter, helper phage κ07 (1×10^{11}) was placed and cultured at 37° C. for 1.5 hour. Then, 800 ml of 2×YTGAK (2×YT, 200 μg/ml ampicillin sulfate, 0.05% glucose, 50 μg/ml kanamycin) was placed and cultured over night at 30° C. This was centrifuged at 8000 rpm for ten minutes so as to prepare 1 l of supernatant. To this, 200 ml of PEG solution (20% polyetyleneglycol 6000, 2.5M NaCl) was mixed and agitated sufficiently. Thereafter, the mixture was centrifuged at 8000 rpm for 10 minutes so as to precipitate phage. This was suspended in 10 ml of PBS/0.05% NaN_3 and the part of it was used so as to examine the number of infected *E. coli*. This is the phase of the I st screening.

[0792] For the 2nd screening, 2×10^7 of cells and 1×10^{10} cfu of the 1st screening phages were used, so that the volume of the reaction solution was made to be 0.8 ml. The reaction solution was 1% BSA-0.1% NaN_3/MEM and the entire scale was carried out equal to that of the 1st screening.

[0793] The 3rd screening was carried out in the same conditions as those of the 2nd screening except that 1×10^9 cfu of 2nd phages were used.

[0794] When the recovering rate of the phages is increased, the screening round is stopped at the time. When the recovering rate is not increased, the 4th screening or later are carried out in the same manner by using the phage recovered immediately before round and by using 1×10^9 cfu of phages.

[0795] The screening of various cell lines was carried out by the same method as that of the screening mentioned above.

5-2 Selection of Antibody Clone

[0796] In the screening of HepG2 as an example, because the recovering rate of HepG2 was increased in the 3rd screening (FIG. **9**), it was judged that HepG2 cell specific antibody clone was concentrated in this stage, and several hundreds clones were picked up. Next, when the base sequence of H-chain portions of these positive clones was analyzed, antibodies obtained by removing the overlap from the kinds of base sequences were classified. These were examined for expression. Furthermore, expression positive clones were selected by the following procedures.

6. Base Sequence Determination of Antibody Clone

[0797] *E. coli*, infected with antibody phage, obtained by screening was diluted and plated on a nutrient agar medium containing 100 Hg/ml of ampicillin. The obtained colonies were picked up and cultured in 2×YTGA culture medium at 30° C. overnight. DNA was extracted by using KURABO PI-50 and the base sequence was determined by a dideoxy method. The overlapped clones having the same base sequence were removed. Furthermore, this culture medium cultured overnight (0.05 ml) was plated on 1.2 ml of 2×YTAI (2×YT, 200 μg/ml ampicillin sulfate, 0.5 mM IPTG) and cultured overnight at 30° C., centrifuged by using a micro-centrifugal machine at 15000 rpm for 5 minutes, and supernatant was obtained.

7. Confirmation of Expression of Antibody Clone

7-1 Selection of Antibody Clone

[0798] Since the antibody was expressed as cp3 fused protein, the expression using the protein was examined. That is to say, firstly, the supernatant obtained in the previous paragraph was reacted in Maxisorp (NUNC) at 37° C. for two hours, liquid was discarded, and blocking was carried out by reacting 5% BSA/PBS/0.05% NaN_3 at 37° C. for two hours. The liquid was discarded and a rabbit anti-cp3 antibody (Medical & Biological Laboratories Co., Ltd.) that had been diluted 5000-fold with 0.05% Tween/PBS was reacted at room temperature for one hour, followed by washing with PBS. Then, a HRP labeled goat anti-rabbit IgG antibody (Medical & Biological Laboratories Co., Ltd.) that had been diluted 2000-fold with 0.05% Tween/PBS was reacted at room temperature for one hour, followed by washing with PBS. Then, 100 μl of OPD solution was reacted at room temperature for 2 to 10 minutes, and the reaction was terminated by using 2N sulfuric acid, and by using SPECTRAmax 340PC (Molecular Devices), the absorbance at 492 nm of wavelength was measured.

[0799] In negative well in which the supernatant was not reacted was made to be a control. It was judged that a control whose absorbance did not become two times or more did not express. Such a control was removed from the later analysis.

7-2 Preparation of Antibody Sample

[0800] 7-2-1 Production of cp Type Antibody Expression *E. coli*

[0801] *E. coli* (10 ml) infected with phage corresponding to expressing antibody clones was introduced was plated on YTGA and shaking cultured at 30° C. one day and one night

(pre-culture solution). This was added to 4 l of YT 0.05GA and cultured at 30° C. When O.D. of the bacterial cells became 0.5, 4 ml of 1M IPTG was added and shaking cultured at 30° C. one day and one night. After the culture was terminated, the bacterial cells were centrifuged by using a cooling centrifugal machine at 10000 g, 4° C. for 10 minutes. To the obtained culture supernatant, an equal amount of saturated ammonium sulfate aqueous solution was added and stirred at room temperature for one hour. This solution was centrifuged by using a cooling centrifugal machine at 10000 g, 4° C. for 15 minutes, then supernatant was discarded, the obtained precipitate was suspended in 20 ml of PBS-NaN_3 solution, centrifuged by using a cooling centrifugal machine at 10000 g, 4° C. for 5 minutes, and supernatant was recovered. This was dialyzed with PBS one day and one night. To this, a supernatant antibody cp3 mouse monoclonal antibody (Medical & Biological Laboratories Co., Ltd.) that had been balanced with 0.05% NaN_3/PBS was chemically immobilized. Antibody affinity column was produced by using sepharose beads. The supernatant was naturally dropped, and the components that had not reacted with beads were allowed to pass through the column. This column was washed with 100 ml of PBS twice, washed with 0.1% Tween 20/PBS (30 ml) four times, and washed with 100 ml of PBS twice. To this, 0.2M Glycine-HCl (pH 3, 4 ml) was slowly added three times and the eluted component was recovered. Then, 3M Tris (80 μl) was added and neutralize (antibody solution). This was filtrated through a MILLEX-GP 0.22 μm filter, O.D. was measured, and the yield of antibodies was calculated.

7-2-2 Production of pp Type Antibody Expressing *E. coli*

[0802] The obtained antibody clone is originally cp3 type clone. This DNA was extracted by using KURABO PI-50, digested with a restriction enzyme SalI, self reconnected, then, introduced into *E. coli* DH 12S for transformation. Then, it was plated on a LBGA plate and cultured at 30° C. overnight at. The obtained *E. coli* colonies were cultured in 2×YTGA overnight and a pp type antibody expressing *E. coli* solution was obtained.

[0803] *E. coli* (10 ml) into which a plasmid expressing pp type antibody clones was introduced was plated on YTGA and shaking cultured at 30° C. one day and one night (pre-culture solution). This was added to 4 l of YT 0.05GA and cultured at 30° C. When O.D. of the bacterial cells became 0.5, 4 ml of 1 M IPTG was added and shaking cultured at 30° C. one day and one night. After the culture was terminated, the bacterial cells were centrifuged by using a cooling centrifugal machine at 10000 g, 4° C. for 10 minutes. To the obtained culture supernatant, an equal amount of saturated ammonium sulfate aqueous solution was added and stirred at room temperature for one hour. This solution was centrifuged by using a cooling centrifugal machine at 10000 g, 4° C. for 15 minutes, then supernatant was discarded, the obtained precipitate was suspended in 20 ml of PBS-NaN_3 solution, centrifuged by using a cooling centrifugal machine at 10000 g, 4° C. for 5 minutes, and supernatant was recovered. This was dialyzed with PBS one day and one night. To this, 2 ml of IgG sepharose 6 Fast Flow (Amersham Biosciences) balanced with 0.05% NaN_3/PBS was added and reacted while shaking at 4° C. one day and one night. This mixture solution was transferred to a column and naturally dropped. The components that were not reacted with beads were allowed to pass through the column. This column was washed with 100 ml of PBS twice, washed with 0.1% Tween 20/PBS (30 ml) four times, and washed with 100 ml of PBS twice. To this, 0.2M Glycine-HCl (pH 3, 4 ml) was slowly added three times and the eluted component was recovered. Then, 3M Tris (80 μl) was added and neutralize (antibody solution). This was filtrated through a MILLEX-GP 0.22 μm filter, O.D. was measured, and the yield of antibodies was calculated.

8. Reactivity to Various Cell Lines of Antibody Clone

8-1 FCM (Flow Cytometry) Analysis

[0804] The reactivity of various isolated antibody clones to various cell lines was confirmed by FCM. Experiment operation was as follows. Firstly, an adherent cell line in 6 well plate (Falcon 3516) and a suspended cell line such as ATL-derived cell line in suspended culture flask (70 ml (slant neck)), which had been cultured in a medium (RPMI-1640: Sigma-Aldrich, 10% fetal calf serum, 1% penicillin-streptomycin solution) in a CO_2 incubator at 37° C., were used.

[0805] i) Adherent cell line was dissociated from a culture plate with 2 mg/ml collagenase I (Gibco BRL)/cell dissociation buffer (Gibco BRL), and then recovered with 10% FBS/DMEM. On the other hand, the suspended cells were, as they were, centrifuged (400×g, 4° C., two minutes) to remove the medium once. After such operation, each cell was washed with 2.5% BSA, 0.05% NaN_3/PBS (BSA solution), suspended in 100 μl of 2.5% normal goat serum/BSA solution and stood still on ice for 30 minutes, dispensed to 10^6 cells/well, and then centrifuged (400×g, 4° C., two minutes) to remove the supernatant.

[0806] ii-1) In the case of cp3 antibodies, they were added so that the concentration became 5 μg/ml and left on ice for one hour. This was washed with a BSA solution once, then suspended in 100 μl of 5 μg/ml BSA solution of anti-cp3 mouse monoclonal antibody (Medical & Biological Laboratories Co., Ltd.) and left on ice for one hour. This was washed with a BSA solution once, then suspended in 100 μl of 5 μg/ml BSA solution of Alexa 488 binding anti-mouse IgG goat antibody (Molecularprobe) and left on ice for one hour. This was washed with BSA solution twice, and then suspended in 500 μl of BSA solution. To this solution, 50 μl of fixation solution (formaldehyde) was added and it was left for 10 minutes. Thereafter, 150 μl of PBS was added, treated by using Cell Strainer (Becton Dickinson), and then the fluorescence intensity of the group of cells was analyzed by using FACScaliver (FCM) (Becton Dickinson) ((1) to (3)).

[0807] ii-2) In the case of the pp type (protein A type) antibodies, they were added so that the concentration became 5 μg/ml and left on ice for one hour. This was washed with a BSA solution once, then suspended in 100 μl of 5 μg/ml BSA solution of Alexa 488 binding anti-mouse IgG goat antibody (Molecularprobe) and left on ice for one hour. This was washed with BSA solution twice, and then suspended in 500 μl of BSA solution. To this solution, 50 μl of fixation solution (formaldehyde) was added and it was left for 10 minutes. Thereafter, 150 μl of PBS was added, treated by using Cell Strainer (Becton Dickinson), and then the fluorescence intensity of the group of cells was analyzed by using FACScaliver (FCM) (Becton Dickinson).

[0808] In the analysis, detection antibody was labeled with fluorescent dye (Alexa 488, etc.) in advance. After sample antibodies and cells were reacted, they were reacted with detection antibodies. The difference in the antibody amount occurs depending upon the amount of antigen existing on the surface of the cell, and as a result, the fluorescence intensity

became different. Thus, the affinity with respect to the antigen existing on the surface of the cells and the amount of antigen can be estimated. Furthermore, in order to remove dead cells and debris, and the like, Forward Scatter: FSC is expressed in X-axis and Side Scatter: SSC is expressed in Y-axis, and a group of living cells (substantially the same group because cultured cells were used) in data obtained by dot plot expansion were gated, the fluorescence intensity only in this gate was measured.

8-2 Production of Panel

[0809] From the results of FCM, a histogram showing the relationship between the antibody binding amount and the number of cells was formed. One-parameter histogram using the antibody binding amount a parameter was drawn. The one-parameter histogram is one of the display methods in the flow cytometry. The one-parameter histogram is generally shown in a graph in which X-axis represents one indicator (parameter) and Y-axis represents the number of cells.

[0810] Typical examples of the results of FCM are shown in FIGS. **10** to **12**. As shown in these figures, basically, the behavior of the FCM becomes unique according to the combination of cells and antibodies. FIGS. **10** and **11** show histogram (right) and cell fluorescence cytology image (left), respectively, which show the reactivity between the scFv antibody and the undifferentiated malignant liver cancer cell line HLF obtained in the above-mentioned method. In all the antibodies (five antibodies), positive patterns are obtained but each has very unique shape of peak. Such shapes of peaks are thought to reflect the uniqueness of epitope of antigen. FIG. **12** shows a plurality of histograms (antibodies to be used was different in each case) which are overwritten. It is shown that the peak of each histogram has its own unique shape. However, during the comprehensive FCM analysis, an antibody group providing histogram having an extremely high similarity as shown in FIGS. **13** to **15** are observed. Furthermore, as shown in FIG. **16**, an antibody group consistently providing histogram having a high similarity regardless of cell lines to be used in the FCM analysis was observed. FIG. **16** show comparison of histograms obtained in three kinds of antibodies (035-234 antibody, 040-107 antibody, and 041-118 antibody). According to the later investigation, it is determined that these three kinds of antibodies recognize ALCAM.

[0811] FIG. **17** shows a method for classifying the antibody group based on the results of the FCM analysis. That is to say regardless of kinds of cells to be used, a plurality of antibodies having similar behavior (shape of histogram) in the FCM analysis are shown as the same group in a panel. Basically, a plurality of antibodies having the same shape of histogram (peaks are overlapped when the shapes are overwritten) are defined as one group. However, a plurality of antibodies may be classified into groups on the basis of the factors such as the median value, mode (peak value), and kurtosis of the histogram.

[0812] A plurality of antibodies are classified based on the above-mentioned technique. Firstly, the histograms obtained in the antibody clones are overwritten for each cell line to be used, and thereby the histograms are compared with each other. Thus, similarly between the antibody clones and the reactivity between antibody clones are obtained. Then, based on the similarity and the reactivity, antibody clones are classified and summarized in table (FIG. **18**). Thus, eight antibody groups (in the description hereinafter, groups are named 1, 2, 3, 4, 5, 6, 7, and 8 sequentially in this order) are obtained. In FIG. **18**, information on antigen identified later is also displayed. Each mark in Table shows a shift amount relative from the histogram (reference histogram) of the negative control antibody. Double circle mark represents that the shift amount is 20 times or more (the peak value of the is 20 times or more of the reference histogram); "o" (circle mark) represents that the shift amount is 10 times or more; "Δ" (triangle mark) represents that the shift amount is 3 times or more; and "x" represents that the shift amount is less than 3, respectively (an oblique line means no data is obtained). The larger the shift amount is, the higher the reactivity is.

[0813] Next, by the following procedure, it is verified that antigens of each antibody group in the produced panel are common.

9. Identification of Protein (Antigen) Recognized by Antibody Clone

9-1 Preparation of Solid Phase Antibody for Immunoprecipitation

[0814] Firstly, a pp type antibody solution was dialyzed with a coupling buffer solution (0.1M $NaHCO_3$—NaOH, pH 9). That is to say, an antibody solution was enclosed with a dialysis membrane (Snake Skin Pleated Dialysis Tubing 10,000 MWCO) and this was allowed to be sunk in 1.5 L of the coupling buffer solution (0.1 M $NaHCO_3$—NaOH, pH 9) and stirred by using a stirrer at 4° C. for two to three hours. Then, the buffer solution was replaced with new one and dialyzed for two to three hours. Thereafter, the buffer solution was replaced with new one again and dialyzed one day and one night.

[0815] Next, activated CNBr-activated Sepharose 4B used for making solid phase was adjusted. That is to say, CNBr-activated Sepharose 4B (Amersham Biosciences) was swollen with 1 mM HCl, then sucked by using an aspirator. To this, 50 ml of coupling buffer solution was added, stirred, and then sucked by using an aspirator. In this sucked state, a coupling buffer solution was added.

[0816] An antibody was made to be solid phased as follows. That is to say, to 5 mg antibody solution (10 ml), activated gel (1 ml) was added to cause a reaction at room temperature for two hours. After the reaction was terminated, the gel was transferred to a column and washed with a coupling buffer solution (1 ml) ten times. The presence of non-reacted antibodies was confirmed by measuring the O.D. The solid phased gel was substituted by 0.2M Glycine-NaOH pH8 solution (5 ml) twice, the same solution (5 ml) was further added and left at room temperature for two hours, this solution was naturally dropped, to this, 0.2M Glycine-HCl (pH 3, 5 ml) was added and substituted, the same solution (5 ml) was further added and left for 5 minutes, and then naturally dropped. Finally, the column was substituted by 20 ml of PBS, then naturally dropped, and 1% NP40, protease inhibitor, and 0.05% NaN_3/PBS were added, and gel was recovered.

9-2 Biotin Label of Protein on Cell Membrane and Production of Cell Lysate

[0817] Biotin labeling of the cultured liver cancer cell line was carried out as follows. That is to say, cultured cells HLF that had been cultured in five 15 cm-dishes were washed with PBS twice, and collagenase I (GIBCO) whose concentration had been adjusted to 5 mg/ml by using a cell dissociation buffer (GIBCO) was added and reacted in a CO_2 incubator at 37° C., so that cells were liberated. Thereafter, cells were

recovered in a culture medium and washed with PBS(−) twice. Then, the number of cells was counted by using a hemocytometer. The cells were suspended in PBS(−) so that the counted number became about 5×10^7/ml. To this, an equal amount of EZ-Link Sulfo-NHS-LC-Biotinylation Kit (PIERCE) was added so that the concentration had been adjusted to 1 mg/ml with PBS, left at room temperature for 30 minutes and then washed with PBS twice.

[0818] The cell lysate of biotin labeled cells was adjusted as follows. That is to say, to the above-mentioned biotin labeled cells, 4 ml of lysis buffer (1% NP40/detergent base solution, the composition of the detergent base solution: 20 mM HEPES, pH 8.0, 140 mM NaCl, protease inhibitor) was added and cells were suspended. This suspension was placed and homogenized in a cooled Dounce homogenizer. To the solution, ½ amount (2 ml) of a detergent mix solution (1% NP40, tritonX-100, b-D-Maltoside, n-Octyl b-D-Glucoside, n-Octyl b-D-Maltoside, n-Decyl b-D-Maltoside, deoxycholic acid, each 0.5%/detergent base solution) was added and mixed at 4° C. for four hours. This solution was centrifuged at 100,000 rpm for 30 minutes and filtrated through MILLEX-GP 0.22 μm filter.

9-3 Immunoprecipitation Reaction

[0819] Firstly, about 60 μl parts (about 150 μl solution parts) of the solid-phased antibodies (hereinafter, referred to as "antibody beads") were placed in a 2 ml-tube and 1/10 volume (about 15 μl) of 4 mM biotin was added to the tube. A mixture of 0.5 culture dishs of lysate (600 μl) and 60 μl of biotin solution was added to the tube and reacted while stirring at 4° C. for several hours. Then, the tube was centrifuged (5500 g, one minute, 4° C.) and supernatant was removed. To this, 800 μl of washing biotin/lysis-T buffer (0.5 mM biotin, 0.1% Tween 20/PBS) was added and mixed while falling two or three times, then the tube was centrifuged (5500 g, one minute, 4° C.), and supernatant was removed. This washing operation was carried out again, then 30 μl of citric acid solution (50 mM citric acid, pH 2.5) for elution was added to the antibody beads and stirred. Then, the tube was centrifuged (5500 g, 1 min, 4° C.) and supernatant was recovered. To the remaining antibody beads, 30 μl of citric acid solution for elution was added and stirred. The tube was centrifuged (5500 g, 1 min, 4° C.) and supernatant was recovered. This elution operation was repeated further three times, and a sample solution was recovered and 3M Tris was added to the solution for neutralization. This sample was migrated by SDS-PAGE so as to confirm the band by silver staining. At the same time, this sample was subjected to western blotting by using streptavidin-HRP (Anti-Streptavidin, IgG Fraction, Conjugated to Peroxidase CORTEX biochem) so as to detect a band of the biotin membrane protein.

9-4 Mass Spectrometry of Cut-Out Band

9-4-1 Trypsin Digestion in Gel

[0820] A portion corresponding to detected membrane protein was digested with trypsin in a gel and peptide was recovered. SDS polyacrylamide gel electrophoresis was carried out in accordance with a usual method and a band that had been obtained by staining with Coomassie Brilliant Blue was cut out. This was soaked in 200 mM ammonium bicarbonate 50% acetonitrile solution, shaken at 37° C. for 45 minutes. Then, the solution was discarded and the operation was repeated twice, thereby removing the Coomassie Brilliant Blue. This gel was dried under reduced pressure, and 4 μl of trypsin (20 μg/ml) dissolved in 40 mM ammonium bicarbonate (pH 8.1)-10% acetonitrile was added per unit area (mm^2) of gel slice, and left at room temperature for one hour and sufficiently infiltrated. To this, a trypsin solution was added in an amount that was 25 times as much as the previously added amount, and left at 37° C. for 18 hours. This was filtrated by a tube having a filter whose power size was 0.22 μm, and peptide in which an antigen had been cut with trypsin was recovered.

9-4-2 Identification of Antigen by Mass Spectrometry

[0821] A specimen obtained by in-gel trypsin digestion was subjected to HPLC linked with an electrospray ionization type ion trap quadrupole mass spectrometer. From the reversed phase chromatography column of HPLC, according to the change of linear concentration gradient of 0% to 80% acetonitrile containing 0.1% TFA, each peptide that had been eluted sequentially depending upon the hydrophobic property was ionized by an electrospray method. The mass of each peptide was analyzed.

[0822] At the same time, the mass of limited digested product of each peptide generated by collision with helium atoms placed in the middle of the fight route of ions was analyzed. When one amino acid is removed by limited digestion, since ion that is smaller by a part of the mass of the removed amino acid is observed, the kind of the removed amino acid can be identified according to the difference in mass. Furthermore, another amino acid is removed, since ion that is smaller by a part of the mass of the removed amino acid is observed, the kind of the removed amino acid can be identified according to the difference in mass. By proceeding the same analysis of the experimental data, an inner amino acid sequence can be determined. The set of the inner sequence of the obtained amino acid was retrieved by using a published amino acid sequence database and antigen was identified. As a result, as shown below, antigen of each antibody clone was identified and it is confirmed that the antibodies in the same group have the common antigen. The identification results was confirmed because the total amount of the identified protein that had been analogized from the amino acid sequence was not contradictory to the experimental data of the molecular weight of the SDS polyacrylamide electrophoresis of antigen before carrying out the trypsin digestion.

[0823] Antigen of antibodies belonging to group 1: HER1 (also known as: ErbB1, c-erbB-1, EGFR (Epidermal Growth Factor Receptor), v-erbB)

[0824] Antigen of antibodies belonging to group 2: HER-2 (also known as: ErbB2, c-erbB-2, neu)

[0825] Antigen of antibodies belonging to group 3: CD46 antigen (also known as: MCP (membrane cofactor protein), gp45-70, HuLY-m5, measles virus receptor, MIC10, TLX-B antigen, TRA2, trophoblast leucocyte common antigen, trophoblast-lymphocyte cross-reactive antigen)

[0826] Antigen of antibodies belonging to group 4: ITGA3 (integrin alpha3) (also known as: alpha3beta1 Epiligrin Receptor, alpha3beta1 Integrin, Epiligrin Receptor, CD49c, VLA-3, Gap b3, Galactoprotein b3, Laminin-5 Receptor)

[0827] Antigen of antibodies belonging to group 5: ICAM1 (Intercellular adhesion molecule-1) (also known as: Intercellular Adhesion Molecule 1, CD54 Antigen)

[0828] Antigen of antibodies belonging to group 6: ALCAM (Activated leukocyte cell adhesion molecule) (also known as: KG-CAM, CD166 Antigen, CD6 Ligand,

Activated Leukocyte Cell Adhesion Molecule, Neurolin)

[0829] Antigen of antibodies belonging to group 7: CD147 antigen (also known as: BSG, TCSF (Tumor cell-derived collagenase stimulatory factor), 5F7 protein, OK blood group protein, basigin protein, collagenase stimulatory factor protein, EMMPRIN (Extracellular matrix metalloproteinase Inducer), M6 activation antigen, human leukocyte activation antigen M6)

[0830] Antigen of antibodies belonging to group 8: IgSF4 (also known as: BL2, ST17, NECL2, TSLC1, IGSF4A, SYNCAM, sTSLC-1)

[0831] From the above-mentioned identification results, it has been clarified that it was possible obtain three antibody clones to HER1 (048-006 antibody, 057-091 antibody, and 059-152 antibody), one antibody clone to HER-2 (015-126 antibody), seven antibody clones to CD46 antigen (035-224 antibody, 045-011 antibody, 051-144 antibody, 052-053 antibody, 052-073 antibody, 053-049 antibody, and 3172-120 antibody), one antibody clone to ITGA3 (015-003 antibody), five antibody clones to ICAM1 (052-033 antibody, 053-042 antibody, 053-051 antibody, 053-059 antibody, and 053-085 antibody), five antibody clones to ALCAM (035-234 antibody, 040-107 antibody, 041-118 antibody, 066-174 antibody, and 083-040 antibody), one antibody clone to CD147 antigen (059-053 antibody), and ten antibody clones to IgSF4. The Note here that the amino acid sequences of the antibody clones have been identified as mentioned below (antibody clones to IgSF4 are omitted).

<Antibodies belonging to group 1>
(1) 048-006 antibody
SEQ ID NO: 1 (VH),

SEQ ID NO: 2 (VH CDR1),

SEQ ID NO: 3 (VH CDR2),

SEQ ID NO: 4 (VH CDR3),

SEQ ID NO: 5 (VL),

SEQ ID NO: 6 (VL CDR1),

SEQ ID NO: 7 (VL CDR2),

SEQ ID NO: 8 (VL CDR3)

(2) 057-091 antibody
SEQ ID NO: 9 (VH),

SEQ ID NO: 10 (VH CDR1),

SEQ ID NO: 11 (VH CDR2),

SEQ ID NO: 12 (VH CDR3),

SEQ ID NO: 13 (VL),

SEQ ID NO: 14 (VL CDR1),

SEQ ID NO: 15 (VL CDR2),

SEQ ID NO: 16 (VL CDR3)

-continued

(3) 059-152 antibody
SEQ ID NO: 17 (VH),

SEQ ID NO: 18 (VH CDR1),

SEQ ID NO: 19 (VH CDR2),

SEQ ID NO: 20 (VH CDR3),

SEQ ID NO: 21 (VL),

SEQ ID NO: 22 (VL CDR1),

SEQ ID NO: 23 (VL CDR2),

SEQ ID NO: 24 (VL CDR3)

<Antibody belonging to group 2>
(1) 015-126 antibody
SEQ ID NO: 25 (VH),

SEQ ID NO: 26 (VH CDR1),

SEQ ID NO: 27 (VH CDR2),

SEQ ID NO: 28 (VH CDR3),

SEQ ID NO: 29 (VL),

SEQ ID NO: 30 (VL CDR1),

SEQ ID NO: 31 (VL CDR2),

SEQ ID NO: 32 (VL CDR3)

<Antibodies belonging to group 3>
(1) 035-224 antibody
SEQ ID NO: 33 (VH),

SEQ ID NO: 34 (VH CDR1),

SEQ ID NO: 35 (VH CDR2),

SEQ ID NO: 36 (VH CDR3),

SEQ ID NO: 37 (VL),

SEQ ID NO: 38 (VL CDR1),

SEQ ID NO: 39 (VL CDR2),

SEQ ID NO: 40 (VL CDR3)

(2) 045-011 antibody
SEQ ID NO: 41 (VH),

SEQ ID NO: 42 (VH CDR1),

SEQ ID NO: 43 (VH CDR2),

SEQ ID NO: 44 (VH CDR3),

SEQ ID NO: 45 (VL),

SEQ ID NO: 46 (VL CDR1),

SEQ ID NO: 47 (VL CDR2),

SEQ ID NO: 48 (VL CDR3)

(3) 051-144 antibody
SEQ ID NO: 49 (VH),

SEQ ID NO: 50 (VH CDR1),

SEQ ID NO: 51 (VH CDR2),

-continued

SEQ ID NO: 52 (VH CDR3),

SEQ ID NO: 53 (VL),

SEQ ID NO: 54 (VL CDR1),

SEQ ID NO: 55 (VL CDR2),

SEQ ID NO: 56 (VL CDR3)

(4) 052-053 antibody
SEQ ID NO: 57 (VH),

SEQ ID NO: 58 (VH CDR1),

SEQ ID NO: 59 (VH CDR2),

SEQ ID NO: 60 (VH CDR3),

SEQ ID NO: 61 (VL),

SEQ ID NO: 62 (VL CDR1),

SEQ ID NO: 63 (VL CDR2),

SEQ ID NO: 64 (VL CDR3)

(5) 052-073 antibody
SEQ ID NO: 65 (VH),

SEQ ID NO: 66 (VH CDR1),

SEQ ID NO: 67 (VH CDR2),

SEQ ID NO: 68 (VH CDR3),

SEQ ID NO: 69 (VL),

SEQ ID NO: 70 (VL CDR1),

SEQ ID NO: 71 (VL CDR2),

SEQ ID NO: 72 (VL CDR3)

(6) 053-049 antibody
SEQ ID NO: 73 (VH),

SEQ ID NO: 74 (VH CDR1),

SEQ ID NO: 75 (VH CDR2),

SEQ ID NO: 76 (VH CDR3),

SEQ ID NO: 77 (VL),

SEQ ID NO: 78 (VL CDR1),

SEQ ID NO: 79 (VL CDR2),

SEQ ID NO: 80 (VL CDR3)

(7) 3172-120 antibody
SEQ ID NO: 81 (VH),

SEQ ID NO: 82 (VH CDR1),

SEQ ID NO: 83 (VH CDR2),

SEQ ID NO: 84 (VH CDR3),

SEQ ID NO: 85 (VL),

SEQ ID NO: 86 (VL CDR1),

SEQ ID NO: 87 (VL CDR2),

SEQ ID NO: 88 (VL CDR3)

-continued

<Antibody belonging to group 4>
(1) 015-003 antibody
SEQ ID NO: 89 (VH),

SEQ ID NO: 90 (VH CDR1),

SEQ ID NO: 91 (VH CDR2),

SEQ ID NO: 92 (VH CDR3),

SEQ ID NO: 93 (VL),

SEQ ID NO: 94 (VL CDR1),

SEQ ID NO: 95 (VL CDR2),

SEQ ID NO: 96 (VL CDR3)

<<Antibodies belonging to group 5>
(1) 052-033 antibody
SEQ ID NO: 97 (VH),

SEQ ID NO: 98 (VH CDR1),

SEQ ID NO: 99 (VH CDR2),

SEQ ID NO: 100 (VH CDR3),

SEQ ID NO: 101 (VL),

SEQ ID NO: 102 (VL CDR1),

SEQ ID NO: 103 (VL CDR2),

SEQ ID NO: 104 (VL CDR3)

(2) 053-042 antibody
SEQ ID NO: 105 (VH),

SEQ ID NO: 106 (VH CDR1),

SEQ ID NO: 107 (VH CDR2),

SEQ ID NO: 108 (VH CDR3),

SEQ ID NO: 109 (VL),

SEQ ID NO: 110 (VL CDR1),

SEQ ID NO: 111 (VL CDR2),

SEQ ID NO: 112 (VL CDR3)

(3) 053-051 antibody
SEQ ID NO: 113 (VH),

SEQ ID NO: 114 (VH CDR1),

SEQ ID NO: 115 (VH CDR2),

SEQ ID NO: 116 (VH CDR3),

SEQ ID NO: 117 (VL),

SEQ ID NO: 118 (VL CDR1),

SEQ ID NO: 119 (VL CDR2),

SEQ ID NO: 120 (VL CDR3)

(4) 053-059 antibody
SEQ ID NO: 121 (VH),

SEQ ID NO: 122 (VH CDR1),

SEQ ID NO: 123 (VH CDR2),

-continued

SEQ ID NO: 124 (VH CDR3),

SEQ ID NO: 125 (VL),

SEQ ID NO: 126 (VL CDR1),

SEQ ID NO: 127 (VL CDR2),

SEQ ID NO: 128 (VL CDR3)

(5) 053-085 antibody
SEQ ID NO: 129 (VH),

SEQ ID NO: 130 (VH CDR1),

SEQ ID NO: 131 (VH CDR2),

SEQ ID NO: 132 (VH CDR3),

SEQ ID NO: 133 (VL),

SEQ ID NO: 134 (VL CDR1),

SEQ ID NO: 135 (VL CDR2),

SEQ ID NO: 136 (VL CDR3)

<Antibodies belonging to group 6>
(1) 035-234 antibody
SEQ ID NO: 137 (VH),

SEQ ID NO: 138 (VH CDR1),

SEQ ID NO: 139 (VH CDR2),

SEQ ID NO: 140 (VH CDR3),

SEQ ID NO: 141 (VL),

SEQ ID NO: 142 (VL CDR1),

SEQ ID NO: 143 (VL CDR2),

SEQ ID NO: 144 (VL CDR3)

(2) 040-107 antibody
SEQ ID NO: 145 (VH),

SEQ ID NO: 146 (VH CDR1),

SEQ ID NO: 147 (VH CDR2),

SEQ ID NO: 148 (VH CDR3),

SEQ ID NO: 149 (VL),

SEQ ID NO: 150 (VL CDR1),

SEQ ID NO: 151 (VL CDR2),

SEQ ID NO: 152 (VL CDR3)

(3) 041-118 antibody
SEQ ID NO: 153 (VH),

SEQ ID NO: 154 (VH CDR1),

SEQ ID NO: 155 (VH CDR2),

SEQ ID NO: 156 (VH CDR3),

SEQ ID NO: 157 (VL),

SEQ ID NO: 158 (VL CDR1),

-continued

SEQ ID NO: 159 (VL CDR2),

SEQ ID NO: 160 (VLCDR3)

(4) 066-174 antibody
SEQ ID NO: 161 (VH),

SEQ ID NO: 162 (VH CDR1),

SEQ ID NO: 163 (VH CDR2),

SEQ ID NO: 164 (VH CDR3),

SEQ ID NO: 165 (VL),

SEQ ID NO: 166 (VL CDR1),

SEQ ID NO: 167 (VL CDR2),

SEQ ID NO: 168 (VLCDR3)

(5) 083-040 antibody
SEQ ID NO: 169 (VH),

SEQ ID NO: 170 (VH CDR1),

SEQ ID NO: 171 (VH CDR2),

SEQ ID NO: 172 (VH CDR3),

SEQ ID NO: 173 (VL),

SEQ ID NO: 174 (VL CDR1),

SEQ ID NO: 175 (VL CDR2),

SEQ ID NO: 176 (VL CDR3)

<<Antibody belonging to group 7>
(1) 059-053 antibody
SEQ ID NO: 177 (VH),

SEQ ID NO: 178 (VH CDR1),

SEQ ID NO: 179 (VH CDR2),

SEQ ID NO: 180 (VH CDR3),

SEQ ID NO: 181 (VL),

SEQ ID NO: 182 (VL CDR1),

SEQ ID NO: 183 (VL CDR2),

SEQ ID NO: 184 (VL CDR3)

10. Confirmation of Antigen by RNAi and Immunostaining

[0832] In order to reconfirm that the isolated antibodies recognize the identified antigen, double stranded oligo RNA was allowed to act on cells so as to carry out antigen gene knockdown. Thus, the immunostaining property of the antibody identified by the isolated antigen with respect to the cell was examined.

[0833] Firstly, cells were cultured in a 6-well culture dish to about 30% confluent. To this, a mixture including Lipofectamin 2000 (5 μl) (Invitrogen) and the following oligo RNA (100 pmol) was acted. At day 2, cells were peeled off by using collagenase and recovered. To this, cp3 type purified antibody for verification was acted at the concentration of 5 μg/ml. After washing, a rabbit anti-cp3 antibody was acted at the concentration of 2 μg/ml. After washing, Alexa488

labeled anti-rabbit IgG was acted at 2 μg/ml. This was washed and then immobilized in OptiLyse (NOTECH) (50 μl) for ten minutes. This was diluted by adding 1 ml of PBS and this was measured by using FACS Caliver (Beckmann). As the antibody reaction solution and washing solution, 2.5% BSA/PBS solution was used.

[0834] Subject antigen: CD147

[0835] Sequence of the used oligo RNA:

CAGAGCUACACAUUGAGAACCUGAA (SEQ ID NO: 441)

[0836] Subject cell: clear cell renal cell carcinoma CCFRC1 cell

[0837] Verified antibody: 059-053 cp3 antibody

[0838] Subject antigen: CD166

[0839] Sequence of the used oligo RNA:

UACCUAUGUGCAGAGGAAUUAUGAU (SEQ ID NO: 442)

[0840] Subject cell: clear cell renal cell carcinoma CCFRC1 cell

[0841] Verified antibody: 035-234 cp3 antibody

[0842] Subject antigen: CD166

[0843] Sequence of the used oligo RNA:

GCAACCAUCUAAACCUGAAAUUGUA (SEQ ID NO: 443)

[0844] Subject cell: hepatic cell carcinoma HLF cell

[0845] Verified antibody: 048-006 cp3 antibody

[0846] Subject antigen: HER2

[0847] Sequence of the used oligo RNA:

UAAUAGAGGUUGUCGAAGGCUGGGC (SEQ ID NO: 444)

[0848] Subject cell: ovarian cancer SKOv-3 cell

[0849] Verified antibody: 015-126 cp3 antibody

[0850] Subject antigen: IgSF4

[0851] Sequence of the used oligo RNA:

CCCAACAGGCAGACCAUUUAUUUCA (SEQ ID NO: 445)

[0852] Subject cell: hepatic cell carcinoma HLF cell

[0853] Verified antibody: 035-273 cp3 antibody Results are shown in FIGS. **19** to **23**. FIG. **19** shows the results of RNAi in which CD147 is a subject antigen. FIG. **20** shows the results of RNAi in which CD166 is a subject antigen. FIG. **21** shows the results of RNAi in which HER1 is a subject antigen. FIG. **22** shows the results of RNAi in which HER2 is a subject antigen. FIG. **23** shows the results of RNAi in which IgSF4 is a subject antigen. As is apparent from these results, in any of the verified antibodies, in the cell population that had been subjected to RNAi, as compared with the cell population that had not been subjected to RNAi, the staining property by antibodies (i.e., reactivity) was significantly reduced. In this way, by RNAi experiment using oligo RNA for knocking down the corresponding antigen it is reconfirmed again that each of the isolated antibodies recognizes the identified antigen.

11. Investigation of Reactivity of Each Antibody by Cell Staining and Tissue Staining

11-1 Experiment Method

(1) Cell Staining

[0854] Cells were dissociated from a culture dish by using 2 mg/ml collagenase I (Gibco BRL)/cell dissociation buffer (Gibco BRL), then collected by using 10% FBS/DMEM, and 1×10^5 of the cells were used. These were washed with 2.5% BSA, 0.05% NaN_3/PBS (BSA solution), then suspended in 100 μl of 2.5% normal goat serum/BSA solution and left on ice for 30 minutes. Thereafter, cp3 type antibodies were added so that the concentration was 5 Hg/ml and left on ice for one hour. This was washed with a BSA solution once, then suspended in 100 μl of 5 μg/ml BSA solution of anti-cp3 mouse monoclonal antibody (Medical & Biological Laboratories Co., Ltd.) and left on ice for one hour. This was washed with a BSA solution once, then suspended in 1001i of 5 μg/ml BSA solution of ALEXA488 binding anti-mouse IgG goat antibody (Molecularprobe), and left on ice for one hour. This was washed with BSA solution twice, and then supernatant was discarded. To this, 5011 of OptiLyse B (BECKMAN COULTER) was added and left at room temperature for ten minutes so as to fix the cells. To this, 950 μl of 1 ng DAPI/BSA solution was added, left at room temperature for 10 minutes, and subjected to centrifugation for collecting cells. The cells were mounted on MULTITEST SLIDE (ICN) and observed under microscopy.

(2) Tissue Staining

(2-1) Preparation of Antibody Sample

[0855] *E. coli* solution cultured overnight (0.5 ml) was planted in 6 ml of 2×YTAI (2×YT, 200 μg/ml ampicillin sulfate, 0.5 mM IPTG), cultured overnight at 30° C. and centrifuged at 10000 rpm for 5 minutes by using a microcentrifugal machine, and supernatant was recovered. To this, an equal amount of saturated ammonium sulfate was added and left at room temperature for 30 minutes. Then, it was centrifuged at room temperature at 10000 rpm for 5 minutes and supernatant was discarded. The obtained precipitates were suspended in 0.6 ml of PBS-0.05% NaN_3, complete solution and centrifuged at 4° C. at 15000 rpm for 5 minutes, and supernatant was recovered.

(2) Production of Section

[0856] The extracted tissue was cut into about 5 mm×5 mm×10 mm, placed in 4% PFA/0.01% glutaraldehyde/0.1 Mcacodylic acid buffer (4° C.) (PFA is a product by Wako Pure Chemical Institute, glutaraldehyde is a product by KANTO CHEMICAL CO., INC., sodium cacodylate is a product by SIGMA). By using a microwave oven (SHARP), it was microwave-fixed. Then, it was fixed again in this fixation solution at 4° C. for one hour. Then, it was transferred into 10% sucrose/PBS and immersed therein at 4° C. for four hours, then substituted by 15% sucrose/PBS and immersed therein at 4° C. for four hours, and then substituted by 20% sucrose/PBS and immersed at one night. It was embedded in an OTC compound and rapidly frozen in dry ice/hexane. This was thinly cut into 4 μm thickness by using cryostat (Reichert-Jung 2800 FRIGCUT E), attached to silane coated slide glass (MATSUNAMI) and dried by using a cold wind drier for 30 minutes.

(2-3) Staining

[0857] The slide glass to which a section was attached was immersed in PBS three times for five minutes each so as to make hydrophilic. Next, 50 μl of 0.3% H_2O_2/0.1% NaN_3 was

dropped so as to cause a reaction at room temperature for ten minutes and blocking of endogenous peroxidase was carried out. Then, it was washed with PBS three times for five minutes each. Then, it was reacted in 2% BSA/PBS at room temperature for 10 minutes, and blocking of a non-specific reaction was carried out. Then, excess liquid was dropped off and 50 μl of antibody sample was dropped thereto so as to cause a reaction at room temperature for one hour, followed by washing with PBS three times for 5 minutes each. Next, 5011 of anti-CP3 rabbit antibody (5 μg/ml) was dropped to cause a secondary antibody reaction at room temperature for 45 minutes, followed by washing with PBS three times for 5 minutes each. Then, 50 μl of peroxidase labeled dextran binding anti-rabbit immunoglobulin-goat polyclonal antibody (DAKO) was dropped so as to cause a tertiary antibody reaction. This was washed with PBS three times for 5 minutes each, and the 50 μl of DAB-H_2O coloring solution was dropped. After the color became brown, this was transferred to a vat filled with distilled water so as to terminate the reaction. Thereafter, obtained product was washed with water for 10 minutes, followed by staining nuclear with hematoxylin. Thereafter, dehydration and penetration were carried out, encapsulation with marinol and observation under microscopy were carried out.

11-2 Experiment Results

(1) Anti-HER1 Antibody Group (Group 1)

[0858] Cancers showing positive in the cell line staining (containing FACS):

[0859] pancreatic cancer cell line PANC-1, kidney cancer cell line CCFRC1, kidney cancer cell line Caki-1, ovarian cancer cell line KF28, stomach cancer cell line SNU-5, lung squamous cell carcinoma line RERF-LC-AI, ovarian cancer cell line RMG-1, undifferentiated hepatic cell carcinoma cell line HLF, ovarian cancer cell line SKOv3, pulmonary adenocarcinoma cell line PCI4, kidney cancer cell line ACHN, lung squamous cell carcinoma line EBC1, vulva mucosal epithelial cell line A431, pulmonary adenocarcinoma cell line H1373, hepatic cell carcinoma cell line HepG2, cell line established from kidney clinical specimen

[0860] Cancers showing negative in the cell line staining (containing FACS):

[0861] breast cancer cell line BT474, hamster ovarian cancer cell line CHO

[0862] Cancers showing positive in the tissue staining:

[0863] kidney cancer, hepatic cell carcinoma, intrahepatic bile duct cancer, lung squamous cell cancer, pulmonary adenocarcinoma, pancreas cancer

(2) Anti-HER2 Antibody Group (Group 2)

[0864] Cancers showing positive in the cell line staining (containing FACS):

[0865] pulmonary adenocarcinoma cell line Calu-3, ovarian cancer cell line SKOv3, breast cancer cell line BT474

[0866] Cancers showing negative in the cell line staining (containing FACS):

[0867] hepatic cell carcinoma cell line. HLF, pulmonary adenocarcinoma cell line PC14, kidney cancer cell line ACHN, kidney cancer cell line 293T, hamster ovarian cancer cell line CHO, kidney cancer cell line Caki-1, kidney and stomach cancer cell line CCFRC1, cell line established from kidney clinical specimen

(3) Anti-CD46 Antibody Group

[0868] Cancers showing positive in the cell line staining (containing FACS):

[0869] large bowel cancer cell line CaCo2, stomach cancer cell line MKN45, undifferentiated hepatic cell carcinoma cell line HLF, liver cancer cell line HepG2, intrahepatic bile duct cell cancer cell line RBE, pancreas cancer cell line PANC1, kidney cancer cell line CCFRC1, kidney cancer cell line Caki-1, pulmonary adenocarcinoma cell line NCI-H441, lung squamous cell cancer EBC1, stomach cancer cell line NCI-N87, stomach cancer cell line SNU-5, lung squamous cell carcinoma line RERF-LC-AI, hepatic cell carcinoma clinical specimen, breast cancer cell line BT474, kidney cancer cell line 293T, pulmonary adenocarcinoma cell line PC14, kidney cancer cell line ACHN, pulmonary adenocarcinoma cell line H1373

[0870] Cancers showing negative in the cell line staining (containing FACS):

[0871] hamster ovarian cancer cell line CHO, vulva mucosal epithelial cell line A431

[0872] Cancers showing positive in the tissue staining:

[0873] kidney cancer, hepatic cell carcinoma, intrahepatic bile duct cancer, pulmonary adenocarcinoma, pancreas cancer

[0874] Specific expression of CD46 in intrahepatic bile duct cancer and pancreas cancer, which had not been particularly reported about the relationship with respect to CD46 was recognized.

(4) Anti-ITGA3 Antibody Group (Group 4)

[0875] Cancers showing positive in the cell line staining (containing FACS):

[0876] undifferentiated hepatic cell carcinoma cell line HLF, ovarian cancer cell line SKOv3, kidney cancer cell line ACHN, kidney cancer cell line Caki-1, pulmonary adenocarcinoma cell line H1373, lung squamous cell cancer EBC1, vulva mucosal epithelial cell line A431, breast cancer cell line BT474, pulmonary adenocarcinoma cell line PCI4, kidney cancer cell line CCFRC1, hepatic cell carcinoma cell line OCTH, intrahepatic bile duct cell cancer cell line RBE, pancreas cancer cell line PANC-1, pancreas cancer cell line MIA-Paca2, pulmonary adenocarcinoma cell line A549, pulmonary adenocarcinoma cell line NCI-N441, pulmonary adenocarcinoma cell line Calu-3, lung squamous cell carcinoma line RERF-LC-AI, stomach cancer cell line SNU5, stomach cancer cell line MKN45, stomach cancer cell line NCI-N87, large bowel cancer cell line CW2, ovarian cancer cell line SKOv3, ovarian cancer cell line KF-28, ovarian cancer cell line RMG-1, ovarian cancer cell line RMG-2

[0877] Cancers showing negative in the cell line staining (containing FACS):

[0878] kidney cancer cell line 293T, hepatic cell carcinoma cell line HepG2, hamster ovarian cancer cell line CHO

[0879] Cancers showing positive in the tissue staining:

[0880] intrahepatic bile duct cancer, pancreas cancer

[0881] Specific expression of ITGA3 in gallbladder and liver cancer and pancreas cancer, which had not been particularly reported about the relationship with respect to ITGA3 was recognized.

(5) Anti-ICAM I Antibody Group (Group 5)

[0882] Cancers showing positive in the cell line staining (containing FACS):

[0883] Liver cancer cell line HepG2, pulmonary adenocarcinoma cell line PC14, cell line established from kidney clinical specimen

[0884] Cancers showing negative in the cell line staining (containing FACS):

[0885] undifferentiated hepatic cell carcinoma cell line HLF, ovarian cancer cell line SKOv3, breast cancer cell line BT474, kidney cancer cell line 293T, kidney cancer cell line ACHN, kidney cancer cell line Caki-1, pulmonary adenocarcinoma cell line PC 14, kidney cancer cell line CCFRC1, hamster ovarian cancer cell line CHO

[0886] Cancers showing positive in the tissue staining:

[0887] hepatic cell carcinoma

(6) Anti-ALCAM Antibody Group (Group 6)

[0888] Cancers showing positive in the cell line staining (containing FACS):

[0889] Liver cancer cell line HepG2, OCTH, Hep3B, and HLF, kidney cancer cell line Caki-1, CCFRC1, ACHN, 293T, and cell line established from clinical specimen, lung cancer cell line PC14, NCI-H441, EBC-1, RERF-LC-AI, A549, and H1373, ovarian cancer cell line SKOv3, KF-28, RMG1, and RMG2, stomach cancer cell line NCI-N87, large bowel cancer cell line CW2, breast cancer cell line BT474, acute myelocytic leukemia AMLclinical specimen, hamster ovarian cancer cell line CHO

[0890] Cancers showing negative in the cell line staining (containing FACS):

[0891] vulva mucosal epithelial cell line A431

[0892] Cancers showing positive in the tissue staining:

[0893] kidney cancer, hepatic cell carcinoma, intrahepatic bile duct cancer, lung squamous cell cancer, alveolar cell carcinoma, adenocarcinoma

[0894] Specific expression of ALCAM in kidney cancer, hepatic cell carcinoma, and gallbladder and liver cancer, which had not been particularly reported about the relationship with respect to ALCAM was recognized.

(7) Anti-CD147 Antibody Group (Group 7)

[0895] Cancers showing positive in the cell line staining (containing FACS):

[0896] liver cancer cell line HepG2, kidney cancer cell line CCFRC1, kidney cancer cell line ACHN, kidney cancer cell line Caki-1, pulmonary adenocarcinoma PCI4, cell line established from kidney cancer clinical specimen

[0897] Cancers showing negative in the cell line staining (containing FACS):

[0898] hamster ovarian cancer cell line CHO

[0899] Cancers showing positive in the tissue staining:

[0900] kidney cancer

[0901] Specific expression of CD147 in kidney cancer, which had not been particularly reported about the relationship with respect to CD147 was recognized.

12. Conversion into IgG Type Antibody

12-1 Construction of IgG Type Antibody Gene

[0902] In order to investigate the efficacy as an antibody medicine, a part of antibodies is converted into IgG type

[0903] Firstly, by using VH and VL genes of scFVcp3 type antibody, it is confirmed that there was not a restriction enzyme site necessary for cloning them to Fc region of IgG1 and the base sequence of the gene. PCR was carried out by using an antibody gene as a template and using a primer for amplifying the H chain and L chain were used. The amplified product was ligated to the downstream of CMV promoter of the IgG1 construction vector and a plasmid DNA containing an IgG type antibody gene was obtained.

12-2 Expression of IgG Type Antibody

[0904] For transfection of plasmid DNA into CHO-K1 cell, GenePORTER Reagent (Gene Therapy Systems: T201007) was used. Firstly, CHO-K1 cells were prepared in a 60 mm-culture dish the day before the transfection so that they became 2×10^4 cells/ml (a medium, in which α-MEM (Invitrogen: 12561-056) to which 10% FCS (Equitech: 268-1) had been added, was used).

[0905] The plasmid DNA (8 μg) was dissolved in 250 μL of serum free medium (hereinafter, abbreviate as "SFM") (Invtrogen: 12052-098 CHO—S—SFMII)) and subjected to 0.22 μm filter. GenePORTER Reagent (40 μL) was added to SFM (250

[0906] The plasmid DNA and GenePORTER Reagent dissolved in SFM were rapidly stirred and stood still at room temperature for 30 minutes.

[0907] The cells were washed with SFM (2 ml) twice, and the plasmid DNA-GenePORTER mixture (Transfection Medium) was slowly poured in a plate containing cells and cultured in an incubator at 37° C. for five hours.

[0908] The medium for transfection was sucked and washed with αMEM 10% FCS twice, then 5 ml of αMEM 10% FCS was added, which was cultured in an incubator at 37° C. for 48 hours.

[0909] The medium was replaced by a medium (10 mL) of αMEM 10% FCS+700 μg/ml G418 (Sigma: G7034) and selection was started (hereinafter, as a medium, αMEM 110% FCS+700 μg/mL G418 was used). After cultured at 37° C. for 48 hours, cells were washed with PBS (10 mL), treated with 0.25% Trypsin-EDTA (Sigma T4049) (750 μL), αMEM (5 mL) was added. Then, cultured product was peeled off and recovered from the plate. The number of cells was measured. Based on the results, limiting dilution was carried out under the conditions of 10 cells/200 μL/well (two sheets of 96 well plates). After culturing for 14 days, ELISA was carried out by using a culture supernatant of each well and the expression of an IgG type antibody was confirmed.

12-3 Purification of Expression Protein (IgG) from Culture Supernatant

[0910] Protein G Sepharose 4 Fast Flow (amersham pharmacia biotech: 17-0618-01) (1 mL) was packed in a column and balanced in PBS (5 mL). The culture supernatant was applied, sent at the flow rate of 1 drop/2 seconds, and allowed the expressed protein (IgG) to be bonded to a column. PBS (10 mL) was sent at the flow rate of 1 drop/2 seconds, non-

adsorbed components were washed, then 6 mL of elute buffer (0.2M glycine-HCl, pH 3) was sent at the flow rate of 1 drop/second, and 1 mL each of eluate was collected in a 1.5 ml tube. To the collection tube, neutralizing buffer (3M Tris-HCl) (400 μL) was added in advance. Neutralization was carried out at the same time of collection. The eluate was collected and concentrated to 750 μL, and solution substitution (PBS, complete, 0.01% NaN_3) was carried out. Then, the concentration of the antibody protein was calculated by SDS-PAGE.

13. Experiment of Inhibition of Binding of EGF by Successfully Obtained Anti-HER1 Antibody (048-006 Antibody)

13-1 Experimental Procedure

[0911] A431 cells were cultured in 15ϕ culture dish (medium: DMEM containing 10% FBS and 1% PS), and the cells were peeled off with the use of cell dissociation buffer (GIBCO: 13151-014) and recovered at 90% confluence. Two ml of PBS containing 1.0% BSA and 0.05% NaN_3 was added and the recovered cells were suspended. The suspension was stood still at 4° C. for 30 minutes and then 100 μl each (about 2.5×10^5 cells) was dispensed into each well of a 96-well V-bottom plate. It was centrifuged (650 G) for 2 minutes, and the cells were precipitated to remove the supernatant. Each antibody solution (HR1-007 [10 μg/ml], 48-006 [10 μg/ml, 5 μg/ml, 1 μg/ml], and 59-152 [10 μg/ml, 5 μg/ml, 1 μg/ml]) (200 μl), which had been prepared by using PBS containing 1.0% BSA, was added and the cells were suspended. The suspension was stood still at 4° C. for one hour, and then, biotin labeled EGF (biotinated EGF: 50 μg/ml) was added to each well so that the final concentration became 1 μg/ml, so that the cells were suspended. Note here that the biotinated EGF was produced by the following method. Firstly, to EGF (prepared to 1 mg/ml with PBS(−); AUSTRAL Biologicals: GF-010-5) (50 μl), EZ-Link Sulfo-NHS-LC-Biotin (prepared to 2 mg/ml with PBS(−); PIERCE: 21335) (25 μl) was added. After it was stood still at room temperature for 30 minutes, 1M glycine (pH=7.0 to 8.0) (10 μl) was added. After it was stood still at room temperature for 30 minutes, PBS(−) (15 μl) was added and stored at 4° C. (final concentration: 500 μg/ml). This was 10-fold diluted with PBS containing 1.0% BSA and used for experiment.

[0912] This was stood still at 4° C. for one hour, and centrifuged (650 G) for 2 minutes so as to remove the supernatant. PBS containing 1.0% BSA (180 μl) was added and centrifuged (650 G) for 2 minutes so as to remove the supernatant. HRP-labeled streptavidin (0.2 μg/ml (PBS containing 1.0% BSA); PIERCE: 21126) (100 μl) was added and cells were suspended at 4° C. for one hour, and centrifuged (650 G) for 2 minutes so as to remove the supernatant. PBS containing 1.0% BSA (180 μl) was added and centrifuged (650 G) for 2 minutes so as to remove the supernatant. This operation was carried out again. OPD (Wako: 154-01673) coloring solution (100 μl) was added and cells were suspended. After four minutes at room temperature, coloring stop solution ($2NH_2SO_4$) (100 μl) was added and centrifuged (650 G) for 2 minutes. Then, the supernatant was transferred to a flat-bottom plate. By using a plate reader, the absorbance at 192 nm (A492) was measured and represented by a numeric value.

13-2 Results

[0913] The results are shown in FIG. **24**. HR1-007 as a control does not affect the binding of EGF. 048-006 antibody and 059-152 antibody inhibit the binding of EGF. 048-006 antibody can inhibit the binding of EGF substantially completely while 059-152 antibody cannot completely inhibit the binding even if the temperature is increased. Note here that 048-006 antibody shows an inhibition effect even at the low level of about 0.02 μg/ml (FIG. **24**C).

[0914] The results suggest that the antagonism activity between each antibody (048-006 antibody and 059-152 antibody) and EGF provides a part of the pharmacological effect such as anti-tumor property.

14. Experiment of Phosphorylation Signal Inhibition of HER1 by Successfully Obtained Anti-HER1 Antibody (048-006 Antibody)

[0915] By using a phosphorylation antibody, it was determined whether or not the successfully obtained anti-HER1 antibody (048-006 antibody) inhibited the phosphorylation signal of HER1. Specifically, by using three kinds of cells (renal cell carcinoma (CCF-RC1, Caki-1) and epidermoid cancer (A431)), the inhibition effect of 048-006 antibody and 059-152 antibody and the inhibition effect of ERBITUX were compared with each other.

14-1 Experimental Procedure

[0916] Each of cells was cultured in 6-well culture dish, and at 60% confluence, a medium (DMEM containing 10% FBS and 1% PS) was substituted to DMEM. After 16 hours, each antibody (HR1-007, 048-006, 059-152 (prepared to 2 mg/ml with PBS(−))) and ERBITUX were added to each well so that the final concentration became 10 μg/ml or 1 μg/ml. After 30 minutes, EGF (prepared to 20 μg/ml with PBS(−)) was added to each well so that the final concentration became 1 μg/ml. After 30 minutes, each well was washed with PBS(−) and quickly frozen together with the culture dish by using liquid nitrogen. To each well, lysis buffer (50 mM Tris (pH 7.4), 150 mM NaCl, 1 mM Na_3VO4, 10 mM NaF, 1% Triton×100, complete (Roche: 11836145001)) were added, and the cells were suspended and transferred to centrifugation tube. Centrifugation (10000G) was carried out for 10 minutes so as to precipitate cell debris. A part of the supernatant was subjected to SDS-PAGE, which was transferred to a membrane. Western blotting using an anti-phosphorylation tyrosine antibody (11 g/ml; upstate: 05-321) or an anti-β-actin antibody (1 μg/ml; abcam: ab25139) as a primary antibody, and a secondary antibody reaction: HRP labeled anti-mouse IgG as a secondary antibody was carried out. A431 cells were required to be exposed to light for 1 to 2 seconds; CCF-RC1 for 10 seconds; and Caki-1 for one minute (there was originally large difference in cell sensitivity to external stimulation).

14-2 Results

[0917] The results are shown in FIG. **25** (A and B: the results of Western blotting using A431 cells; C to E: comparison effect of inhibiting HER1 phosphorylation signal between the successfully obtained antibody and ERBITUX). In CCF-RC1 and A-431 cell lines, HR1-007 as a control does not affect the phosphorylation signal of HER1. However, 048-006 antibody and 059-152 antibody inhibit signal in a concentration-dependent manner. 048-006 antibody can inhibits the binding of EGF substantially completely and also inhibit self phosphorylation of HER1 substantially completely. 059-152 antibody inhibits the binding of EGF about 50%. Furthermore, 059-152 antibody inhibits self phospho-

rylation of HER1 although it is weaker than 048-006 antibody. 048-006 antibody and 059-152 antibody have inhibition capabilities superior to that by ERBITUX. In particular, the inhibition capability of 048-006 antibody is remarkable.

[0918] The sensitivity to external stimulation by EGF differs depending upon the kinds of cells. Therefore, when a cell like Caki-1 that does not show sensitivity to external stimulation by EGF is used, the difference in signal inhibition effect by the antibody is not observed.

[0919] The results suggest that each antibody (048-006 antibody and 059-152 antibody) has an activity of suppress the tyrosine kinase circuit of HER1 with respect to sensitive cells of HER1 by EGF, and exhibits pharmacological effects such as proliferation suppression and anti-tumor property.

15. Measurement of Binding Constant by BIAcore

[0920] As to the successfully obtained antibodies 048-006 and 059-152, the dissociation constant with respect to the expression Her1 was measured.

15-1 Experimental Procedure

(1) Forced Expression of Partial Sequence of Her1

[0921] A sequence from a region after the signal of HER1 to immediately before the transmembrane region (621 amino acid of the expression sites from positions 26 to 645 (SEQ ID NO: 943) was cloned. For cloning and expression, a pSecTagII vector (Invitrogen) was used. When this vector is inserted, myc and his tags are added.

(2) Recovering of Expressed Cells

[0922] One 15φ-culture dish (80 confluent) in which 293T cells were cultured was prepared. The medium was replaced with new one so that cells were not peeled off, and then cultured. Thus, a state in which cells were aggregated at 90-100% confluence was formed. The day before recovering cells, final medium replacement was carried out. DNA (75 μl) was added to D-MEM (serum free) (1.9 ml) and subjected to tapping adjustment so as to make the solution A. Furthermore, Lipo (75 μl) was added to D-MEM (serum free) (1.9 ml) and subjected to tapping adjustment (50 ml, Falcon) so as to make the solution B.

[0923] One minute after the formation of the solution B, the solution B was added to the solution A by using a 5 ml-pipette, subjected to pipetting, and incubated at room temperature for 20 minutes. 22.5 ml of D-MEM (serum free) was measured and taken out into a 50 ml culture container (Falcon) and 2.5 ml of serum was added thereto, which was incubated at 37° C. for 15 minutes so as to obtain D-MEM (containing serum).

[0924] The medium was removed from a 15φ-culture dish in which 293T cells were aggregated, and D-MEM (serum free) (25 ml) was added along the wall of the dish carefully so that cells are not peeled off. The added D-MEM (serum free) was sucked by using an aspirator and D-MEM (containing serum) (25 ml) was added. Twenty minutes after D-MEM (containing serum) was formed, the mixture solution (3.8 ml) of solution A and solution B was added to the cells by using 25 ml-pipette and the cells were peeled off. The cells were separated from each other by pipetting, the cells were stood still in a CO_2 incubator for 2 days. Two days after, the supernatant was recovered and subjected to protein purification.

(3) Secretory Protein Purification (Ni-NTA)

[0925] Ni-NTA agarose gel (QIAGEN) (2 ml) (bed volume of 1 ml) was packed in a column and balanced in PBS. Then, the culture supernatant recovered in (2) was applied thereto. A flow-through solution was again applied to a column. The column was washed with 5 ml of PBS, and eluted in stages with 20, 50, 100, 250, and 500 mM imidazole/PBS (5 ml each) so that the absorbance (280 nm)<0.005 was satisfied. Furthermore, it was eluted with 0.5M EDTA/PBS (10 ml). The solution was replaced by new one by dialysis so as to obtain BIAcore immobilized sample.

(4) BIAcore Measurement

[0926] The interaction between the antibody clone and the expressed Her1 was examined so as to determine KD (dissociation constant; kd/ka). For analysis, BIAcore 1000 biosensor device was used.

[0927] A carboxymethyldextran (Sensor Chip CM5, Research grade, BIACORE) sensor chip was used. With the electrostatic adsorption to a CM5 matrix and a covalent linkage between a lysyl group on CM5 and an activated carboxyl group, antigen (Her1) was immobilized on the chip. By EDC/NHS coupling chemical reaction, a carboxyl group was activated.

[0928] In the condition of HBS-EP (BIACORE) at a flow rate of 5 μL/minute by using EDC/NHS (amine coupling kit, BIACORE was mixed with equal amount of EDC and NHS), after the lysyl group on CM5 was activated (contact time: 2.4 minutes), chip was washed with HBS-EP (BIACORE). Subsequently, Her1 (20 μg/mL: Sigma, 0.6 mg protein/ml was diluted with 10 mM acetic acid (pH 4.0)) was added to the chip. The chip was washed with HBS-EP, then, 1M ethanolamine (pH 8.5) was added so as to deactivate the remaining activated carboxyl group. Thereafter, the chip was washed with 50 mM NaOH so as to remove all Her1 that were not linked covalently. Note here that all the analysis experiments were carried out under the conditions of HBS-EP (BIACORE) at a flow rate of 35 μl/minute at 25° C. Reproduction was carried out by using 50 mM NaOH (one minute).

[0929] 059-152 antibody or 048-006 antibody were reacted at each concentration shown in the figure and HBS-EP at flow rate of 35 μl/minute, so that the binding constant was analyzed.

15-2 Results

[0930] The results are shown in FIG. **26**. 048-006 antibody shows extremely strong binding force of more than KD=10−11 (M) at every measurement point. The actual value of Global fitting based on each detection value was 4.8×10^{-13} (M). This is beyond the reliable measurement limit of BIAcore. As to 059-152 antibody, a bond dissociation curve cannot be detected. This is thought to be because this antibody cannot recognize the higher-order structure of artificially produced forced expression product. In other words, it is suggested that this antibody recognize a higher-order structure of a complex or a higher-order structure that can be observed only on an intact membrane.

16. Cytotoxicity test of anti-HER1 antibody, anti-HER2 antibody, anti-ITGA3 antibody, Anti-ALCAM Antibody, and Anti-ICAM Antibody (ADCC Activity Measurement)

[0931] Antibody-Dependent Cell-mediated Cytotoxicity (ADCC) is an immune reaction of killing and attacking cells

harmful to a human body, for example, virus infected cells, in which "effector cells" mainly consisting of natural-killer cell or monocyte attacks cells to which antibodies are bonded widely on the membrane surface as a target. The cytotoxicity by ADCC occurs depending upon the combination of an antibody specifically bonded to a surface of the cell membrane antigen and an effector cell.

[0932] Some of antibodies specifically bonded to a tumor surface antigen have an anti-tumor effect and a therapeutic effect to cancer and sold as antibody medicine. It has been reported that the main mechanism of action of these antibodies are ADCC. Then, in order to evaluate whether or not the cancer antigen specific antibodies successfully isolated by the present inventor have an anti-tumor effect, that is, they have promising as a cancer treatment antibody, the detection of ADCC was carried out. In the below-mentioned experiments, human IgG type antibody clone recognizing a subject antigen is reacted to a target cell to present it to an effector cell. In the detection of ADCC, the degree of cytotoxicity is calculated by using a cytotoxicity detection kit which, in principle, detects the enzymatic activity of lactate dehydrogenase leaking into the medium from the target cancer cell attached by the effector cell by using the coloring of the reagent.

16-1 Induction of ADCC I (Case of 015-003 Antibody as Anti-ITGA3 Antibody: scFVcp3 Type Antibody is Used)

[0933] Regarding 015-003 antibody as anti-ITGA3 antibody, a scFVcp3 type antibody was used and the ADCC activity was investigated by an assay combining an anti-M13 pIII rabbit antibody. Furthermore, liver cancer HLF cell is used as the target subject cultured cell. The operation procedure is described below.

[0934] (1) By the following procedures, peripheral blood is collected from a volunteer and mononucleosis is separated. Firstly, heparin-added peripheral blood (30 ml) collected from a volunteer is diluted with PBS to 80 ml and superposed quietly on 10 ml each of lymphocyte isolation reagent Ficoll Paque Plus (Amersham Bioscience), which have been dispensed in four centrifugation tubes, and centrifuged (400×g, 20° C. for 40 minutes). The mononucleosis fractions (including lymphocyte and monocyte) are recovered, diluted with cooled PBS to 80 ml and centrifuged (200×g, 4° C. for 15 minutes).

[0935] (2) (1) is suspended in a cooled cytotoxicity test medium (Cytotoxic Medium, hereinafter, abbreviated as "CTM", RPMI-1640 medium, 1% (v/v) fetal calf serum, 1% (v/v) Penicillin-Streptomycin Solution, 1% (v/v) 1M HEPES buffer (pH 7.0): Invitrogen) so that the final density becomes 5.0×10^6 cells/ml to obtain an effector cell.

[0936] (3) In a culture dish having a diameter of 150 mm, a target subject cultured cell is grown in a culture medium I (Minimum Essential Medium Alpha Medium:Invitrogen, 10% (v/v) fetal calf serum: Equitic-Bio, 1% (v/v) Penicillin-Streptomycin Solution Sigma-Aldrich). A liquid medium is removed and cells are washed with PBS (10 ml) twice so as to remove the solution. Thereafter, 4% (w/v) collagenase Type IV (Invitrogen) (5 ml) is added and stored keeping warm at 37° C. for 10 minutes, so that cells are peeled off from the culture dish. Furthermore, 5 ml of liquid medium 2 (RPMI-1640, 10% (v/v) fetal calf serum, 1% (v/v) Penicillin—Streptomycin Solution:Sigma-Aldrich) (RPMI-1640: Sigma-Aldrich, 10% fetal calf serum, 1% penicillin-streptomycin solution) is added to stop a collagenase reaction. Then, suspended cells are recovered to obtain cell suspension.

(4) The cell density of the cell suspension of (3) is measured. The supernatant is removed by centrifugation and the cells are suspended in a cooled CTM medium so that the final density becomes 1.5×10^5 cells/ml.

(5) 100 μl each of target cells is dispensed in a 96-well V-bottom multi plate on ice.

(6) 2 μg/ml scFv-pIII phage antibody-CTM solution (100 μl each) is dispensed and reacted on ice for 60 minutes.

(7) Centrifugation (Swing rotor: 500×g, 4° C. for 10 min) is carried out to remove the supernatant.

(8) Cell pellet is suspended in 5 μg/ml anti-M13 pill rabbit polyclonal antibody-CTM solution (150 μl each), a part of 100 μl is transferred to a 96-well U-bottom multi plate.

(9) The effector cell of (2) (or 2% Triton X-100-CTM solution) is added and then centrifuged (Swing rotor: 50×g, 4° C. for 5 min).

(10) Reaction is carried out in 5% CO_2 at 37° C. for 4 hours.

(11) After the reaction, centrifugation (Swing rotor: 500×g, 4° C. for 10 min) is carried out and the supernatant (100 μl) is transferred to a flat-bottom 96 well multi plate.

(12) LDH activity measurement reagent (Roche) (100 μl) is added and reaction is carried out at room temperature for 30 min.

(13) OD490 and OD690 are measured by using a micro plate absorptiometer.

16-2 Induction of ADCC 2 (case of 048-006 antibody as anti-HER1 antibody, 015-126 antibody as anti-HER2 antibody, 066-174 antibody, 035-234 antibody and 041-118 antibody as anti-ALCAM antibody, 053-051 antibody, 053-059 antibody and 053-085 antibody as anti-ICAM1 antibody, 067-153 antibody as anti-EpCAM antibody, 067-133 antibody as anti-HGFR antibody: IgG type antibody is used)

[0937] Regarding 048-006 antibody as anti-HER1 antibody, an IgG type antibody was used and the ADCC activity was investigated. A-431 and A549 (epidermoid tumor), ACHN and CCF-RC-1 (kidney cancer), NCI-H1373 (lung cancer), as well as SK-OV-3 (ovarian cancer) were used as the target subject cultured cell.

[0938] Also regarding 015-126 antibody as anti-HER2 antibody, an IgG type antibody was used, and the ADCC activity was investigated. Breast cancer BT-474 was used as the target subject cultured cell.

[0939] Regarding 066-174 antibody and 035-234 antibody as anti-ALCAM antibody, an IgG type antibody was used, and the ADCC activity was investigated. NCI-H1373 (pulmonary adenocarcinoma), CW2 (large bowel cancer), or NCI-H441 (lung cancer) was used as the target subject cultured cell.

[0940] Regarding 053-051 antibody, 053-059 antibody and 053-085 antibody as anti-ICAM1 antibody, an IgG type antibody was used, and the ADCC activity was investigated. HepG2 (hepatic cell carcinoma) and NCI-H441 (lung cancer) were used as the target subject cultured cell.

[0941] Furthermore, regarding the effect of 048-006 antibody or 059-152 antibody as anti-HER1 antibody on CCF-RC-1 (kidney cancer), NCI-H1373 (lung cancer) and A-431 (epidermoid cancer), the antibody dosage dependence of the ADCC activity was investigated so that the final concentration of the IgG type antibody was in the range from 0.01 to 10 μg/ml.

[0942] Regarding 041-118 antibody as anti-ALCAM antibody, an IgG type antibody was used and the antibody dosage dependence of the ADCC activity was investigated. NCI-H1373 (pulmonary adenocarcinoma) was used as the target subject cultured cell.

[0943] Regarding 067-153 antibody as anti-EpCAM antibody, an IgG type antibody was used and the antibody dosage dependence of the ADCC activity was investigated. MKN-45 (solid-type gastric adenocarcinoma), HT-29 (colon adenocarcinoma) and NCI-H1373 (lung cancer) were used as the target subject cultured cell.

[0944] Regarding 067-133 antibody as anti-HGFR antibody, an IgG type antibody was used and the antibody dosage dependence of the ADCC activity was investigated. NCI-H1373 (lung cancer) was used as antibody dosage dependence of the ADCC activity.

[0945] The antibody dosage dependence of the ADCC activity was basically measured at the E/T Ratio (ratio of effector cell:target cell) of 80:1 at final antibody concentration in the solution of 0.01 μg/ml to 10 μg/ml or 10^{-6} μg/ml to 10 μg/ml.

[0946] At each measurement point, the antibody and the effector cell were added to the target cell, and four hours later, the ADCC activity was measured. Regarding NCI-H1373, the ADCC activity was measured at the E/T Ratio of 100:1.

[0947] The operation procedure was carried out in accordance with the procedures described in 16-1. The detail of the reaction was made to be as follows. 66 μl/well of the target cells (2×10^4 cells) were placed in 96-well U-bottom plate (Becton Dickinson) and 66 μl of IgG type antibody (3 μg/ml) was added and then 66 μl of peripheral blood mononucleosis suspension (7.5×10^5 cells) was added. The E/T

[0948] Ratio (ratio of effector cell:target cell) was made to be 20. In order to promote the association of cells, centrifugation (60×g, 4° C., 5 minutes) so as to allow the cells to sink, which was stored keeping warm 240 minutes in a culture container that had been set to the conditions of 37° C. and 5% CO_2. Thus ADCC reaction was induced. Each antibody sample was prepared as a CTM solution. Furthermore, in each sample, CTM was used as a negative control and target cell to which 100 μl of 2% Triton X-100-CTM solution was added was used as a control of maximum liberation of lactate dehydrogenase (cells had been destroyed by Triton X-100 in advance). Furthermore, three wells were used for each experiment groups.

16-3 Measurement of ADCC Activity

[0949] In both the assay using a scFVcp3 type antibody and assay using an IgG type antibody, the ADCC activity was an indicator of the damage to the target cell, which is in proportion to the degree of coloring, that is, the concentration of lactate dehydrogenase liberating to the culture supernatant. Thirty minutes after the coloring starts, absorbance (OD490-OD620 (background absorbance)) was measured by using a spectrophotometer. In each experiment group, absorbance values in the three wells were averaged to calculate the cytotoxic Index. In advance, the absorbance of only a medium was subtracted and the calculation was carried out by the following calculation equation.

Relative LDH activity=OD490−OD690

LDH activity derived from cell=experimental value−(control containing only solution)

Cytotoxicity (%)=(experimental value−effector cell control−target cell control)/(cell+Triton X-100 control−target cell control)×100 [Equation 1]

[0950] Note here that when the antibody does not have any cytotoxic activity, the cytotoxicity calculated by this method may be minus value due to a measurement error because the measurement is carried in experiments using the living body components.

16-4 Measurement Result

[0951] The measurement results of the ADCC activity are shown in FIG. **27** (anti-ITGA3 antibody was used; the target culture cell was HLF), FIG. **28** (anti-HER1 antibody was used; the target culture cell was A-431), FIG. **29** (anti-HER1 antibody was used; the target culture cell was A549), FIG. **30** (anti-HER1 antibody was used; the target culture cell was ACHN), FIG. **31** (anti-HER1 antibody was used; the target culture cell was CCF-RC-1), FIG. **32** (anti-HER1 antibody was used; the target culture cell was NCI-H1373), FIG. **33** (anti-HER1 antibody was used; the target culture cell was SK-OV-3), FIG. **34** (anti-HER2 antibody was used; the target culture cell was BT-474), FIG. **35** (066-174 as anti-ALCAM antibody was used; the target culture cell was NCI-H1373, CW2, or NCI-H441), FIG. **36** (035-234 as anti-ALCAM antibody was used; the target culture cell was CW2 or NCI-H441), FIG. **37** (053-051 as anti-ICAM1 antibody was used; the target culture cell was NCI-H441 and HepG2), FIG. **38** (053-059 as anti-ICAM1 antibody was used; the target culture cell was NCI-H441 and HepG2), and FIG. **39** (053-085 as anti-ICAM1 antibody was used; the target culture cell was NCI-H441 and HepG2). I

[0952] The measurement results of the antibody dosage dependence of the ADCC activity are shown in FIG. **40** (048-006 or 059-152 antibody as anti-HER I antibody was used; the target culture cell was CCF-RC-1), FIG. **41** (048-006 or 059-152 antibody as anti-HER1 antibody was used; the target culture cell was NCI-H1373), FIG. **42** (048-006 or 059-152 antibody as anti-HER1 antibody was used; the target culture cell was A-431), FIG. **43** (041-118 antibody as anti-ALCAM antibody was used; the target culture cell was NCI-H1373), FIG. **44** (067-153 antibody as anti-EpCAM antibody was used; the target culture cell was MKN-45), FIG. **45** (067-153 antibody as anti-EpCAM antibody was used; the target culture cell was HT-29), FIG. **46** (067-153 antibody as anti-EpCAM antibody was used; the target culture cell was NCI-H1373), and FIG. **47** (067-133 antibody as anti-HGFR antibody was used; the target culture cell was NCI-H1373).

[0953] Similarly, the measurement results of the antibody dosage dependence of the ADCC activity are shown in FIG. **48** (055-147 antibody or 059-173 antibody as anti-HER1 antibody was used; the target culture cell was CCF-RC1), FIG. **49** (048-006 antibody, 059-152 antibody, 055-147 antibody or 059-173 antibody as anti-HER1 antibody was used; the target culture cell was HT-29), FIG. **50** (048-006 antibody, 055-147 antibody or 059-173 antibody as anti-HER1 antibody was used; the target culture cell was A431), FIG. **51** (048-006 antibody or 059-152 antibody as anti-HER1 antibody was used; the target culture cell was ACHN), FIG. **52** (035-234 antibody or 066-174 antibody as anti-ALCAM antibody was used; the target culture cell was NCI-H1373), FIG. **53** (035-234 antibody or 066-174 antibody as anti-ALCAM antibody was used; the target culture cell was target cell SKOv3), FIG. **54** (035-234 antibody or 066-174 antibody as anti-ALCAM antibody was used; the target culture cell was CW-2), FIG. **55** (041-118 antibody as anti-ALCAM antibody was used; the target culture cell was EBC-1), FIG. **56** (080-040 antibody as anti-ALCAM antibody was used; the target culture cell was NCI-H1373), FIG. **57** (053-042 antibody as anti-ICAM1 antibody was used; the target culture cell was

NCI-H1373), FIG. **58** (053-051 antibody, 053-059 antibody or 053-085 antibody as anti-ICAM I antibody was used; the target culture cell was NCI-H1373), FIG. **59** (067-153 antibody as anti-EpCAM antibody was used; the target culture cell was EBC-1), FIG. **60** (067-133 antibody as anti-HGFR antibody was used; the target culture cell was MKN-45), FIG. **61** (067-133 antibody as anti-HGFR antibody was used; the target culture cell was EBC-1), FIG. **62** (015-003 antibody as anti-ITGA3 antibody was used; the target culture cell was ACHN), FIG. **63** (059-053 antibody as anti-CD147 antibody was used; the target culture cell was CCF-RC1), FIG. **64** (059-053 antibody as anti-CD147 antibody was used; the target culture cell was ACHN), FIG. **65** (064-044 antibody or 079-085 antibody as anti-PTP-LAR antibody was used; the target culture cell was PC-14), and FIG. **66** (064-003 antibody as anti-CD44 antibody was used; the target culture cell was PC-14).

[0954] In any of anti-ITGA3 antibody (015-003), anti-HER1 antibody (048-006) and anti-HER2 antibody (015-126), anti-CD44 antibody (064-003), the cytotoxicity was increased in the experiment groups in which the effector cell was added. That is to say, in any of the antibodies, the cytotoxic activity caused by the effector cell that recognizes an antibody to which a target cell has been specifically-bound and attacks the target cell was observed.

[0955] Note here that an anti-habu venom antibody (control antibody) HR1-007 that is not related to the surface antigen or the experiment group in which the antibody clone is not added, the increase in the cytotoxicity is not observed. In any of anti-ALCAM antibodies (066-174, 035-234, 041-118, and 083-040), anti-ICAM1 antibody (053-051, 053-059, 053-085, and 053-042), and anti-CD147 antibody (059-053), the cytotoxicity is increased more significantly than in the anti-habu venom antibody (control antibody) HR1-007 experiment group. As mentioned above, it is clearly shown that the antibody dependent cytotoxicity is higher than that of the control antibody (HR1-007) with a significant difference.

[0956] From the above-mentioned results, it has been confirmed that an antibody capable of specifically recognizing a cancer cell and exhibiting a damaging effect by the ADCC activity has been obtained for each of HER1, HER2, ITGA3, ALCAM, ICAM, CD44, CD147, EPCAM and HGFR. In other words, an antibody that is a promising as the antibody medicine targeting each of cancer cells has been obtained.

[0957] In the results of the antibody dosage dependence test, anti-HER1 antibody (048-006) shows a significant effect even if the dosage is 0.01 μg/ml. It is determined that the effect is expected with low dosage.

[0958] It is observed that the 048-006 antibody and 059-152 antibody tend to have a strong ADCC activity in the cell line in which HER1 is expressed. However, the activity differs depending upon the concentration range of the antibody to be used or the kinds of antibodies. To A431 cell, with 0.001 Hg/ml, the difference in the activity was observed. Generally, in the low concentration range, the activity of 059-152 antibody was more significant than that of 048-006 antibody. Furthermore, 055-147 antibody and 059-173 antibody shows higher ADCC activity than ERBITUX™ that is commercially available drug and is more useful.

[0959] Furthermore, 067-153 antibody as anti-EpCAM antibody shows an excellent ADCC activity to MKN-45 (solid-type gastric adenocarcinoma) cell line at the concentration of 0.01 μg/ml or more, and it shows an excellent ADCC activity to HT-29 (colon adenocarcinoma) cell line at the concentration of 10 μg/ml or more with an amazing score of 80% or more in the ADCC activity in the concentration range of about 1 μg/ml. It shows an amazing score of 50% or more in the ADCC activity in NCI-H1373 (pulmonary adenocarcinoma) cell line at the concentration of 0.01 μg/ml or more.

[0960] Furthermore, 041-118 antibody as anti-ALCAM antibody shows a remarkable effect to NCI-H1373 (pulmonary adenocarcinoma) cell line at the concentration of 0.01 μg/ml or more. It is determined that the effect can be expected with low dosage.

[0961] Furthermore, 066-174 antibody as anti-ALCAM antibody shows high ADCC activity to various cells such as NCI-H1373 (pulmonary adenocarcinoma) cell line, SKOv3 (ovarian cancer) cell line, and CW-2 (large bowel cancer) cell line. Wide application is expected.

[0962] Furthermore, 067-133 antibody as anti-HGFR antibody shows a remarkable effect to NCI-H1373 (pulmonary adenocarcinoma) cell line at the concentration of 0.01 μg/ml or more with strong activity of 40% or more at the concentration of 10 μg/ml or more.

[0963] Furthermore, 059-053 antibody as anti-CD147 antibody shows an excellent ADCC effect to CCF-RC1 (kidney cancer) cell line and ACHN (kidney cancer) cell line, which shows near the upper limit value at the low concentration. Therefore, it can be expected to show the maximum activity at a low concentration.

[0964] From the above-mentioned results, it is confirmed that a promising antibody group showing a sufficient ADCC activity even with low dosage (at low concentration) can be obtained successfully. Also in the similar experiments using a plurality of lymphocyte fractions derived from human, the same results as mentioned above can be obtained. The high reproducibility is confirmed.

17. Cancer Cell Proliferation Inhibition Test

[0965] Some antibody medicines exhibit the efficacy by an effect of inhibiting the proliferation of cancer instead of the ADCC effect (or in addition to the ADCC effect). Thus, in order to further investigate the efficacy of antibody medicine, the activity of inhibiting the proliferation of cancer by antibodies that have been successfully isolated have been investigated according to the following procedure.

17-1 Testing Method

[0966] (1) Target culture cells that have grown in a culture dish are peeled off with 4% Collagenase and suspended in the used medium.

(2) The cell density is measured and then the supernatant is removed by centrifugation and suspended in a RPMI-1640 (10% FBS, 1% Penicillin—Streptomycin) medium so that the final density is 1.0×10^4 cells/ml.

(3) 100 μl each of target cells is dispensed in a flat-bottom 96 well multi plate.

(4) 100 μl each of 20 μg/ml human IgG monoclonal antibody solution is dispensed.

(5) Reaction is carried out in 5% CO_2 at 37° C. for 5 days.

(6) Medium is removed, and living cell measurement reagent (XTT: Roche) is dispensed in each well (150 μl each).

(7) Reaction is carried out in 5% CO_2 at 37° C. for 4 hours.

(8) After reaction, OD490 and OD690 are measured by using a micro plate absorptiometer. Then, the number of living cells is calculated according to the following equation.

XTT reduction amount (degree of coloring)=OD490−OD690

XTT reducing activity derived from cells=(experimental value)−(control value using only a solution) [Equation 2]

[0967] Note here that the XTT reducing activity derived from cells is in proportion to the number of living cells.

17-2 Results

[0968] The results are shown in FIG. **67** (anti-HER1 antibody (048-006) was used; the target subject cultured cell was A-431), FIG. **68** (anti-HER1 antibody (048-006) was used; the target subject cultured cell was ACHN), FIG. **69** (anti-HER1 antibody (048-006) was used; the target subject cultured cell was NCI-H1373), FIG. **70** (anti-HER1 antibody (048-006) was used; the target subject cultured cell wasSK-OV-3), and FIG. **71** (anti-HER2 antibody (015-126) was used; the target subject cultured cell was BT-474).

[0969] As is apparent from these drawings, it is confirmed that the antibodies inhibiting the proliferation of cancer cell can be successfully obtained. In other words, it is shown that these antibodies may be effective as antibody medicine of suppressing the proliferation of cancer cells.

18. Antitumor Experiment Using Mouse

[0970] Next, whether or not the antibodies that have been successfully isolated show an anti-tumor activity in vivo is confirmed by using a cancer cell-transplanted mouse.

18-1 Animals and Cell Line to be Used

[0971] Four-week old female BALB/c nude mouse (Charles River Japan) was acclimated and bred for one week and then used for experiment. The animals were bred under the SPF environment and fed with sterilized water and feed.

[0972] Human lung cancer cell H1373 or epidermoid tumor A-431, which had been subcultured in a RPMI medium containing 10% FBS at 37° C. in the presence of 5% CO_2, were used.

18-2 Method of Antitumor Experiment

[0973] Human lung cancer cells, H1373 cells (1×10^7 cells) were transplanted in the dorsolateral subcutaneous portion of a nude mouse so as to produce a tumor. At the time the tumor volume was 1 cm^3, the tumor was cut into a size of 3 mm×3 mm, and is was successive-transplanted to the dorsal subcutaneous portion of the prepared nude mouse. After transplantation, when a volume of the tumor was estimated to be 200 mm^3, administration of the antibody was started. The diameter of the tumor and body weight were measure twice a week, estimated tumor volume was calculated from the equation: $W=a\times b^2/2$ (W: estimated tumor volume (mm^3), a: major axis (mm), b: minor axis (mm)). The experiment group was divided into a control group (PBS was administered) and 048-006 IgG administered group (0.5 mg/individual). The administration pathway was made to be an intraperitoneal administration. Administration was carried out twice a week eight times in total. Then, the anti-tumor effect was examined.

[0974] Furthermore, ERBITUX (Cetuximab, Bristol-Myers Squibb Company) was used as a comparative group or an additivity examining group. When ERBITUX is used singly, the dosage amount was made to be 0.25 mg/individual. ERBITUX was used together with 048-006 IgG, the dosage amount of ERBITUX was made to be 0.25 mg/individual and the dosage amount of 048-006 IgG was made to be 0.25 mg/individual. After administration, the follow-up was carried out.

[0975] When epidermoid tumor A-431 is used, epidermoid tumors A-431 (5×10^6) were similarly transplanted in the dorsolateral subcutaneous portion of a five-week old female BALB/c nude mouse nude mouse so as to produce a tumor. At the time the tumor volume was estimated to be 200 mm^3, administration of the antibody was started. The administration pathway was made to be an intraperitoneal administration. 048-006 IgG type antibody was administered twice a week six times in total. Then, the anti-tumor effect was examined. 059-152 IgG type antibody administered group (0.25 mg or 1.00 mg of antibody was diluted in 0.5 ml PBS/individual) twice a week six times in total. Then, the anti-tumor effect was examined. And the follow up was also carried out.

18-3 Results

[0976] In the antibody (048-006 IgG type antibody) administered group, estimated tumor volume was significantly reduced as compared with the control group (PBS was administered), showing a clear anti-tumor effect. It was confirmed that the effect was comparative to ERBITUX (see FIGS. **72** to **75**). On the other hand, in the antibody (059-152 IgG type antibody) administered group, estimated tumor volume was significantly reduced as compared with the control group (PBS was administered), showing a clear anti-tumor effect. The effect was more excellent than that of ERBITUX (see FIG. **75**). 059-152 antibody shows stronger tumor suppression effect than 048-006 antibody and commercially available ERBITUX. Thus, it was confirmed that the successfully obtained antibodies exhibited the anti-tumor effect in also in vivo model. In other words, they are shown to be an extremely promising as the antibody medicine.

[0977] 19. Analysis by Three Dimensional ELISA

(1) Expression of Antibody by Culturing Screened Clone Group and Preparation of Antibody Mixture

[0978] Clones (about 4000 clones) of phage-infected *E. coli*, which were screened by the methods described in 1 to 5, were transferred to 41 sheets of 96-well plates at 1 clone/well, and they were shaking cultured in 100 μl/well YTGA medium (YT medium+1% Glucose+200 μg/ml Ampicillin) at 30° C. overnight. Next, 10 μl each of culture solution was mixed in all wells of the first to sixth columns for each plate to make one group (however, as to the 28th plate, the first to seventh columns are made to be one group). Forty-one plates of the mixed antibodies were obtained in total. As to 7th to 12th columns were also made into one group (excluding the 28th plate and 35th plate). Thirty-nine plates of the mixed antibodies in total were obtained. Furthermore, after the plates were divided into 7 groups (3, 6 or 7 sheets per group), for each group, 10 μl each of culture solution was mixed in all wells in each row and they were made to one group. Thus, 56 rows of the mixed antibodies in total were obtained. Finally, after the plates were divided into 5 groups (3, 9 or 10 sheets per group), for each group, 10 μl each of culture solution was mixed in all wells in each column and they were made to one group. Thus, 54 columns of the mixed antibodies in total (in a part, two columns were made to one group) were obtained.

[0979] A YT0.05GA medium (YT medium+0.05% Glucose+200 μg/ml Ampicillin) (100 ml) was added to each mixed antibody, and shaking cultured at 30° C. until OD600 nm was about 0.3 to 0.5. Thereafter, IPTG was added so that the final concentration was 0.5 mM and further shaking cultured at 30° C. The mixture was centrifuged at 10000 rpm at 4° C. for 15 minutes, and the culture supernatant was recovered. Then, ammonium sulfate (29.1 g) was slowly added and mixed, mixture was centrifuged at 10000 rpm at 4° C. for 20 minutes, and sediment was recovered. The sediment was

suspended in 5 ml of PBS/NaN_3/complete. The suspension was centrifuged at 10000 rpm at 4° C. for 20 minutes, and the culture supernatant was recovered. Thus, 20-fold concentrated mixed antibodies (190 types) were obtained.

(2) Measurement by Three-Dimensional ELISA

[0980] Three dimensional ELISA was carried out by using the obtained 20-fold concentrated mixed antibodies (190 types). Firstly, 50 μl/well of antigen whose concentration was adjusted to be 20 μg/ml with PBS was added to Maxisorp (Nunc) and reacted at 37° C. for two hours to be sensitized. After the liquid in each well was removed, 5% skim milk/PBS (200 μg/well) was added and reacted at 37° C. for two hours for blocking. The liquid in each well was removed and washed with PBS, and 20-fold concentrated mixed antibody (100 μl/well) was added and reacted at 37° C. for one hour. The reacted product was washed with PBS, and a rabbit anti-cp3 antibody (MBL) that had been 5000-fold diluted with 0.05% Tween/PBS was added (100 μl/well) and reacted at 37° C. for one hour. The mixture was washed with PBS, and an HRP labeled goat anti-rabbit IgG antibody (MBL) that had been 2000-fold diluted with 0.05% Tween/PBS was added (100 μl/well) and reacted at 37° C. for one hour. The reacted product was washed with PBS and a substrate solution (100 μl/well) was added. The substrate solution was produced as followed. That is to say, to 12 ml of 0.1 M citric acid-disodium hydrogen-phosphate (pH 5.1), H_2O_2 was added so that the final concentration became 0.01% and furthermore, OPD tablet (Wako Pure Chemical) was added.

[0981] 2N sulfuric acid (100 μl/well) was added to stop the reaction and the absorbance at 492 nm was measured by using a plate reader (Wako Pure Chemical, SUNRISE Remote).

[0982] The measurement results are shown in FIGS. **79** to **81** (ELISA using CK147 as an antigen) and FIGS. **82** to **84** (ELISA using HER1 as an antigen).

[0983] Based on the results of the above-mentioned three dimensional ELISA, positive clones were selected. That is to say, from information of plate, row and column providing positive results, intersection point was searched and antibody clones existing in the intersection point were selected. The selected antibody clones were shaking cultured in 75 μl/well YTGA medium at 30° C. overnight. In 200 μl/well YT0. 05GA medium, the culture solution was plated and standing cultured at 37° C. for four hours. Thereafter, IPTG was added so that the final concentration became 1 mM and shaking cultured at 30° C. overnight. The culture was centrifuged at 3000 rpm at 4° C. for 10 minutes and the culture supernatant was recovered.

(3) Reactivity of Selected Antibody Clones

[0984] 50 μl/well of antigen (CD147 or HER1) whose concentration was adjusted to be 10 μg/ml with PBS was added to Maxisorp (Nunc) and reacted at 37° C. for two hours to be sensitized. After the liquid in each well was removed, 5% skim milk/PBS (200 μl/well) was added and reacted at 37° C. for two hours for blocking. The liquid in each well was removed and washed with PBS. The culture supernatant of the selected clones (100 μl/well) was added and reacted at 37° C. for one hour. The reacted product was washed with PBS, and a rabbit anti-cp3 antibody (MBL) that had been 5000-fold diluted with 0.05% Tween/PBS was added (1001l/well) and reacted at 37° C. for one hour. The mixture was washed with PBS, and an HRP labeled goat anti-rabbit IgG antibody (MBL) that had been 2000-fold diluted with 0.05% Tween/PBS was added (100 μl/well) and reacted at 37° C. for one hour. The reacted product was washed with PBS and a substrate solution (100 μl/well) was added. 2N sulfuric acid (100 μl/well) was added to stop the reaction and the absorbance at 492 nm was measured by using a plate reader (Wako Pure Chemical, SUNRISE Remote). The results of ELISA using HER1 as an antigen is show in FIG. **85**. As is apparent from the graph of FIG. **85**, a large number of monoclonal antibodies to HER1 were obtained.

20. Newly Obtained Antibodies

[0985] By using the classifying method and identification method of the present invention, it was possible to obtain the following antibodies successfully.

(1) Antibody to C1qR

[0986] 070-016 antibody

(a) Amino Acid Sequence

[0987] SEQ ID NO: 451 (VH); SEQ ID NO: (VH CDR1) 452; SEQ ID NO: 453 (VH CDR2); SEQ ID NO: 454 (VH CDR3), SEQ ID NO: 455 (VL); SEQ ID NO: (VL CDR1) 456; SEQ ID NO: 457 (VL CDR2); and SEQ ID NO: 458 (VL CDR3)

(b) Base Sequence

[0988] SEQ ID NO: 843 (VH); and SEQ ID NO: 844 (VL)

(2) Antibody to CD44

[0989] 064-003 antibody

(a) Amino Acid Sequence

[0990] SEQ ID NO: 459 (VH); SEQ ID NO: 460 (VH CDR1); SEQ ID NO: 461 (VH CDR2); SEQ ID NO: 462 (VH CDR3); SEQ ID NO: 463 (VL); SEQ ID NO: 464 (VL CDR1); SEQ ID NO: 465 (VL CDR2); and SEQ ID NO: 466 (VL CDR3)

(b) Base Sequence

[0991] SEQ ID NO: 845 (VH); and SEQ ID NO: 846 (VL)

(3) Antibody to CD73

[0992] 067-213 antibody

(a) Amino Acid Sequence

[0993] SEQ ID NO: 467 (VH); SEQ ID NO: 468 (VH CDR1); SEQ ID NO: 469 (VH CDR2); SEQ ID NO: 470 (VH CDR3); SEQ ID NO: 471 (VL); SEQ ID NO: 472 (VL CDR1); SEQ ID NO: 473 (VL CDR2); and SEQ ID NO: 474 (VL CDR3)

(b) Base Sequence

[0994] SEQ ID NO: 847 (VH); and SEQ ID NO: 848 (VL)

(4) Antibody to EpCAM

[0995] 067-153 Antibody

(a) Amino Acid Sequence

[0996] SEQ ID NO: 475 (VH); SEQ ID NO: 476 (VH CDR1); SEQ ID NO: 477 (VH CDR2); SEQ ID NO: 478 (VH

CDR3); SEQ ID NO: 479 (VL); SEQ ID NO: 480 (VL CDR1); SEQ ID NO: 481 (VL CDR2); and SEQ ID NO: 482 (VL CDR3)

(b) Base Sequence

[0997] SEQ ID NO: 849 (VH); and SEQ ID NO: 850 (VL)

(5) Antibody to HER1

[0998] 048-040 antibody

(a) Amino Acid Sequence

[0999] SEQ ID NO: 483 (VH); SEQ ID NO: 484 (VH CDR1); SEQ ID NO: 485 (VH CDR2); SEQ ID NO: 486 (VH CDR3); SEQ ID NO: 487 (VL); SEQ ID NO: 488 (VL CDR1); SEQ ID NO: 489 (VL CDR2); and SEQ ID NO: 490 (VL CDR3)

(b) Base Sequence

[1000] SEQ ID NO: 851 (VH); and SEQ ID NO: 852 (VL)
[1001] 054-101 antibody

(a) Amino Acid Sequence

[1002] SEQ ID NO: 491 (VH); SEQ ID NO: 492 (VH CDR1); SEQ ID NO: 493 (VH CDR2); SEQ ID NO: 494 (VH CDR3); SEQ ID NO: 495 (VL); SEQ ID NO: 496 (VL CDR1); SEQ ID NO: 497 (VL CDR2); and SEQ ID NO: 498 (VL CDR3)

(b) Base Sequence

[1003] SEQ ID NO: 853 (VH); and SEQ ID NO: 854 (VL)
[1004] 055-147 antibody

(a) Amino Acid Sequence

[1005] SEQ ID NO: 499 (VH); SEQ ID NO: 500 (VH CDR1); SEQ ID NO: 501 (VH CDR2); SEQ ID NO: 502 (VH CDR3); SEQ ID NO: 503 (VL); SEQ ID NO: 504 (VL CDR1); SEQ ID NO: 505 (VL CDR2); and SEQ ID NO: 506 (VL CDR3)

(b) Base Sequence

[1006] SEQ ID NO: 855 (VH); and SEQ ID NO: 856 (VL)
[1007] 059-173 antibody

(a) Amino Acid Sequence

[1008] SEQ ID NO: 507 (VH); SEQ ID NO: 508 (VH CDR1); SEQ ID NO: 509 (VH CDR2); SEQ ID NO: 510 (VH CDR3); SEQ ID NO: 511 (VL); SEQ ID NO: 512 (VL CDR1); SEQ ID NO: 513 (VL CDR2); and SEQ ID NO: 514 (VL CDR3)

(b) Base Sequence

[1009] SEQ ID NO: 857 (VH); and SEQ ID NO: 858 (VL)
[1010] 067-149 antibody

(a) Amino Acid Sequence

[1011] SEQ ID NO: 515 (VH); SEQ ID NO: 516 (VH CDR1); SEQ ID NO: 517 (VH CDR2); SEQ ID NO: 518 (VH CDR3); SEQ ID NO: 519 (VL); SEQ ID NO: 520 (VL CDR1); SEQ ID NO: 521 (VL CDR2); and SEQ ID NO: 522 (VL CDR3)

(b) Base Sequence

[1012] SEQ ID NO: 859 (VH); and SEQ ID NO: 860 (VL)
[1013] 067-176 antibody

(a) Amino Acid Sequence

[1014] SEQ ID NO: 523 (VH); SEQ ID NO: 524 (VH CDR1); SEQ ID NO: 525 (VH CDR2); SEQ ID NO: 526 (VH CDR3); SEQ ID NO: 527 (VL); SEQ ID NO: 528 (VL CDR1); SEQ ID NO: 529 (VL CDR2); and SEQ ID NO: 530 (VL CDR3)

(b) Base Sequence

[1015] SEQ ID NO: 861 (VH); and SEQ ID NO: 862 (VL)

(6) Antibody to HER2

[1016] 015-044 antibody

(a) Amino Acid Sequence

[1017] SEQ ID NO: 531 (VH); SEQ ID NO: 532 (VH CDR1); SEQ ID NO: 533 (VH CDR2); SEQ ID NO: 534 (VH CDR3); SEQ ID NO: 535 (VL); SEQ ID NO: 536 (VL CDR1); SEQ ID NO: 537 (VL CDR2); and SEQ ID NO: 538 (VL CDR3)

(b) Base Sequence

[1018] SEQ ID NO: 863 (VH); and SEQ ID NO: 864 (VL)
[1019] 015-102 antibody

(a) Amino Acid Sequence

[1020] SEQ ID NO: 539 (VH); SEQ ID NO: 540 (VH CDR1); SEQ ID NO: 541 (VH CDR2); SEQ ID NO: 542 (VH CDR3); SEQ ID NO: 543 (VL); SEQ ID NO: 544 (VL CDR1); SEQ ID NO: 545 (VL CDR2); and SEQ ID NO: 546 (VL CDR3)

(b) Base Sequence

[1021] SEQ ID NO: 865 (VH); and SEQ ID NO: 866 (VL)
[1022] 015-136 antibody

(a) Amino Acid Sequence

[1023] SEQ ID NO: 547 (VH); SEQ ID NO: 548 (VH CDR1); SEQ ID NO: 549 (VH CDR2); SEQ ID NO: 550 (VH CDR3); SEQ ID NO: 551 (VL); SEQ ID NO: 552 (VL CDR1); SEQ ID NO: 553 (VL CDR2); and SEQ ID NO: 554 (VL CDR3)

(b) Base Sequence

[1024] SEQ ID NO: 867 (VH); SEQ ID NO: 868 (VL)
[1025] 015-143 antibody

(a) Amino Acid Sequence

[1026] SEQ ID NO: 555 (VH); SEQ ID NO: 556 (VH CDR1); SEQ ID NO: 557 (VH CDR2); SEQ ID NO: 558 (VH

CDR3); SEQ ID NO: 559 (VL); SEQ ID NO: 560 (VL CDR1); SEQ ID NO: 561 (VL CDR2); SEQ ID NO: 562 (VL CDR3)

(b) Base Sequence

[1027] SEQ ID NO: 869 (VH); SEQ ID NO: 870 (VL)

[1028] 015-209 antibody

(a) Amino Acid Sequence

[1029] SEQ ID NO: 563 (VH); SEQ ID NO: 564 (VH CDR1); SEQ ID NO: 565 (VH CDR2); SEQ ID NO: 566 (VH CDR3); SEQ ID NO: 567 (VL); SEQ ID NO: 568 (VL CDR1); SEQ ID NO: 569 (VL CDR2); SEQ ID NO: 570 (VL CDR3)

(b) Base Sequence

[1030] SEQ ID NO: 871 (VH); SEQ ID NO: 872 (VL)

[1031] 039-016 antibody

(a) Amino Acid Sequence

[1032] SEQ ID NO: 571 (VH); SEQ ID NO: 572 (VH CDR1); SEQ ID NO: 573 (VH CDR2); SEQ ID NO: 574 (VH CDR3); SEQ ID NO: 575 (VL); SEQ ID NO: 576 (VL CDR1); SEQ ID NO: 577 (VL CDR2); SEQ ID NO: 578 (VL CDR3)

(b) Base Sequence

[1033] SEQ ID NO: 873 (VH); SEQ ID NO: 874 (VL)

[1034] 053-216 antibody

(a) Amino Acid Sequence

[1035] SEQ ID NO: 579 (VH); SEQ ID NO: 580 (VH CDR1); SEQ ID NO: 581 (VH CDR2); SEQ ID NO: 582 (VH CDR3); SEQ ID NO: 583 (VL); SEQ ID NO: 584 (VL CDR1); SEQ ID NO: 585 (VL CDR2); SEQ ID NO: 586 (VL CDR3)

(b) Base Sequence

[1036] SEQ ID NO: 875 (VH); SEQ ID NO: 876 (VL)

[1037] 075-024 antibody

(a) Amino Acid Sequence

[1038] SEQ ID NO: 587 (VH); SEQ ID NO: 588 (VH CDR1); SEQ ID NO: 589 (VH CDR2); SEQ ID NO: 590 (VH CDR3); SEQ ID NO: 591 (VL); SEQ ID NO: 592 (VL CDR1); SEQ ID NO: 593 (VL CDR2); SEQ ID NO: 594 (VL CDR3)

(b) Base Sequence

[1039] SEQ ID NO: 877 (VH); SEQ ID NO: 878 (VL)

[1040] 075-110 antibody

(a) Amino Acid Sequence

[1041] SEQ ID NO: 595 (VH); SEQ ID NO: 596 (VH CDR1); SEQ ID NO: 597 (VH CDR2); SEQ ID NO: 598 (VH CDR3); SEQ ID NO: 599 (VL); SEQ ID NO: 600 (VL CDR1); SEQ ID NO: 601 (VL CDR2); SEQ ID NO: 602 (VL CDR3)

(b) Base Sequence

[1042] SEQ ID NO: 879 (VH); SEQ ID NO: 880 (VL)

[1043] 086-032 antibody

(a) Amino Acid Sequence

[1044] SEQ ID NO: 603 (VH); SEQ ID NO: 604 (VH CDR1); SEQ ID NO: 605 (VH CDR2); SEQ ID NO: 606 (VH CDR3); SEQ ID NO: 607 (VL); SEQ ID NO: 608 (VL CDR1); SEQ ID NO: 609 (VL CDR2); SEQ ID NO: 610 (VL CDR3)

(b) Base Sequence

[1045] SEQ ID NO: 881 (VH); SEQ ID NO: 882 (VL)

[1046] 086-035 antibody

(a) Amino Acid Sequence

[1047] SEQ ID NO: 611 (VH); SEQ ID NO: 612 (VH CDR1); SEQ ID NO: 613 (VH CDR2); SEQ ID NO: 614 (VH CDR3); SEQ ID NO: 615 (VL); SEQ ID NO: 616 (VL CDR1); SEQ ID NO: 617 (VL CDR2); SEQ ID NO: 618 (VL CDR3)

(b) Base Sequence

[1048] SEQ ID NO: 883 (VH); SEQ ID NO: 884 (VL)

[1049] 086-036 antibody

(a) Amino Acid Sequence

[1050] SEQ ID NO: 619 (VH); SEQ ID NO: 620 (VH CDR1); SEQ ID NO: 621 (VH CDR2); SEQ ID NO: 622 (VH CDR3); SEQ ID NO: 623 (VL); SEQ ID NO: 624 (VL CDR1); SEQ ID NO: 625 (VL CDR2); SEQ ID NO: 626 (VL CDR3)

(b) Base Sequence

[1051] SEQ ID NO: 885 (VH); SEQ ID NO: 886 (VL)

[1052] 086-061 antibody

(a) Amino Acid Sequence

[1053] SEQ ID NO: 627 (VH); SEQ ID NO: 628 (VH CDR1); SEQ ID NO: 629 (VH CDR2); SEQ ID NO: 630 (VH CDR3); SEQ ID NO: 631 (VL); SEQ ID NO: 632 (VL CDR1); SEQ ID NO: 633 (VL CDR2); SEQ ID NO: 634 (VL CDR3)

(b) Base Sequence

[1054] SEQ ID NO: 887 (VH); SEQ ID NO: 888 (VL)

[1055] 086-138 antibody

(a) Amino Acid Sequence

[1056] SEQ ID NO: 635 (VH); SEQ ID NO: 636 (VH CDR1); SEQ ID NO: 637 (VH CDR2); SEQ ID NO: 638 (VH

CDR3); SEQ ID NO: 639 (VL); SEQ ID NO: 640 (VL CDR1); SEQ ID NO: 641 (VL CDR2); SEQ ID NO: 642 (VL CDR3)

(b) Base Sequence

[1057] SEQ ID NO: 889 (VH); SEQ ID NO: 890 (VL)

[1058] 086-182 antibody

(a) Amino Acid Sequence

[1059] SEQ ID NO: 643 (VH); SEQ ID NO: 644 (VH CDR1); SEQ ID NO: 645 (VH CDR2); SEQ ID NO: 646 (VH CDR3); SEQ ID NO: 647 (VL); SEQ ID NO: 648 (VL CDR1); SEQ ID NO: 649 (VL CDR2); SEQ ID NO: 650 (VL CDR3,

(b) Base Sequence

[1060] SEQ ID NO: 891 (VH); SEQ ID NO: 892 (VL)

(7) Antibody to HGFR 067-126 antibody

(a) Amino Acid Sequence

[1061] SEQ ID NO: 651 (VH); SEQ ID NO: 652 (VH CDR1); SEQ ID NO: 653 (VH CDR2); SEQ ID NO: 654 (VH CDR3); SEQ ID NO: 655 (VL); SEQ ID NO: 656 (VL CDR1); SEQ ID NO: 657 (VL CDR2); SEQ ID NO: 658 (VL CDR3)

(b) Base Sequence

[1062] SEQ ID NO: 893 (VH); SEQ ID NO: 894 (VL)

[1063] 067-133 antibody

(a) Amino Acid Sequence

[1064] SEQ ID NO: 659 (VH); SEQ ID NO: 660 (VH CDR1); SEQ ID NO: 661 (VH CDR2); SEQ ID NO: 662 (VH CDR3); SEQ ID NO: 663 (VL); SEQ ID NO: 664 (VL CDR1); SEQ ID NO: 665 (VL CDR2); SEQ ID NO: 666 (VL CDR3)

(b) Base Sequence

[1065] SEQ ID NO: 895 (VH); SEQ ID NO: 896 (VL)

[1066] 067-287 antibody

(a) Amino Acid Sequence

[1067] SEQ ID NO: 667 (VH); SEQ ID NO: 668 (VH CDR1); SEQ ID NO: 669 (VH CDR2); SEQ ID NO: 670 (VH CDR3); SEQ ID NO: 671 (VL); SEQ ID NO: 672 (VL CDR1); SEQ ID NO: 673 (VL CDR2); SEQ ID NO: 674 (VL CDR3)

(b) Base Sequence

[1068] SEQ ID NO: 897 (VH); SEQ ID NO: 898 (VL)

(8) Antibody to ITGA3

[1069] 064-002 antibody

(a) Amino Acid Sequence

[1070] SEQ ID NO: 675 (VH); SEQ ID NO: 676 (VH CDR1); SEQ ID NO: 677 (VH CDR2); SEQ ID NO: 678 (VH CDR3); SEQ ID NO: 679 (VL); SEQ ID NO: 680 (VL CDR1); SEQ ID NO: 681 (VL CDR2); SEQ ID NO: 682 (VL CDR3)

(b) Base Sequence

[1071] SEQ ID NO: 899 (VH); SEQ ID NO: 900 (VL)

[1072] 064-006 antibody

(a) Amino Acid Sequence

[1073] SEQ ID NO: 683 (VH); SEQ ID NO: 684 (VH CDR1); SEQ ID NO: 685 (VH CDR2); SEQ ID NO: 686 (VH CDR3); SEQ ID NO: 687 (VL); SEQ ID NO: 688 (VL CDR1); SEQ ID NO: 689 (VL CDR2); SEQ ID NO: 690 (VL CDR3)

(b) Base Sequence

[1074] SEQ ID NO: 901 (VH); SEQ ID NO: 902 (VL)

[1075] 064-012a antibody

(a) Amino Acid Sequence

[1076] SEQ ID NO: 691 (VH); SEQ ID NO: 692 (VH CDR1); SEQ ID NO: 693 (VH CDR2); SEQ ID NO: 694 (VH CDR3); SEQ ID NO: 695 (VL); SEQ ID NO: 696 (VL CDR1); SEQ ID NO: 697 (VL CDR2); SEQ ID NO: 698 (VL CDR3)

(b) Base Sequence

[1077] SEQ ID NO: 903 (VH); SEQ ID NO: 904 (VL)

[1078] 064-012b antibody

(a) Amino Acid Sequence

[1079] SEQ ID NO: 699 (VH); SEQ ID NO: 700 (VH CDR1); SEQ ID NO: 701 (VH CDR2); SEQ ID NO: 702 (VH CDR3); SEQ ID NO: 703 (VL); SEQ ID NO: 704 (VL CDR1); SEQ ID NO: 705 (VL CDR2); SEQ ID NO: 706 (VL CDR3)

(b) Base Sequence

[1080] SEQ ID NO: 905 (VH); SEQ ID NO: 906 (VL)

[1081] 064-014 antibody

(a) Amino Acid Sequence

[1082] SEQ ID NO: 707 (VH); SEQ ID NO: 708 (VH CDR1); SEQ ID NO: 709 (VH CDR2); SEQ ID NO: 710 (VH CDR3); SEQ ID NO: 711 (VL); SEQ ID NO: 712 (VL CDR1); SEQ ID NO: 713 (VL CDR2); SEQ ID NO: 714 (VL CDR3)

(b) Base Sequence

[1083] SEQ ID NO: 907 (VH); SEQ ID NO: 908 (VL)

[1084] 064-054 antibody

(a) Amino Acid Sequence

[1085] SEQ ID NO: 715 (VH); SEQ ID NO: 716 (VH CDR1); SEQ ID NO: 717 (VH CDR2); SEQ ID NO: 718 (VH

CDR3); SEQ ID NO: 719 (VL); SEQ ID NO: 720 (VL CDR1); SEQ ID NO: 721 (VL CDR2); SEQ ID NO: 722 (VL CDR3)

(b) Base Sequence

[1086] SEQ ID NO: 909 (VH); SEQ ID NO: 910 (VL)

[1087] 064-085 antibody

(a) Amino Acid Sequence

[1088] SEQ ID NO: 723 (VH); SEQ ID NO: 724 (VH CDR1); SEQ ID NO: 725 (VH CDR2); SEQ ID NO: 726 (VH CDR3); SEQ ID NO: 727 (VL); SEQ ID NO: 728 (VL CDR1); SEQ ID NO: 729 (VL CDR2); SEQ ID NO: 730 (VL CDR3)

(b) Base Sequence

[1089] SEQ ID NO: 911 (VH); SEQ ID NO: 912 (VL)

[1090] 064-093 antibody

(a) Amino Acid Sequence

[1091] SEQ ID NO: 731 (VH); SEQ ID NO: 732 (VH CDR1); SEQ ID NO: 733 (VH CDR2); SEQ ID NO: 734 (VH CDR3); SEQ ID NO: 735 (VL); SEQ ID NO: 736 (VL CDR1); SEQ ID NO: 737 (VL CDR2); SEQ ID NO: 738 (VL CDR3)

(b) Base Sequence

[1092] SEQ ID NO: 913 (VH); SEQ ID NO: 914 (VL)

[1093] 064-116 antibody

(a) Amino Acid Sequence

[1094] SEQ ID NO: 739 (VH); SEQ ID NO: 740 (VH CDR1); SEQ ID NO: 741 (VH CDR2); SEQ ID NO: 742 (VH CDR3); SEQ ID NO: 743 (VL); SEQ ID NO: 744 (VL CDR1); SEQ ID NO: 745 (VL CDR2); SEQ ID NO: 746 (VL CDR3)

(b) Base Sequence

[1095] SEQ ID NO: 915 (VH); SEQ ID NO: 916 (VL)

[1096] 065-183 antibody

(a) Amino Acid Sequence

[1097] SEQ ID NO: 747 (VH); SEQ ID NO: 748 (VH CDR1); SEQ ID NO: 749 (VH CDR2); SEQ ID NO: 750 (VH CDR3); SEQ ID NO: 751 (VL); SEQ ID NO: 752 (VL CDR1); SEQ ID NO: 753 (VL CDR2); SEQ ID NO: 754 (VL CDR3)

(b) Base Sequence

[1098] SEQ ID NO: 917 (VH); SEQ ID NO: 918 (VL)

[1099] 067-142 antibody

(a) Amino Acid Sequence

[1100] SEQ ID NO: 763 (VH); SEQ ID NO: 764 (VH CDR1); SEQ ID NO: 765 (VH CDR2); SEQ ID NO: 766 (VH CDR3); SEQ ID NO: 767 (VL); SEQ ID NO: 768 (VL CDR1); SEQ ID NO: 769 (VL CDR2); SEQ ID NO: 770 (VL CDR3)

(b) Base Sequence

[1101] SEQ ID NO: 921 (VH); SEQ ID NO: 922 (VL)

[1102] 068-007 antibody

(a) Amino Acid Sequence

[1103] SEQ ID NO: 771 (VH); SEQ ID NO: 772 (VH CDR1); SEQ ID NO: 773 (VH CDR2); SEQ ID NO: 774 (VH CDR3); SEQ ID NO: 775 (VL); SEQ ID NO: 776 (VL CDR1); SEQ ID NO: 777 (VL CDR2); SEQ ID NO: 778 (VL CDR3)

(b) Base Sequence

[1104] SEQ ID NO: 923 (VH); SEQ ID NO: 924 (VL)

(9) Antibody to ALCAM 029-143 antibody

(a) Amino Acid Sequence

[1105] SEQ ID NO: 779 (VH); SEQ ID NO: 780 (VH CDR1); SEQ ID NO: 781 (VH CDR2); SEQ ID NO 782 (VH CDR3); SEQ ID NO: 783 (VL); SEQ ID NO: 784 (VL CDR1); SEQ ID NO: 785 (VL CDR2); SEQ ID NO: 786 (VL CDR3)

(b) Base Sequence

[1106] SEQ ID NO: 925 (VH); SEQ ID NO: 926 (VL)

[1107] 045-1.34 antibody

(a) Amino Acid Sequence

[1108] SEQ ID NO: 787 (VH); SEQ ID NO: 788 (VH CDR1); SEQ ID NO: 789 (VH CDR2); SEQ ID NO: 790 (VH CDR3); SEQ ID NO: 791 (VL); SEQ ID NO: 792 (VL CDR1); SEQ ID NO: 793 (VL CDR2); SEQ ID NO: 794 (VL CDR3)

(b) Base Sequence

[1109] SEQ ID NO: 927 (VH); SEQ ID NO: 928 (VL)

[1110] 062-101 antibody

(a) Amino Acid Sequence

[1111] SEQ ID NO: 795 (VH); SEQ ID NO: 796 (VH CDR1); SEQ ID NO: 797 (VH CDR2); SEQ ID NO: 798 (VH CDR3); SEQ ID NO: 799 (VL); SEQ ID NO: 800 (VL CDR1); SEQ ID NO: 801 (VL CDR2); SEQ ID NO: 802 (VL CDR3)

(b) Base Sequence

[1112] SEQ ID NO: 929 (VH); SEQ ID NO: 930 (VL)

[1113] 062-109 antibody

(a) Amino Acid Sequence

[1114] SEQ ID NO: 803 (VH); SEQ ID NO: 804 (VH CDR1); SEQ ID NO: 805 (VH CDR2); SEQ ID NO: 806 (VH

CDR3); SEQ ID NO: 807 (VL); SEQ ID NO: 808 (VL CDR1); SEQ ID NO: 809 (VL CDR2); SEQ ID NO: 810 (VL CDR3)

(b) Base Sequence

[1115] SEQ ID NO: 931 (VH); SEQ ID NO: 932 (VL)
[1116] 084-103 antibody

(a) Amino Acid Sequence

[1117] SEQ ID NO: 811 (VH); SEQ ID NO: 812 (VH CDR1); SEQ ID NO: 813 (VH CDR2); SEQ ID NO: 814 (VH CDR3); SEQ ID NO: 815 (VL); SEQ ID NO: 816 (VL CDR1); SEQ ID NO: 817 (VL CDR2); SEQ ID NO: 818 (VL CDR3)

(b) Base Sequence

[1118] SEQ ID NO: 933 (VH); SEQ ID NO: 934 (VL)
[1119] 052-274 antibody

(a) Amino Acid Sequence

[1120] SEQ ID NO: 819 (VH); SEQ ID NO: 820 (VH CDR1); SEQ ID NO: 821 (VH CDR2); SEQ ID NO: 822 (VH CDR3); SEQ ID NO: 823 (VL); SEQ ID NO: 824 (VL CDR1); SEQ ID NO: 825 (VL CDR2); SEQ ID NO: 826 (VL CDR3)

(b) Base Sequence

[1121] SEQ ID NO: 935 (VH); SEQ ID NO: 936 (VL)
[1122] 029-067 antibody

(a) Amino Acid Sequence

[1123] SEQ ID NO: 827 (VH); SEQ ID NO: 828 (VH CDR1); SEQ ID NO: 829 (VH CDR2); SEQ ID NO: 830 (VH CDR3); SEQ ID NO: 831 (VL); SEQ ID NO: 832 (VL CDR1); SEQ ID NO: 833 (VL CDR2); SEQ ID NO: 834 (VL CDR3)

(b) Base Sequence

[1124] SEQ ID NO: 937 (VH); SEQ ID NO: 938 (VL)
[1125] 083-131 antibody

(a) Amino Acid Sequence

[1126] SEQ ID NO: 835 (VH); SEQ ID NO: 836 (VH CDR1); SEQ ID NO: 837 (VH CDR2); SEQ ID NO: 838 (VH CDR3); SEQ ID NO: 839 (VL); SEQ ID NO: 840 (VL CDR1); SEQ ID NO: 841 (VL CDR2); SEQ ID NO: 842 (VL CDR3)

(b) Base Sequence

[1127] SEQ ID NO: 939 (VH); SEQ ID NO: 940 (VL)

(10) Antibody to CD46

[1128] 066-069 antibody

(a) Amino Acid Sequence

[1129] SEQ ID NO: 755 (VH); SEQ ID NO: 756 (VH CDR1); SEQ ID NO: 757 (VH CDR2); SEQ ID NO: 758 (VH CDR3); SEQ ID NO: 759 (VL); SEQ ID NO: 760 (VL CDR1); SEQ ID NO: 761 (VL CDR2); SEQ ID NO: 762 (VL CDR3)

(b) Base Sequence

[1130] SEQ ID NO: 919 (VH); SEQ ID NO: 920 (VL)

(11) Antibody to LAR 064-044 antibody

(a) Amino Acid Sequence

[1131] SEQ ID NO: 944 (VH); SEQ ID NO: 945 (VL)

(b) Base Sequence

[1132] SEQ ID NO: 956 (VH); SEQ ID NO: 957 (VL)
[1133] 065-030 antibody

(a) Amino Acid Sequence

[1134] SEQ ID NO: 946 (VH); SEQ ID NO: 947 (VL)

(b) Base Sequence

[1135] SEQ ID NO: 958 (VH); SEQ ID NO: 959 (VL)
[1136] 065-358 antibody

(a) Amino Acid Sequence

[1137] SEQ ID NO: 948 (VH); SEQ ID NO: 949 (VL)

(b) Base Sequence

[1138] SEQ ID NO: 960 (VH); SEQ ID NO: 961 (VL)
[1139] 066-019 antibody

(a) Amino Acid Sequence

[1140] SEQ ID NO: 950 (VH); SEQ ID NO: 951 (VL)

(b) Base Sequence

[1141] SEQ ID NO: 962 (VH); SEQ ID NO: 963 (VL)
[1142] 079-085 antibody

(a) Amino Acid Sequence

[1143] SEQ ID NO: 952 (VH); SEQ ID NO: 953 (VL)

(b) Base Sequence

[1144] SEQ ID NO: 964 (VH); SEQ ID NO: 965 (VL)

(12) Antibody to BCAM 067-024 antibody

(a) Amino Acid Sequence

[1145] SEQ ID NO: 954 (VH); SEQ ID NO: 955 (VL)

(b) Base Sequence

[1146] SEQ ID NO: 966 (VH); SEQ ID NO: 967 (VL)

(13) Antibody to IgSF4

[1147] 076-048 antibody

(a) Amino Acid Sequence

[1148] SEQ ID NO: 968 (VH); SEQ ID NO: 969 (VL)

(b) Base Sequence

[1149] SEQ ID NO: 970 (VH); SEQ ID NO: 971 (VL)

21. Experiment to Confirm ITGA3 Antibody

[1150] From the results of the immunoprecipitation-mass spectrometry, a part of the antibody group, it was shown that

the antibody included therein recognized a VLA complex. However, in a strict sense, it was not possible to determine what the antibody was, that is, whether the antigen was ITGA3 or ITGB1 or other molecules forming a complex such as CD151. Then, the antibody clones (015-003, 064-002, 064-006, 064-012, 064-014, 064-054, 064-085, 064-091, 064-093, 064-116, 065-183, 067-142, and 068-007) were subjected to RNAI in order to confirm antigens.

21-1 Experiment Procedure

[1151] ITGA3 stealth oligo RNA (400 pmol) purchased from Invitrogen and lipofect RNAi MAX (100 μl) (product of Invitrogen) were mixed with Opti-MEMI (8 ml) (product of GIBCO-BRL) and the mixture was stood still at a room temperature for 10 minutes. To this mixture, 4 ml of SKOv-3 cell solution (2×10^6 cells) and 28 ml of RPMI1640-10% FBS were added. This mixture was planted on four 10-cm culture dishes and cultured in a CO_2 incubator for two days. 1% trypsin solution was allowed to act on the cultured cells so as to liberate cells. The cells were recovered in 5% BSA/PBS solution so as to produce 1 ml of cell suspension. The same experiment was carried out with respect to ITGB1. As to a group without RNAi (control group), the same experiment was carried out except that stealth oligo is not allowed to act.

[1152] To the recovered cells (50 μl), 2.5 μl of normal goat serum was added, and then primary antibody solution was added, so that the final amount was made to be 100 μl by using 5% BSA/PBS. The using amount of the primary antibody (anti-ITGA3 antibody or anti-ITGB1 antibody (mouse monoclonal antibody, product of CHEMICON)) was made to be 1 μl. As to the subjected sample (for example, 015-003 cp3 type antibody), 7 μl of 10-fold concentrated supernatant was used.

[1153] Next, the mixture was stood still at a room temperature for 10 minutes and then subjected to centrifugation. The supernatant was discarded, followed by washing with 5% BSA/PBS (200 μl). Next, as to the sample 015-003 cp3 type antibody, 100 μl of anti-cp3 mouse monoclonal antibody (MBL), which had been diluted with 5% BSA/PBS so that the concentration became 5 μg/ml, was added. The mixture was stood still at a room temperature for 10 minutes. After centrifugation, the supernatant was discarded, followed by washing with 5% BSA/PBS (200 μl). Then, ALEXA488 labeled anti-mouse IgG goat antibody (100 μl), which had been 1000-folded diluted with 5% BSA/PBS, was reacted. The reacted product was stood still at a room temperature for 10 minutes and then subjected to centrifugation. The supernatant was discarded, followed by washing with 5% BSA/PBS (200 μl). The thus obtained cells were suspended in 50 μl of OptilyseB (BECKMAN COULTER). This was stood still for 10 minutes, and then 600 μl of PBS was added to be diluted. Subsequently, the diluted product was treated with Cell-Strainer (BD Falcon) and subjected to measurement using FACS Caliber (BECKMAN COULTER).

21-2 Results

[1154] The results of the above-mentioned RNAi experiment are shown in FIG. **86**. It is shown that A (results of FCM using anti-ITGA3 antibody) and B (results of FCM using anti-ITGB1 antibody) have different peak patterns. The samples (015-003, 064-002, 064-006, 064-012, 064-014, 064-054, 064-085, 064-091, 064-093, 064-116, 065-183, 067-142, and 068-007) show the peak patterns (C) similar to A. From this result, it is confirmed that antigen recognized by these antibody clones is ITGA3.

[1155] When the same RNAi experiment is carried out in each antibody obtained as an anti-HER1 antibody, an anti-HER2 antibody, an anti-HGFR antibody, an anti-IgSF4 antibody, an anti-EpCAM antibody, an anti-CD147 antibody, an anti-CD166 antibody, or anti-MCP antibody, antigen is not wrong, and it is confirmed that the method (method using a panel, three-dimensional ELISA)) of the present invention is useful.

22. Cancer Tissue Specificity of Each Antibody Clone

[1156] When the immunostaining property of the obtained antibody clones with respect to clinical cancer specimens were examined by the same method as described in the above column 11, results shown in FIG. **87** were obtained. These antibody clones are useful for studying and diagnosing the corresponding cancers. Furthermore, clinical specimens in different stages in some cancers were prepared and the immunostaining property of the antibody clones with respect to the specimens was obtained. As a result, some antibody clones showed the staining property specific to stages in addition to the staining property specific to cancer (see FIG. **88**). Thus, in the actual clinical tissues, there are differences in the reactivity to each antibody clone even if the tissue is from the same cancer or in the same grade of malignancy. This results show that the use of the antibody set provided by the present invention enables new tailor-maid diagnosis in cancers to be carried out and diagnosis that is more detail than conventional criterion to be carried out. In other words, it is shown that staging of cancer and re-classification of pathologic conditions can be realized. On the other hand, the staging of cancer and the re-classification of pathologic conditions by using the antibody set are useful for determining a treatment plan. Furthermore, antibodies recognized to have specific reactivity can be useful as antibodies for treatment and useful as a tool for drug screening. Thus, the antibody set provided by the present invention can realize not only tailor-made diagnosis of cancers but also tailor-made treatment of cancers. Thus, the antibody set provides extremely great values and significance.

INDUSTRIAL APPLICABILITY

[1157] The present invention provides a method of classifying a plurality of antibodies to cell surface antigens rapidly. Also, the present invention provides a method of rapidly identifying an antigen to an antibody. The use of these methods makes it possible to obtain an antibody useful for treatment and diagnosis of cancers, or study of the onset mechanism of cancers, and the like. Furthermore, when the classifying method and the identification method of an antigen of the present invention are used, a panel on which a useful antibody set and its characteristics are displayed can be provided, which is expected to greatly contribute to tailor-made medicine. On the other hand, the present invention provides antibodies recognizing antigens expressing in a cancer-specific manner. Such antibodies are expected to be used as antibody for treatment, antibody for diagnosis, antibody for study, and the like, which target cancer cells specifically expressing cancer surface membrane protein recognized by the antibodies.

[1158] The present invention is not limited only to the description of the above embodiments. A variety of modifications which are within the scopes of the following claims and which are achieved easily by a person skilled in the art are included in the present invention.

[1159] Contents of the theses, Publication of Patent Applications, Patent Publications, and other published documents referred to in this specification are herein incorporated by reference in its entity.

SEQUENCE LISTING

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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
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Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Thr Pro Trp Glu Leu Leu Ala Phe Asp Ile Trp Gly Gln
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Gly Thr Met Val Thr Val Ser Arg
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Ser Gly Gly Tyr Tyr Trp Ser
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            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45

Tyr Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
    50                  55                  60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
                85                  90                  95

Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105


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Gln Val Trp Asp Ser Ser Ser Asp His
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Ser Phe Ser Ser Ser
            20                  25                  30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly His Gly Leu Glu Trp Leu
        35                  40                  45

Gly Gly Ile Ile Pro Thr Phe Gly Thr Pro Asn His Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Gly Thr Ala Tyr
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65                  70                  75                  80

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


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<400> SEQUENCE: 12

Ala His Cys Gly Gly Gly Arg Cys Tyr Asp Tyr Thr Asp Ala Phe His
1               5                   10                  15

Phe


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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 13

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Lys
1               5                   10                  15

Thr Ala Arg Ile Thr Cys Gly Gly Asp Asn Ile Gly Asn Arg Ser Val
            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Leu Ile Tyr
        35                  40                  45

Tyr Asp Ser Asp Arg Pro Ser Gly Ile Pro Lys Arg Phe Ser Gly Ser
    50                  55                  60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Thr Ser Asp His
                85                  90                  95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Arg
            100                 105
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Gln Val Trp Asp Ser Thr Ser Asp His
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1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
20 25 30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Leu Pro Met Val Thr Met Ser Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Arg
115 120

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Ser Ser Ser Tyr Tyr Trp Gly
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1 5 10 15

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 21

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1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Tyr Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105

<210> SEQ ID NO 22
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 22

Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
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Tyr Asp Ser Asp Arg Pro Ser
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<210> SEQ ID NO 24

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Gln Val Trp Asp Ser Ser Ser Asp His
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<213> ORGANISM: Homo sapiens

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1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Leu Thr Leu Ser Tyr Ser Ser Ser Trp Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Arg
115 120

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Ser Tyr Trp Ile Gly
1 5

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Gly

<210> SEQ ID NO 28
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<213> ORGANISM: Homo sapiens

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Gln Thr Val Val Thr Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Leu Ser Ser Gly Ser Val Ser Thr Ser
20 25 30

Tyr Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
35 40 45

Leu Ile Tyr Ser Thr Asn Thr Arg Ser Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Ile Leu Gly Asn Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Ala Asp Asp Glu Ser Asp Tyr Tyr Cys Val Leu Tyr Met Gly Ser
85 90 95

Gly Ile Ser Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

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<400> SEQUENCE: 30

Gly Leu Ser Ser Gly Ser Val Ser Thr Ser Tyr Tyr Pro Ser
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<210> SEQ ID NO 31
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<400> SEQUENCE: 31

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<210> SEQ ID NO 32
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 32

Val Leu Tyr Met Gly Ser Gly Ile
1 5

<210> SEQ ID NO 33
<211> LENGTH: 118
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<400> SEQUENCE: 33

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Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

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Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Leu Leu Gly Ile Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr
            100                 105                 110

Thr Val Thr Val Ser Arg
        115


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<400> SEQUENCE: 34

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1               5


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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 35

Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln
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Gly


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Leu Leu Gly Ile Gly Ala Phe Asp Ile
1               5


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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 37

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Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
            20                  25                  30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
    50                  55                  60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80
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Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
                85                  90                  95

His Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
            100                 105                 110


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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 38

Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser
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<210> SEQ ID NO 39
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<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 39

Gly Lys Asn Asn Arg Pro Ser
1               5


<210> SEQ ID NO 40
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Asn Ser Arg Asp Ser Ser Gly Asn His His
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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 41

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1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr
            20                  25                  30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Ser Val Tyr Thr Gly Lys Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Leu Asp Leu Arg Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Gly Asp His His Glu Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Arg
        115


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Ser Tyr Gly Ile Thr
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<400> SEQUENCE: 43

Trp Ile Ser Val Tyr Thr Gly Lys Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 44
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 44

Gly Gly Asp His His Glu Tyr
1 5

<210> SEQ ID NO 45
<211> LENGTH: 107
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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 45

Asn Phe Met Leu Thr Gln Pro Leu Ser Val Ser Val Ala Leu Gly Gln
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Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Asn Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Arg Asp Ser Asn Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Ala Gln Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Thr Val Val
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Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105

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<213> ORGANISM: Homo sapiens

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Gly Gly Asn Asn Ile Gly Ser Lys Asn Val His
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<210> SEQ ID NO 47
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Arg Asp Ser Asn Arg Pro Ser
1 5

<210> SEQ ID NO 48
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<400> SEQUENCE: 48

Gln Val Trp Asp Ser Ser Thr
1 5

<210> SEQ ID NO 49
<211> LENGTH: 128
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 49

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Gly Ser Gly Gly Arg Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Asp Pro Leu Ala Leu Arg Asp Phe Asp Trp Leu Ser Pro Gly
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Arg Asp Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg
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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 50

Ser Tyr Ala Met Ser
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<400> SEQUENCE: 51

Gly Ile Ser Gly Ser Gly Gly Arg Thr Tyr Tyr Ala Asp Ser Val Lys
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Gly

<210> SEQ ID NO 52
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<212> TYPE: PRT

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 52

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Phe Asp Tyr

<210> SEQ ID NO 53
<211> LENGTH: 111
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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 53

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1 5 10 15

Lys Val Thr Ile Ser Cys Ser Gly Ser His Ser Asn Ile Gly Asn Asn
20 25 30

Tyr Val Ser Trp Ser Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Asp Ile Ala Gly Leu Gln
65 70 75 80

Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Gly Ala Trp Asp Thr Ser Leu
85 90 95

Ser Ser Tyr Val Phe Gly Ala Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 54
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 54

Ser Gly Ser His Ser Asn Ile Gly Asn Asn Tyr Val Ser
1 5 10

<210> SEQ ID NO 55
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 55

Asp Asn Asn Lys Arg Pro Ser
1 5

<210> SEQ ID NO 56
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 56

Gly Ala Trp Asp Thr Ser Leu Ser Ser
1 5

<210> SEQ ID NO 57
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 57

Glu Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Leu Ser Gly Gly Tyr Gly Met Asp Val Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 58
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 58

Ser Tyr Ala Ile Ser
1 5

<210> SEQ ID NO 59
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 59

Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 60
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 60

Glu Gly Leu Ser Gly Gly Tyr Gly Met Asp Val
1 5 10

<210> SEQ ID NO 61
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 61

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
20 25 30

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```
Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
        35                  40                  45

Leu Ile Tyr Arg Asn Asn Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
    50                  55                  60

Ser Gly Ser Asn Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65                  70                  75                  80

Arg Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
                85                  90                  95

Leu Ser Ser Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 62
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 62

Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His
1               5                   10


<210> SEQ ID NO 63
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 63

Arg Asn Asn Asn Arg Pro Ser
1               5


<210> SEQ ID NO 64
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 64

Gln Ser Tyr Asp Ser Ser Leu Ser Ser
1               5


<210> SEQ ID NO 65
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 65

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Asn Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ala Tyr Tyr Asp Ile Leu Thr Gly Tyr Phe Tyr Asn Gly Met
            100                 105                 110
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```
Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120                 125


<210> SEQ ID NO 66
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 66

Ser Tyr Ala Met Ser
1               5


<210> SEQ ID NO 67
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 67

Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1               5                   10                  15

Gly


<210> SEQ ID NO 68
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 68

Ala Tyr Tyr Asp Ile Leu Thr Gly Tyr Phe Tyr Asn Gly Met Asp Val
1               5                   10                  15


<210> SEQ ID NO 69
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 69

Gln Ala Val Leu Thr Gln Pro Ser Ser Val Ser Gly Ser Pro Gly Gln
1               5                   10                  15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
            20                  25                  30

Asp Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35                  40                  45

Met Ile His Asp Val Arg Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
    50                  55                  60

Ser Gly Ser Lys Phe Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80

Gln Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
                85                  90                  95

Ser Thr His Val Leu Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 70
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 70
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Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asp Tyr Val Ser
1 5 10

<210> SEQ ID NO 71
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 71

Asp Val Arg Asn Arg Pro Ser
1 5

<210> SEQ ID NO 72
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 72

Ser Ser Tyr Thr Ser Ser Ser Thr His
1 5

<210> SEQ ID NO 73
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 73

Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Ser Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ala Lys Gly His Ser Pro Tyr Ser Ser Gly Trp Ser Asp Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 74
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 74

Asp Tyr Ala Met His
1 5

<210> SEQ ID NO 75
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 75

-continued

Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 76
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 76

Gly His Ser Pro Tyr Ser Ser Gly Trp Ser Asp Phe Asp Tyr
1 5 10

<210> SEQ ID NO 77
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 77

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
20 25 30

Tyr Asp Val Gln Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
35 40 45

Leu Ile His Ala Asn Lys Asn Arg Pro Ser Gly Val Pro Asp Arg Ile
50 55 60

Ser Gly Ser Lys Ser Gly Thr Thr Ala Ser Leu Ala Ile Thr Gly Phe
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
85 90 95

Leu Thr Gly Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 78
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 78

Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val Gln
1 5 10

<210> SEQ ID NO 79
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 79

Ala Asn Lys Asn Arg Pro Ser
1 5

<210> SEQ ID NO 80
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 80

Gln Ser Tyr Asp Ser Ser Leu Thr Gly

-continued

1 5

<210> SEQ ID NO 81
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 81

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Trp Asn Ser Gly Ser Ile Ala Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ala Lys Ala Ser Ala Ala Gly Thr Glu Tyr Tyr His Tyr Tyr Gly Met
100 105 110

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Arg
115 120 125

<210> SEQ ID NO 82
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 82

Asp Tyr Ala Met His
1 5

<210> SEQ ID NO 83
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 83

Ser Ile Ser Trp Asn Ser Gly Ser Ile Ala Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 84
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 84

Ala Ser Ala Ala Gly Thr Glu Tyr Tyr His Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> SEQ ID NO 85
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 85

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Ser Tyr Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1               5                   10                  15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
            20                  25                  30

Thr Ile Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
        35                  40                  45

Ile Tyr Asn Asn His Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65                  70                  75                  80

Ser Ala Asp Glu Ala Asp Tyr Tyr Cys Gly Ala Trp Asn Asp Ser Leu
                85                  90                  95

Asn Val Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 86
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 86

Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Ile Asn
1               5                   10


<210> SEQ ID NO 87
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 87

Asn Asn His Gln Arg Pro Ser
1               5


<210> SEQ ID NO 88
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 88

Gly Ala Trp Asn Asp Ser Leu Asn Val
1               5


<210> SEQ ID NO 89
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 89

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
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65                  70                  75                  80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Thr Ala Ala Ser Leu Lys Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr
            100                 105                 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg
        115                 120


<210> SEQ ID NO 90
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 90

Ser Tyr Gly Ile Ser
1               5


<210> SEQ ID NO 91
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 91

Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
1               5                   10                  15

Gly


<210> SEQ ID NO 92
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 92

Ala Ala Ser Leu Lys Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr
1               5                   10                  15


<210> SEQ ID NO 93
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 93

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1               5                   10                  15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
            20                  25                  30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Ser
        35                  40                  45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
    50                  55                  60

Ser Ser Gly Asp Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80

Asp Glu Ala Asn Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Tyr Pro
                85                  90                  95

Ser Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110
```

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<210> SEQ ID NO 94
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 94

Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser
1 5 10

<210> SEQ ID NO 95
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 95

Gly Lys Asn Asn Arg Pro Ser
1 5

<210> SEQ ID NO 96
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 96

Asn Ser Arg Asp Ser Ser Gly Tyr Pro Ser
1 5 10

<210> SEQ ID NO 97
<211> LENGTH: 130
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 97

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Gly Ser Gly Tyr Val Phe Asn Ser Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Tyr Thr Asp Tyr Ala Gln Lys Val
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Glu Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Tyr Asp Ser Ser Thr Tyr Tyr Ser Ser Asp Tyr Phe
100 105 110

Gln Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val
115 120 125

Ser Ser
130

<210> SEQ ID NO 98
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 98

Ser Tyr Gly Ile Thr

-continued

1 5

<210> SEQ ID NO 99
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 99

Trp Ile Ser Ala Tyr Asn Gly Tyr Thr Asp Tyr Ala Gln Lys Val Gln
1 5 10 15

Gly

<210> SEQ ID NO 100
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 100

Asp Tyr Tyr Asp Ser Ser Thr Tyr Tyr Ser Ser Asp Tyr Phe Gln Tyr
1 5 10 15

Tyr Gly Met Asp Val
20

<210> SEQ ID NO 101
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 101

Gln Ala Val Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ala Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Ser Asp Val Ser Arg Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Asn Thr Val Leu Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 102
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 102

Thr Gly Thr Ser Ser Asp Val Gly Ala Tyr Asn Tyr Val Ser
1 5 10

<210> SEQ ID NO 103
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 103

-continued

Asp Val Ser Arg Arg Pro Ser
1 5

<210> SEQ ID NO 104
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 104

Ser Ser Tyr Thr Ser Ser Asn Thr
1 5

<210> SEQ ID NO 105
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 105

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Asn Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ala Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Met Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Arg Gly Ser Arg Ser Ser Gly Glu Asp Ala Phe Glu Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 106
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 106

Asn Tyr Trp Ile Gly
1 5

<210> SEQ ID NO 107
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 107

Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 108
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 108

Arg Gly Ser Arg Ser Ser Gly Glu Asp Ala Phe Glu Val
1 5 10

<210> SEQ ID NO 109
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 109

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Lys
1 5 10 15

Thr Ala Thr Ile Thr Cys Gly Gly Asp Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Val Leu Val Ile Asn
35 40 45

Tyr Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Glu Asp Arg Arg Gly Gly Tyr
85 90 95

His Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 110
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 110

Gly Gly Asp Asn Ile Gly Ser Lys Ser Val His
1 5 10

<210> SEQ ID NO 111
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 111

Tyr Asp Ser Asp Arg Pro Ser
1 5

<210> SEQ ID NO 112
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 112

Gln Val Glu Asp Arg Arg Gly Gly Tyr His
1 5 10

<210> SEQ ID NO 113
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 113

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```
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
            20                  25                  30

Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Glu Gly Tyr Cys Ser Gly Gly Ser Cys Tyr Ser Tyr Gly Ala Phe
            100                 105                 110

Asp Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125


<210> SEQ ID NO 114
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 114

Ser Asn Tyr Met Ser
1               5


<210> SEQ ID NO 115
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 115

Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly
1               5                   10                  15


<210> SEQ ID NO 116
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 116

Glu Gly Tyr Cys Ser Gly Gly Ser Cys Tyr Ser Tyr Gly Ala Phe Asp
1               5                   10                  15

Ile


<210> SEQ ID NO 117
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 117

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asn Ile Ala Asn Trp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
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```
Tyr Ala Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Ser Tyr Tyr Cys Gln Gln Gly Asn Ser Phe Pro Arg
                85                  90                  95

Val Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> SEQ ID NO 118
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 118

Arg Ala Ser Gln Asn Ile Ala Asn Trp Leu Ala
1               5                   10


<210> SEQ ID NO 119
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 119

Ala Ala Ser Asn Leu Gln Ser
1               5


<210> SEQ ID NO 120
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 120

Gln Gln Gly Asn Ser Phe Pro Arg
1               5


<210> SEQ ID NO 121
<211> LENGTH: 130
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 121

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Val Phe Asn Ser Tyr
            20                  25                  30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Ser Ala Tyr Asn Gly Tyr Thr Asp Tyr Ala Gln Lys Val
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Thr Glu Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Tyr Tyr Asp Ser Ser Thr Tyr Tyr Ser Ser Asp Tyr Phe
            100                 105                 110

Lys Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val
        115                 120                 125
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-continued

Ser Ser
130

<210> SEQ ID NO 122
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 122

Ser Tyr Gly Ile Thr
1 5

<210> SEQ ID NO 123
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 123

Trp Ile Ser Ala Tyr Asn Gly Tyr Thr Asp Tyr Ala Gln Lys Val Gln
1 5 10 15

Gly

<210> SEQ ID NO 124
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 124

Asp Tyr Tyr Asp Ser Ser Thr Tyr Tyr Ser Ser Asp Tyr Phe Lys Tyr
1 5 10 15

Tyr Gly Met Asp Val
20

<210> SEQ ID NO 125
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 125

Gln Ala Val Leu Thr Gln Pro Ser Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Ser Gly Thr Ser Ser Asp Val Gly Ala Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Arg Leu
35 40 45

Leu Thr Phe Asp Val Asn Arg Arg Pro Ser Gly Ser Ser Ser Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Asn Ser
85 90 95

Asn Thr Val Val Phe Gly Gly Gly Thr Arg Leu Thr Val Leu Ser
100 105 110

<210> SEQ ID NO 126
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 126

Ser Gly Thr Ser Ser Asp Val Gly Ala Tyr Asn Tyr Val Ser
1 5 10

<210> SEQ ID NO 127
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 127

Asp Val Asn Arg Arg Pro Ser
1 5

<210> SEQ ID NO 128
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 128

Ser Ser Tyr Thr Asn Ser Asn Thr
1 5

<210> SEQ ID NO 129
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 129

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ala Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Asn Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Asp Ile Glu Asn Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Asp Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Asp Ser Arg Val Ile Arg Phe Leu Glu Gly Tyr Ser Tyr Tyr Tyr
100 105 110

Gly Val Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 130
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 130

Asn Tyr Tyr Trp Ser
1 5

<210> SEQ ID NO 131
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 131

Tyr Ile Tyr Asp Ile Glu Asn Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 132
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 132

Asp Ser Arg Val Ile Arg Phe Leu Glu Gly Tyr Ser Tyr Tyr Tyr Gly
1 5 10 15

Val Asp Val

<210> SEQ ID NO 133
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 133

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Thr Val Ile Ile Ser Cys Ser Gly Ser Arg Ser Asn Ile Gly Gly His
20 25 30

Gly Val Asn Trp His Gln Gln Val Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Arg Asn Asp Arg Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Val Ile Ser Gly Leu Gln
65 70 75 80

Phe Glu Asp Glu Ala Asp Tyr Tyr Cys Val Ala Trp Glu Asp Ser Leu
85 90 95

Asp Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 134
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 134

Ser Gly Ser Arg Ser Asn Ile Gly Gly His Gly Val Asn
1 5 10

<210> SEQ ID NO 135
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 135

Arg Asn Asp Arg Arg Pro Ser
1 5

<210> SEQ ID NO 136
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 136

Val Ala Trp Glu Asp Ser Leu Asp Gly
1 5

<210> SEQ ID NO 137
<211> LENGTH: 115
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 137

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ile Val Ala Thr Ser Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Arg
115

<210> SEQ ID NO 138
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 138

Ser Tyr Ala Met Ser
1 5

<210> SEQ ID NO 139
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 139

Thr Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 140
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 140

Gly Ile Val Ala Thr Ser
1 5

<210> SEQ ID NO 141
<211> LENGTH: 108
<212> TYPE: PRT

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 141

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Lys Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Gln Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Leu Asp Arg Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys His Leu Trp Asp Ser Gly Ser Asp Gln
85 90 95

Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105

<210> SEQ ID NO 142
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 142

Gly Gly Asn Lys Ile Gly Ser Lys Ser Val His
1 5 10

<210> SEQ ID NO 143
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 143

Leu Asp Arg Asp Arg Pro Ser
1 5

<210> SEQ ID NO 144
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 144

His Leu Trp Asp Ser Gly Ser Asp
1 5

<210> SEQ ID NO 145
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 145

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Phe Asp Val Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Val Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Leu Ile Asn Gly Asp Gly Gly Leu Arg Tyr Tyr Ala Asp Ser Val

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    50                  55                  60

Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Ser Arg Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95

Val Lys Gly Asn Phe Gln Gln Trp Gly Gln Gly Thr Leu Val Thr Val
            100                 105                 110

Ser Arg


<210> SEQ ID NO 146
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 146

Val Tyr Gly Met Asn
1               5


<210> SEQ ID NO 147
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 147

Leu Ile Asn Gly Asp Gly Gly Leu Arg Tyr Tyr Ala Asp Ser Val Lys
1               5                   10                  15

Gly


<210> SEQ ID NO 148
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 148

Gly Asn Phe Gln Gln
1               5


<210> SEQ ID NO 149
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 149

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Lys
1               5                   10                  15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45

Tyr Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
    50                  55                  60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
                85                  90                  95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105
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<210> SEQ ID NO 150
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 150

Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1 5 10

<210> SEQ ID NO 151
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 151

Tyr Asp Ser Asp Arg Pro Ser
1 5

<210> SEQ ID NO 152
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 152

Gln Val Trp Asp Ser Ser Ser Asp His
1 5

<210> SEQ ID NO 153
<211> LENGTH: 115
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 153

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Leu Ile Ser Gly Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Arg
115

<210> SEQ ID NO 154
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 154

Asp Tyr Ala Met His
1 5

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<210> SEQ ID NO 155
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 155

Leu Ile Ser Gly Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Asp

<210> SEQ ID NO 156
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 156

Gly Asn Tyr Phe Asp Tyr
1 5

<210> SEQ ID NO 157
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 157

Ser Tyr Glu Leu Thr Gln Pro Leu Ser Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Asn Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Arg Asp Ser Asn Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Ala Gln Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Val Val Phe
85 90 95

Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105

<210> SEQ ID NO 158
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 158

Gly Gly Asn Asn Ile Gly Ser Lys Asn Val His
1 5 10

<210> SEQ ID NO 159
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 159

Arg Asp Ser Asn Arg Pro Ser
1 5

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<210> SEQ ID NO 160
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 160

Gln Val Trp Asp Ser Ser
1 5

<210> SEQ ID NO 161
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 161

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Met Pro Ser Tyr Tyr Tyr Tyr Tyr Gly Met Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 162
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 162

Ser Tyr Ser Met Asn
1 5

<210> SEQ ID NO 163
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 163

Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 164
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 164

Val Met Pro Ser Tyr Tyr Tyr Tyr Tyr Gly Met Asp Val

-continued

1 5 10

<210> SEQ ID NO 165
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 165

Asn Phe Met Leu Thr Gln Pro His Ser Val Ser Glu Ser Pro Gly Lys
1 5 10 15

Thr Val Thr Ile Ser Cys Thr Gly Ser Ser Gly Ser Ile Ala Ser Asn
20 25 30

Tyr Val Gln Trp Tyr Gln Gln Arg Pro Gly Ser Ala Pro Thr Thr Val
35 40 45

Ile Tyr Glu Asp Ser Glu Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Ile Asp Ser Ser Ser Asn Ser Ala Ser Leu Thr Ile Ser Gly
65 70 75 80

Leu Lys Thr Gln Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Gly
85 90 95

Val Asn Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 166
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 166

Thr Gly Ser Ser Gly Ser Ile Ala Ser Asn Tyr Val Gln
1 5 10

<210> SEQ ID NO 167
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 167

Glu Asp Ser Glu Arg Pro Ser
1 5

<210> SEQ ID NO 168
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 168

Gln Ser Tyr Asp Gly Val Asn
1 5

<210> SEQ ID NO 169
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 169

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr

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            20                  25                  30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Asp Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val
            100                 105                 110

Ser Arg


<210> SEQ ID NO 170
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 170

Ser Tyr Gly Met His
1               5


<210> SEQ ID NO 171
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 171

Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
1               5                   10                  15

Gly


<210> SEQ ID NO 172
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 172

Tyr Gly Met Asp Val
1               5


<210> SEQ ID NO 173
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 173

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
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Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Val
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 174
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 174

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> SEQ ID NO 175
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 175

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> SEQ ID NO 176
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 176

Gln Gln Ser Tyr Ser Thr Pro
1 5

<210> SEQ ID NO 177
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 177

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Asp Arg Gly Thr Gly Asp Ala Phe Asp Ile Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 178
<211> LENGTH: 7
<212> TYPE: PRT

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 178

Ser Gly Gly Tyr Tyr Trp Ser
1 5

<210> SEQ ID NO 179
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 179

Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 180
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 180

Asp Arg Gly Thr Gly Asp Ala Phe Asp Ile
1 5 10

<210> SEQ ID NO 181
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 181

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Arg Gln
1 5 10 15

Thr Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Gln Asn
20 25 30

Ser Val Thr Trp Tyr Gln Arg Leu Pro Gly Glu Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Tyr Asp Asp Leu Leu His Ser Gly Val Ser Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Ser Trp Asp Asp Ser Leu
85 90 95

Lys Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 182
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 182

Ser Gly Ser Ser Ser Asn Ile Gly Gln Asn Ser Val Thr
1 5 10

<210> SEQ ID NO 183
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 183

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Tyr Asp Asp Leu Leu His Ser
1 5

<210> SEQ ID NO 184
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 184

Ala Ser Trp Asp Asp Ser Leu Lys Gly
1 5

<210> SEQ ID NO 185
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 185

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcacagac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagc agtggtggtt actactggag ctggatccgc 120

cagcacccag ggaagggcct ggagtggatt gggtacatct attacagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagtcacc atatcagtag acacgtctaa gaaccagttc 240

tccctgaagc tgagctctgt gactgccgcg gacacggccg tgtattactg tgcgaggaca 300

ccgtgggagc tactagcttt tgatatctgg ggccaaggga caatggtcac cgtctcgaga 360

<210> SEQ ID NO 186
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 186

agtggtggtt actactggag c 21

<210> SEQ ID NO 187
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 187

tacatctatt acagtgggag cacctactac aacccgtccc tcaagagt 48

<210> SEQ ID NO 188
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 188

acaccgtggg agctactagc ttttgatatc 30

<210> SEQ ID NO 189
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 189

tcctatgagc tgactcagcc accctcagtg tcagtggccc caggaaagac gaccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa agtgcgcact ggtaccagca gaagccaggc 120

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caggcccctg tgctggtcat ctattatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcattg ggtgttcggc 300

ggagggacca agctgaccgt cctaggt 327

<210> SEQ ID NO 190
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 190

gggggaaaca acattggaag taaaagtgcg cac 33

<210> SEQ ID NO 191
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 191

tatgatagcg accggccctc a 21

<210> SEQ ID NO 192
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 192

caggtgtggg atagtagtag tgatcat 27

<210> SEQ ID NO 193
<211> LENGTH: 378
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 193

caggtgcagc tggtgcagtc tggggctgag gtgaagaaga ctgggtcctc ggtgaaggtc 60

tcctgcaagg cctctggagg ctccttcagc agctctgcaa tcagctgggt gcgacaggcc 120

cctggacacg ggcttgaatg gctgggaggg atcatcccta cctttggtac accaaaccac 180

gcacagaagt tccagggcag agtcacaatt accgcggacg aatcaacggg cacagcctac 240

atggagctga gtggcctgag atctgaggac acggccgtgt attactgtgc gagagcccat 300

tgtggtggtg gtaggtgtta cgactacact gatgcttttc atttctgggg ccaagggaca 360

atggtcaccg tctcgaga 378

<210> SEQ ID NO 194
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 194

agctctgcaa tcagc 15

<210> SEQ ID NO 195
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 195

gggatcatcc ctacctttgg tacaccaaac cacgcacaga agttccaggg c 51

<210> SEQ ID NO 196
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 196

gcccattgtg gtggtggtag gtgttacgac tacactgatg cttttcattt c 51

<210> SEQ ID NO 197
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 197

tcctatgagc tgactcagcc accctcagtg tcagtggccc caggaaagac ggccaggatt 60

acctgtgggg gagacaacat tggaaataga agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctgcttat ctattatgat agcgaccggc cctcagggat ccctaagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtacta gtgatcatgt ggtattcggc 300

ggagggacca agctgaccgt cctacgt 327

<210> SEQ ID NO 198
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 198

gggggagaca acattggaaa tagaagtgtg cac 33

<210> SEQ ID NO 199
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 199

tatgatagcg accggccctc a 21

<210> SEQ ID NO 200
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 200

caggtgtggg atagtactag tgatcat 27

<210> SEQ ID NO 201
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 201

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagc agtagtagtt actactgggg ctggatccgc 120

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cagcccccag ggaaggggct ggagtggatt gggagtatct attatagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gaccgccgca gacacggctg tgtattactg tgcgagactt 300

cctatggtta cgatgtcctt tgactactgg ggccagggaa ccctggtcac cgtctcgaga 360

<210> SEQ ID NO 202
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 202

agtagtagtt actactgggg c 21

<210> SEQ ID NO 203
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 203

agtatctatt atagtgggag cacctactac aacccgtccc tcaagagt 48

<210> SEQ ID NO 204
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 204

cttcctatgg ttacgatgtc ctttgactac 30

<210> SEQ ID NO 205
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 205

tcctatgtgc tgactcagcc accctcagtg tcagtggccc caggaaagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcat ctattatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgt ggtattcggc 300

ggagggacca agctgaccgt cctaggt 327

<210> SEQ ID NO 206
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 206

gggggaaaca acattggaag taaaagtgtg cac 33

<210> SEQ ID NO 207
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 207

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tatgatagcg accggccctc a 21

<210> SEQ ID NO 208
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 208

caggtgtggg atagtagtag tgatcat 27

<210> SEQ ID NO 209
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 209

caggtgcagc tggtgcagtc tggagcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcggctgggt gcgccagatg 120

cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag caccgcctac 240

ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagacttact 300

ttgtcttata gcagcagctg gtttgactac tggggccagg gaaccctggt caccgtctcg 360

aga 363

<210> SEQ ID NO 210
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 210

agctactgga tcggc 15

<210> SEQ ID NO 211
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 211

atcatctatc ctggtgactc tgataccaga tacagcccgt ccttccaagg c 51

<210> SEQ ID NO 212
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 212

cttactttgt cttatagcag cagctggttt gactac 36

<210> SEQ ID NO 213
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 213

cagactgtgg tgacccagga gccatcgttc tcagtgtccc ctggagggac agtcacactc 60

acttgtggct tgagctctgg ctcagtctct actagttact accccagctg gtaccagcag 120

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accccaggcc aggctccacg cacgctcatc tacagcacaa acactcgctc ttctggggtc 180

cctgatcgct tctctggctc catccttggg aacaaagctg ccctcaccat cacgggggcc 240

caggcagatg atgaatctga ttattactgt gtgctgtata tgggtagtgg catttcggtg 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 214
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 214

ggcttgagct ctggctcagt ctctactagt tactacccca gc 42

<210> SEQ ID NO 215
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 215

agcacaaaca ctcgctcttc t 21

<210> SEQ ID NO 216
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 216

gtgctgtata tgggtagtgg catt 24

<210> SEQ ID NO 217
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 217

caggtgcagc tggtgcagtc tggagcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcggctgggt gcgccagatg 120

cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag caccgcctac 240

ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagacttctg 300

gggataggcg cttttgatat ctggggccaa gggaccacgg tcaccgtctc gaga 354

<210> SEQ ID NO 218
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 218

agctactgga tcggc 15

<210> SEQ ID NO 219
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 219

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atcatctatc ctggtgactc tgataccaga tacagcccgt ccttccaagg c 51

<210> SEQ ID NO 220
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 220

cttctgggga taggcgcttt tgatatc 27

<210> SEQ ID NO 221
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 221

tcttctgagc tgactcagga ccctgctgtg tctgtggcct tgggacagac agtcaggatc 60

acatgccaag gagacagcct cagaagctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctatggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacagcagtg gtaaccatca ttatgtcttc 300

ggaactggga ccaaggtcac cgtcctaggt 330

<210> SEQ ID NO 222
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 222

caaggagaca gcctcagaag ctattatgca agc 33

<210> SEQ ID NO 223
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 223

ggtaaaaaca accggccctc a 21

<210> SEQ ID NO 224
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 224

aactcccggg acagcagtgg taaccatcat 30

<210> SEQ ID NO 225
<211> LENGTH: 678
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 225

caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgtaagg cttctggtta cacctttaat agctatggta ttacttgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgttt acactggtaa gacaaactat 180

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gcacagaagt tccagggcag agtcaccatg accacagaca catccacgag tacagcctac 240

ctggacctga ggagcctgac atctgacgac acggccgttt attactgtgc gagaggaggg 300

gatcaccatg aatattgggg ccagggaacc ctggtcaccg tctcgagatc ttctgagctg 360

actcaggacc ctgctgtgtc tgtggccttg ggacagacag tcaggatcac atgccaagga 420

gacagcctca gaagctatta tgcaagctgg taccagcaga agccaggaca ggcccctgta 480

cttgtcatct atggtaaaaa caaccggccc tcagggatcc cagaccgatt ctctggctcc 540

agctcaggaa acacagcttc cttgaccatc actggggctc aggcggaaga tgaggctgac 600

tattactgta actcccggga cagcagtggt aaccatcatt atgtcttcgg aactgggacc 660

aaggtcaccg tcctaggt 678

<210> SEQ ID NO 226
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 226

agctatggta ttact 15

<210> SEQ ID NO 227
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 227

tggatcagcg tttacactgg taagacaaac tatgcacaga agttccaggg c 51

<210> SEQ ID NO 228
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 228

ggaggggatc accatgaata t 21

<210> SEQ ID NO 229
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 229

aattttatgc tgactcagcc actctcagtg tcagtggccc tgggacagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa aatgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcat ctatagggat agcaaccggc cctctgggat ccctgagcga 180

ttctctggct ccaactcggg gaacacggcc accctgacca tcagcagagc ccaagccggg 240

gatgaggctg actattactg tcaggtgtgg gacagcagca ctgtggtatt cggcggaggg 300

accaagctga ccgtcctagg t 321

<210> SEQ ID NO 230
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 230

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gggggaaaca acattggaag taaaaatgtg cac 33

<210> SEQ ID NO 231
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 231

agggatagca accggccctc t 21

<210> SEQ ID NO 232
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 232

caggtgtggg acagcagcac t 21

<210> SEQ ID NO 233
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 233

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc cgggggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcaggt attagtggta gtggtggtag aacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attctaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagatccc 300

ctcgcattac gagattttga ctggttatcc cccgggcggg actttgatta ctggggccag 360

ggaaccctgg tcaccgtctc gaga 384

<210> SEQ ID NO 234
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 234

agctatgcca tgagc 15

<210> SEQ ID NO 235
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 235

ggtattagtg gtagtggtgg tagaacatac tacgcagact ccgtgaaggg c 51

<210> SEQ ID NO 236
<211> LENGTH: 57
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 236

gatcccctcg cattacgaga ttttgactgg ttatcccccg ggcgggactt tgattac 57

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<210> SEQ ID NO 237
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 237

cagtctgtgt tgacgcagcc gccctcagtg tctgcggccc cgggacagaa ggtcaccatc 60

tcctgctctg gaagccactc caacattgga aataattatg tatcgtggtc ccagcaactc 120

ccaggaacag cccccaaact cctcatttat gacaataata agcgaccctc agggattcct 180

gaccgattct ctggctccaa gtctggcacg tcagccaccc tggacatcgc cgggctccag 240

actggggacg aggccgatta ttactgcgga gcatgggata ccagcctgag ttcttatgtc 300

ttcggagctg ggaccaaggt caccgtccta ggt 333

<210> SEQ ID NO 238
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 238

tctggaagcc actccaacat tggaaataat tatgtatcg 39

<210> SEQ ID NO 239
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 239

gacaataata agcgaccctc a 21

<210> SEQ ID NO 240
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 240

ggagcatggg ataccagcct gagttct 27

<210> SEQ ID NO 241
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 241

gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttggtac agcaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagaaggt 300

ttatcgggtg ggtacggtat ggacgtctgg ggccaaggga ccacggtcac cgtctcgagc 360

<210> SEQ ID NO 242
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 242

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agctatgcta tcagc 15

<210> SEQ ID NO 243
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 243

gggatcatcc ctatctttgg tacagcaaac tacgcacaga agttccaggg c 51

<210> SEQ ID NO 244
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 244

gaaggtttat cgggtgggta cggtatggac gtc 33

<210> SEQ ID NO 245
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 245

cagtctgtgt tgacgcagcc gccctcagtg tctggggccc cagggcagag ggtcaccatc 60

tcctgcactg ggagcagctc caacatcggg gcaggttatg atgtacactg gtaccagcag 120

cttccaggaa cagccccaa actcctcatc tatcgtaaca acaatcggcc ctcaggggtc 180

cctgaccgat tctctggctc caactctggc acctcagcct ccctggccat cactgggctc 240

cgggctgaag atgaggctga ttattactgc cagtcctatg acagcagcct gagtagttat 300

gtcttcggaa ctgggaccaa ggtcaccgtc ctaggt 336

<210> SEQ ID NO 246
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 246

actgggagca gctccaacat cggggcaggt tatgatgtac ac 42

<210> SEQ ID NO 247
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 247

cgtaacaaca atcggccctc a 21

<210> SEQ ID NO 248
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 248

cagtcctatg acagcagcct gagtagt 27

<210> SEQ ID NO 249
<211> LENGTH: 375

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<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 249

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccaac tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagcgtat 300

tacgatattt tgactggtta tttttacaac ggtatggacg tctggggcca agggacaatg 360

gtcaccgtct cgagc 375

<210> SEQ ID NO 250
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 250

agctatgcca tgagc 15

<210> SEQ ID NO 251
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 251

gctattagtg gtagtggtgg tagcacatac tacgcagact ccgtgaaggg c 51

<210> SEQ ID NO 252
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 252

gcgtattacg atattttgac tggttatttt tacaacggta tggacgtc 48

<210> SEQ ID NO 253
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 253

caggctgtgc tcactcagcc gtcttccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt ggttatgact atgtctcctg gtaccaacaa 120

cacccaggca aagcccccaa actcatgatt catgatgtca ggaatcggcc ctcaggggtt 180

tctaatcgct tctctggctc caagtttggc aacacggcct ccctgaccat ctctgggctc 240

cagactgagg acgaggctga ttattactgc agttcatata caagcagcag cactcatgtg 300

ctattcggcg gagggaccaa gctgaccgtc ctaggt 336

<210> SEQ ID NO 254
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 254

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actggaacca gcagtgacgt tggtggttat gactatgtct cc 42

<210> SEQ ID NO 255
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 255

gatgtcagga atcggccctc a 21

<210> SEQ ID NO 256
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 256

agttcatata caagcagcag cactcat 27

<210> SEQ ID NO 257
<211> LENGTH: 369
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 257

caggtgcagc tggtgcagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120

ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag cataggctat 180

gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagag ctccctgtat 240

ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaaggccac 300

tctccgtata gcagtggctg gtctgacttt gactactggg gccagggaac cctggtcacc 360

gtctcgagc 369

<210> SEQ ID NO 258
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 258

gattatgcca tgcac 15

<210> SEQ ID NO 259
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 259

ggtattagtt ggaatagtgg tagcataggc tatgcggact ctgtgaaggg c 51

<210> SEQ ID NO 260
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 260

ggccactctc cgtatagcag tggctggtct gactttgact ac 42

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<210> SEQ ID NO 261
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 261

cagtctgtgt tgacgcagcc gccctcagtg tctggggccc cagggcagag ggtcaccatc 60

tcctgcaccg ggagcagctc caacatcggg gcaggttatg atgttcagtg gtaccagcag 120

ctcccaggaa cagccccaa actcctcatc catgctaaca agaatcggcc ctcaggggtc 180

cctgaccgaa tctctggctc caagtctggc accacagcct ccctggccat cactgggttc 240

caggctgagg atgaggctga ttattactgc cagtcctatg acagcagcct gactggttat 300

gtcttcggaa ctgggaccaa ggtcaccgtc ctaggt 336

<210> SEQ ID NO 262
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 262

accgggagca gctccaacat cggggcaggt tatgatgttc ag 42

<210> SEQ ID NO 263
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 263

gctaacaaga atcggccctc a 21

<210> SEQ ID NO 264
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 264

cagtcctatg acagcagcct gactggt 27

<210> SEQ ID NO 265
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 265

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttgct gattatgcca tgcactgggt ccggcaagct 120

ccagggaagg gcctggagtg ggtctcaagt attagttgga atagtggtag catagcctat 180

gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240

ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagcctca 300

gcagctggta ctgaatacta ccactactac ggtatggacg tctggggcca agggaccacg 360

gtcaccgtct cgaga 375

<210> SEQ ID NO 266
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 266

gattatgcca tgcac 15

<210> SEQ ID NO 267
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 267

agtattagtt ggaatagtgg tagcatagcc tatgcggact ctgtgaaggg c 51

<210> SEQ ID NO 268
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 268

gcctcagcag ctggtactga atactaccac tactacggta tggacgtc 48

<210> SEQ ID NO 269
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 269

tcctatgtgc tgactcagcc accctcagcg tctgggaccc ccgggcagag ggtcaccatc 60

tcttgttctg gaagcagctc caacatcgga agtaatacta taaactggta ccagcagctc 120

ccaggaacgg cccccaaact cctcatctat aataatcatc agcggccctc aggggtccct 180

gaccgattct ctggctcaaa gtctggcacc tcagcctccc tggccatcag tgggctccag 240

tctgcggatg aggctgatta ttactgtgga gcgtggaatg acagcctgaa tgtctatgtc 300

ttcggaactg ggaccaaggt caccgtccta ggt 333

<210> SEQ ID NO 270
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 270

tctggaagca gctccaacat cggaagtaat actataaac 39

<210> SEQ ID NO 271
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 271

aataatcatc agcggccctc a 21

<210> SEQ ID NO 272
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 272

ggagcgtgga atgacagcct gaatgtc 27

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<210> SEQ ID NO 273
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 273

caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggtta cacctttacc agctatggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gacagcagca 300

agcctaaagt attactatga tagtagtggt tattactact ggggccaggg aaccctggtc 360

accgtctcga ga 372

<210> SEQ ID NO 274
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 274

agctatggta tcagc 15

<210> SEQ ID NO 275
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 275

tggatcagcg cttacaatgg taacacaaac tatgcacaga agctccaggg c 51

<210> SEQ ID NO 276
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 276

gcagcaagcc taaagtatta ctatgatagt agtggttatt actac 45

<210> SEQ ID NO 277
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 277

tcttctgagc tgactcagga ccctgctgtg tctgtggcct tgggacagac agtcaggatc 60

acatgccaag gagacagcct cagaagctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctctggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg agacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggcta actattactg taactctcgg gacagcagtg gttacccctc ttgggtgttc 300

ggcggaggga ccaagctgac cgtcctaggc 330

<210> SEQ ID NO 278
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 278

caaggagaca gcctcagaag ctattatgca agc 33

<210> SEQ ID NO 279
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 279

ggtaaaaaca accggccctc a 21

<210> SEQ ID NO 280
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 280

aactctcggg acagcagtgg ttacccctct 30

<210> SEQ ID NO 281
<211> LENGTH: 390
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 281

caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg gttctggtta cgtttttaac agttatggta ttacctgggt gcgacaggcc 120

ccaggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtta cacagactat 180

gcacagaagg tccagggcag agtcaccatg accacagaga catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgttt attattgtgc gagggattac 300

tatgatagta gtacttatta ctccagtgat tacttccagt actacggtat ggacgtctgg 360

ggccaaggga ccacggtcac cgtctcgagc 390

<210> SEQ ID NO 282
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 282

agttatggta ttacc 15

<210> SEQ ID NO 283
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 283

tggatcagcg cttacaatgg ttacacagac tatgcacaga aggtccaggg c 51

<210> SEQ ID NO 284
<211> LENGTH: 63
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 284

gattactatg atagtagtac ttattactcc agtgattact tccagtacta cggtatggac 60

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gtc 63

<210> SEQ ID NO 285
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 285

caggctgtgc tgactcagcc ggcttccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt gcttataact atgtctcctg gtaccaacaa 120

cacccaggca aagcccccaa actcatgatt tctgatgtca gtaggcggcc ctcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

cagactgagg acgaggctga ttattactgc agctcatata caagcagcaa cactgtctta 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 286
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 286

actggaacca gcagtgacgt tggtgcttat aactatgtct cc 42

<210> SEQ ID NO 287
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 287

gatgtcagta ggcggccctc a 21

<210> SEQ ID NO 288
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 288

agctcatata caagcagcaa cact 24

<210> SEQ ID NO 289
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 289

caggctgtgc tgactcagcc ggcttccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt gcttataact atgtctcctg gtaccaacaa 120

cacccaggca aagcccccaa actcatgatt tctgatgtca gtaggcggcc ctcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

cagactgagg acgaggctga ttattactgc agctcatata caagcagcaa cactgtctta 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 290
<211> LENGTH: 15

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<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 290

aactactgga tcggc 15

<210> SEQ ID NO 291
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 291

atcatctatc ctggtgactc tgataccagg tacagtccgt cattccaagg c 51

<210> SEQ ID NO 292
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 292

cggggctccc gtagtagtgg tgaagatgct tttgaagtc 39

<210> SEQ ID NO 293
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 293

tcctatgagc tgactcagcc accctcagtg tcagtggccc caggaaagac ggccacaatt 60

acgtgtgggg gcgacaacat tggaagtaag agtgtgcact ggtaccagca gaggccaggc 120

caggcccctg tgttggtcat caattatgat agtgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtggaa gatcgccgtg gtggttatca tgtggtattc 300

ggcggaggga ccaagctgac cgtcctaggt 330

<210> SEQ ID NO 294
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 294

gggggcgaca acattggaag taagagtgtg cac 33

<210> SEQ ID NO 295
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 295

tatgatagtg accggccctc a 21

<210> SEQ ID NO 296
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 296

caggtggaag atcgccgtgg tggttatcat 30

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<210> SEQ ID NO 297
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 297

caggtgcagc tggtgcagtc tgggggaggc ttggtccagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt caccgtcagt agcaactaca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagtt atttatagcg gtggtagcac atactacgca 180

gactccgtga agggcagatt caccatctcc agagacaatt ccaagaacac gctgtatctt 240

caaatgaaca gcctgagagc cgaggacacg gctgtgtatt actgtgcgag ggaaggatat 300

tgtagtggtg gtagctgcta ctcctacggc gcttttgata tctggggcca agggaccacg 360

gtcaccgtct cgagc 375

<210> SEQ ID NO 298
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 298

agcaactaca tgagc 15

<210> SEQ ID NO 299
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 299

gttatttata gcggtggtag cacatactac gcagactccg tgaagggc 48

<210> SEQ ID NO 300
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 300

gaaggatatt gtagtggtgg tagctgctac tcctacggcg cttttgatat c 51

<210> SEQ ID NO 301
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 301

caggtgcagc tggtgcagtc tgggggaggc ttggtccagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt caccgtcagt agcaactaca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagtt atttatagcg gtggtagcac atactacgca 180

gactccgtga agggcagatt caccatctcc agagacaatt ccaagaacac gctgtatctt 240

caaatgaaca gcctgagagc cgaggacacg gctgtgtatt actgtgcgag ggaaggatat 300

tgtagtggtg gtagctgcta ctcctacggc gcttttgata tctggggcca agggaccacg 360

gtcaccgtct cgagc 375

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<210> SEQ ID NO 302
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 302

cgggcgagtc agaatattgc caactggtta gcc 33

<210> SEQ ID NO 303
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 303

gctgcatcca atttgcaaag t 21

<210> SEQ ID NO 304
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 304

caacagggta acagtttccc tcgg 24

<210> SEQ ID NO 305
<211> LENGTH: 390
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 305

caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggtta cgtttttaac agttatggta ttacctgggt gcgacaggcc 120

ccaggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtta cacagactat 180

gcacagaagg tccagggcag agtcaccatg accacagaga catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgttt attattgtgc gagggactac 300

tatgatagta gtacttatta ctccagtgat tacttcaagt actacggtat ggacgtctgg 360

ggccaaggga ccacggtcac cgtctcgagc 390

<210> SEQ ID NO 306
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 306

agttatggta ttacc 15

<210> SEQ ID NO 307
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 307

tggatcagcg cttacaatgg ttacacagac tatgcacaga aggtccaggg c 51

<210> SEQ ID NO 308
<211> LENGTH: 63
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 308

gactactatg atagtagtac ttattactcc agtgattact tcaagtacta cggtatggac 60

gtc 63

<210> SEQ ID NO 309
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 309

caggctgtgc tcactcagcc gtcttccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgctctg gaaccagcag tgacgttggt gcttataact atgtctcctg gtaccaacaa 120

cacccaggca aagcccccag actcctgact tttgatgtca ataggcgtcc ctcagggtct 180

tctagtcgct tctctggctc caagtctggc aacacggcct ccctgactat ctctgggctc 240

caggctgagg acgaggctga ctattactgc agttcatata caaacagcaa cactgtcgtg 300

ttcggcggag ggaccaggct gaccgtccta agt 333

<210> SEQ ID NO 310
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 310

tctggaacca gcagtgacgt tggtgcttat aactatgtct cc 42

<210> SEQ ID NO 311
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 311

gatgtcaata ggcgtccctc a 21

<210> SEQ ID NO 312
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 312

agttcatata caaacagcaa cact 24

<210> SEQ ID NO 313
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 313

caggtgcagc tgcaggagtc ggggccagga ctggtgaagc cgtcggagac cctggccctc 60

acctgcactg tctctggtgg ctccatcagt aactactact ggagttggat ccggcagccc 120

ccagggaagg gactggagtg gattgggtat atctatgaca ttgagaatac caactacaac 180

ccctccctca agagtcgagt caccatatca gtggacacgt ccaagaacca gttctccctg 240

aagttgagct ctgtgaccgc tgatgacacg gccgtatatt actgtgcgag agattcaagg 300

gtcattcgat ttttggaggg gtactcctac tactacggtg tggacgtctg gggccaaggg 360

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acaatggtca ccgtctcgag c 381

<210> SEQ ID NO 314
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 314

aactactact ggagt 15

<210> SEQ ID NO 315
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 315

tatatctatg acattgagaa taccaactac aacccctccc tcaagagt 48

<210> SEQ ID NO 316
<211> LENGTH: 57
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 316

gattcaaggg tcattcgatt tttggagggg tactcctact actacggtgt ggacgtc 57

<210> SEQ ID NO 317
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 317

tcctatgagc tgactcagcc accctcagcg tctgggaccc ccgggcagac ggtcatcatc 60

tcttgttctg gaagcaggtc caacatcgga ggtcatggtg taaattggca ccagcaggtt 120

ccaggaacgg cccccaaact cctcatctac cgtaatgatc gccggccctc aggggtcccg 180

gaccgattct ctggctccaa gtctggcact tcagcctccc tggtcatcag tggactgcag 240

tttgaggatg aggctgatta ttactgtgta gcatgggaag acagcctgga tggtccggtg 300

ttcggcggag ggaccaagct gactgtccta ggt 333

<210> SEQ ID NO 318
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 318

tctggaagca ggtccaacat cggaggtcat ggtgtaaat 39

<210> SEQ ID NO 319
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 319

cgtaatgatc gccggccctc a 21

<210> SEQ ID NO 320
<211> LENGTH: 27

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<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 320

gtagcatggg aagacagcct ggatggt 27

<210> SEQ ID NO 321
<211> LENGTH: 345
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 321

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcaact attagtggta gtggtggtag tacatactac 180

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctatat 240

cttcaaatga acagcctgag agccgaggac acggccgtct attattgtgc gagaggtata 300

gtggctacta gctggggcca gggaaccctg gtcaccgtct cgaga 345

<210> SEQ ID NO 322
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 322

agctatgcca tgagc 15

<210> SEQ ID NO 323
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 323

actattagtg gtagtggtgg tagtacatac tacgcagact ccgtgaaggg c 51

<210> SEQ ID NO 324
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 324

ggtatagtgg ctactagc 18

<210> SEQ ID NO 325
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 325

tcctatgagc tgactcagcc accctcagtg tcagtggccc caggacagac ggccagaatt 60

acctgtgggg gaaacaagat tggaagcaaa agtgtgcact ggtaccagca gaagcaaggc 120

caggcccctg tattggtcat ctatttggat cgcgaccggc cctcagggat ccctgaacga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcaccagggt cgaagccgag 240

gatgaggccg actattattg tcacctgtgg gatagtggta gtgatcaggt gttcggcgga 300

gggaccaaac tgaccgtcct gggt 324

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<210> SEQ ID NO 326
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 326

ggggggaaaca agattggaag caaaagtgtg cac 33

<210> SEQ ID NO 327
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 327

ttggatcgcg accggccctc a 21

<210> SEQ ID NO 328
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 328

cacctgtggg atagtggtag tgat 24

<210> SEQ ID NO 329
<211> LENGTH: 342
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 329

gaggtgcagc tggtggagtc tgggggaggc gtagtacagc ctggggggtc cctgagactc 60

tcctgtgcag cctcaggatt caactttgat gtttatggca tgaactgggt ccgtcaagtt 120

ccagggaagg gtctggagtg ggtctctctt atcaacgggg atggcggttt aagatattac 180

gcagactctg tgaagggccg attcaccgtc tccagagaca acagcaggaa ttccctatat 240

ctgcaaatga acagtctcag aagtgaggac accgccctgt attattgtgt aaagggaaac 300

ttccagcagt ggggccaggg aaccctggtc accgtctcga ga 342

<210> SEQ ID NO 330
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 330

gtttatggca tgaac 15

<210> SEQ ID NO 331
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 331

cttatcaacg gggatggcgg tttaagatat tacgcagact ctgtgaaggg c 51

<210> SEQ ID NO 332
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 332

ggaaacttcc agcag 15

<210> SEQ ID NO 333
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 333

tcctatgtgc tgactcagcc accctcagtg tcagtggccc caggaaagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcat ctattatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgt ggtattcggc 300

ggagggacca agctgaccgt cctaggt 327

<210> SEQ ID NO 334
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 334

gggggaaaca acattggaag taaaagtgtg cac 33

<210> SEQ ID NO 335
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 335

tatgatagcg accggccctc a 21

<210> SEQ ID NO 336
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 336

caggtgtggg atagtagtag tgatcat 27

<210> SEQ ID NO 337
<211> LENGTH: 345
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 337

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccgtcaagct 120

ccagggaagg gtctggagtg ggtctctctt attagtgggg atggtggtag cacatactat 180

gcagactctg tgaaggaccg attcaccatc tccagagaca acagcaaaaa ctccctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gaggggaaac 300

tactttgact actggggcca gggaaccctg gtcaccgtct cgaga 345

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<210> SEQ ID NO 338
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 338

gattatgcca tgcac 15

<210> SEQ ID NO 339
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 339

cttattagtg gggatggtgg tagcacatac tatgcagact ctgtgaagga c 51

<210> SEQ ID NO 340
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 340

ggaaactact ttgactac 18

<210> SEQ ID NO 341
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 341

tcctatgagc tgactcagcc actctcagtg tcagtggccc tgggacagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa aatgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcat ctatagggat agcaaccggc cctctgggat ccctgagcga 180

ttctctggct ccaactcggg gaacacggcc accctgacca tcagcagagc ccaagccggg 240

gatgaggctg actattactg tcaggtgtgg gacagcagcg tggtattcgg cggagggacc 300

aagctgaccg tcctaggt 318

<210> SEQ ID NO 342
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 342

gggggaaaca acattggaag taaaaatgtg cac 33

<210> SEQ ID NO 343
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 343

agggatagca accggccctc t 21

<210> SEQ ID NO 344
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 344

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caggtgtggg acagcagc 18

<210> SEQ ID NO 345
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 345

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt caccttcagt agctatagca tgaactgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtttcatac attagtagta gtagtagtac catatactac 180

gcagactctg tgaagggccg attcaccatc tccagagaca atgccaagaa ctcactgtat 240

ctgcagatga acagcctgag agacgaggac acggctgtgt attactgtgc gagagtgatg 300

ccgagttact actactacta cggtatggac gtctggggcc aagggaccac ggtcaccgtc 360

tcgaga 366

<210> SEQ ID NO 346
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 346

agctatagca tgaac 15

<210> SEQ ID NO 347
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 347

tacattagta gtagtagtag taccatatac tacgcagact ctgtgaaggg c 51

<210> SEQ ID NO 348
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 348

gtgatgccga gttactacta ctactacggt atggacgtc 39

<210> SEQ ID NO 349
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 349

aattttatgc tgactcagcc ccactctgtg tcggagtctc cggggaagac ggtaaccatc 60

tcctgcaccg gcagcagtgg cagcattgcc agcaactatg tgcagtggta ccagcagcgc 120

ccgggcagtg cccccaccac tgtgatctat gaggatagtg aaagaccctc tggggtccct 180

gatcggttct ctggctccat cgacagctcc tccaactctg cctccctcac catctctgga 240

ctgaagactc aggacgaggc tgactactac tgtcagtctt atgatggcgt caattgggtg 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

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<210> SEQ ID NO 350
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 350

accggcagca gtggcagcat tgccagcaac tatgtgcag 39

<210> SEQ ID NO 351
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 351

gaggatagtg aaagaccctc t 21

<210> SEQ ID NO 352
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 352

cagtcttatg atggcgtcaa t 21

<210> SEQ ID NO 353
<211> LENGTH: 342
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 353

gaggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60

tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120

ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtaa taaatactat 180

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc ggactacggt 300

atggacgtct ggggccaagg gaccacggtc accgtctcga ga 342

<210> SEQ ID NO 354
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 354

agctatggca tgcac 15

<210> SEQ ID NO 355
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 355

gttatatcat atgatggaag taataaatac tatgcagact ccgtgaaggg c 51

<210> SEQ ID NO 356
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 356

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tacggtatgg acgtc 15

<210> SEQ ID NO 357
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 357

gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180

aggttcagtg gcagtggatc tgggactgat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg caacttacta ctgtcaacag agttacagta cccccgtgac gttcggccaa 300

gggaccaagg tggaaatcaa a 321

<210> SEQ ID NO 358
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 358

cgggcaagtc agagcattag cagctattta aat 33

<210> SEQ ID NO 359
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 359

gctgcatcca gtttgcaaag t 21

<210> SEQ ID NO 360
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 360

caacagagtt acagtacccc c 21

<210> SEQ ID NO 361
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 361

caggtgcagc tgcaggagtc gggcccggga ctggtgaagc cttcacagac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagc agtggtggtt actactggag ctggatccgc 120

cagcacccag ggaagggcct ggagtggatt gggtacatct attacagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagttacc atatcagtag acacgtctaa gaaccagttc 240

tccctgaagc tgagctctgt gactgccgcg gacacggccg tgtattactg tgcgagagat 300

cgggggactg gggatgcttt tgatatctgg ggccaaggga caatggtcac cgtctcgaga 360

<210> SEQ ID NO 362
<211> LENGTH: 21

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<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 362

agtggtggtt actactggag c 21

<210> SEQ ID NO 363
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 363

tacatctatt acagtgggag cacctactac aacccgtccc tcaagagt 48

<210> SEQ ID NO 364
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 364

gatcgggggga ctggggatgc ttttgatatc 30

<210> SEQ ID NO 365
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 365

cagtctgtgt tgacgcagcc gccctcggtg tctggggccc cccggcagac ggtcaccatc 60

tcctgctctg ggagcagctc caacatcgga caaaattctg ttacctggta ccagcgcctc 120

ccgggtgagg ctcccaaact cctcatctac tatgatgatc tcttgcactc aggagtctct 180

gaccgattct ctggctccaa gtctggcacc tcagcctcac tggccatcag tggactccag 240

tctgaggatg aggctgagta ctactgtgcg tcatgggatg acagcctgaa aggtccggta 300

ttcggcggag ggaccaaact gaccgtccta ggt 333

<210> SEQ ID NO 366
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 366

tctgggagca gctccaacat cggacaaaat tctgttacc 39

<210> SEQ ID NO 367
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 367

tatgatgatc tcttgcactc a 21

<210> SEQ ID NO 368
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 368

gcgtcatggg atgacagcct gaaaggt 27

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<210> SEQ ID NO 369
<211> LENGTH: 1200
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 369

Met Arg Pro Ser Gly Thr Ala Gly Ala Ala Leu Leu Ala Leu Leu Ala
1 5 10 15

Ala Leu Cys Pro Ala Ser Arg Ala Leu Glu Glu Lys Lys Val Cys Gln
20 25 30

Gly Thr Ser Asn Lys Leu Thr Gln Leu Gly Thr Phe Glu Asp His Phe
35 40 45

Leu Ser Leu Gln Arg Met Phe Asn Asn Cys Glu Val Val Leu Gly Asn
50 55 60

Leu Glu Ile Thr Tyr Val Gln Arg Asn Tyr Asp Leu Ser Phe Leu Lys
65 70 75 80

Thr Ile Gln Glu Val Ala Gly Tyr Val Leu Ile Ala Leu Asn Thr Val
85 90 95

Glu Arg Ile Pro Leu Glu Asn Leu Gln Ile Ile Arg Gly Asn Met Tyr
100 105 110

Tyr Glu Asn Ser Tyr Ala Leu Ala Gly Leu Lys Glu Leu Pro Met Arg
115 120 125

Asn Leu Gln Glu Ile Leu His Gly Ala Val Arg Phe Ser Asn Asn Pro
130 135 140

Ala Leu Cys Asn Val Glu Ser Ile Gln Trp Arg Asp Ile Val Ser Ser
145 150 155 160

Asp Phe Leu Ser Asn Met Ser Met Asp Phe Gln Asn His Leu Gly Ser
165 170 175

Cys Gln Lys Cys Asp Pro Ser Cys Pro Asn Gly Ser Cys Trp Gly Ala
180 185 190

Gly Glu Glu Asn Cys Gln Lys Leu Thr Lys Ile Ile Cys Ala Gln Gln
195 200 205

Cys Ser Gly Arg Cys Arg Gly Lys Ser Pro Ser Asp Cys Cys His Asn
210 215 220

Gln Cys Ala Ala Gly Cys Thr Gly Pro Arg Glu Ser Asp Cys Leu Val
225 230 235 240

Cys Arg Lys Phe Arg Asp Glu Ala Thr Cys Lys Asp Thr Cys Pro Pro
245 250 255

Leu Met Leu Tyr Asn Pro Thr Thr Tyr Gln Met Asp Val Asn Pro Glu
260 265 270

Gly Lys Tyr Ser Phe Gly Ala Thr Cys Val Lys Lys Cys Pro Arg Asn
275 280 285

Tyr Val Val Thr Asp His Gly Ser Cys Val Arg Ala Cys Gly Ala Asp
290 295 300

Ser Tyr Glu Met Glu Glu Asp Gly Val Arg Lys Cys Lys Lys Cys Glu
305 310 315 320

Gly Pro Cys Arg Lys Val Cys Asn Gly Ile Gly Ile Gly Glu Phe Lys
325 330 335

Asp Ser Leu Ser Ile Asn Ala Thr Asn Ile Lys His Phe Lys Asn Cys
340 345 350

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

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        355                 360                 365

Asp Ser Phe Thr His Thr Pro Pro Leu Asp Pro Gln Glu Leu Asp Ile
    370                 375                 380

Leu Lys Thr Val Lys Glu Ile Thr Gly Phe Leu Leu Ile Gln Ala Trp
385                 390                 395                 400

Pro Glu Asn Arg Thr Asp Leu His Ala Phe Glu Asn Leu Glu Ile Ile
                405                 410                 415

Arg Gly Arg Thr Lys Gln His Gly Gln Phe Ser Leu Ala Val Val Ser
            420                 425                 430

Leu Asn Ile Thr Ser Leu Gly Leu Arg Ser Leu Lys Glu Ile Ser Asp
        435                 440                 445

Gly Asp Val Ile Ile Ser Gly Asn Lys Asn Leu Cys Tyr Ala Asn Thr
    450                 455                 460

Ile Asn Trp Lys Lys Leu Phe Gly Thr Ser Gly Gln Lys Thr Lys Ile
465                 470                 475                 480

Ile Ser Asn Arg Gly Glu Asn Ser Cys Lys Ala Thr Gly Gln Val Cys
                485                 490                 495

His Ala Leu Cys Ser Pro Glu Gly Cys Trp Gly Pro Glu Pro Arg Asp
            500                 505                 510

Cys Val Ser Cys Arg Asn Val Ser Arg Gly Arg Glu Cys Val Asp Lys
        515                 520                 525

Cys Asn Leu Leu Glu Gly Glu Pro Arg Glu Phe Val Glu Asn Ser Glu
    530                 535                 540

Cys Ile Gln Cys His Pro Glu Cys Leu Pro Gln Ala Met Asn Ile Thr
545                 550                 555                 560

Cys Thr Gly Arg Gly Pro Asp Asn Cys Ile Gln Cys Ala His Tyr Ile
                565                 570                 575

Asp Gly Pro His Cys Val Lys Thr Cys Pro Ala Gly Val Met Gly Glu
            580                 585                 590

Asn Asn Thr Leu Val Trp Lys Tyr Ala Asp Ala Gly His Val Cys His
        595                 600                 605

Leu Cys His Pro Asn Cys Thr Tyr Gly Cys Thr Gly Pro Gly Leu Glu
    610                 615                 620

Gly Cys Pro Thr Asn Gly Pro Lys Ile Pro Ser Ile Ala Thr Gly Met
625                 630                 635                 640

Val Gly Ala Leu Leu Leu Leu Leu Val Val Ala Leu Gly Ile Gly Leu
                645                 650                 655

Phe Met Arg Arg Arg His Ile Val Arg Lys Arg Thr Leu Arg Arg Leu
            660                 665                 670

Leu Gln Glu Arg Glu Leu Val Glu Pro Leu Thr Pro Ser Gly Glu Ala
        675                 680                 685

Pro Asn Gln Ala Leu Leu Arg Ile Leu Lys Glu Thr Glu Phe Lys Lys
    690                 695                 700

Ile Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys Gly Leu
705                 710                 715                 720

Trp Ile Pro Glu Gly Glu Lys Val Lys Ile Pro Val Ala Ile Lys Glu
                725                 730                 735

Leu Arg Glu Ala Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu
            740                 745                 750

Ala Tyr Val Met Ala Ser Val Asp Asn Pro His Val Cys Arg Leu Leu
        755                 760                 765
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Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Ile Thr Gln Leu Met Pro
    770                 775                 780

Phe Gly Cys Leu Leu Asp Tyr Val Arg Glu His Lys Asp Asn Ile Gly
785                 790                 795                 800

Ser Gln Tyr Leu Leu Asn Trp Cys Val Gln Ile Ala Lys Gly Met Asn
                805                 810                 815

Tyr Leu Glu Asp Arg Arg Leu Val His Arg Asp Leu Ala Ala Arg Asn
            820                 825                 830

Val Leu Val Lys Thr Pro Gln His Val Lys Ile Thr Asp Phe Gly Leu
        835                 840                 845

Ala Lys Leu Leu Gly Ala Glu Glu Lys Glu Tyr His Ala Glu Gly Gly
    850                 855                 860

Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu His Arg Ile
865                 870                 875                 880

Tyr Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val Trp Glu
                885                 890                 895

Leu Met Thr Phe Gly Ser Lys Pro Tyr Asp Gly Ile Pro Ala Ser Glu
            900                 905                 910

Ile Ser Ser Ile Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile
        915                 920                 925

Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met Ile Asp
    930                 935                 940

Ala Asp Ser Arg Pro Lys Phe Arg Glu Leu Ile Ile Glu Phe Ser Lys
945                 950                 955                 960

Met Ala Arg Asp Pro Gln Arg Tyr Leu Val Ile Gln Gly Asp Glu Arg
                965                 970                 975

Met His Leu Pro Ser Pro Thr Asp Ser Asn Phe Tyr Arg Ala Leu Met
            980                 985                 990

Asp Glu Glu Asp Met Asp Asp Val  Val Asp Ala Asp Glu  Tyr Leu Ile
        995                 1000                1005

Pro Gln  Gln Gly Phe Phe Ser  Ser Pro Ser Thr Ser  Arg Thr Pro
    1010                1015                1020

Leu Leu  Ser Ser Leu Ser Ala  Thr Ser Asn Asn Ser  Thr Val Ala
    1025                1030                1035

Cys Ile  Asp Arg Asn Gly Leu  Gln Ser Cys Pro Ile  Lys Glu Asp
    1040                1045                1050

Ser Phe  Leu Gln Arg Tyr Ser  Ser Asp Pro Thr Gly  Ala Leu Thr
    1055                1060                1065

Glu Asp  Ser Ile Asp Asp Thr  Phe Leu Pro Val Pro  Glu Tyr Ile
    1070                1075                1080

Asn Gln  Ser Val Pro Lys Arg  Pro Ala Gly Ser Val  Gln Asn Pro
    1085                1090                1095

Val Tyr  His Asn Gln Pro Leu  Asn Pro Ala Pro Ser  Arg Asp Pro
    1100                1105                1110

His Tyr  Gln Asp Pro His Ser  Thr Ala Val Gly Asn  Pro Glu Tyr
    1115                1120                1125

Leu Asn  Thr Val Gln Pro Thr  Cys Val Asn Ser Thr  Phe Asp Ser
    1130                1135                1140

Pro Ala  His Trp Ala Gln Lys  Gly Ser His Gln Ile  Ser Leu Asp
    1145                1150                1155
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Asn Pro  Asp Tyr Gln Gln Asp  Phe Phe Pro Lys Glu  Ala Lys Pro
    1160                1165                1170

Asn Gly  Ile Phe Lys Gly Ser  Thr Ala Glu Asn Ala  Glu Tyr Leu
    1175                1180                1185

Arg Val  Ala Pro Gln Ser Ser  Glu Phe Ile Gly Ala
    1190                1195                1200


<210> SEQ ID NO 370
<211> LENGTH: 1255
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 370

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1               5                   10                  15

Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
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Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
               325                 330                 335

Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
           340                 345                 350

Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
       355                 360                 365

Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
   370                 375                 380

Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385                 390                 395                 400

Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
               405                 410                 415

Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
           420                 425                 430

Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
       435                 440                 445

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
   450                 455                 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465                 470                 475                 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
               485                 490                 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
           500                 505                 510

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
       515                 520                 525

Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
   530                 535                 540

Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545                 550                 555                 560

Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
               565                 570                 575

Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
           580                 585                 590

Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
       595                 600                 605

Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
   610                 615                 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625                 630                 635                 640

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser
               645                 650                 655

Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly
           660                 665                 670

Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
       675                 680                 685

Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly
   690                 695                 700

Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
705                 710                 715                 720
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Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
                725                 730                 735

Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
            740                 745                 750

Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
        755                 760                 765

Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
    770                 775                 780

Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
785                 790                 795                 800

Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
                805                 810                 815

Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
            820                 825                 830

Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala
        835                 840                 845

Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
    850                 855                 860

Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
865                 870                 875                 880

Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
                885                 890                 895

Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
            900                 905                 910

Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
        915                 920                 925

Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
    930                 935                 940

Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met
945                 950                 955                 960

Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe
                965                 970                 975

Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu
            980                 985                 990

Asp Leu Gly Pro Ala Ser Pro Leu  Asp Ser Thr Phe Tyr  Arg Ser Leu
        995                 1000                1005

Leu Glu  Asp Asp Asp Met Gly  Asp Leu Val Asp Ala  Glu Glu Tyr
    1010                1015                1020

Leu Val  Pro Gln Gln Gly Phe  Phe Cys Pro Asp Pro  Ala Pro Gly
    1025                1030                1035

Ala Gly  Gly Met Val His His  Arg His Arg Ser Ser  Ser Thr Arg
    1040                1045                1050

Ser Gly  Gly Gly Asp Leu Thr  Leu Gly Leu Glu Pro  Ser Glu Glu
    1055                1060                1065

Glu Ala  Pro Arg Ser Pro Leu  Ala Pro Ser Glu Gly  Ala Gly Ser
    1070                1075                1080

Asp Val  Phe Asp Gly Asp Leu  Gly Met Gly Ala Ala  Lys Gly Leu
    1085                1090                1095

Gln Ser  Leu Pro Thr His Asp  Pro Ser Pro Leu Gln  Arg Tyr Ser
    1100                1105                1110

Glu Asp  Pro Thr Val Pro Leu  Pro Ser Glu Thr Asp  Gly Tyr Val
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    1115                1120                1125

Ala Pro  Leu Thr Cys Ser Pro  Gln Pro Glu Tyr Val  Asn Gln Pro
    1130                1135                1140

Asp Val  Arg Pro Gln Pro Pro  Ser Pro Arg Glu Gly  Pro Leu Pro
    1145                1150                1155

Ala Ala  Arg Pro Ala Gly Ala  Thr Leu Glu Arg Pro  Lys Thr Leu
    1160                1165                1170

Ser Pro  Gly Lys Asn Gly Val  Val Lys Asp Val Phe  Ala Phe Gly
    1175                1180                1185

Gly Ala  Val Glu Asn Pro Glu  Tyr Leu Thr Pro Gln  Gly Gly Ala
    1190                1195                1200

Ala Pro  Gln Pro His Pro Pro  Pro Ala Phe Ser Pro  Ala Phe Asp
    1205                1210                1215

Asn Leu  Tyr Tyr Trp Asp Gln  Asp Pro Pro Glu Arg  Gly Ala Pro
    1220                1225                1230

Pro Ser  Thr Phe Lys Gly Thr  Pro Thr Ala Glu Asn  Pro Glu Tyr
    1235                1240                1245

Leu Gly  Leu Asp Val Pro Val
    1250                1255


<210> SEQ ID NO 371
<211> LENGTH: 392
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 371

Met Glu Pro Pro Gly Arg Arg Glu Cys Pro Phe Pro Ser Trp Arg Phe
1               5                   10                  15

Pro Gly Leu Leu Leu Ala Ala Met Val Leu Leu Leu Tyr Ser Phe Ser
            20                  25                  30

Asp Ala Cys Glu Glu Pro Pro Thr Phe Glu Ala Met Glu Leu Ile Gly
        35                  40                  45

Lys Pro Lys Pro Tyr Tyr Glu Ile Gly Glu Arg Val Asp Tyr Lys Cys
    50                  55                  60

Lys Lys Gly Tyr Phe Tyr Ile Pro Pro Leu Ala Thr His Thr Ile Cys
65                  70                  75                  80

Asp Arg Asn His Thr Trp Leu Pro Val Ser Asp Asp Ala Cys Tyr Arg
                85                  90                  95

Glu Thr Cys Pro Tyr Ile Arg Asp Pro Leu Asn Gly Gln Ala Val Pro
            100                 105                 110

Ala Asn Gly Thr Tyr Glu Phe Gly Tyr Gln Met His Phe Ile Cys Asn
        115                 120                 125

Glu Gly Tyr Tyr Leu Ile Gly Glu Glu Ile Leu Tyr Cys Glu Leu Lys
    130                 135                 140

Gly Ser Val Ala Ile Trp Ser Gly Lys Pro Pro Ile Cys Glu Lys Val
145                 150                 155                 160

Leu Cys Thr Pro Pro Pro Lys Ile Lys Asn Gly Lys His Thr Phe Ser
                165                 170                 175

Glu Val Glu Val Phe Glu Tyr Leu Asp Ala Val Thr Tyr Ser Cys Asp
            180                 185                 190

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

Val Val Lys Cys Arg Phe Pro Val Val Glu Asn Gly Lys Gln Ile Ser
225                 230                 235                 240

Gly Phe Gly Lys Lys Phe Tyr Tyr Lys Ala Thr Val Met Phe Glu Cys
                245                 250                 255

Asp Lys Gly Phe Tyr Leu Asp Gly Ser Asp Thr Ile Val Cys Asp Ser
            260                 265                 270

Asn Ser Thr Trp Asp Pro Pro Val Pro Lys Cys Leu Lys Val Leu Pro
        275                 280                 285

Pro Ser Ser Thr Lys Pro Pro Ala Leu Ser His Ser Val Ser Thr Ser
    290                 295                 300

Ser Thr Thr Lys Ser Pro Ala Ser Ser Ala Ser Gly Pro Arg Pro Thr
305                 310                 315                 320

Tyr Lys Pro Pro Val Ser Asn Tyr Pro Gly Tyr Pro Lys Pro Glu Glu
                325                 330                 335

Gly Ile Leu Asp Ser Leu Asp Val Trp Val Ile Ala Val Ile Val Ile
            340                 345                 350

Ala Ile Val Val Gly Val Ala Val Ile Cys Val Val Pro Tyr Arg Tyr
        355                 360                 365

Leu Gln Arg Arg Lys Lys Lys Gly Thr Tyr Leu Thr Asp Glu Thr His
    370                 375                 380

Arg Glu Val Lys Phe Thr Ser Leu
385                 390


<210> SEQ ID NO 372
<211> LENGTH: 1066
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 372

Met Gly Pro Gly Pro Ser Arg Ala Pro Arg Ala Pro Arg Leu Met Leu
1               5                   10                  15

Cys Ala Leu Ala Leu Met Val Ala Ala Gly Gly Cys Val Val Ser Ala
            20                  25                  30

Phe Asn Leu Asp Thr Arg Phe Leu Val Val Lys Glu Ala Gly Asn Pro
        35                  40                  45

Gly Ser Leu Phe Gly Tyr Ser Val Ala Leu His Arg Gln Thr Glu Arg
    50                  55                  60

Gln Gln Arg Tyr Leu Leu Leu Ala Gly Ala Pro Arg Glu Leu Ala Val
65                  70                  75                  80

Pro Asp Gly Tyr Thr Asn Arg Thr Gly Ala Val Tyr Leu Cys Pro Leu
                85                  90                  95

Thr Ala His Lys Asp Asp Cys Glu Arg Met Asn Ile Thr Val Lys Asn
            100                 105                 110

Asp Pro Gly His His Ile Ile Glu Asp Met Trp Leu Gly Val Thr Val
        115                 120                 125

Ala Ser Gln Gly Pro Ala Gly Arg Val Leu Val Cys Ala His Arg Tyr
    130                 135                 140

Thr Gln Val Leu Trp Ser Gly Ser Glu Asp Gln Arg Arg Met Val Gly
145                 150                 155                 160

Lys Cys Tyr Val Arg Gly Asn Asp Leu Glu Leu Asp Ser Ser Asp Asp
                165                 170                 175
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Trp Gln Thr Tyr His Asn Glu Met Cys Asn Ser Asn Thr Asp Tyr Leu
            180                 185                 190

Glu Thr Gly Met Cys Gln Leu Gly Thr Ser Gly Gly Phe Thr Gln Asn
        195                 200                 205

Thr Val Tyr Phe Gly Ala Pro Gly Ala Tyr Asn Trp Lys Gly Asn Ser
    210                 215                 220

Tyr Met Ile Gln Arg Lys Glu Trp Asp Leu Ser Glu Tyr Ser Tyr Lys
225                 230                 235                 240

Asp Pro Glu Asp Gln Gly Asn Leu Tyr Ile Gly Tyr Thr Met Gln Val
                245                 250                 255

Gly Ser Phe Ile Leu His Pro Lys Asn Ile Thr Ile Val Thr Gly Ala
            260                 265                 270

Pro Arg His Arg His Met Gly Ala Val Phe Leu Leu Ser Gln Glu Ala
        275                 280                 285

Gly Gly Asp Leu Arg Arg Arg Gln Val Leu Glu Gly Ser Gln Val Gly
    290                 295                 300

Ala Tyr Phe Gly Ser Ala Ile Ala Leu Ala Asp Leu Asn Asn Asp Gly
305                 310                 315                 320

Trp Gln Asp Leu Leu Val Gly Ala Pro Tyr Tyr Phe Glu Arg Lys Glu
                325                 330                 335

Glu Val Gly Gly Ala Ile Tyr Val Phe Met Asn Gln Ala Gly Thr Ser
            340                 345                 350

Phe Pro Ala His Pro Ser Leu Leu Leu His Gly Pro Ser Gly Ser Ala
        355                 360                 365

Phe Gly Leu Ser Val Ala Ser Ile Gly Asp Ile Asn Gln Asp Gly Phe
    370                 375                 380

Gln Asp Ile Ala Val Gly Ala Pro Phe Glu Gly Leu Gly Lys Val Tyr
385                 390                 395                 400

Ile Tyr His Ser Ser Ser Lys Gly Leu Leu Arg Gln Pro Gln Gln Val
                405                 410                 415

Ile His Gly Glu Lys Leu Gly Leu Pro Gly Leu Ala Thr Phe Gly Tyr
            420                 425                 430

Ser Leu Ser Gly Gln Met Asp Val Asp Glu Asn Phe Tyr Pro Asp Leu
        435                 440                 445

Leu Val Gly Ser Leu Ser Asp His Ile Val Leu Leu Arg Ala Arg Pro
    450                 455                 460

Val Ile Asn Ile Val His Lys Thr Leu Val Pro Arg Pro Ala Val Leu
465                 470                 475                 480

Asp Pro Ala Leu Cys Thr Ala Thr Ser Cys Val Gln Val Glu Leu Cys
                485                 490                 495

Phe Ala Tyr Asn Gln Ser Ala Gly Asn Pro Asn Tyr Arg Arg Asn Ile
            500                 505                 510

Thr Leu Ala Tyr Thr Leu Glu Ala Asp Arg Asp Arg Arg Pro Pro Arg
        515                 520                 525

Leu Arg Phe Ala Gly Ser Glu Ser Ala Val Phe His Gly Phe Phe Ser
    530                 535                 540

Met Pro Glu Met Arg Cys Gln Lys Leu Glu Leu Leu Leu Met Asp Asn
545                 550                 555                 560

Leu Arg Asp Lys Leu Arg Pro Ile Ile Ile Ser Met Asn Tyr Ser Leu
                565                 570                 575
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Pro Leu Arg Met Pro Asp Arg Pro Arg Leu Gly Leu Arg Ser Leu Asp
            580                 585                 590

Ala Tyr Pro Ile Leu Asn Gln Ala Gln Ala Leu Glu Asn His Thr Glu
        595                 600                 605

Val Gln Phe Gln Lys Glu Cys Gly Pro Asp Asn Lys Cys Glu Ser Asn
    610                 615                 620

Leu Gln Met Arg Ala Ala Phe Val Ser Glu Gln Gln Gln Lys Leu Ser
625                 630                 635                 640

Arg Leu Gln Tyr Ser Arg Asp Val Arg Lys Leu Leu Leu Ser Ile Asn
                645                 650                 655

Val Thr Asn Thr Arg Thr Ser Glu Arg Ser Gly Glu Asp Ala His Glu
            660                 665                 670

Ala Leu Leu Thr Leu Val Val Pro Pro Ala Leu Leu Leu Ser Ser Val
        675                 680                 685

Arg Pro Pro Gly Ala Cys Gln Ala Asn Glu Thr Ile Phe Cys Glu Leu
    690                 695                 700

Gly Asn Pro Phe Lys Arg Asn Gln Arg Met Glu Leu Leu Ile Ala Phe
705                 710                 715                 720

Glu Val Ile Gly Val Thr Leu His Thr Arg Asp Leu Gln Val Gln Leu
                725                 730                 735

Gln Leu Ser Thr Ser Ser His Gln Asp Asn Leu Trp Pro Met Ile Leu
            740                 745                 750

Thr Leu Leu Val Asp Tyr Thr Leu Gln Thr Ser Leu Ser Met Val Asn
        755                 760                 765

His Arg Leu Gln Ser Phe Phe Gly Gly Thr Val Met Gly Glu Ser Gly
    770                 775                 780

Met Lys Thr Val Glu Asp Val Gly Ser Pro Leu Lys Tyr Glu Phe Gln
785                 790                 795                 800

Val Gly Pro Met Gly Glu Gly Leu Val Gly Leu Gly Thr Leu Val Leu
                805                 810                 815

Gly Leu Glu Trp Pro Tyr Glu Val Ser Asn Gly Lys Trp Leu Leu Tyr
            820                 825                 830

Pro Thr Glu Ile Thr Val His Gly Asn Gly Ser Trp Pro Cys Arg Pro
        835                 840                 845

Pro Gly Asp Leu Ile Asn Pro Leu Asn Leu Thr Leu Ser Asp Pro Gly
    850                 855                 860

Asp Arg Pro Ser Ser Pro Gln Arg Arg Arg Arg Gln Leu Asp Pro Gly
865                 870                 875                 880

Gly Gly Gln Gly Pro Pro Pro Val Thr Leu Ala Ala Ala Lys Lys Ala
                885                 890                 895

Lys Ser Glu Thr Val Leu Thr Cys Ala Thr Gly Arg Ala His Cys Val
            900                 905                 910

Trp Leu Glu Cys Pro Ile Pro Asp Ala Pro Val Val Thr Asn Val Thr
        915                 920                 925

Val Lys Ala Arg Val Trp Asn Ser Thr Phe Ile Glu Asp Tyr Arg Asp
    930                 935                 940

Phe Asp Arg Val Arg Val Asn Gly Trp Ala Thr Leu Phe Leu Arg Thr
945                 950                 955                 960

Ser Ile Pro Thr Ile Asn Met Glu Asn Lys Thr Thr Trp Phe Ser Val
                965                 970                 975

Asp Ile Asp Ser Glu Leu Val Glu Glu Leu Pro Ala Glu Ile Glu Leu
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            980                 985                 990

Trp Leu Val Leu Val Ala Val Gly  Ala Gly Leu Leu Leu  Leu Gly Leu
        995                 1000                1005

Ile Ile  Leu Leu Leu Trp Lys  Cys Gly Phe Phe Lys  Arg Thr Arg
    1010                1015                1020

Tyr Tyr  Gln Ile Met Pro Lys  Tyr His Ala Val Arg  Ile Arg Glu
    1025                1030                1035

Glu Glu  Arg Tyr Pro Pro Pro  Gly Ser Thr Leu Pro  Thr Lys Lys
    1040                1045                1050

His Trp  Val Thr Ser Trp Gln  Thr Arg Asp Gln Tyr  Tyr
    1055                1060                1065


<210> SEQ ID NO 373
<211> LENGTH: 532
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 373

Met Ala Pro Ser Ser Pro Arg Pro Ala Leu Pro Ala Leu Leu Val Leu
1               5                   10                  15

Leu Gly Ala Leu Phe Pro Gly Pro Gly Asn Ala Gln Thr Ser Val Ser
            20                  25                  30

Pro Ser Lys Val Ile Leu Pro Arg Gly Gly Ser Val Leu Val Thr Cys
        35                  40                  45

Ser Thr Ser Cys Asp Gln Pro Lys Leu Leu Gly Ile Glu Thr Pro Leu
    50                  55                  60

Pro Lys Lys Glu Leu Leu Leu Pro Gly Asn Asn Arg Lys Val Tyr Glu
65                  70                  75                  80

Leu Ser Asn Val Gln Glu Asp Ser Gln Pro Met Cys Tyr Ser Asn Cys
                85                  90                  95

Pro Asp Gly Gln Ser Thr Ala Lys Thr Phe Leu Thr Val Tyr Trp Thr
            100                 105                 110

Pro Glu Arg Val Glu Leu Ala Pro Leu Pro Ser Trp Gln Pro Val Gly
        115                 120                 125

Lys Asn Leu Thr Leu Arg Cys Gln Val Glu Gly Gly Ala Pro Arg Ala
    130                 135                 140

Asn Leu Thr Val Val Leu Leu Arg Gly Glu Lys Glu Leu Lys Arg Glu
145                 150                 155                 160

Pro Ala Val Gly Glu Pro Ala Glu Val Thr Thr Thr Val Leu Val Arg
                165                 170                 175

Arg Asp His His Gly Ala Asn Phe Ser Cys Arg Thr Glu Leu Asp Leu
            180                 185                 190

Arg Pro Gln Gly Leu Glu Leu Phe Glu Asn Thr Ser Ala Pro Tyr Gln
        195                 200                 205

Leu Gln Thr Phe Val Leu Pro Ala Thr Pro Pro Gln Leu Val Ser Pro
    210                 215                 220

Arg Val Leu Glu Val Asp Thr Gln Gly Thr Val Val Cys Ser Leu Asp
225                 230                 235                 240

Gly Leu Phe Pro Val Ser Glu Ala Gln Val His Leu Ala Leu Gly Asp
                245                 250                 255

Gln Arg Leu Asn Pro Thr Val Thr Tyr Gly Asn Asp Ser Phe Ser Ala
            260                 265                 270
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Lys Ala Ser Val Ser Val Thr Ala Glu Asp Glu Gly Thr Gln Arg Leu
        275                 280                 285

Thr Cys Ala Val Ile Leu Gly Asn Gln Ser Gln Glu Thr Leu Gln Thr
    290                 295                 300

Val Thr Ile Tyr Ser Phe Pro Ala Pro Asn Val Ile Leu Thr Lys Pro
305                 310                 315                 320

Glu Val Ser Glu Gly Thr Glu Val Thr Val Lys Cys Glu Ala His Pro
                325                 330                 335

Arg Ala Lys Val Thr Leu Asn Gly Val Pro Ala Gln Pro Leu Gly Pro
            340                 345                 350

Arg Ala Gln Leu Leu Leu Lys Ala Thr Pro Glu Asp Asn Gly Arg Ser
        355                 360                 365

Phe Ser Cys Ser Ala Thr Leu Glu Val Ala Gly Gln Leu Ile His Lys
    370                 375                 380

Asn Gln Thr Arg Glu Leu Arg Val Leu Tyr Gly Pro Arg Leu Asp Glu
385                 390                 395                 400

Arg Asp Cys Pro Gly Asn Trp Thr Trp Pro Glu Asn Ser Gln Gln Thr
                405                 410                 415

Pro Met Cys Gln Ala Trp Gly Asn Pro Leu Pro Glu Leu Lys Cys Leu
            420                 425                 430

Lys Asp Gly Thr Phe Pro Leu Pro Ile Gly Glu Ser Val Thr Val Thr
        435                 440                 445

Arg Asp Leu Glu Gly Thr Tyr Leu Cys Arg Ala Arg Ser Thr Gln Gly
    450                 455                 460

Glu Val Thr Arg Lys Val Thr Val Asn Val Leu Ser Pro Arg Tyr Glu
465                 470                 475                 480

Ile Val Ile Ile Thr Val Val Ala Ala Ala Val Ile Met Gly Thr Ala
                485                 490                 495

Gly Leu Ser Thr Tyr Leu Tyr Asn Arg Gln Arg Lys Ile Lys Lys Tyr
            500                 505                 510

Arg Leu Gln Gln Ala Gln Lys Gly Thr Pro Met Lys Pro Asn Thr Gln
        515                 520                 525

Ala Thr Pro Pro
    530


<210> SEQ ID NO 374
<211> LENGTH: 583
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 374

Met Glu Ser Lys Gly Ala Ser Ser Cys Arg Leu Leu Phe Cys Leu Leu
1               5                   10                  15

Ile Ser Ala Thr Val Phe Arg Pro Gly Leu Gly Trp Tyr Thr Val Asn
            20                  25                  30

Ser Ala Tyr Gly Asp Thr Ile Ile Ile Pro Cys Arg Leu Asp Val Pro
        35                  40                  45

Gln Asn Leu Met Phe Gly Lys Trp Lys Tyr Glu Lys Pro Asp Gly Ser
    50                  55                  60

Pro Val Phe Ile Ala Phe Arg Ser Ser Thr Lys Lys Ser Val Gln Tyr
65                  70                  75                  80

Asp Asp Val Pro Glu Tyr Lys Asp Arg Leu Asn Leu Ser Glu Asn Tyr
                85                  90                  95
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```
Thr Leu Ser Ile Ser Asn Ala Arg Ile Ser Asp Glu Lys Arg Phe Val
            100                 105                 110

Cys Met Leu Val Thr Glu Asp Asn Val Phe Glu Ala Pro Thr Ile Val
        115                 120                 125

Lys Val Phe Lys Gln Pro Ser Lys Pro Glu Ile Val Ser Lys Ala Leu
    130                 135                 140

Phe Leu Glu Thr Glu Gln Leu Lys Lys Leu Gly Asp Cys Ile Ser Glu
145                 150                 155                 160

Asp Ser Tyr Pro Asp Gly Asn Ile Thr Trp Tyr Arg Asn Gly Lys Val
                165                 170                 175

Leu His Pro Leu Glu Gly Ala Val Val Ile Ile Phe Lys Lys Glu Met
            180                 185                 190

Asp Pro Val Thr Gln Leu Tyr Thr Met Thr Ser Thr Leu Glu Tyr Lys
        195                 200                 205

Thr Thr Lys Ala Asp Ile Gln Met Pro Phe Thr Cys Ser Val Thr Tyr
    210                 215                 220

Tyr Gly Pro Ser Gly Gln Lys Thr Ile His Ser Glu Gln Ala Val Phe
225                 230                 235                 240

Asp Ile Tyr Tyr Pro Thr Glu Gln Val Thr Ile Gln Val Leu Pro Pro
                245                 250                 255

Lys Asn Ala Ile Lys Glu Gly Asp Asn Ile Thr Leu Lys Cys Leu Gly
            260                 265                 270

Asn Gly Asn Pro Pro Pro Glu Glu Phe Leu Phe Tyr Leu Pro Gly Gln
        275                 280                 285

Pro Glu Gly Ile Arg Ser Ser Asn Thr Tyr Thr Leu Met Asp Val Arg
    290                 295                 300

Arg Asn Ala Thr Gly Asp Tyr Lys Cys Ser Leu Ile Asp Lys Lys Ser
305                 310                 315                 320

Met Ile Ala Ser Thr Ala Ile Thr Val His Tyr Leu Asp Leu Ser Leu
                325                 330                 335

Asn Pro Ser Gly Glu Val Thr Arg Gln Ile Gly Asp Ala Leu Pro Val
            340                 345                 350

Ser Cys Thr Ile Ser Ala Ser Arg Asn Ala Thr Val Val Trp Met Lys
        355                 360                 365

Asp Asn Ile Arg Leu Arg Ser Ser Pro Ser Phe Ser Ser Leu His Tyr
    370                 375                 380

Gln Asp Ala Gly Asn Tyr Val Cys Glu Thr Ala Leu Gln Glu Val Glu
385                 390                 395                 400

Gly Leu Lys Lys Arg Glu Ser Leu Thr Leu Ile Val Glu Gly Lys Pro
                405                 410                 415

Gln Ile Lys Met Thr Lys Lys Thr Asp Pro Ser Gly Leu Ser Lys Thr
            420                 425                 430

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

Ile Thr Gly Ser Gly Ser Val Ile Asn Gln Thr Glu Glu Ser Pro Tyr
    450                 455                 460

Ile Asn Gly Arg Tyr Tyr Ser Lys Ile Ile Ile Ser Pro Glu Glu Asn
465                 470                 475                 480

Val Thr Leu Thr Cys Thr Ala Glu Asn Gln Leu Glu Arg Thr Val Asn
                485                 490                 495
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```
Ser Leu Asn Val Ser Ala Ile Ser Ile Pro Glu His Asp Glu Ala Asp
            500                 505                 510

Glu Ile Ser Asp Glu Asn Arg Glu Lys Val Asn Asp Gln Ala Lys Leu
        515                 520                 525

Ile Val Gly Ile Val Val Gly Leu Leu Leu Ala Ala Leu Val Ala Gly
    530                 535                 540

Val Val Tyr Trp Leu Tyr Met Lys Lys Ser Lys Thr Ala Ser Lys His
545                 550                 555                 560

Val Asn Lys Asp Leu Gly Asn Met Glu Glu Asn Lys Lys Leu Glu Glu
                565                 570                 575

Asn Asn His Lys Thr Glu Ala
            580


<210> SEQ ID NO 375
<211> LENGTH: 385
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 375

Met Ala Ala Ala Leu Phe Val Leu Leu Gly Phe Ala Leu Leu Gly Thr
1               5                   10                  15

His Gly Ala Ser Gly Ala Ala Gly Phe Val Gln Ala Pro Leu Ser Gln
            20                  25                  30

Gln Arg Trp Val Gly Gly Ser Val Glu Leu His Cys Glu Ala Val Gly
        35                  40                  45

Ser Pro Val Pro Glu Ile Gln Trp Trp Phe Glu Gly Gln Gly Pro Asn
    50                  55                  60

Asp Thr Cys Ser Gln Leu Trp Asp Gly Ala Arg Leu Asp Arg Val His
65                  70                  75                  80

Ile His Ala Thr Tyr His Gln His Ala Ala Ser Thr Ile Ser Ile Asp
                85                  90                  95

Thr Leu Val Glu Glu Asp Thr Gly Thr Tyr Glu Cys Arg Ala Ser Asn
            100                 105                 110

Asp Pro Asp Arg Asn His Leu Thr Arg Ala Pro Arg Val Lys Trp Val
        115                 120                 125

Arg Ala Gln Ala Val Val Leu Val Leu Glu Pro Gly Thr Val Phe Thr
    130                 135                 140

Thr Val Glu Asp Leu Gly Ser Lys Ile Leu Leu Thr Cys Ser Leu Asn
145                 150                 155                 160

Asp Ser Ala Thr Glu Val Thr Gly His Arg Trp Leu Lys Gly Gly Val
                165                 170                 175

Val Leu Lys Glu Asp Ala Leu Pro Gly Gln Lys Thr Glu Phe Lys Val
            180                 185                 190

Asp Ser Asp Asp Gln Trp Gly Glu Tyr Ser Cys Val Phe Leu Pro Glu
        195                 200                 205

Pro Met Gly Thr Ala Asn Ile Gln Leu His Gly Pro Pro Arg Val Lys
    210                 215                 220

Ala Val Lys Ser Ser Glu His Ile Asn Glu Gly Glu Thr Ala Met Leu
225                 230                 235                 240

Val Cys Lys Ser Glu Ser Val Pro Pro Val Thr Asp Trp Ala Trp Tyr
                245                 250                 255

Lys Ile Thr Asp Ser Glu Asp Lys Ala Leu Met Asn Gly Ser Glu Ser
            260                 265                 270
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```
Arg Phe Phe Val Ser Ser Ser Gln Gly Arg Ser Glu Leu His Ile Glu
        275                 280                 285

Asn Leu Asn Met Glu Ala Asp Pro Gly Gln Tyr Arg Cys Asn Gly Thr
    290                 295                 300

Ser Ser Lys Gly Ser Asp Gln Ala Ile Ile Thr Leu Arg Val Arg Ser
305                 310                 315                 320

His Leu Ala Ala Leu Trp Pro Phe Leu Gly Ile Val Ala Glu Val Leu
                325                 330                 335

Val Leu Val Thr Ile Ile Phe Ile Tyr Glu Lys Arg Arg Lys Pro Glu
            340                 345                 350

Asp Val Leu Asp Asp Asp Asp Ala Gly Ser Ala Pro Leu Lys Ser Ser
        355                 360                 365

Gly Gln His Gln Asn Asp Lys Gly Lys Asn Val Arg Gln Arg Asn Ser
    370                 375                 380

Ser
385


<210> SEQ ID NO 376
<211> LENGTH: 442
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 376

Met Ala Ser Val Val Leu Pro Ser Gly Ser Gln Cys Ala Ala Ala Ala
1               5                   10                  15

Ala Ala Ala Ala Pro Pro Gly Leu Arg Leu Arg Leu Leu Leu Leu Leu
            20                  25                  30

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

Thr Lys Asp Val Thr Val Ile Glu Gly Glu Val Ala Thr Ile Ser Cys
    50                  55                  60

Gln Val Asn Lys Ser Asp Asp Ser Val Ile Gln Leu Leu Asn Pro Asn
65                  70                  75                  80

Arg Gln Thr Ile Tyr Phe Arg Asp Phe Arg Pro Leu Lys Asp Ser Arg
                85                  90                  95

Phe Gln Leu Leu Asn Phe Ser Ser Ser Glu Leu Lys Val Ser Leu Thr
            100                 105                 110

Asn Val Ser Ile Ser Asp Glu Gly Arg Tyr Phe Cys Gln Leu Tyr Thr
        115                 120                 125

Asp Pro Pro Gln Glu Ser Tyr Thr Thr Ile Thr Val Leu Val Pro Pro
    130                 135                 140

Arg Asn Leu Met Ile Asp Ile Gln Arg Asp Thr Ala Val Glu Gly Glu
145                 150                 155                 160

Glu Ile Glu Val Asn Cys Thr Ala Met Ala Ser Lys Pro Ala Thr Thr
                165                 170                 175

Ile Arg Trp Phe Lys Gly Asn Thr Glu Leu Lys Gly Lys Ser Glu Val
            180                 185                 190

Glu Glu Trp Ser Asp Met Tyr Thr Val Thr Ser Gln Leu Met Leu Lys
        195                 200                 205

Val His Lys Glu Asp Asp Gly Val Pro Val Ile Cys Gln Val Glu His
    210                 215                 220

Pro Ala Val Thr Gly Asn Leu Gln Thr Gln Arg Tyr Leu Glu Val Gln
```

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225                 230                 235                 240

Tyr Lys Pro Gln Val His Ile Gln Met Thr Tyr Pro Leu Gln Gly Leu
                245                 250                 255

Thr Arg Glu Gly Asp Ala Leu Glu Leu Thr Cys Glu Ala Ile Gly Lys
            260                 265                 270

Pro Gln Pro Val Met Val Thr Trp Val Arg Val Asp Asp Glu Met Pro
        275                 280                 285

Gln His Ala Val Leu Ser Gly Pro Asn Leu Phe Ile Asn Asn Leu Asn
    290                 295                 300

Lys Thr Asp Asn Gly Thr Tyr Arg Cys Glu Ala Ser Asn Ile Val Gly
305                 310                 315                 320

Lys Ala His Ser Asp Tyr Met Leu Tyr Val Tyr Asp Pro Pro Thr Thr
                325                 330                 335

Ile Pro Pro Pro Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr
            340                 345                 350

Thr Ile Leu Thr Ile Ile Thr Asp Ser Arg Ala Gly Glu Glu Gly Ser
        355                 360                 365

Ile Arg Ala Val Asp His Ala Val Ile Gly Gly Val Val Ala Val Val
    370                 375                 380

Val Phe Ala Met Leu Cys Leu Leu Ile Ile Leu Gly Arg Tyr Phe Ala
385                 390                 395                 400

Arg His Lys Gly Thr Tyr Phe Thr His Glu Ala Lys Gly Ala Asp Asp
                405                 410                 415

Ala Ala Asp Ala Asp Thr Ala Ile Ile Asn Ala Glu Gly Gly Gln Asn
            420                 425                 430

Asn Ser Glu Glu Lys Lys Glu Tyr Phe Ile
        435                 440


<210> SEQ ID NO 377
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 377

caggaaacag ctatgac                                                  17


<210> SEQ ID NO 378
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 378

cggctccaag tcgacgtcgt ca                                            22


<210> SEQ ID NO 379
<211> LENGTH: 83
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 379

cagctgcagc agtctggggc agagcttgtg aagccagggg cctcagtcaa gttgtcctgc     60
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acagcttctg gcttcaacat taa 83

<210> SEQ ID NO 380
<211> LENGTH: 81
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 380

agaccgaagt tgtaatttct gtggatatac gtgacccact tcgtctccgg acttttccca 60

gatctcacct aaccttccta a 81

<210> SEQ ID NO 381
<211> LENGTH: 84
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 381

aagggtctag agtggattgg aaggattgat cctgcgagtg gtaatactaa atatgacccg 60

aaggacaagg ccactataac agca 84

<210> SEQ ID NO 382
<211> LENGTH: 66
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 382

ttcctgttcc ggtgatattg tcgtctgtgt aggaggttgt gtcggatgga tgtcgactta 60

agggac 66

<210> SEQ ID NO 383
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 383

cagctgaatt ccctgacatc tgaggacact gccgtctatt actgtgctgg t 51

<210> SEQ ID NO 384
<211> LENGTH: 73
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 384

cagataatga cacgaccaat actaatgccg ttgaaactga tgaccccggt tccgtggtgc 60

cagtggcaca agg 73

<210> SEQ ID NO 385
<211> LENGTH: 54
<212> TYPE: DNA
<213> ORGANISM: Artificial

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<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 385

ggttctctaa cagtagtggt agtagtggta attattctcg atagggccct cgaa 54

<210> SEQ ID NO 386
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 386

gacatcgagc tcacccagtc tccagcctcc ctttctgcgt ctgtgggaga aactgtcacc 60

atcacatgt 69

<210> SEQ ID NO 387
<211> LENGTH: 63
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 387

tgacagtggt agtgtacagc tcgttcaccc ttataagtgt taataaatcg taccatggtc 60

gtc 63

<210> SEQ ID NO 388
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 388

gcatggtacc agcagaaacc agggaaatct cctcagctcc tggtctat 48

<210> SEQ ID NO 389
<211> LENGTH: 81
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 389

ggagtcgagg accagatatt acgtttttgg aatcgtctac cacacggtag ttccaagtca 60

ccgtcaccta ggccttgtgt t 81

<210> SEQ ID NO 390
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 390

tcatgaggca cctgcaagcc acctccgtgg ttcgagctct agttt 45

<210> SEQ ID NO 391
<211> LENGTH: 45

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<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 391

agtactccgt ggacgttcgg tggaggcacc aagctcgaga tcaaa 45

<210> SEQ ID NO 392
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 392

atcgacagct 10

<210> SEQ ID NO 393
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 393

aagccacctc catggttcga gctctagttt 30

<210> SEQ ID NO 394
<211> LENGTH: 44
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 394

tcgaagttgt ccttactcac aagccgcgcg gtcagctgag gtaa 44

<210> SEQ ID NO 395
<211> LENGTH: 55
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 395

accctggtca ccgtctcctc agcctccacc aagggcccat cggtcttccc cctgg 55

<210> SEQ ID NO 396
<211> LENGTH: 37
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 396

gggagtcgtc gcagcactgg cacgggaggt cgtcgaa 37

<210> SEQ ID NO 397
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

-continued

<400> SEQUENCE: 397

ggactctact ccctcagcag cgtcgtgacc gtgccc 36

<210> SEQ ID NO 398
<211> LENGTH: 63
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 398

gggtcgttgt ggttccacct gttctttcaa ctcgggttta gaacagtagt ggtagtagtg 60

gta 63

<210> SEQ ID NO 399
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 399

gggtttagaa cagtagtggt agtagtggta attattctcg atagggccct cgaacg 56

<210> SEQ ID NO 400
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 400

ggcaccacgg tcaccgtctc gagcgcctcc acc 33

<210> SEQ ID NO 401
<211> LENGTH: 1916
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Insert sequence of pscFvCA9-E8VHdVLd

<400> SEQUENCE: 401

aagcttgcat gcaaattcta tttcaaggag acagtcataa tgaaatacct attgcctacg 60

gcagccgctg gattgttatt actcgctgcc caaccagcga tggcccaggt gcagctgcag 120

cagtctgggg cagagcttgt gaagccaggg gcctcagtca agttgtcctg cacagcttct 180

ggcttcaaca ttaaagacac ctatatgcac tgggtgaagc agaggcctga aaagggtcta 240

gaattccctg acatctgagg acactgccgt ctattactgt gctggttatg attacggcaa 300

ctttgactac tggggccaag gcaccacggt caccgtctcg agaggcggtg gcggatcagg 360

tggcggtgga agtggcggtg gtgggtccat ggccgacatc gagctcaccc agtctccagc 420

ctccctttct gcgtctgtgg gagaaactgt caccatcaca tgtcgagcaa gtgggaatat 480

tcacaattat ttagcatggt accaagctcg agatcaaacg ggctgatgct gcaccaactg 540

tatccatctt cccaccatcc agtgagcagt taacatctgg aggtgcctca gtcgtgtgct 600

tcttgaacag cttctacccc aaagacatca atgtcaagtg gaagattgat ggcagtgaac 660

gacaaaatgg cgtcctgaac agttggactg atcaggacag caaagacagc acctacagca 720

-continued

tgagcagcac cctcacgttg accaaggacg agtatgaacg acataacagc tatacctgtg 780

aggccactca caagacatca acttcaccca ttgtcaagag cttcaacagg aatgagtgtt 840

cggcgcgcca gtcgactcca ttcgtttgtg aatatcaagg ccaatcgtct gacctgcctc 900

aacctcctgt caatgctggc ggcggctctg gtggtggttc tggtggcggc tctgagggtg 960

gtggctctga gggtggcggt tctgagggtg gcggctctga gggaggcggt tccggtggtg 1020

gctctggttc cggtgatttt gattatgaaa agatggcaaa cgctaataag ggggctatga 1080

ccgaaaatgc cgatgaaaac gcgctacagt cagacgctaa aggcaaactt gattctgtcg 1140

ctactgatta cggtgctgct atcgatggtt tcattggtga cgtttccggc cttgctaatg 1200

gtaatggtgc tactggtgat tttgctggct ctaattccca aatggctcaa gtcggtgacg 1260

gtgataattc acctttaatg aataatttcc gtcaatattt accttccctc cctcaatcgg 1320

ttgaatgtcg ccctttttgtc tttggcgctg gtaaaccata tgaattttct attgattgtg 1380

acaaaataaa cttattccgt ggtgtctttg cgtttctttt atatgttgcc acctttatgt 1440

atgtattttc tacgtttgct aacatactgc gtaataagga gtcttaatca tgccagttct 1500

tttgggtgct agctgtcgac tgcgcaacac gatgaagccg tagacaacaa attcaacaaa 1560

gaacaacaaa acgcgttcta tgagatctta catttaccta acttaaacga agaacaacga 1620

aacgccttca tccaaagttt aaaagatgac ccaagccaaa gcgctaacct tttagcagaa 1680

gctaaaaagc taaatgatgc tcaggcgccg aaagtagaca acaaattcaa caaagaacaa 1740

caaaacgcgt tctatgagat cttacattta cctaacttaa acgaagaaca acgaaacgcc 1800

ttcatccaaa gtttaaaaga tgacccaagc caaagcgcta acctttttagc agaagctaaa 1860

aagctaaatg atgctcaggc gccgaaagta gacgcgaatt agctgggaat taattc 1916

<210> SEQ ID NO 402
<211> LENGTH: 66
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Amino acid sequence encoded by insert sequence of pscFvCA9-E8VHdVLd

<400> SEQUENCE: 402

Met Lys Tyr Leu Leu Pro Thr Ala Ala Ala Gly Leu Leu Leu Leu Ala
1 5 10 15

Ala Gln Pro Ala Met Ala Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
20 25 30

Leu Val Lys Pro Gly Ala Ser Val Lys Leu Ser Cys Thr Ala Ser Gly
35 40 45

Phe Asn Ile Lys Asp Thr Tyr Met His Trp Val Lys Gln Arg Pro Glu
50 55 60

Lys Gly
65

<210> SEQ ID NO 403
<211> LENGTH: 77
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 403

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gtcaccgtct cgagaggcgg tggcggatca ggtggcggtg gaagtggcgg tggtgggtcc 60

atggccgaca tcgagct 77

<210> SEQ ID NO 404
<211> LENGTH: 68
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 404

cgatgtcggc catggaccca ccaccgccac ttccaccgcc acctgatccg ccaccgcctc 60

tcgagacg 68

<210> SEQ ID NO 405
<211> LENGTH: 1774
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Insert sequence of pscFvCA-E8VHd

<400> SEQUENCE: 405

aagcttgcat gcaaattcta tttcaaggag acagtcataa tgaaatacct attgcctacg 60

gcagccgctg gattgttatt actcgcggcc cagccggcca tggcccaggt gcagctgcag 120

cagtctgggg cagagcttgt gaagccaggg gcctcagtca agttgtcctg cacagcttct 180

ggcttcaaca ttaaagacac ctatatgcac tgggtgaagc agaggcctga aaagggtcta 240

gaattccctg acatctgagg acactgccgt ctattactgt gctggttatg attacggcaa 300

ctttgactac tggggccaag gcaccacggt caccgtctcc tcaggcggtg gcggatcagg 360

tggcggtgga agtggcggtg gtgggtctac tagtgacatc gagctcaccc agtctccagc 420

ctccctttct gcgtctgtgg gagaaactgt caccatcaca tgtcgagcaa gtgggaatat 480

tcacaattat ttagcatggt accagcagaa accagggaaa tctcctcagc tcctggtcta 540

taatgcaaaa accttagcag atggtgtgcc atcaaggttc agtggcagtg gatccggaac 600

acaatattct ctcaagatca acagcctgca gcctgaagat tttgggagtt attactgtca 660

acatttttgg agtactccgt ggacgttcgg tggaggtacc aagctcgagt cgactccatt 720

cgtttgtgaa tatcaaggcc aatcgtctga cctgcctcaa cctcctgtca atgctggcgg 780

cggctctggt ggtggttctg gtggcggctc tgagggtggt ggctctgagg gtggcggttc 840

tgagggtggc ggctctgagg gaggcggttc cggtggtggc tctggttccg gtgattttga 900

ttatgaaaag atggcaaacg ctaataaggg ggctatgacc gaaaatgccg atgaaaacgc 960

gctacagtca gacgctaaag gcaaacttga ttctgtcgct actgattacg gtgctgctat 1020

cgatggtttc attggtgacg tttccggcct tgctaatggt aatggtgcta ctggtgattt 1080

tgctggctct aattcccaaa tggctcaagt cggtgacggt gataattcac ctttaatgaa 1140

taatttccgt caatatttac cttccctccc tcaatcggtt gaatgtcgcc cttttgtctt 1200

tggcgctggt aaaccatatg aattttctat tgattgtgac aaaataaact tattccgtgg 1260

tgtctttgcg tttcttttat atgttgccac ctttatgtat gtattttcta cgtttgctaa 1320

catactgcgt aataaggagt cttaatcatg ccagttcttt tgggtgctag ctgtcgactg 1380

cgcaacacga tgaagccgta gacaacaaat tcaacaaaga acaacaaaac gcgttctatg 1440

-continued

agatcttaca tttacctaac ttaaacgaag aacaacgaaa cgccttcatc caaagtttaa 1500

aagatgaccc aagccaaagc gctaaccttt tagcagaagc taaaaagcta aatgatgctc 1560

aggcgccgaa agtagacaac aaattcaaca aagaacaaca aaacgcgttc tatgagatct 1620

tacatttacc taacttaaac gaagaacaac gaaacgcctt catccaaagt ttaaaagatg 1680

acccaagcca aagcgctaac cttttagcag aagctaaaaa gctaaatgat gctcaggcgc 1740

cgaaagtaga cgcgaattag ctgggaatta attc 1774

<210> SEQ ID NO 406
<211> LENGTH: 66
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Amino acid sequence encoded by insert sequence of pscFvCA-E8VHd

<400> SEQUENCE: 406

Met Lys Tyr Leu Leu Pro Thr Ala Ala Ala Gly Leu Leu Leu Leu Ala
1 5 10 15

Ala Gln Pro Ala Met Ala Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
20 25 30

Leu Val Lys Pro Gly Ala Ser Val Lys Leu Ser Cys Thr Ala Ser Gly
35 40 45

Phe Asn Ile Lys Asp Thr Tyr Met His Trp Val Lys Gln Arg Pro Glu
50 55 60

Lys Gly
65

<210> SEQ ID NO 407
<211> LENGTH: 91
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 407

caccacggtc accgtctcct caggcggtgg cggatcaggt ggcggtggaa gtggcggtgg 60

tgggtctact agtgacatcg agctcaccca g 91

<210> SEQ ID NO 408
<211> LENGTH: 91
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 408

gtggtgccag tggcagagga gtccgccacc gcctagtcca ccgccacctt caccgccacc 60

acccagatga tcactgtagc tcgagtgggt c 91

<210> SEQ ID NO 409
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 409

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caggaaacag ctatgac 17

<210> SEQ ID NO 410
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 410

gacgccgggt cggccggtac cggctccaag tcgacgtcgt ca 42

<210> SEQ ID NO 411
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 411

gtcctcgcaa ctgcggccca gccggccatg gccgacatcc agatgaccca gtctcc 56

<210> SEQ ID NO 412
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 412

gtcctcgcaa ctgcggccca gccggccatg gccgatgttg tgatgactca gtctcc 56

<210> SEQ ID NO 413
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 413

gtcctcgcaa ctgcggccca gccggccatg gccgaaattg tgttgacgca gtctcc 56

<210> SEQ ID NO 414
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 414

gtcctcgcaa ctgcggccca gccggccatg gccgacatcg tgatgaccca gtctcc 56

<210> SEQ ID NO 415
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 415

gtcctcgcaa ctgcggccca gccggccatg gccgaaacga cactcacgca gtctcc 56

-continued

<210> SEQ ID NO 416
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 416

gtcctcgcaa ctgcggccca gccggccatg gccgaaattg tgctgactca gtctcc 56

<210> SEQ ID NO 417
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 417

gtcctcgcaa ctgcggccca gccggccatg gcccagtctg tgttgacgca gccgcc 56

<210> SEQ ID NO 418
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 418

gtcctcgcaa ctgcggccca gccggccatg gcccagtctg ccctgactca gcctgc 56

<210> SEQ ID NO 419
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 419

gtcctcgcaa ctgcggccca gccggccatg gcctcctatg tgctgactca gccacc 56

<210> SEQ ID NO 420
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 420

gtcctcgcaa ctgcggccca gccggccatg gcctcttctg agctgactca ggaccc 56

<210> SEQ ID NO 421
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 421

gtcctcgcaa ctgcggccca gccggccatg gcccacgtta tactgactca accgcc 56

<210> SEQ ID NO 422
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial

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<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 422

gtcctcgcaa ctgcggccca gccggccatg gcccaggctg tgctcactca gccgcc 56

<210> SEQ ID NO 423
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 423

gtcctcgcaa ctgcggccca gccggccatg gccaatttta tgctgactca gcccca 56

<210> SEQ ID NO 424
<211> LENGTH: 44
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 424

tcgactggcg cgccgaacac tctcccctgt tgaagctctt tgtg 44

<210> SEQ ID NO 425
<211> LENGTH: 43
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 425

tcgactggcg cgccgaacat tctgtagggg ccactgtctt ctc 43

<210> SEQ ID NO 426
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 426

atggagtcgg gaaggaagtc 20

<210> SEQ ID NO 427
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 427

gtcctcgcaa ctgcggccca gccggccatg gcccaggtgc agctggtgca gtctgg 56

<210> SEQ ID NO 428
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 428

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gtcctcgcaa ctgcggccca gccggccatg gcccaggtca acttaaggga gtctgg 56

<210> SEQ ID NO 429
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 429

gtcctcgcaa ctgcggccca gccggccatg gccgaggtgc agctggtgga gtctgg 56

<210> SEQ ID NO 430
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 430

gtcctcgcaa ctgcggccca gccggccatg gcccaggtgc agctgcagga gtcggg 56

<210> SEQ ID NO 431
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 431

gtcctcgcaa ctgcggccca gccggccatg gcccaggtgc agctgttgca gtctgc 56

<210> SEQ ID NO 432
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 432

gtcctcgcaa ctgcggccca gccggccatg gcccaggtac agctgcagca gtcagg 56

<210> SEQ ID NO 433
<211> LENGTH: 59
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 433

gtcctcgcaa ctgcggccca gccggccatg gcccagrtca ccttgaagga gtctggtcc 59

<210> SEQ ID NO 434
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 434

gtcctcgcaa ctgcggccca gccggccatg gcccaggtgc agctacagca gtgggg 56

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<210> SEQ ID NO 435
<211> LENGTH: 56
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 435

gtcctcgcaa ctgcggccca gccggccatg gccgaggtgc agctggtgca gtctgg 56

<210> SEQ ID NO 436
<211> LENGTH: 64
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 436

gtcctcgcaa ctgcggccca gccggccatg gcccaggtgc agctggtgca atctgggtct 60

gagt 64

<210> SEQ ID NO 437
<211> LENGTH: 32
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 437

ggtggaggca ctcgagacgg tgaccagggt gc 32

<210> SEQ ID NO 438
<211> LENGTH: 32
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 438

ggtggaggca ctcgagacgg tgaccattgt cc 32

<210> SEQ ID NO 439
<211> LENGTH: 32
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 439

ggtggaggca ctcgagacgg tgaccagggt tc 32

<210> SEQ ID NO 440
<211> LENGTH: 32
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: An artificially synthesized primer sequence

<400> SEQUENCE: 440

ggtggaggca ctcgagacgg tgaccgtggt cc 32

<210> SEQ ID NO 441
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligo RNA

<400> SEQUENCE: 441

cagagcuaca cauugagaac cugaa 25

<210> SEQ ID NO 442
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligo RNA

<400> SEQUENCE: 442

uaccuaugug cagaggaauu augau 25

<210> SEQ ID NO 443
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligo RNA

<400> SEQUENCE: 443

gcaaccaucu aaaccugaaa uugua 25

<210> SEQ ID NO 444
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligo RNA

<400> SEQUENCE: 444

uaauagaggu ugucgaaggc ugggc 25

<210> SEQ ID NO 445
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligo RNA

<400> SEQUENCE: 445

cccaacaggc agaccauuua uuuca 25

<210> SEQ ID NO 446
<211> LENGTH: 652
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 446

Met Ala Thr Ser Met Gly Leu Leu Leu Leu Leu Leu Leu Leu Leu Thr
1 5 10 15

Gln Pro Gly Ala Gly Thr Gly Ala Asp Thr Glu Ala Val Val Cys Val
20 25 30

Gly Thr Ala Cys Tyr Thr Ala His Ser Gly Lys Leu Ser Ala Ala Glu
35 40 45

Ala Gln Asn His Cys Asn Gln Asn Gly Gly Asn Leu Ala Thr Val Lys
50 55 60

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Ser Lys Glu Glu Ala Gln His Val Gln Arg Val Leu Ala Gln Leu Leu
65                  70                  75                  80

Arg Arg Glu Ala Ala Leu Thr Ala Arg Met Ser Lys Phe Trp Ile Gly
                85                  90                  95

Leu Gln Arg Glu Lys Gly Lys Cys Leu Asp Pro Ser Leu Pro Leu Lys
            100                 105                 110

Gly Phe Ser Trp Val Gly Gly Gly Glu Asp Thr Pro Tyr Ser Asn Trp
        115                 120                 125

His Lys Glu Leu Arg Asn Ser Cys Ile Ser Lys Arg Cys Val Ser Leu
    130                 135                 140

Leu Leu Asp Leu Ser Gln Pro Leu Leu Pro Ser Arg Leu Pro Lys Trp
145                 150                 155                 160

Ser Glu Gly Pro Cys Gly Ser Pro Gly Ser Pro Gly Ser Asn Ile Glu
                165                 170                 175

Gly Phe Val Cys Lys Phe Ser Phe Lys Gly Met Cys Arg Pro Leu Ala
            180                 185                 190

Leu Gly Gly Pro Gly Gln Val Thr Tyr Thr Thr Pro Phe Gln Thr Thr
        195                 200                 205

Ser Ser Ser Leu Glu Ala Val Pro Phe Ala Ser Ala Ala Asn Val Ala
    210                 215                 220

Cys Gly Glu Gly Asp Lys Asp Glu Thr Gln Ser His Tyr Phe Leu Cys
225                 230                 235                 240

Lys Glu Lys Ala Pro Asp Val Phe Asp Trp Gly Ser Ser Gly Pro Leu
                245                 250                 255

Cys Val Ser Pro Lys Tyr Gly Cys Asn Phe Asn Asn Gly Gly Cys His
            260                 265                 270

Gln Asp Cys Phe Glu Gly Gly Asp Gly Ser Phe Leu Cys Gly Cys Arg
        275                 280                 285

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

Pro Cys Ser Ser Ser Pro Cys Arg Gly Gly Ala Thr Cys Ala Leu Gly
305                 310                 315                 320

Pro His Gly Lys Asn Tyr Thr Cys Arg Cys Pro Gln Gly Tyr Gln Leu
                325                 330                 335

Asp Ser Ser Gln Leu Asp Cys Val Asp Val Asp Glu Cys Gln Asp Ser
            340                 345                 350

Pro Cys Ala Gln Glu Cys Val Asn Thr Pro Gly Gly Phe Arg Cys Glu
        355                 360                 365

Cys Trp Val Gly Tyr Glu Pro Gly Gly Pro Gly Glu Gly Ala Cys Gln
    370                 375                 380

Asp Val Asp Glu Cys Ala Leu Gly Arg Ser Pro Cys Ala Gln Gly Cys
385                 390                 395                 400

Thr Asn Thr Asp Gly Ser Phe His Cys Ser Cys Glu Glu Gly Tyr Val
                405                 410                 415

Leu Ala Gly Glu Asp Gly Thr Gln Cys Gln Asp Val Asp Glu Cys Val
            420                 425                 430

Gly Pro Gly Gly Pro Leu Cys Asp Ser Leu Cys Phe Asn Thr Gln Gly
        435                 440                 445

Ser Phe His Cys Gly Cys Leu Pro Gly Trp Val Leu Ala Pro Asn Gly
    450                 455                 460
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Val Ser Cys Thr Met Gly Pro Val Ser Leu Gly Pro Pro Ser Gly Pro
465                 470                 475                 480

Pro Asp Glu Glu Asp Lys Gly Glu Lys Glu Gly Ser Thr Val Pro Arg
                485                 490                 495

Ala Ala Thr Ala Ser Pro Thr Arg Gly Pro Glu Gly Thr Pro Lys Ala
            500                 505                 510

Thr Pro Thr Thr Ser Arg Pro Ser Leu Ser Ser Asp Ala Pro Ile Thr
        515                 520                 525

Ser Ala Pro Leu Lys Met Leu Ala Pro Ser Gly Ser Ser Gly Val Trp
    530                 535                 540

Arg Glu Pro Ser Ile His His Ala Thr Ala Ala Ser Gly Pro Gln Glu
545                 550                 555                 560

Pro Ala Gly Gly Asp Ser Ser Val Ala Thr Gln Asn Asn Asp Gly Thr
                565                 570                 575

Asp Gly Gln Lys Leu Leu Leu Phe Tyr Ile Leu Gly Thr Val Val Ala
            580                 585                 590

Ile Leu Leu Leu Leu Ala Leu Ala Leu Gly Leu Leu Val Tyr Arg Lys
        595                 600                 605

Arg Arg Ala Lys Arg Glu Glu Lys Lys Glu Lys Lys Pro Gln Asn Ala
    610                 615                 620

Ala Asp Ser Tyr Ser Trp Val Pro Glu Arg Ala Glu Ser Arg Ala Met
625                 630                 635                 640

Glu Asn Gln Tyr Ser Pro Thr Pro Gly Thr Asp Cys
                645                 650


<210> SEQ ID NO 447
<211> LENGTH: 719
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 447

Leu Asn Ile Thr Cys Arg Phe Ala Gly Val Phe His Val Glu Lys Asn
1               5                   10                  15

Gly Arg Tyr Ser Ile Ser Arg Thr Glu Ala Ala Asp Leu Cys Lys Ala
            20                  25                  30

Phe Asn Ser Thr Leu Pro Thr Met Ala Gln Met Glu Lys Ala Leu Ser
        35                  40                  45

Ile Gly Phe Glu Thr Cys Arg Tyr Gly Phe Ile Glu Gly His Val Val
    50                  55                  60

Ile Pro Arg Ile His Pro Asn Ser Ile Cys Ala Ala Asn Asn Thr Gly
65                  70                  75                  80

Val Tyr Ile Leu Thr Ser Asn Thr Ser Gln Tyr Asp Thr Tyr Cys Phe
                85                  90                  95

Asn Ala Ser Ala Pro Pro Glu Glu Asp Cys Thr Ser Val Thr Asp Leu
            100                 105                 110

Pro Asn Ala Phe Asp Gly Pro Ile Thr Ile Thr Ile Val Asn Arg Asp
        115                 120                 125

Gly Thr Arg Tyr Val Gln Lys Gly Glu Tyr Arg Thr Asn Pro Glu Asp
    130                 135                 140

Ile Tyr Pro Ser Asn Pro Thr Asp Asp Asp Val Ser Ser Gly Ser Ser
145                 150                 155                 160

Ser Glu Arg Ser Ser Thr Ser Gly Gly Tyr Ile Phe Tyr Thr Phe Ser
                165                 170                 175
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```
Thr Val His Pro Ile Pro Asp Glu Asp Ser Pro Trp Ile Thr Asp Ser
            180                 185                 190

Thr Asp Arg Ile Pro Ala Thr Thr Leu Met Ser Thr Ser Ala Thr Ala
        195                 200                 205

Thr Glu Thr Ala Thr Lys Arg Gln Glu Thr Trp Asp Trp Phe Ser Trp
    210                 215                 220

Leu Phe Leu Pro Ser Glu Ser Lys Asn His Leu His Thr Thr Thr Gln
225                 230                 235                 240

Met Ala Gly Thr Ser Ser Asn Thr Ile Ser Ala Gly Trp Glu Pro Asn
                245                 250                 255

Glu Glu Asn Glu Asp Glu Arg Asp Arg His Leu Ser Phe Ser Gly Ser
            260                 265                 270

Gly Ile Asp Asp Asp Glu Asp Phe Ile Ser Ser Thr Ile Ser Thr Thr
        275                 280                 285

Pro Arg Ala Phe Asp His Thr Lys Gln Asn Gln Asp Trp Thr Gln Trp
    290                 295                 300

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

Met Thr Asp Val Asp Arg Asn Gly Thr Thr Ala Tyr Glu Gly Asn Trp
                325                 330                 335

Asn Pro Glu Ala His Pro Pro Leu Ile His His Glu His His Glu Glu
            340                 345                 350

Glu Glu Thr Pro His Ser Thr Ser Thr Ile Gln Ala Thr Pro Ser Ser
        355                 360                 365

Thr Thr Glu Glu Thr Ala Thr Gln Lys Glu Gln Trp Phe Gly Asn Arg
    370                 375                 380

Trp His Glu Gly Tyr Arg Gln Thr Pro Lys Glu Asp Ser His Ser Thr
385                 390                 395                 400

Thr Gly Thr Ala Ala Ala Ser Ala His Thr Ser His Pro Met Gln Gly
                405                 410                 415

Arg Thr Thr Pro Ser Pro Glu Asp Ser Ser Trp Thr Asp Phe Phe Asn
            420                 425                 430

Pro Ile Ser His Pro Met Gly Arg Gly His Gln Ala Gly Arg Arg Met
        435                 440                 445

Asp Met Asp Ser Ser His Ser Ile Thr Leu Gln Pro Thr Ala Asn Pro
    450                 455                 460

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

Thr Thr Gln Gln Ser Asn Ser Gln Ser Phe Ser Thr Ser His Glu Gly
                485                 490                 495

Leu Glu Glu Asp Lys Asp His Pro Thr Thr Ser Thr Leu Thr Ser Ser
            500                 505                 510

Asn Arg Asn Asp Val Thr Gly Gly Arg Arg Asp Pro Asn His Ser Glu
        515                 520                 525

Gly Ser Thr Thr Leu Leu Glu Gly Tyr Thr Ser His Tyr Pro His Thr
    530                 535                 540

Lys Glu Ser Arg Thr Phe Ile Pro Val Thr Ser Ala Lys Thr Gly Ser
545                 550                 555                 560

Phe Gly Val Thr Ala Val Thr Val Gly Asp Ser Asn Ser Asn Val Asn
                565                 570                 575
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```
Arg Ser Leu Ser Gly Asp Gln Asp Thr Phe His Pro Ser Gly Gly Ser
            580                 585                 590

His Thr Thr His Gly Ser Glu Ser Asp Gly His Ser His Gly Ser Gln
        595                 600                 605

Glu Gly Gly Ala Asn Thr Thr Ser Gly Pro Ile Arg Thr Pro Gln Ile
    610                 615                 620

Pro Glu Trp Leu Ile Ile Leu Ala Ser Leu Leu Ala Leu Ala Leu Ile
625                 630                 635                 640

Leu Ala Val Cys Ile Ala Val Asn Ser Arg Arg Arg Cys Gly Gln Lys
                645                 650                 655

Lys Lys Leu Val Ile Asn Ser Gly Asn Gly Ala Val Glu Asp Arg Lys
            660                 665                 670

Pro Ser Gly Leu Asn Gly Glu Ala Ser Lys Ser Gln Glu Met Val His
        675                 680                 685

Leu Val Asn Lys Glu Ser Ser Glu Thr Pro Asp Gln Phe Met Thr Ala
    690                 695                 700

Asp Glu Thr Arg Asn Leu Gln Asn Val Asp Met Lys Ile Gly Val
705                 710                 715


<210> SEQ ID NO 448
<211> LENGTH: 574
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 448

Met Cys Pro Arg Ala Ala Arg Ala Pro Ala Thr Leu Leu Leu Ala Leu
1               5                   10                  15

Gly Ala Val Leu Trp Pro Ala Ala Gly Ala Trp Glu Leu Thr Ile Leu
            20                  25                  30

His Thr Asn Asp Val His Ser Arg Leu Glu Gln Thr Ser Glu Asp Ser
        35                  40                  45

Ser Lys Cys Val Asn Ala Ser Arg Cys Met Gly Gly Val Ala Arg Leu
    50                  55                  60

Phe Thr Lys Val Gln Gln Ile Arg Arg Ala Glu Pro Asn Val Leu Leu
65                  70                  75                  80

Leu Asp Ala Gly Asp Gln Tyr Gln Gly Thr Ile Trp Phe Thr Val Tyr
                85                  90                  95

Lys Gly Ala Glu Val Ala His Phe Met Asn Ala Leu Arg Tyr Asp Ala
            100                 105                 110

Met Ala Leu Gly Asn His Glu Phe Asp Asn Gly Val Glu Gly Leu Ile
        115                 120                 125

Glu Pro Leu Leu Lys Glu Ala Lys Phe Pro Ile Leu Ser Ala Asn Ile
    130                 135                 140

Lys Ala Lys Gly Pro Leu Ala Ser Gln Ile Ser Gly Leu Tyr Leu Pro
145                 150                 155                 160

Tyr Lys Val Leu Pro Val Gly Asp Glu Val Val Gly Ile Val Gly Tyr
                165                 170                 175

Thr Ser Lys Glu Thr Pro Phe Leu Ser Asn Pro Gly Thr Asn Leu Val
            180                 185                 190

Phe Glu Asp Glu Ile Thr Ala Leu Gln Pro Glu Val Asp Lys Leu Lys
        195                 200                 205

Thr Leu Asn Val Asn Lys Ile Ile Ala Leu Gly His Ser Gly Phe Glu
    210                 215                 220
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```
Met Asp Lys Leu Ile Ala Gln Lys Val Arg Gly Val Asp Val Val Val
225                 230                 235                 240

Gly Gly His Ser Asn Thr Phe Leu Tyr Thr Gly Asn Pro Pro Ser Lys
                245                 250                 255

Glu Val Pro Ala Gly Lys Tyr Pro Phe Ile Val Thr Ser Asp Asp Gly
            260                 265                 270

Arg Lys Val Pro Val Val Gln Ala Tyr Ala Phe Gly Lys Tyr Leu Gly
        275                 280                 285

Tyr Leu Lys Ile Glu Phe Asp Glu Arg Gly Asn Val Ile Ser Ser His
    290                 295                 300

Gly Asn Pro Ile Leu Leu Asn Ser Ser Ile Pro Glu Asp Pro Ser Ile
305                 310                 315                 320

Lys Ala Asp Ile Asn Lys Trp Arg Ile Lys Leu Asp Asn Tyr Ser Thr
                325                 330                 335

Gln Glu Leu Gly Lys Thr Ile Val Tyr Leu Asp Gly Ser Ser Gln Ser
            340                 345                 350

Cys Arg Phe Arg Glu Cys Asn Met Gly Asn Leu Ile Cys Asp Ala Met
        355                 360                 365

Ile Asn Asn Asn Leu Arg His Thr Asp Glu Met Phe Trp Asn His Val
    370                 375                 380

Ser Met Cys Ile Leu Asn Gly Gly Gly Ile Arg Ser Pro Ile Asp Glu
385                 390                 395                 400

Arg Asn Asn Gly Thr Ile Thr Trp Glu Asn Leu Ala Ala Val Leu Pro
                405                 410                 415

Phe Gly Gly Thr Phe Asp Leu Val Gln Leu Lys Gly Ser Thr Leu Lys
            420                 425                 430

Lys Ala Phe Glu His Ser Val His Arg Tyr Gly Gln Ser Thr Gly Glu
        435                 440                 445

Phe Leu Gln Val Gly Gly Ile His Val Val Tyr Asp Leu Ser Arg Lys
    450                 455                 460

Pro Gly Asp Arg Val Val Lys Leu Asp Val Leu Cys Thr Lys Cys Arg
465                 470                 475                 480

Val Pro Ser Tyr Asp Pro Leu Lys Met Asp Glu Val Tyr Lys Val Ile
                485                 490                 495

Leu Pro Asn Phe Leu Ala Asn Gly Gly Asp Gly Phe Gln Met Ile Lys
            500                 505                 510

Asp Glu Leu Leu Arg His Asp Ser Gly Asp Gln Asp Ile Asn Val Val
        515                 520                 525

Ser Thr Tyr Ile Ser Lys Met Lys Val Ile Tyr Pro Ala Val Glu Gly
    530                 535                 540

Arg Ile Lys Phe Ser Thr Gly Ser His Cys His Gly Ser Phe Ser Leu
545                 550                 555                 560

Ile Phe Leu Ser Leu Trp Ala Val Ile Phe Val Leu Tyr Gln
                565                 570


<210> SEQ ID NO 449
<211> LENGTH: 314
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 449

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

Thr Ala Thr Phe Ala Ala Ala Gln Glu Glu Cys Val Cys Glu Asn Tyr
            20                  25                  30

Lys Leu Ala Val Asn Cys Phe Val Asn Asn Asn Arg Gln Cys Gln Cys
        35                  40                  45

Thr Ser Val Gly Ala Gln Asn Thr Val Ile Cys Ser Lys Leu Ala Ala
    50                  55                  60

Lys Cys Leu Val Met Lys Ala Glu Met Asn Gly Ser Lys Leu Gly Arg
65                  70                  75                  80

Arg Ala Lys Pro Glu Gly Ala Leu Gln Asn Asn Asp Gly Leu Tyr Asp
                85                  90                  95

Pro Asp Cys Asp Glu Ser Gly Leu Phe Lys Ala Lys Gln Cys Asn Gly
            100                 105                 110

Thr Ser Thr Cys Trp Cys Val Asn Thr Ala Gly Val Arg Arg Thr Asp
        115                 120                 125

Lys Asp Thr Glu Ile Thr Cys Ser Glu Arg Val Arg Thr Tyr Trp Ile
    130                 135                 140

Ile Ile Glu Leu Lys His Lys Ala Arg Glu Lys Pro Tyr Asp Ser Lys
145                 150                 155                 160

Ser Leu Arg Thr Ala Leu Gln Lys Glu Ile Thr Thr Arg Tyr Gln Leu
                165                 170                 175

Asp Pro Lys Phe Ile Thr Ser Ile Leu Tyr Glu Asn Asn Val Ile Thr
            180                 185                 190

Ile Asp Leu Val Gln Asn Ser Ser Gln Lys Thr Gln Asn Asp Val Asp
        195                 200                 205

Ile Ala Asp Val Ala Tyr Tyr Phe Glu Lys Asp Val Lys Gly Glu Ser
    210                 215                 220

Leu Phe His Ser Lys Lys Met Asp Leu Thr Val Asn Gly Glu Gln Leu
225                 230                 235                 240

Asp Leu Asp Pro Gly Gln Thr Leu Ile Tyr Tyr Val Asp Glu Lys Ala
                245                 250                 255

Pro Glu Phe Ser Met Gln Gly Leu Lys Ala Gly Val Ile Ala Val Ile
            260                 265                 270

Val Val Val Val Met Ala Val Val Ala Gly Ile Val Val Leu Val Ile
        275                 280                 285

Ser Arg Lys Lys Arg Met Ala Lys Tyr Glu Lys Ala Glu Ile Lys Glu
    290                 295                 300

Met Gly Glu Met His Arg Glu Leu Asn Ala
305                 310


<210> SEQ ID NO 450
<211> LENGTH: 1390
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 450

Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
1               5                   10                  15

Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
            20                  25                  30

Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
        35                  40                  45
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Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
    50                  55                  60

Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65                  70                  75                  80

Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
                85                  90                  95

Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
            100                 105                 110

Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
        115                 120                 125

Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
    130                 135                 140

Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145                 150                 155                 160

Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
                165                 170                 175

Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
            180                 185                 190

Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
        195                 200                 205

His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
    210                 215                 220

Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225                 230                 235                 240

Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255

Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270

Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285

His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300

Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320

Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335

Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350

Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365

Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380

Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400

Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415

Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430

Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445

Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
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    450                 455                 460

Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480

Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495

Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510

Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525

Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540

Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560

Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575

Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590

Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605

Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610                 615                 620

Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640

Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
                645                 650                 655

Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
            660                 665                 670

Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
        675                 680                 685

His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn
    690                 695                 700

Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Phe
705                 710                 715                 720

Ala Val Lys Leu Lys Ile Asp Leu Ala Asn Arg Glu Thr Ser Ile Phe
                725                 730                 735

Ser Tyr Arg Glu Asp Pro Ile Val Tyr Glu Ile His Pro Thr Lys Ser
            740                 745                 750

Phe Ile Ser Gly Gly Ser Thr Ile Thr Gly Val Gly Lys Asn Leu Asn
        755                 760                 765

Ser Val Ser Val Pro Arg Met Val Ile Asn Val His Glu Ala Gly Arg
    770                 775                 780

Asn Phe Thr Val Ala Cys Gln His Arg Ser Asn Ser Glu Ile Ile Cys
785                 790                 795                 800

Cys Thr Thr Pro Ser Leu Gln Gln Leu Asn Leu Gln Leu Pro Leu Lys
                805                 810                 815

Thr Lys Ala Phe Phe Met Leu Asp Gly Ile Leu Ser Lys Tyr Phe Asp
            820                 825                 830

Leu Ile Tyr Val His Asn Pro Val Phe Lys Pro Phe Glu Lys Pro Val
        835                 840                 845

Met Ile Ser Met Gly Asn Glu Asn Val Leu Glu Ile Lys Gly Asn Asp
    850                 855                 860
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Ile Asp Pro Glu Ala Val Lys Gly Glu Val Leu Lys Val Gly Asn Lys
865                 870                 875                 880

Ser Cys Glu Asn Ile His Leu His Ser Glu Ala Val Leu Cys Thr Val
                885                 890                 895

Pro Asn Asp Leu Leu Lys Leu Asn Ser Glu Leu Asn Ile Glu Trp Lys
            900                 905                 910

Gln Ala Ile Ser Ser Thr Val Leu Gly Lys Val Ile Val Gln Pro Asp
        915                 920                 925

Gln Asn Phe Thr Gly Leu Ile Ala Gly Val Val Ser Ile Ser Thr Ala
    930                 935                 940

Leu Leu Leu Leu Leu Gly Phe Phe Leu Trp Leu Lys Lys Arg Lys Gln
945                 950                 955                 960

Ile Lys Asp Leu Gly Ser Glu Leu Val Arg Tyr Asp Ala Arg Val His
                965                 970                 975

Thr Pro His Leu Asp Arg Leu Val Ser Ala Arg Ser Val Ser Pro Thr
            980                 985                 990

Thr Glu Met Val Ser Asn Glu Ser  Val Asp Tyr Arg Ala  Thr Phe Pro
        995                 1000                1005

Glu Asp  Gln Phe Pro Asn Ser  Ser Gln Asn Gly Ser  Cys Arg Gln
    1010                1015                1020

Val Gln  Tyr Pro Leu Thr Asp  Met Ser Pro Ile Leu  Thr Ser Gly
    1025                1030                1035

Asp Ser  Asp Ile Ser Ser Pro  Leu Leu Gln Asn Thr  Val His Ile
    1040                1045                1050

Asp Leu  Ser Ala Leu Asn Pro  Glu Leu Val Gln Ala  Val Gln His
    1055                1060                1065

Val Val  Ile Gly Pro Ser Ser  Leu Ile Val His Phe  Asn Glu Val
    1070                1075                1080

Ile Gly  Arg Gly His Phe Gly  Cys Val Tyr His Gly  Thr Leu Leu
    1085                1090                1095

Asp Asn  Asp Gly Lys Lys Ile  His Cys Ala Val Lys  Ser Leu Asn
    1100                1105                1110

Arg Ile  Thr Asp Ile Gly Glu  Val Ser Gln Phe Leu  Thr Glu Gly
    1115                1120                1125

Ile Ile  Met Lys Asp Phe Ser  His Pro Asn Val Leu  Ser Leu Leu
    1130                1135                1140

Gly Ile  Cys Leu Arg Ser Glu  Gly Ser Pro Leu Val  Val Leu Pro
    1145                1150                1155

Tyr Met  Lys His Gly Asp Leu  Arg Asn Phe Ile Arg  Asn Glu Thr
    1160                1165                1170

His Asn  Pro Thr Val Lys Asp  Leu Ile Gly Phe Gly  Leu Gln Val
    1175                1180                1185

Ala Lys  Gly Met Lys Tyr Leu  Ala Ser Lys Lys Phe  Val His Arg
    1190                1195                1200

Asp Leu  Ala Ala Arg Asn Cys  Met Leu Asp Glu Lys  Phe Thr Val
    1205                1210                1215

Lys Val  Ala Asp Phe Gly Leu  Ala Arg Asp Met Tyr  Asp Lys Glu
    1220                1225                1230

Tyr Tyr  Ser Val His Asn Lys  Thr Gly Ala Lys Leu  Pro Val Lys
    1235                1240                1245
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Trp Met  Ala Leu Glu Ser Leu  Gln Thr Gln Lys Phe  Thr Thr Lys
    1250                1255                1260

Ser Asp  Val Trp Ser Phe Gly  Val Val Leu Trp Glu  Leu Met Thr
    1265                1270                1275

Arg Gly  Ala Pro Pro Tyr Pro  Asp Val Asn Thr Phe  Asp Ile Thr
    1280                1285                1290

Val Tyr  Leu Leu Gln Gly Arg  Arg Leu Leu Gln Pro  Glu Tyr Cys
    1295                1300                1305

Pro Asp  Pro Leu Tyr Glu Val  Met Leu Lys Cys Trp  His Pro Lys
    1310                1315                1320

Ala Glu  Met Arg Pro Ser Phe  Ser Glu Leu Val Ser  Arg Ile Ser
    1325                1330                1335

Ala Ile  Phe Ser Thr Phe Ile  Gly Glu His Tyr Val  His Val Asn
    1340                1345                1350

Ala Thr  Tyr Val Asn Val Lys  Cys Val Ala Pro Tyr  Pro Ser Leu
    1355                1360                1365

Leu Ser  Ser Glu Asp Asn Ala  Asp Asp Glu Val Asp  Thr Arg Pro
    1370                1375                1380

Ala Ser  Phe Trp Glu Thr Ser
    1385                1390


<210> SEQ ID NO 451
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 451

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Asp Ile Leu Thr Gly Tyr Tyr Ala Phe Asp Ile Trp Gly
            100                 105                 110

Gln Gly Thr Met Val Thr Val Ser Arg
        115                 120


<210> SEQ ID NO 452
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 452

Gly Tyr Tyr Met His
1               5


<210> SEQ ID NO 453
<211> LENGTH: 17
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-continued

<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 453

Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 454
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 454

Ser Asp Ile Leu Thr Gly Tyr Tyr Ala Phe Asp Ile
1 5 10

<210> SEQ ID NO 455
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 455

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Thr Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 456
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 456

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> SEQ ID NO 457
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 457

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> SEQ ID NO 458
<211> LENGTH: 7
<212> TYPE: PRT

-continued

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 458

Gln Gln Ser Tyr Ser Thr Thr
1 5

<210> SEQ ID NO 459
<211> LENGTH: 129
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 459

Glu Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Trp Tyr Tyr Tyr Gly Ser Gly Ser Ser Leu Tyr Tyr
100 105 110

Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
115 120 125

Arg

<210> SEQ ID NO 460
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 460

Gly Tyr Tyr Met His
1 5

<210> SEQ ID NO 461
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 461

Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 462
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 462

Asp Leu Trp Tyr Tyr Tyr Gly Ser Gly Ser Ser Leu Tyr Tyr Tyr Tyr
1 5 10 15

-continued

Gly Met Asp Val
20

<210> SEQ ID NO 463
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 463

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
20 25 30

Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
35 40 45

Leu Ile Tyr Gly Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
85 90 95

Leu Ser Gly Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 464
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 464

Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His
1 5 10

<210> SEQ ID NO 465
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 465

Gly Asn Ser Asn Arg Pro Ser
1 5

<210> SEQ ID NO 466
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 466

Gln Ser Tyr Asp Ser Ser Leu Ser Gly
1 5

<210> SEQ ID NO 467
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 467

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95

Val Arg Ser Gly Ser Tyr Asn Tyr Tyr Tyr Tyr Gly Met Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Arg
        115                 120


<210> SEQ ID NO 468
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 468

Asp Tyr Ala Met His
1               5


<210> SEQ ID NO 469
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 469

Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val Lys
1               5                   10                  15

Gly


<210> SEQ ID NO 470
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 470

Ser Gly Ser Tyr Asn Tyr Tyr Tyr Tyr Gly Met Asp Val
1               5                   10


<210> SEQ ID NO 471
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 471

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1               5                   10                  15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
            20                  25                  30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
        35                  40                  45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
    50                  55                  60
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Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65                  70                  75                  80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
                85                  90                  95

Asn Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 472
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 472

Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Val Asn
1               5                   10


<210> SEQ ID NO 473
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 473

Ser Asn Asn Gln Arg Pro Ser
1               5


<210> SEQ ID NO 474
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 474

Ala Ala Trp Asp Asp Ser Leu Asn Gly
1               5


<210> SEQ ID NO 475
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 475

Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Thr Thr Ser Gly Phe Thr Phe Thr Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ser Ile Ser Gly Ser Gly Gly Ile Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Asp Arg Val Leu Val Pro Ala Ser Ser Ser Tyr Phe Asp Tyr
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg
        115                 120


<210> SEQ ID NO 476
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-continued

<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 476

Ser Tyr Ala Met Ser
1 5

<210> SEQ ID NO 477
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 477

Ser Ile Ser Gly Ser Gly Gly Ile Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 478
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 478

Asp Arg Val Leu Val Pro Ala Ser Ser Ser Tyr Phe Asp Tyr
1 5 10

<210> SEQ ID NO 479
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 479

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50 55 60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105

<210> SEQ ID NO 480
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 480

Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser
1 5 10

<210> SEQ ID NO 481
<211> LENGTH: 7

-continued

<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 481

Gly Lys Asn Asn Arg Pro Ser
1 5

<210> SEQ ID NO 482
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 482

Asn Ser Arg Asp Ser Ser Gly Asn His
1 5

<210> SEQ ID NO 483
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 483

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
20 25 30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Arg Pro Leu Thr Phe Asn Ala Phe Asp Ile Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 484
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 484

Ser Ser Ser Tyr Tyr Trp Gly
1 5

<210> SEQ ID NO 485
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 485

Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 486
<211> LENGTH: 10

-continued

<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 486

Arg Pro Leu Thr Phe Asn Ala Phe Asp Ile
1 5 10

<210> SEQ ID NO 487
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 487

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Lys
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Tyr Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105

<210> SEQ ID NO 488
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 488

Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1 5 10

<210> SEQ ID NO 489
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 489

Tyr Asp Ser Asp Arg Pro Ser
1 5

<210> SEQ ID NO 490
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 490

Gln Val Trp Asp Ser Ser Ser Asp His
1 5

<210> SEQ ID NO 491
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 491

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
20 25 30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Ile Pro Met Tyr Ser Ser Ser Val Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 492
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 492

Ser Ser Ser Tyr Tyr Trp Gly
1 5

<210> SEQ ID NO 493
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 493

Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 494
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 494

Ile Pro Met Tyr Ser Ser Ser Val Asp Tyr
1 5 10

<210> SEQ ID NO 495
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 495

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Lys
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

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Tyr Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
    50                  55                  60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
                85                  90                  95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105


<210> SEQ ID NO 496
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 496

Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1               5                   10


<210> SEQ ID NO 497
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 497

Tyr Asp Ser Asp Arg Pro Ser
1               5


<210> SEQ ID NO 498
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 498

Gln Val Trp Asp Ser Ser Ser Asp His
1               5


<210> SEQ ID NO 499
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 499

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Arg Pro Leu Thr Phe Asn Ala Phe Asp Ile Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Arg
        115                 120
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<210> SEQ ID NO 500
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 500

Ser Ser Ser Tyr Tyr Trp Gly
1 5

<210> SEQ ID NO 501
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 501

Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 502
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 502

Arg Pro Leu Thr Phe Asn Ala Phe Asp Ile
1 5 10

<210> SEQ ID NO 503
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 503

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Lys
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Tyr Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105

<210> SEQ ID NO 504
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 504

Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1 5 10

<210> SEQ ID NO 505

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<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 505

Tyr Asp Ser Asp Arg Pro Ser
1 5

<210> SEQ ID NO 506
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 506

Gln Val Trp Asp Ser Ser Ser Asp His
1 5

<210> SEQ ID NO 507
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 507

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Asp Gly Gly Trp Phe Gly Glu Leu Asp Tyr Phe Gln His Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 508
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 508

Ser Tyr Ala Met Ser
1 5

<210> SEQ ID NO 509
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 509

Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

-continued

<210> SEQ ID NO 510
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 510

Asp Gly Gly Trp Phe Gly Glu Leu Asp Tyr Phe Gln His
1 5 10

<210> SEQ ID NO 511
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 511

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Ala Ala Pro Gly Gln
1 5 10 15

Lys Val Thr Val Ser Cys Thr Gly Ser Asn Ser Asn Ile Glu Lys Asn
20 25 30

Asp Val Ser Trp Tyr Gln Gln Gly Pro Gly Ala Ala Pro Lys Leu Leu
35 40 45

Ile Ser Asp Thr Asp Arg Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Ala Ile Ala Gly Leu Gln
65 70 75 80

Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser His Asp Thr Thr Leu
85 90 95

Ser Gly Pro Ile Phe Gly Gly Gly Thr Gln Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 512
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 512

Thr Gly Ser Asn Ser Asn Ile Glu Lys Asn Asp Val Ser
1 5 10

<210> SEQ ID NO 513
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 513

Asp Thr Asp Arg Arg Pro Ser
1 5

<210> SEQ ID NO 514
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 514

Gln Ser His Asp Thr Thr Leu Ser Gly
1 5

<210> SEQ ID NO 515
<211> LENGTH: 124

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<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 515

Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Ser Tyr Ile Thr Ser Ser Ser Ser Asp Thr Asp Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Tyr Tyr Tyr Asp Tyr Tyr Tyr Tyr Tyr Tyr Met Asp
100 105 110

Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 516
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 516

Asp Tyr Tyr Met Ser
1 5

<210> SEQ ID NO 517
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 517

Tyr Ile Thr Ser Ser Ser Ser Asp Thr Asp Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 518
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 518

Val Gly Tyr Tyr Tyr Asp Tyr Tyr Tyr Tyr Tyr Tyr Met Asp Val
1 5 10 15

<210> SEQ ID NO 519
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 519

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

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

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            20                  25                  30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
        35                  40                  45

Asp Glu Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
    50                  55                  60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ile Asn Leu Asp Trp
                85                  90                  95

Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105


<210> SEQ ID NO 520
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 520

Gln Gly Asp Ser Leu Arg Gly Tyr Tyr Ala Ser
1               5                   10


<210> SEQ ID NO 521
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 521

Asp Glu Asn Asn Arg Pro Ser
1               5


<210> SEQ ID NO 522
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 522

Asn Ser Arg Asp Ile Asn Leu Asp
1               5


<210> SEQ ID NO 523
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 523

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95
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Cys Ala Arg Arg Val Ile Val Trp Gly Ser Tyr Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Arg
        115                 120


<210> SEQ ID NO 524
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 524

Ser Ser Ser Tyr Tyr Trp Gly
1               5


<210> SEQ ID NO 525
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 525

Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1               5                   10                  15


<210> SEQ ID NO 526
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 526

Arg Val Ile Val Trp Gly Ser Tyr Asp Tyr
1               5                   10


<210> SEQ ID NO 527
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 527

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Lys
1               5                   10                  15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45

Tyr Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
    50                  55                  60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
                85                  90                  95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105


<210> SEQ ID NO 528
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 528
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Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1               5                   10


<210> SEQ ID NO 529
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 529

Tyr Asp Ser Asp Arg Pro Ser
1               5


<210> SEQ ID NO 530
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 530

Gln Val Trp Asp Ser Ser Ser Asp His
1               5


<210> SEQ ID NO 531
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 531

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Met Arg Ala Tyr Gly Ser Gly Ser Tyr Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Arg
        115                 120


<210> SEQ ID NO 532
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 532

Ser Ser Ser Tyr Tyr Trp Gly
1               5


<210> SEQ ID NO 533
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 533
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Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1               5                   10                  15


<210> SEQ ID NO 534
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 534

Arg Ala Tyr Gly Ser Gly Ser Tyr Asp Tyr
1               5                   10


<210> SEQ ID NO 535
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 535

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1               5                   10                  15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
            20                  25                  30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95

Leu Gln Thr Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
            100                 105                 110


<210> SEQ ID NO 536
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 536

Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
1               5                   10                  15


<210> SEQ ID NO 537
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 537

Leu Gly Ser Asn Arg Ala Ser
1               5


<210> SEQ ID NO 538
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 538

Met Gln Ala Leu Gln Thr Pro
1               5
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<210> SEQ ID NO 539
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 539

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ala Tyr Tyr Cys
85 90 95

Ala Lys Gly Leu Arg Tyr Ser Ser Ala Trp Thr Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 540
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 540

Ser Tyr Ala Met Ser
1 5

<210> SEQ ID NO 541
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 541

Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 542
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 542

Gly Leu Arg Tyr Ser Ser Ala Trp Thr Phe Asp Tyr
1 5 10

<210> SEQ ID NO 543
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 543

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln

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1               5                   10                  15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
            20                  25                  30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35                  40                  45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
    50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
                85                  90                  95

Ser Thr Pro Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 544
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 544

Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1               5                   10


<210> SEQ ID NO 545
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 545

Asp Val Ser Asn Arg Pro Ser
1               5


<210> SEQ ID NO 546
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 546

Ser Ser Tyr Thr Ser Ser Ser Thr Pro
1               5


<210> SEQ ID NO 547
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 547

Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Arg Tyr
            20                  25                  30

Gly Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Thr Asn Thr Gly Asn Pro Thr Tyr Ala Gln Gly Phe
    50                  55                  60

Thr Gly Arg Val Val Phe Ser Leu Asp Thr Ser Val Ser Thr Ala Tyr
65                  70                  75                  80
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Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Ile Ser Ser Gly Phe Gly Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Arg
115

<210> SEQ ID NO 548
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 548

Arg Tyr Gly Ile Asn
1 5

<210> SEQ ID NO 549
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 549

Trp Ile Asn Thr Asn Thr Gly Asn Pro Thr Tyr Ala Gln Gly Phe Thr
1 5 10 15

Gly

<210> SEQ ID NO 550
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 550

Ser Ser Gly Phe Gly Tyr Tyr Phe Asp Tyr
1 5 10

<210> SEQ ID NO 551
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 551

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Arg Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Phe Leu Ile
35 40 45

Tyr Ala Gly Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Asn Ser Phe Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 552
<211> LENGTH: 11

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<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 552

Arg Ala Ser Gln Ser Ile Ser Arg Trp Leu Ala
1 5 10

<210> SEQ ID NO 553
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 553

Ala Gly Ser Ser Leu Gln Ser
1 5

<210> SEQ ID NO 554
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 554

Gln Gln Thr Asn Ser Phe Pro
1 5

<210> SEQ ID NO 555
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 555

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Phe Arg Asp Trp Gly Ser Leu Arg Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 556
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 556

Ser Tyr Gly Ile Ser
1 5

<210> SEQ ID NO 557
<211> LENGTH: 17

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<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 557

Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> SEQ ID NO 558
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 558

Ala Phe Arg Asp Trp Gly Ser Leu Arg Asp Tyr
1 5 10

<210> SEQ ID NO 559
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 559

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Ala Ala Pro Gly Gln
1 5 10 15

Lys Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Asn Asn
20 25 30

Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
65 70 75 80

Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Gly Thr Trp Asp Ser Ser Leu
85 90 95

Ser Ala Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 560
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 560

Ser Gly Ser Ser Ser Asn Ile Gly Asn Asn Tyr Val Ser
1 5 10

<210> SEQ ID NO 561
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 561

Asp Asn Asn Lys Arg Pro Ser
1 5

<210> SEQ ID NO 562
<211> LENGTH: 9
<212> TYPE: PRT

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 562

Gly Thr Trp Asp Ser Ser Leu Ser Ala
1 5

<210> SEQ ID NO 563
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 563

Glu Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Leu Ala Val Gly Ala Tyr Gln Tyr Tyr Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 564
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 564

Ser Tyr Trp Ile Gly
1 5

<210> SEQ ID NO 565
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 565

Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 566
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 566

Leu Ala Val Gly Ala Tyr Gln Tyr Tyr Phe Asp Tyr
1 5 10

<210> SEQ ID NO 567

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<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 567

Gln Thr Val Val Thr Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Leu Ser Ser Gly Ser Val Ser Thr Ser
20 25 30

Tyr Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
35 40 45

Leu Ile Tyr Ser Thr Asn Thr Arg Ser Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Ile Leu Gly Asn Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Ala Asp Asp Glu Ser Asp Tyr Tyr Cys Val Leu Tyr Met Gly Ser
85 90 95

Gly Ile Ser Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 568
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 568

Gly Leu Ser Ser Gly Ser Val Ser Thr Ser Tyr Tyr Pro Ser
1 5 10

<210> SEQ ID NO 569
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 569

Ser Thr Asn Thr Arg Ser Ser
1 5

<210> SEQ ID NO 570
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 570

Val Leu Tyr Met Gly Ser Gly Ile
1 5

<210> SEQ ID NO 571
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 571

Glu Val Gln Leu Val Glu Ser Gly Gly Asn Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
20 25 30

Trp Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

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Ser Ser Val Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Tyr Trp Pro Gly Trp Tyr Phe Asp Leu Trp Gly Arg Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Arg
        115


<210> SEQ ID NO 572
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 572

Arg Tyr Trp Met Thr
1               5


<210> SEQ ID NO 573
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 573

Ser Val Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1               5                   10                  15

Gly


<210> SEQ ID NO 574
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 574

Asp Tyr Trp Pro Gly Trp Tyr Phe Asp Leu
1               5                   10


<210> SEQ ID NO 575
<211> LENGTH: 116
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 575

Gln Ala Val Leu Thr Gln Pro Ser Ser Leu Ser Ala Ser Pro Gly Ala
1               5                   10                  15

Ser Ala Ser Leu Thr Cys Thr Phe Arg Ser Asp Ile Ser Val Gly Ser
            20                  25                  30

Tyr Arg Ile Tyr Trp Tyr Gln Gln Lys Pro Gly Ser Pro Pro Gln Phe
        35                  40                  45

Leu Leu Lys Tyr Thr Ser Asp Ser Asp Lys Gln Gln Gly Ser Gly Val
    50                  55                  60

Pro Ser Arg Phe Ser Gly Ser Lys Asp Val Ser Ala Asn Ala Gly Ile
65                  70                  75                  80

Leu Leu Ile Ser Gly Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys
                85                  90                  95
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Met Thr Trp His Asn Thr Ala Ser Val Phe Gly Gly Gly Thr Lys Leu
100 105 110

Ala Val Leu Gly
115

<210> SEQ ID NO 576
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 576

Thr Phe Arg Ser Asp Ile Ser Val Gly Ser Tyr Arg Ile Tyr
1 5 10

<210> SEQ ID NO 577
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 577

Tyr Thr Ser Asp Ser Asp Lys Gln Gln Gly Ser
1 5 10

<210> SEQ ID NO 578
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 578

Met Thr Trp His Asn Thr Ala
1 5

<210> SEQ ID NO 579
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 579

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ile Arg Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Thr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Ser Tyr Ile Ser Gly Gly Ser Gly Thr Lys Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Glu Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Leu Val Ser Tyr Ser Ser Pro Gly Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 580
<211> LENGTH: 5
<212> TYPE: PRT

-continued

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 580

Ser Tyr Thr Met Asn
1 5

<210> SEQ ID NO 581
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 581

Tyr Ile Ser Gly Gly Ser Gly Thr Lys Phe Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 582
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 582

Val Ser Tyr Ser Ser Pro Gly Phe Asp Tyr
1 5 10

<210> SEQ ID NO 583
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 583

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
1 5 10 15

Thr Ala Ser Ile Thr Cys Ser Gly Asp Lys Leu Gly Asp Lys Tyr Val
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Ile Leu Leu Ile Phe
35 40 45

Gln Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ala Trp Asp Ser Ser Ala Ala Val
85 90 95

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105

<210> SEQ ID NO 584
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 584

Ser Gly Asp Lys Leu Gly Asp Lys Tyr Val Tyr
1 5 10

<210> SEQ ID NO 585
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 585

Gln Asp Ser Glu Arg Pro Ser
1 5

<210> SEQ ID NO 586
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 586

Gln Ala Trp Asp Ser Ser Ala
1 5

<210> SEQ ID NO 587
<211> LENGTH: 115
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 587

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Arg
115

<210> SEQ ID NO 588
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 588

Ser Tyr Gly Ile Ser
1 5

<210> SEQ ID NO 589
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 589

Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> SEQ ID NO 590
<211> LENGTH: 6

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<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 590

Gly Gly Ala Phe Asp Ile
1 5

<210> SEQ ID NO 591
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 591

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
20 25 30

Tyr His Val Tyr Trp Tyr Gln Gln Leu Pro Gly Lys Ala Pro Lys Leu
35 40 45

Leu Ile Tyr Val Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65 70 75 80

Gln Ala Asp Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
85 90 95

Leu Ser Gly Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 592
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 592

Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr His Val Tyr
1 5 10

<210> SEQ ID NO 593
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 593

Val Asn Ser Asn Arg Pro Ser
1 5

<210> SEQ ID NO 594
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 594

Gln Ser Tyr Asp Ser Ser Leu Ser Gly
1 5

<210> SEQ ID NO 595
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 595

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ser Ala Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Trp Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Ser Ser Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Trp Pro Gly Trp Tyr Phe Asp Leu Trp Gly Arg Gly
100 105 110

Thr Leu Val Thr Val Ser Arg
115

<210> SEQ ID NO 596
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 596

Asn Tyr Trp Met Thr
1 5

<210> SEQ ID NO 597
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 597

Ser Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 598
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 598

Asp Tyr Trp Pro Gly Trp Tyr Phe Asp Leu
1 5 10

<210> SEQ ID NO 599
<211> LENGTH: 116
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 599

Gln Ala Val Leu Thr Gln Pro Ser Ser Leu Ser Ala Ser Pro Gly Ala
1 5 10 15

Ser Ala Ser Leu Thr Cys Thr Phe Arg Ser Asp Ile Ser Val Gly Ser
20 25 30

Tyr Arg Ile Tyr Trp Tyr Gln Gln Lys Pro Gly Ser Pro Pro Gln Phe

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        35                  40                  45

Leu Leu Lys Tyr Thr Ser Asp Ser Asp Lys Gln Gln Gly Ser Gly Val
    50                  55                  60

Pro Ser Arg Phe Ser Gly Ser Lys Asp Val Ser Ala Asn Ala Gly Ile
65                  70                  75                  80

Leu Leu Ile Ser Gly Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys
                85                  90                  95

Met Thr Trp His Asn Thr Ala Ser Val Phe Gly Gly Gly Thr Lys Leu
            100                 105                 110

Ala Val Leu Gly
        115


<210> SEQ ID NO 600
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 600

Thr Phe Arg Ser Asp Ile Ser Val Gly Ser Tyr Arg Ile Tyr
1               5                   10


<210> SEQ ID NO 601
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 601

Tyr Thr Ser Asp Ser Asp Lys Gln Gln Gly Ser
1               5                   10


<210> SEQ ID NO 602
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 602

Met Thr Trp His Asn Thr Ala
1               5


<210> SEQ ID NO 603
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 603

Gln Val Gln Leu Val Gln Ser Gly Ser Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Thr Ser Gly Tyr Ile Phe Thr Asp Tyr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Tyr Tyr Ala Gln Lys Phe
    50                  55                  60

His Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
                85                  90                  95
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Ala Arg Glu Asp Tyr Asp Ile Leu Thr Gly Tyr Tyr Pro Ala Ser Gly
            100                 105                 110

His Gly Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg
        115                 120                 125


<210> SEQ ID NO 604
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 604

Asp Tyr Tyr Met His
1               5


<210> SEQ ID NO 605
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 605

Trp Ile Asn Pro Asn Ser Gly Gly Thr Tyr Tyr Ala Gln Lys Phe His
1               5                   10                  15

Gly


<210> SEQ ID NO 606
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 606

Glu Asp Tyr Asp Ile Leu Thr Gly Tyr Tyr Pro Ala Ser Gly His Gly
1               5                   10                  15

Asp Tyr


<210> SEQ ID NO 607
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 607

Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1               5                   10                  15

Thr Val Thr Leu Thr Cys Ala Ser Ser Thr Gly Ala Val Thr Ser Gly
            20                  25                  30

Phe Leu Ala Asn Trp Phe Gln Gln Lys Pro Gly Gln Thr Pro Arg Ser
        35                  40                  45

Leu Ile Tyr Lys Thr Ser Asn Lys His Pro Trp Thr Pro Ala Arg Phe
    50                  55                  60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65                  70                  75                  80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Leu Leu Leu Ser Gly Gly
                85                  90                  95

Ala Trp Val Phe Gly Gly Gly Thr Lys Leu Ser Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 608
<211> LENGTH: 14
<212> TYPE: PRT
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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 608

Ala Ser Ser Thr Gly Ala Val Thr Ser Gly Phe Leu Ala Asn
1 5 10

<210> SEQ ID NO 609
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 609

Lys Thr Ser Asn Lys His Pro
1 5

<210> SEQ ID NO 610
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 610

Leu Leu Leu Ser Gly Gly Ala
1 5

<210> SEQ ID NO 611
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 611

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Glu Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Asp Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg His Asp Val Val Asp Gly Tyr Asn Thr Gly Met Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 612
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 612

Ser Tyr Trp Ile Gly
1 5

<210> SEQ ID NO 613
<211> LENGTH: 17
<212> TYPE: PRT

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 613

Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 614
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 614

His Asp Val Val Asp Gly Tyr Asn Thr Gly Met Asp Val
1 5 10

<210> SEQ ID NO 615
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 615

Gln Thr Val Val Thr Gln Glu Pro Ser Phe Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Leu Ser Ser Gly Ser Val Ser Thr Ser
            20 25 30

Tyr Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
        35 40 45

Leu Ile Ser Ser Thr Asn Thr Arg Ser Ser Gly Val Pro Asp Arg Phe
    50 55 60

Ser Gly Ser Ile Leu Gly Asn Arg Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Ala Asp Asp Glu Ser Asp Tyr Tyr Cys Val Leu Tyr Met Gly Ser
                85 90 95

Gly Ile Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100 105 110

<210> SEQ ID NO 616
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 616

Gly Leu Ser Ser Gly Ser Val Ser Thr Ser Tyr Tyr Pro Ser
1 5 10

<210> SEQ ID NO 617
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 617

Ser Thr Asn Thr Arg Ser Ser
1 5

<210> SEQ ID NO 618
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 618

Val Leu Tyr Met Gly Ser Gly Ile
1 5

<210> SEQ ID NO 619
<211> LENGTH: 128
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 619

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Ala Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Leu Thr Gly Ser Ser Tyr Tyr Asp Ser Ser Gly Tyr Ser Ser
100 105 110

Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Arg
115 120 125

<210> SEQ ID NO 620
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 620

Ser Tyr Trp Ile Gly
1 5

<210> SEQ ID NO 621
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 621

Ile Ile Tyr Pro Gly Asp Ser Asp Ala Arg Tyr Ser Pro Ser Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 622
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 622

Leu Thr Gly Ser Ser Tyr Tyr Asp Ser Ser Gly Tyr Ser Ser Tyr Gly
1 5 10 15

Met Asp Val

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<210> SEQ ID NO 623
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 623

Gln Thr Val Val Thr Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Leu Ser Ser Gly Ser Val Ser Thr Ser
20 25 30

Tyr Tyr Pro Ser Trp Phe Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
35 40 45

Leu Ile Tyr Ser Thr Asn Thr Arg Ser Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Ile Leu Gly Asn Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Ala Asp Asp Glu Ser Asp Tyr Tyr Cys Val Leu Tyr Met Gly Ser
85 90 95

Gly Ile Ser Val Phe Gly Gly Gly Thr Gln Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 624
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 624

Gly Leu Ser Ser Gly Ser Val Ser Thr Ser Tyr Tyr Pro Ser
1 5 10

<210> SEQ ID NO 625
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 625

Ser Thr Asn Thr Arg Ser Ser
1 5

<210> SEQ ID NO 626
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 626

Val Leu Tyr Met Gly Ser Gly Ile
1 5

<210> SEQ ID NO 627
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 627

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met

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        35                  40                  45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg His Asn Ser Asn Tyr Tyr Tyr Tyr Tyr Met Asp Val Trp Gly
            100                 105                 110

Lys Gly Thr Leu Val Thr Val Ser Arg
        115                 120


<210> SEQ ID NO 628
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 628

Ser Tyr Trp Ile Gly
1               5


<210> SEQ ID NO 629
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 629

Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln
1               5                   10                  15

Gly


<210> SEQ ID NO 630
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 630

His Asn Ser Asn Tyr Tyr Tyr Tyr Tyr Met Asp Val
1               5                   10


<210> SEQ ID NO 631
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 631

Gln Thr Val Val Thr Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1               5                   10                  15

Thr Val Thr Leu Thr Cys Gly Leu Ser Ser Gly Ser Val Ser Thr Ser
            20                  25                  30

Tyr Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
        35                  40                  45

Leu Ile Tyr Ser Thr Asn Thr Arg Ser Ser Gly Val Pro Asp Arg Phe
    50                  55                  60

Ser Gly Ser Ile Leu Gly Asn Lys Ala Ala Leu Thr Ile Thr Gly Ala
65                  70                  75                  80

Gln Ala Asp Asp Glu Ser Asp Tyr Tyr Cys Val Leu Tyr Met Gly Ser
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                85                  90                  95

Gly Ile Ser Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 632
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 632

Gly Leu Ser Ser Gly Ser Val Ser Thr Ser Tyr Tyr Pro Ser
1               5                   10


<210> SEQ ID NO 633
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 633

Ser Thr Asn Thr Arg Ser Ser
1               5


<210> SEQ ID NO 634
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 634

Val Leu Tyr Met Gly Ser Gly Ile
1               5


<210> SEQ ID NO 635
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 635

Gln Val Gln Leu Val Gln Ser Gly Ser Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Thr Ser Gly Tyr Ile Phe Thr Asp Tyr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Tyr Tyr Ala Gln Lys Phe
    50                  55                  60

His Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Asp Tyr Asp Ile Leu Thr Gly Phe Tyr Pro Ala Ser Gly
            100                 105                 110

His Gly Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg
        115                 120                 125


<210> SEQ ID NO 636
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
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<400> SEQUENCE: 636

Asp Tyr Tyr Met His
1 5

<210> SEQ ID NO 637
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 637

Trp Ile Asn Pro Asn Ser Gly Gly Thr Tyr Tyr Ala Gln Lys Phe His
1 5 10 15

Gly

<210> SEQ ID NO 638
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 638

Glu Asp Tyr Asp Ile Leu Thr Gly Phe Tyr Pro Ala Ser Gly His Gly
1 5 10 15

Asp Tyr

<210> SEQ ID NO 639
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 639

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 640
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 640

Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
1 5 10

<210> SEQ ID NO 641
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 641

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> SEQ ID NO 642
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 642

Gln Gln Tyr Gly Ser Ser
1 5

<210> SEQ ID NO 643
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 643

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg His Gly Met Thr Ser Gly Tyr Val Ala His Asn Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 644
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 644

Ser Tyr Trp Ile Gly
1 5

<210> SEQ ID NO 645
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 645

Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 646
<211> LENGTH: 13

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<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 646

His Gly Met Thr Ser Gly Tyr Val Ala His Asn Asp Tyr
1 5 10

<210> SEQ ID NO 647
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 647

Gln Thr Val Val Thr Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Leu Ser Ser Gly Ser Val Ser Thr Ser
20 25 30

Tyr Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
35 40 45

Leu Ile Tyr Ser Thr Asn Thr Arg Ser Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Ile Leu Gly Asn Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Ala Asp Asp Glu Ser Asp Tyr Tyr Cys Val Leu Tyr Met Gly Ser
85 90 95

Gly Ile Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 648
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 648

Gly Leu Ser Ser Gly Ser Val Ser Thr Ser Tyr Tyr Pro Ser
1 5 10

<210> SEQ ID NO 649
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 649

Ser Thr Asn Thr Arg Ser Ser
1 5

<210> SEQ ID NO 650
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 650

Val Leu Tyr Met Gly Ser Gly Ile
1 5

<210> SEQ ID NO 651
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 651

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gly
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Ile Ser Ser Ser
20 25 30

Asn Trp Trp Ser Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
35 40 45

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

Lys Ser Arg Val Thr Ile Ser Val Asp Lys Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Ser Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Arg
115

<210> SEQ ID NO 652
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 652

Ser Ser Asn Trp Trp Ser
1 5

<210> SEQ ID NO 653
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 653

Glu Ile Tyr His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 654
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 654

Gly Gly Ser Tyr Tyr Phe Asp Tyr
1 5

<210> SEQ ID NO 655
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 655

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ile Ser Asp Val Gly Gly Tyr
20 25 30

Asp Phe Val Ser Trp Tyr Gln His His Pro Gly Lys Ala Pro Lys Leu
35 40 45

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Leu Ile Tyr Asp Val Asn Asn Arg Pro Ser Gly Val Ser His Arg Phe
    50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Thr Tyr Tyr Cys Ser Ser Tyr Ser Asn Arg
                85                  90                  95

His Ser Leu Ile Val Phe Gly Ser Gly Thr Gln Val Val Gly Leu Gly
            100                 105                 110


<210> SEQ ID NO 656
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 656

Thr Gly Thr Ile Ser Asp Val Gly Gly Tyr Asp Phe Val Ser
1               5                   10


<210> SEQ ID NO 657
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 657

Asp Val Asn Asn Arg Pro Ser
1               5


<210> SEQ ID NO 658
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 658

Ser Ser Tyr Ser Asn Arg His Ser Leu
1               5


<210> SEQ ID NO 659
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 659

Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
            20                  25                  30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Gly Glu Ile Asn His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
    50                  55                  60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Gly Gly Gly Val Glu Ala Leu Asn Tyr Gly Met Asp Val Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Arg
        115                 120
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<210> SEQ ID NO 660
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 660

Gly Tyr Tyr Trp Ser
1 5

<210> SEQ ID NO 661
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 661

Glu Ile Asn His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 662
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 662

Gly Gly Gly Val Glu Ala Leu Asn Tyr Gly Met Asp Val
1 5 10

<210> SEQ ID NO 663
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 663

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Thr Ile Thr Ile Ser Cys Thr Gly Thr Ile Ser Asp Val Gly Gly Tyr
20 25 30

Asp Phe Val Ser Trp Tyr Gln His His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Leu Ile Tyr Asp Val Asn Asn Arg Pro Ser Gly Val Ser His Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Thr Tyr Tyr Cys Ser Ser Tyr Ser Asn Arg
85 90 95

His Ser Leu Ile Val Phe Gly Ser Gly Thr Gln Val Val Gly Leu Gly
100 105 110

<210> SEQ ID NO 664
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 664

Thr Gly Thr Ile Ser Asp Val Gly Gly Tyr Asp Phe Val Ser
1 5 10

<210> SEQ ID NO 665

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<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 665

Asp Val Asn Asn Arg Pro Ser
1 5

<210> SEQ ID NO 666
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 666

Ser Ser Tyr Ser Asn Arg His Ser Leu
1 5

<210> SEQ ID NO 667
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 667

Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val His Gly Gly Ser Phe Asp Asp Tyr
20 25 30

Tyr Trp Thr Trp Ile Arg Gln Pro Pro Gly Gly Gly Leu Glu Trp Ile
35 40 45

Gly Glu Met Asn Ser Gly Arg Thr Tyr Asn Tyr Asn Pro Phe Leu Glu
50 55 60

Ser Arg Ala Ser Ile Asp Val Asp Thr Phe Lys Lys Gln Phe Ser Leu
65 70 75 80

Ala Leu Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Gly Ala Tyr Val Asn Tyr Tyr Tyr Ile Asp Val Trp Gly Asp Gly
100 105 110

Thr Thr Val Thr Val Ser Arg
115

<210> SEQ ID NO 668
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 668

Asp Tyr Tyr Trp Thr
1 5

<210> SEQ ID NO 669
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 669

Glu Met Asn Ser Gly Arg Thr Tyr Asn Tyr Asn Pro Phe Leu Glu Ser
1 5 10 15

<210> SEQ ID NO 670

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<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 670

Gly Ala Tyr Val Asn Tyr Tyr Tyr Ile Asp Val
1 5 10

<210> SEQ ID NO 671
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 671

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Thr Ile Thr Ile Ser Cys Thr Gly Thr Ile Ser Asp Val Gly Gly Tyr
20 25 30

Asp Phe Val Ser Trp Tyr Gln His His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Leu Ile Tyr Asp Val Asn Asn Arg Pro Ser Gly Val Ser His Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Thr Tyr Tyr Cys Ser Ser Tyr Ser Asn Arg
85 90 95

His Ser Leu Ile Val Phe Gly Ser Gly Thr Gln Val Val Gly Leu Gly
100 105 110

<210> SEQ ID NO 672
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 672

Thr Gly Thr Ile Ser Asp Val Gly Gly Tyr Asp Phe Val Ser
1 5 10

<210> SEQ ID NO 673
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 673

Asp Val Asn Asn Arg Pro Ser
1 5

<210> SEQ ID NO 674
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 674

Ser Ser Tyr Ser Asn Arg His Ser Leu
1 5

<210> SEQ ID NO 675
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 675

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Ala Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Arg Ile Tyr Thr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Glu Arg Ala Tyr Cys Ser Ser Thr Ser Cys Tyr Arg Asn Ala Phe
100 105 110

Asp Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Arg
115 120 125

<210> SEQ ID NO 676
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 676

Ser Tyr Tyr Trp Ser
1 5

<210> SEQ ID NO 677
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 677

Arg Ile Tyr Thr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 678
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 678

Glu Arg Ala Tyr Cys Ser Ser Thr Ser Cys Tyr Arg Asn Ala Phe Asp
1 5 10 15

Ile

<210> SEQ ID NO 679
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 679

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Asn Ile Ser Cys Ala Gly Ser Ser Ser Asn Ile Gly Ala Gly
20 25 30

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Tyr Asp Val His Trp Tyr Gln Gln Ile Pro Gly Thr Ala Pro Lys Leu
        35                  40                  45

Leu Met Tyr Gly Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
    50                  55                  60

Ser Gly Ser Lys Ser Gly Ala Ser Ala Ser Leu Ala Ile Thr Arg Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
                85                  90                  95

Leu Ser Gly Ser Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
            100                 105                 110

Gly


<210> SEQ ID NO 680
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 680

Ala Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His
1               5                   10


<210> SEQ ID NO 681
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 681

Gly Asn Ser Asn Arg Pro Ser
1               5


<210> SEQ ID NO 682
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 682

Gln Ser Tyr Asp Ser Ser Leu Ser Gly Ser
1               5                   10


<210> SEQ ID NO 683
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 683

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Thr Val Ile Ser Phe Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
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Ala Lys Ala Tyr Thr Asn Thr Trp Trp Pro Asp Ala Phe Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Arg
        115                 120


<210> SEQ ID NO 684
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 684

Ser Tyr Gly Met His
1               5


<210> SEQ ID NO 685
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 685

Val Ile Ser Phe Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
1               5                   10                  15

Gly


<210> SEQ ID NO 686
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 686

Ala Tyr Thr Asn Thr Trp Trp Pro Asp Ala Phe Asp Ile
1               5                   10


<210> SEQ ID NO 687
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 687

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Ser Asn Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Asp Ala Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Asn Leu Pro Pro
                85                  90                  95

Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
            100                 105


<210> SEQ ID NO 688
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
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<400> SEQUENCE: 688

Gln Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

<210> SEQ ID NO 689
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 689

Asp Ala Ser Asn Leu Glu Thr
1 5

<210> SEQ ID NO 690
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 690

Gln Gln Tyr Asp Asn Leu Pro
1 5

<210> SEQ ID NO 691
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 691

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ser Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Asp Leu Tyr Trp Asn Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Arg
115

<210> SEQ ID NO 692
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 692

Ser Tyr Tyr Trp Ser
1 5

<210> SEQ ID NO 693
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 693

Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 694
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 694

Asp Leu Tyr Trp Asn Asp Ala Phe Asp Ile
1 5 10

<210> SEQ ID NO 695
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 695

Gln Ser Ala Leu Thr Gln Pro Leu Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
85 90 95

Asn Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 696
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 696

Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Val Asn
1 5 10

<210> SEQ ID NO 697
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 697

Ser Asn Asn Gln Arg Pro Ser
1 5

<210> SEQ ID NO 698
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 698

Ala Ala Trp Asp Asp Ser Leu Asn Gly

-continued

1 5

<210> SEQ ID NO 699
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 699

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ser Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Asp Leu Tyr Trp Asn Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Arg
115

<210> SEQ ID NO 700
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 700

Ser Tyr Tyr Trp Ser
1 5

<210> SEQ ID NO 701
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 701

Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 702
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 702

Asp Leu Tyr Trp Asn Asp Ala Phe Asp Ile
1 5 10

<210> SEQ ID NO 703
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 703

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln

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1               5                   10                  15

Ser Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
            20                  25                  30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
        35                  40                  45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65                  70                  75                  80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
                85                  90                  95

Asn Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 704
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 704

Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Val Asn
1               5                   10


<210> SEQ ID NO 705
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 705

Ser Asn Asn Gln Arg Pro Ser
1               5


<210> SEQ ID NO 706
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 706

Ala Ala Trp Asp Asp Ser Leu Asn Gly
1               5


<210> SEQ ID NO 707
<211> LENGTH: 126
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 707

Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
            20                  25                  30

Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
        35                  40                  45

Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala
    50                  55                  60

Val Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn
65                  70                  75                  80
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Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
                85                  90                  95

Tyr Tyr Cys Ala Arg Glu Ser Trp Leu Trp Gly Ile Gly Gly Asp Ala
            100                 105                 110

Phe Asp Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Arg
        115                 120                 125


<210> SEQ ID NO 708
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 708

Ser Asn Ser Ala Ala Trp Asn
1               5


<210> SEQ ID NO 709
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 709

Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala Val Ser Val
1               5                   10                  15

Lys Ser


<210> SEQ ID NO 710
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 710

Glu Ser Trp Leu Trp Gly Ile Gly Gly Asp Ala Phe Asp Ile
1               5                   10


<210> SEQ ID NO 711
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 711

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Arg Gln
1               5                   10                  15

Thr Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Gln Asn
            20                  25                  30

Ser Val Thr Trp Tyr Gln Arg Leu Pro Gly Glu Ala Pro Lys Leu Leu
        35                  40                  45

Ile Tyr Tyr Asp Asp Leu Leu His Ser Gly Val Ser Asp Arg Phe Ser
    50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65                  70                  75                  80

Ser Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Ser Trp Asp Asp Ser Leu
                85                  90                  95

Lys Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 712
<211> LENGTH: 13
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<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 712

Ser Gly Ser Ser Ser Asn Ile Gly Gln Asn Ser Val Thr
1 5 10

<210> SEQ ID NO 713
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 713

Tyr Asp Asp Leu Leu His Ser
1 5

<210> SEQ ID NO 714
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 714

Ala Ser Trp Asp Asp Ser Leu Lys Gly
1 5

<210> SEQ ID NO 715
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 715

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
20 25 30

Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Glu Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg
100 105 110

<210> SEQ ID NO 716
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 716

Ser Asn Tyr Met Ser
1 5

<210> SEQ ID NO 717
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 717

Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly
1 5 10 15

<210> SEQ ID NO 718
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 718

Glu Phe Asp Tyr
1

<210> SEQ ID NO 719
<211> LENGTH: 105
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 719

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Asn Pro Ala Phe
85 90 95

Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 720
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 720

Gln Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

<210> SEQ ID NO 721
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 721

Asp Ala Ser Asn Leu Glu Thr
1 5

<210> SEQ ID NO 722
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 722

Gln Gln Tyr Asp Asn

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1 5

<210> SEQ ID NO 723
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 723

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Tyr Tyr Gly Ser Gly Phe Gly Met Asp Val Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 724
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 724

Ser Tyr Gly Ile Ser
1 5

<210> SEQ ID NO 725
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 725

Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> SEQ ID NO 726
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 726

Asp Arg Tyr Tyr Gly Ser Gly Phe Gly Met Asp Val
1 5 10

<210> SEQ ID NO 727
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 727

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Ser Ser Glu Leu Thr Gln Asp Pro Ala Met Ser Val Ala Leu Gly Gln
1               5                   10                  15

Thr Val Lys Ile Thr Cys Gln Gly Asp Ser Leu Thr Asn Tyr Tyr Pro
            20                  25                  30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Met Tyr
        35                  40                  45

Gly Lys Asp Ser Arg Pro Ser Gly Ile Ser Asp Arg Phe Ser Gly Ser
    50                  55                  60

Ser Ser Gly Ile Ser Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Gly Ser Ala His Arg
                85                  90                  95

Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105


<210> SEQ ID NO 728
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 728

Gln Gly Asp Ser Leu Thr Asn Tyr Tyr Pro Ser
1               5                   10


<210> SEQ ID NO 729
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 729

Gly Lys Asp Ser Arg Pro Ser
1               5


<210> SEQ ID NO 730
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 730

Asn Ser Arg Asp Gly Ser Ala His Arg
1               5


<210> SEQ ID NO 731
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 731

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30

Gly Leu Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Ser Thr Tyr Asn Ser Asn Thr Asn Tyr Ala Glu Lys Leu
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
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65                  70                  75                  80

Met Glu Leu Arg Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Pro Thr Tyr Ser Phe Asp Ser Ser Gly Tyr Phe Phe Asp
            100                 105                 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg
        115                 120


<210> SEQ ID NO 732
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 732

Asn Tyr Gly Leu Thr
1               5


<210> SEQ ID NO 733
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 733

Trp Ile Ser Thr Tyr Asn Ser Asn Thr Asn Tyr Ala Glu Lys Leu Gln
1               5                   10                  15

Gly


<210> SEQ ID NO 734
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 734

Gly Pro Thr Tyr Ser Phe Asp Ser Ser Gly Tyr Phe Phe Asp Tyr
1               5                   10                  15


<210> SEQ ID NO 735
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 735

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1               5                   10                  15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
            20                  25                  30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
    50                  55                  60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
                85                  90                  95

Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105
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<210> SEQ ID NO 736
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 736

Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser
1 5 10

<210> SEQ ID NO 737
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 737

Gly Lys Asn Asn Arg Pro Ser
1 5

<210> SEQ ID NO 738
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 738

Asn Ser Arg Asp Ser Ser Gly Asn His
1 5

<210> SEQ ID NO 739
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 739

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Thr Tyr Ser Ser Gly Trp Tyr Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 740
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 740

Ser Tyr Gly Ile Ser
1 5

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<210> SEQ ID NO 741
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 741

Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> SEQ ID NO 742
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 742

Asp Thr Tyr Ser Ser Gly Trp Tyr Phe Asp Tyr
1 5 10

<210> SEQ ID NO 743
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 743

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Asn Tyr Tyr Ala
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50 55 60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
85 90 95

Leu Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 744
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 744

Gln Gly Asp Ser Leu Arg Asn Tyr Tyr Ala Ser
1 5 10

<210> SEQ ID NO 745
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 745

Gly Lys Asn Asn Arg Pro Ser
1 5

<210> SEQ ID NO 746

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<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 746

Asn Ser Arg Asp Ser Ser Gly Asn His Leu
1 5 10

<210> SEQ ID NO 747
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 747

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Thr Leu Asn Ile Ser Gly Ser Tyr Tyr Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 748
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 748

Ser Tyr Gly Ile Ser
1 5

<210> SEQ ID NO 749
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 749

Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> SEQ ID NO 750
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 750

Leu Asn Ile Ser Gly Ser Tyr Tyr Phe Asp Tyr
1 5 10

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<210> SEQ ID NO 751
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 751

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20 25 30

Thr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Ser
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50 55 60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Tyr Pro
85 90 95

Ser Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 752
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 752

Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Thr
1 5 10

<210> SEQ ID NO 753
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 753

Gly Lys Asn Asn Arg Pro Ser
1 5

<210> SEQ ID NO 754
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 754

Asn Ser Arg Asp Ser Ser Gly Tyr Pro Ser
1 5 10

<210> SEQ ID NO 755
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 755

Gln Val Gln Leu Val Gln Ser Glu Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

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Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Thr Ile Gly Leu Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr
            100                 105                 110

Thr Val Thr Val Ser Arg
        115


<210> SEQ ID NO 756
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 756

Ser Tyr Trp Ile Gly
1               5


<210> SEQ ID NO 757
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 757

Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln
1               5                   10                  15

Gly


<210> SEQ ID NO 758
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 758

Thr Ile Gly Leu Gly Ala Phe Asp Ile
1               5


<210> SEQ ID NO 759
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 759

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1               5                   10                  15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
            20                  25                  30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
    50                  55                  60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80
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```
Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
                85                  90                  95

His Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 760
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 760

Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser
1               5                   10


<210> SEQ ID NO 761
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 761

Gly Lys Asn Asn Arg Pro Ser
1               5


<210> SEQ ID NO 762
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 762

Asn Ser Arg Asp Ser Ser Gly Asn His His
1               5                   10


<210> SEQ ID NO 763
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 763

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg His Trp Gly Asn Tyr Ala Phe Asp Ile Trp Gly Gln Gly
            100                 105                 110

Thr Thr Val Thr Val Ser Arg
        115


<210> SEQ ID NO 764
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
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<400> SEQUENCE: 764

Ser Ser Ser Tyr Tyr Trp Gly
1 5

<210> SEQ ID NO 765
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 765

Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 766
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 766

His Trp Gly Asn Tyr Ala Phe Asp Ile
1 5

<210> SEQ ID NO 767
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 767

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
85 90 95

Ser Gly Gln Val Phe Gly Gly Gly Thr Gln Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 768
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 768

Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Tyr Val Tyr
1 5 10

<210> SEQ ID NO 769
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 769

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Ser Asn Asn Gln Arg Pro Ser
1 5

<210> SEQ ID NO 770
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 770

Ala Ala Trp Asp Asp Ser Leu Ser Gly
1 5

<210> SEQ ID NO 771
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 771

Glu Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

Gly Thr Leu Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 772
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 772

Ser Tyr Gly Ile Ser
1 5

<210> SEQ ID NO 773
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 773

Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> SEQ ID NO 774
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 774

Glu Lys Tyr Ser Ser Gly Trp Tyr Phe Asp Tyr
1 5 10

<210> SEQ ID NO 775
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 775

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50 55 60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
85 90 95

His Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 776
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 776

Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser
1 5 10

<210> SEQ ID NO 777
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 777

Gly Lys Asn Asn Arg Pro Ser
1 5

<210> SEQ ID NO 778
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 778

Asn Ser Arg Asp Ser Ser Gly Asn His His
1 5 10

<210> SEQ ID NO 779
<211> LENGTH: 115
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 779

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

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1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Ser Ile Ala Ala Asp Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Arg
115

<210> SEQ ID NO 780
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 780

Ser Tyr Ala Met Ser
1 5

<210> SEQ ID NO 781
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 781

Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 782
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 782

Gly Ser Ile Ala Ala Asp
1 5

<210> SEQ ID NO 783
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 783

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser

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    50                  55                  60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn Val
                85                  90                  95

Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105


<210> SEQ ID NO 784
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 784

Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser
1               5                   10


<210> SEQ ID NO 785
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 785

Gly Lys Asn Asn Arg Pro Ser
1               5


<210> SEQ ID NO 786
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 786

Asn Ser Arg Asp Ser Ser Gly Asn
1               5


<210> SEQ ID NO 787
<211> LENGTH: 115
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 787

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

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

Val Ser Arg
        115
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<210> SEQ ID NO 788
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 788

Ser Tyr Ala Met Ser
1 5

<210> SEQ ID NO 789
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 789

Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 790
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 790

Glu Gln Ala Gly Asp Tyr
1 5

<210> SEQ ID NO 791
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 791

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Arg Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ala
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
65 70 75 80

Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Gly Thr Trp Asp Ser Ser Leu
85 90 95

Ser Ala Gly Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 792
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 792

Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Tyr Val Tyr
1 5 10

-continued

<210> SEQ ID NO 793
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 793

Arg Asn Asn Gln Arg Pro Ser
1 5

<210> SEQ ID NO 794
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 794

Gly Thr Trp Asp Ser Ser Leu Ser Ala
1 5

<210> SEQ ID NO 795
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 795

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Leu Ser Ala Ala Thr Ala Phe Asp Ile Trp Gly Gln Gly
100 105 110

Thr Met Val Thr Val Ser Arg
115

<210> SEQ ID NO 796
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 796

Ser Tyr Tyr Met His
1 5

<210> SEQ ID NO 797
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 797

Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

-continued

<210> SEQ ID NO 798
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 798

Glu Leu Ser Ala Ala Thr Ala Phe Asp Ile
1 5 10

<210> SEQ ID NO 799
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 799

Glu Thr Thr Leu Thr Gln Ser Pro Phe Ser Val Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Ser Arg Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ala Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Val
85 90 95

Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> SEQ ID NO 800
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 800

Arg Ala Ser Gln Tyr Ile Ser Arg Trp Leu Ala
1 5 10

<210> SEQ ID NO 801
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 801

Ala Ala Ala Ser Leu Gln Ser
1 5

<210> SEQ ID NO 802
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 802

Gln Gln Ala Asn Ser Phe Pro
1 5

<210> SEQ ID NO 803

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<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 803

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85 90 95

Ala Arg Val Gly Tyr Tyr Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln
            100 105 110

Gly Thr Thr Val Thr Val Ser Arg
        115 120

<210> SEQ ID NO 804
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 804

Ser Tyr Gly Ile Ser
1 5

<210> SEQ ID NO 805
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 805

Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> SEQ ID NO 806
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 806

Val Gly Tyr Tyr Tyr Tyr Tyr Gly Met Asp Val
1 5 10

<210> SEQ ID NO 807
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 807

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

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Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ser Tyr
            20                  25                  30

Asn Leu Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35                  40                  45

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
    50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
                85                  90                  95

Ser Thr Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 808
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 808

Thr Gly Thr Ser Ser Asp Val Gly Ser Tyr Asn Leu Val Ser
1               5                   10


<210> SEQ ID NO 809
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 809

Glu Gly Ser Lys Arg Pro Ser
1               5


<210> SEQ ID NO 810
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 810

Ser Ser Tyr Thr Ser Ser Ser Thr
1               5


<210> SEQ ID NO 811
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 811

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
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Ala Arg Asp Val Gly Ile Gly Val Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Arg
        115


<210> SEQ ID NO 812
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 812

Ser Tyr Ala Ile Ser
1               5


<210> SEQ ID NO 813
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 813

Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe Gln
1               5                   10                  15

Gly


<210> SEQ ID NO 814
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 814

Asp Val Gly Ile Gly Val Phe Asp Tyr
1               5


<210> SEQ ID NO 815
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 815

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Lys
1               5                   10                  15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45

Tyr Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
    50                  55                  60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
                85                  90                  95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105


<210> SEQ ID NO 816
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
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<400> SEQUENCE: 816

Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1 5 10

<210> SEQ ID NO 817
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 817

Tyr Asp Ser Asp Arg Pro Ser
1 5

<210> SEQ ID NO 818
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 818

Gln Val Trp Asp Ser Ser Ser Asp His
1 5

<210> SEQ ID NO 819
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 819

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Thr Ser Gly Ser Gly Gly Ser Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Ser Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Thr Leu Pro His Tyr Tyr Asp Ser Ser Gly Ile Gly Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 820
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 820

Asp Tyr Ala Met Asn
1 5

<210> SEQ ID NO 821
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 821

Ala Thr Ser Gly Ser Gly Gly Ser Thr Phe Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 822
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 822

Gly Thr Leu Pro His Tyr Tyr Asp Ser Ser Gly Ile
1 5 10

<210> SEQ ID NO 823
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 823

Gln Ala Val Leu Thr Gln Pro Ser Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Asp Val Gly Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Arg Ala Glu Asp Glu Ala Asn Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Trp Phe Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

Gly

<210> SEQ ID NO 824
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 824

Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> SEQ ID NO 825
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 825

Asp Val Gly Lys Arg Pro Ser
1 5

<210> SEQ ID NO 826
<211> LENGTH: 10
<212> TYPE: PRT

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 826

Ser Ser Tyr Thr Ser Ser Ser Thr Trp Phe
1 5 10

<210> SEQ ID NO 827
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 827

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Gly Glu Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Thr Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Phe Ile Gly Thr Arg Gly Gly Gly Leu Asp Val Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 828
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 828

Thr Tyr Tyr Met His
1 5

<210> SEQ ID NO 829
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 829

Ile Ile Asn Pro Ser Gly Glu Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 830
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 830

Ser Phe Ile Gly Thr Arg Gly Gly Gly Leu Asp Val
1 5 10

<210> SEQ ID NO 831

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<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 831

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Asn Ile Ser Cys Ala Gly Ser Ser Ser Asn Ile Gly Ala Gly
20 25 30

Tyr Asp Val His Trp Tyr Gln Gln Ile Pro Gly Thr Ala Pro Lys Leu
35 40 45

Leu Met Tyr Gly Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Ala Ser Ala Ser Leu Ala Ile Thr Arg Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
85 90 95

Leu Ser Gly Ser Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105 110

Gly

<210> SEQ ID NO 832
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 832

Ala Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His
1 5 10

<210> SEQ ID NO 833
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 833

Gly Asn Ser Asn Arg Pro Ser
1 5

<210> SEQ ID NO 834
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 834

Gln Ser Tyr Asp Ser Ser Leu Ser Gly Ser
1 5 10

<210> SEQ ID NO 835
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 835

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

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Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Thr Glu Glu Trp Trp Arg Phe Asp Leu Trp Gly Arg Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Arg
        115


<210> SEQ ID NO 836
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 836

Asp Tyr Ala Met His
1               5


<210> SEQ ID NO 837
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 837

Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val Lys
1               5                   10                  15

Gly


<210> SEQ ID NO 838
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 838

Glu Glu Trp Trp Arg Phe Asp Leu
1               5


<210> SEQ ID NO 839
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 839

Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1               5                   10                  15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Asp Asp Tyr
            20                  25                  30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35                  40                  45

Met Ile Tyr Glu Val Thr Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
    50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80
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Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Val Gly Ser
85 90 95

Asp Asn Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Pro Gly
100 105 110

<210> SEQ ID NO 840
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 840

Thr Gly Thr Ser Ser Asp Val Asp Asp Tyr Asn Tyr Val Ser
1 5 10

<210> SEQ ID NO 841
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 841

Glu Val Thr Lys Arg Pro Ser
1 5

<210> SEQ ID NO 842
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 842

Ser Ser Tyr Val Gly Ser Asp Asn
1 5

<210> SEQ ID NO 843
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 843

caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggata caccttcacc ggctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtggtgg cacaaactat 180

gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcag cacagcctac 240

atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gagatccgat 300

attttgactg gttattatgc ttttgatatc tggggccaag ggacaatggt caccgtctcg 360

aga 363

<210> SEQ ID NO 844
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 844

gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

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gaagattttg caacttacta ctgtcaacag agttacagta ccacgtggac gttcggccaa 300

gggaccaagg tggaaatcaa a 321

<210> SEQ ID NO 845
<211> LENGTH: 387
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 845

gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggata caccttcacc ggctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtggtgg cacaaactat 180

gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcag cacagcctac 240

atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gagagattta 300

tggtattact atggttcggg gagttcactg tactactact acggtatgga cgtctggggc 360

caagggacca cggtcaccgt ctcgaga 387

<210> SEQ ID NO 846
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 846

cagtctgtgt tgacgcagcc gccctcagtg tctggggccc cagggcagag ggtcaccatc 60

tcctgcactg ggagcagctc caacatcggg gcaggttatg atgtacactg gtaccagcag 120

cttccaggaa cagccccaa actcctcatc tatggtaaca gcaatcggcc ctcaggggtc 180

cctgaccgat tctctggctc caagtctggc acctcagcct ccttggccat cactgggctc 240

caggctgagg atgaggctga ttattactgc cagtcctatg acagcagcct gagtggtgtg 300

gtattcggcg gagggaccaa gctgaccgtc ctaggt 336

<210> SEQ ID NO 847
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 847

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120

ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag cataggctat 180

gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240

ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgt acggagtggg 300

agctacaact actactacta cggtatggac gtctggggcc aagggaccac ggtcaccgtc 360

tcgaga 366

<210> SEQ ID NO 848
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 848

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cagtctgtgt tgacgcagcc gccctcagcg tctgggaccc ccgggcagag ggtcaccatc 60

tcttgttctg gaagcagctc caacatcgga agtaatactg taaactggta ccagcagctc 120

ccaggaacgg cccccaaact cctcatctat agtaataatc agcggccctc aggggtccct 180

gaccgattct ctggctccaa gtctggcacc tcagcctccc tggccatcag tgggctccag 240

tctgaggatg aggctgatta ttactgtgca gcatgggatg acagcctgaa tggttgggtg 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 849
<211> LENGTH: 369
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 849

caggtgcagc tgcaggagtc gggggggaggc ttggtacagc ctgggggggtc cctgagactc 60

tcctgtacaa cctctggatt cacctttacc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcatct attagtggta gtggtggtat cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacactgtat 240

ctgcaaatga acagcctaag agccgaggac acggccgtat attactgtgc gaaagatagg 300

gttctagtcc cagcttcctc ttcgtacttt gactactggg gccagggaac cctggtcacc 360

gtctcgaga 369

<210> SEQ ID NO 850
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 850

tcttctgagc tgactcagga ccctgctgtg tctgtggcct tgggacagac agtcaggatc 60

acatgccaag gagacagcct cagaagctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctatggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacagcagtg gtaaccatgt ggtattcggc 300

ggagggacca agctgaccgt cctaggt 327

<210> SEQ ID NO 851
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 851

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagc agtagtagtt actactgggg ctggatccgc 120

cagcccccag ggaaggggct ggagtggatt gggagtatct attatagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gaccgccgca gacacggctg tgtattactg tgcgagacgt 300

cccttaacct ttaatgcttt tgatatctgg ggccaaggga caatggtcac cgtctcgaga 360

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<210> SEQ ID NO 852
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 852

tcctatgtgc tgactcagcc accctcagtg tcagtggccc caggaaagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcat ctattatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgt ggtattcggc 300

ggagggacca agctgaccgt cctaggt 327

<210> SEQ ID NO 853
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 853

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagc agtagtagtt actactgggg ctggatccgc 120

cagccccag ggaaggggct ggagtggatt gggagtatct attatagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gaccgccgca gacacggctg tgtattactg tgcgaggatt 300

cccatgtata gcagctcggt tgactactgg ggccagggaa ccctggtcac cgtctcgaga 360

<210> SEQ ID NO 854
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 854

tcctatgtgc tgactcagcc accctcagtg tcagtggccc caggaaagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcat ctattatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgt ggtattcggc 300

ggagggacca agctgaccgt cctaggt 327

<210> SEQ ID NO 855
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 855

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagc agtagtagtt actactgggg ctggatccgc 120

cagccccag ggaaggggct ggagtggatt gggagtatct attatagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gaccgccgca gacacggctg tgtattactg tgcgagacgt 300

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ccttaacct ttaatgcttt tgatatctgg ggccaaggga ccacggtcac cgtctcgaga 360

<210> SEQ ID NO 856
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 856

tcctatgtgc tgactcagcc accctcagtg tcagtggccc caggaaagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcat ctattatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgt ggtattcggc 300

ggagggacca agctgaccgt cctaggt 327

<210> SEQ ID NO 857
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 857

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagatggg 300

ggatggttcg gggagttaga ttacttccag cactggggcc agggcaccct ggtcaccgtc 360

tcgaga 366

<210> SEQ ID NO 858
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 858

cagtctgtgt tgacgcagcc gccctcagtg tctgcggccc caggacagaa ggtcaccgtc 60

tcctgcactg gaagcaactc caacattgag aagaatgatg tttcctggta ccagcaggga 120

ccaggagcag cccccaaact cctcatttct gacactgata ggcgaccctc agggattcct 180

gaccgattct ctggctccaa gtctggcacg tcagccaccc tggccatcgc tgggctccag 240

gctgaggatg aggctgatta ttactgccag tcccatgaca ccactctgag tggtccgatc 300

ttcggcgggg ggacccagct gaccgtccta ggt 333

<210> SEQ ID NO 859
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 859

caggtgcagc tgcaggagtc gggggggaggc ttggtcaagc ctggagggtc cctgagactc 60

tcctgtgcag cctctggatt cagtttcagt gactactaca tgagctgggt ccgccaggct 120

-continued

ccagggaagg ggctggagtg gatttcatat attactagta gtagtagtga cacagactac 180

gcagactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactatat 240

ctgcaaatga acagcctgag agccgacgac acggccgtgt attactgtgc gagagtgggc 300

tattattatg attactacta ctactactac atggacgtct ggggcaaagg gaccacggtc 360

accgtctcga ga 372

<210> SEQ ID NO 860
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 860

tcttctgagc tgactcagga ccctgctgtg tctgtggcct tgggacagac agtcaggatc 60

acatgccaag gagacagcct cagaggctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tccttgtcgt ctatgatgaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacattaacc ttgattgggt gttcggcgga 300

gggaccaagt tgaccgtcct aggt 324

<210> SEQ ID NO 861
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 861

caggtgcagc tgcaggattc gggcccagga ctggtgaagc cttcggatac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagc agtattagtt actactgggg ctggatccgc 120

cagccccag ggaaggggct ggagtgtatt gggagtatct attatagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gaccgccgca gacacggctg tgtattactg tgcgagacgg 300

gtcatagtgt gggggagtga tgactactgg ggccagggaa ccctggtcac cgtctcgaga 360

<210> SEQ ID NO 862
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 862

tcctatgtgc tgactcagcc accctcagtg tcagtggccc caggaaagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcat ctattatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgt ggtattcggc 300

ggagggacca agctgaccgt cctaggt 327

<210> SEQ ID NO 863
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 863

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagc agtagtagtt actactgggg ctggatccgc 120

cagcccccag ggaaggggct ggagtggatt gggagtatct attatagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gaccgccgca gacacggctg tgtattactg tgcgatgcgg 300

gcctatggtt cagggagtta tgactactgg ggccagggaa ccctggtcac cgtctcgaga 360

<210> SEQ ID NO 864
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 864

gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60

atctcctgca ggtctagtca gagcctcctc catagtaatg gatacaacta tttggattgg 120

tacctgcaga agccagggca gtctccgcag ctcctgatct atttgggttc taatcgggcc 180

tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240

agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaacccca 300

ttcactttcg gccctgggac caaagtggat atcaaa 336

<210> SEQ ID NO 865
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 865

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatattac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgcat attactgtgc gaaaggtctt 300

aggtatagca gtgcctggac gtttgactac tggggccagg gaaccctggt caccgtctcg 360

aga 363

<210> SEQ ID NO 866
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 866

cagtctgccc tgactcagcc tgcctccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtaccaacaa 120

cacccaggca aagcccccaa actcatgatt tatgatgtca gtaatcggcc ctcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctggactc 240

caggctgagg acgaggctga ttattactgc agctcatata caagcagtag cactcctgtg 300

gtattcggcg gagggaccaa gctgaccgtc ctaggt 336

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<210> SEQ ID NO 867
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 867

caggtgcagc tggtgcaatc tgggtctgag ttgaagaagc ctggggcctc agtgaaggtt 60

tcctgcaagg cttctggata catcttcact agatatggca taaattgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaacacca acactgggaa cccaacgtat 180

gcccagggct tcacaggccg ggttgtcttc tccttggaca cctctgtcag cacggcatat 240

ctgcagatca gcagcctaaa ggctgaggac actgccatgt attactgtgc gatcagcagt 300

ggctttgggt actactttga ctactggggc cagggaaccc tggtcaccgt ctcgaga 357

<210> SEQ ID NO 868
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 868

gacatccaga tgacccagtc tccatcgtcc gtgtctgcat ctgtgggaga cagagtcacc 60

atcacttgtc gggcgagtca aagtattagt aggtggttag cctggtatca gcagaaacca 120

gggaaagccc ctaagttcct gatctatgct ggatccagtt tgcaaagtgg ggtcccatcg 180

aggttcagcg gcagtgggtc tgggacagat ttcactctca ccatcagcag cctgcagcct 240

gaagactttg caacttatta ttgtcaacag actaacagtt tccctctcac cttcggcgga 300

gggaccaagg tggagatcaa a 321

<210> SEQ ID NO 869
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 869

caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggtta cacctttacc agctacggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagctttt 300

agggactggg gatctcttag ggactactgg ggccagggca ccctggtcac cgtctcgaga 360

<210> SEQ ID NO 870
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 870

cagtctgtgt tgacgcagcc gccctcagtg tctgcggccc caggacagaa ggtcaccatc 60

tcctgctctg gaagcagctc caacattggg aataattatg tatcctggta ccagcagctc 120

ccaggaacag cccccaaact cctcatttat gacaataata agcgaccctc agggattcct 180

gaccgattct ctggctccaa gtctggcacg tcagccaccc tgggcatcac cggactccag 240

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actggggacg aggccgatta ttactgcgga acatgggata gcagcctgag tgccgtggta 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 871
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 871

gaggtgcagc tggtggagtc tggagcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcggctgggt gcgccagatg 120

cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag caccgcctac 240

ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagactggca 300

gtgggagcct accagtacta ctttgactac tggggccagg gaaccctggt caccgtctcg 360

aga 363

<210> SEQ ID NO 872
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 872

cagactgtgg tgacccagga gccatcgttc tcagtgtccc ctggagggac agtcacactc 60

acttgtggct tgagctctgg ctcagtctct actagttact accccagctg gtaccagcag 120

accccaggcc aggctccacg cacgctcatc tacagcacaa acactcgctc ttctggggtc 180

cctgatcgct tctctggctc catccttggg aacaaagctg ccctcaccat cacggggcc 240

caggcagatg atgaatctga ttattactgt gtgctgtata tgggtagtgg catttcggtg 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 873
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 873

gaggtgcagc tggtggagtc tgggggaaac ttggtccagc cgggggggtc cctgagactc 60

tcctgtgcag cctctggatt caccttcagt aggtattgga tgacctgggt ccgccaggct 120

ccagggaagg ggctggagtg gatttcatcc gttagtagta gcggcagtac catatactac 180

gcagactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat 240

ctgcaaatga acagcctgag agtcgaggac acggctgttt attactgtgc gcgagactat 300

tggcctggct ggtacttcga tctctggggc cgtggaaccc tggtcaccgt ctcgaga 357

<210> SEQ ID NO 874
<211> LENGTH: 348
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 874

caggctgtgc tcactcagcc gtcttccctc tctgcatctc ctggagcatc agccagtctc 60

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acctgcacct tccgcagtga catcagtgtt ggttcctata ggatatactg gtaccagcag 120

aagccaggga gtcctcccca gtttctcctg aaatatacgt cagactcaga taagcagcag 180

ggctctggag tccccagccg cttctctgga tccaaagatg tttcggccaa tgctggcatt 240

ttactcatct ctgggctcca gtctgaggat gaggctgact attactgtat gacttggcac 300

aacaccgctt cggtattcgg cggagggacc aagctggccg tcctaggt 348

<210> SEQ ID NO 875
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 875

gaggtacagc tggtggagtc tgggggaggt ttgataaggc cgggggggtc cctgagactc 60

tcctgtacag cctctggatt caccttcagt agttatacta tgaattgggt ccgccaggct 120

ccagggaagg ggctggagtg gctttcatat ataagtggtg gcagtggtac caaattctac 180

gcagactctg tgaagggccg gttcaccgtc tccagagaca atgccaagaa ttcattgtat 240

ctggaaatga acagcctgag acccgaggac acggctgtct attactgtgc gctagtgtca 300

tatagttcgc cgggctttga ctactggggc cagggcaccc tggtcaccgt ctcgagc 357

<210> SEQ ID NO 876
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 876

tcctatgagc tgactcagcc accctcagtg tccgtgtccc caggacagac agccagcatc 60

acctgctctg gagataaatt gggcgataaa tatgtttact ggtatcaaca gaagccaggc 120

cagtccccta tattgctcat ctttcaagat agcgagcggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacagcc actctgacca tcagcgggac ccaggctatg 240

gatgaggctg actattactg tcaggcgtgg gacagcagcg ctgcggtgtt cggcggaggg 300

accaagctga ccgtcctagg t 321

<210> SEQ ID NO 877
<211> LENGTH: 345
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 877

caggtgcagc tggtgcagtc tggagcagag gtgaaaaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggtta cacctttacc agctatggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagaggggtt 300

gcttttgata tctggggcca agggaccacg gtcaccgtct cgaga 345

<210> SEQ ID NO 878
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 878

cagtctgtgt tgacgcagcc gccctcagtg tctggggccc cagggcagag ggtcaccatc 60

tcctgcactg ggagcagctc caacatcggg gcaggttatc atgtatactg gtaccagcag 120

cttccaggaa aagccccaa actcctcatc tacgttaaca gcaatcggcc ctcaggggtc 180

cctgaccgat tctctggctc caagtctggc acctcagcct ccctggccat cactgggctc 240

caggctgacg atgaggctga ttactactgc cagtcctatg acagcagcct gagtggtagg 300

gttttcggcg gagggaccaa gctgaccgtc ttaggt 336

<210> SEQ ID NO 879
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 879

gaggtgcagc tggtggagtc tgggggcggc ttggtccagc cgggggggtc cctgagactc 60

tcctgttcag cctctggatt cacctttagt aactattgga tgacctgggt ccgtcaggct 120

ccagggaagg ggctggagtg gatttcatcc attagtagta gcggcagtac catatactac 180

gcagactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat 240

ctgcaaatga acagcctgag agtcgaggac acggctgttt attactgtgc gcgagactat 300

tggcctggct ggtacttcga tctctggggc cgtggcaccc tggtcaccgt ctcgaga 357

<210> SEQ ID NO 880
<211> LENGTH: 348
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 880

caggctgtgc tcactcagcc gtcttccctc tctgcatctc ctggagcatc agccagtctc 60

acctgcacct tccgcagtga catcagtgtt ggttcctata ggatatactg gtaccagcag 120

aagccaggga gtcctcccca gtttctcctg aaatatacgt cagactcaga taagcagcag 180

ggctctggag tccccagccg cttctctgga tccaaagatg tttcggccaa tgctggcatt 240

ttactcatct ctgggctcca gtctgaggat gaggctgact attactgtat gacttggcac 300

aacaccgctt cggtattcgg cggagggacc aagctggccg tcctaggt 348

<210> SEQ ID NO 881
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 881

caggtgcagc tggtgcagtc tgggtctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaaga cttctggata catcttcacc gactactata tgcactgggt gcgacaggcc 120

cctggaaaag ggcttgagtg gatgggatgg attaacccta acagtggtgg cacatactat 180

gcacagaagt ttcacggcag ggtcaccatg accagtgaca cgtccatcag cacagcctac 240

atggagctga gcagtctgag atctgacgac acggccatat attactgtgc gagagaggat 300

tacgatattt tgactggtta ttatcccgcg tccggccacg gggactactg gggccaggga 360

accctggtca ccgtctcgag a 381

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<210> SEQ ID NO 882
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 882

caggctgtgg tgactcagga gccctcactg actgtgtccc caggagggac agtcactctc 60

acctgtgcat ccagcactgg agcagtcacc agtggtttcc ttgcaaactg gttccagcag 120

aaacctggac aaacacccag gtcactgatt tataaaacaa gcaacaaaca tccctggacc 180

cctgcccggt tctcaggctc cctccttggg ggcaaagctg ccctgacact gtcaggtgtg 240

cagcctgagg acgaggctga ctattactgc ctgctcttat ctggtggtgc atgggtgttt 300

ggcggaggga ccaagctgag tgtcctaggt 330

<210> SEQ ID NO 883
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 883

caggtgcagc tggtgcagtc tggagcagag gtgaaaaagc ccggagagtc tctgaagatc 60

tcgtgtgagg gttctggata cacctttacc agctactgga tcggctgggt gcgccagatg 120

cccgggaaag acctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagtcgaca agtctatcag caccgcctac 240

ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagacacgac 300

gtagttgatg gctacaatac cggtatggac gtctggggcc aagggaccac ggtcaccgtc 360

tcgaga 366

<210> SEQ ID NO 884
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 884

cagactgtgg tgacccagga gccatcgttc acagtgtccc ctggagggac agtcacactc 60

acttgtggct tgagctctgg ctcagtctct actagttact accccagctg gtaccagcag 120

accccaggcc aggctccacg cacgctcatc tccagcacaa acactcgctc ttctggggtc 180

cctgatcgct tctctggctc catccttggg aacagagctg ccctcaccat cacgggggcc 240

caggcagatg atgagtctga ttattactgt gtgctgtata tgggtagtgg catttgggtg 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 885
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 885

caggtgcagc tggtgcagtc tggagcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcggctgggt gcgccagatg 120

cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga tgccagatac 180

-continued

agcccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag caccgcctac 240

ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagactcacg 300

ggcagttctt actatgatag tagtggttat tcctcctacg gtatggacgt ctggggccaa 360

gggaccacgg tcaccgtctc gaga 384

<210> SEQ ID NO 886
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 886

cagactgtgg tgacccagga gccatcgttc tcagtgtccc ctggagggac agtcacactc 60

acttgtggct tgagctctgg ctcagtctct actagttact accccagctg gttccagcag 120

accccaggcc aggctccacg cacgctcatc tacagcacaa acactcgctc ttctggggtc 180

cctgatcgct tctctggctc catccttggg aacaaagctg ccctcaccat cacgggggcc 240

caggcagatg atgaatctga ttattactgt gtgctgtata tgggtagtgg catttctgtg 300

ttcggaggag gcacccagct gaccgtcctc ggt 333

<210> SEQ ID NO 887
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 887

caggtgcagc tggtgcagtc tggagcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcggctgggt gcgccagatg 120

cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag caccgcctac 240

ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagacataac 300

agtaactact actactacta catggacgtc tggggcaaag gaaccctggt caccgtctcg 360

aga 363

<210> SEQ ID NO 888
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 888

cagactgtgg tgacccagga gccatcgttc tcagtgtccc ctggagggac agtcacactc 60

acttgtggct tgagctctgg ctcagtctct actagttact accccagctg gtaccagcag 120

accccaggcc aggctccacg cacgctcatc tacagcacaa acactcgctc ttctggggtc 180

cctgatcgct tctctggctc catccttggg aacaaagctg ccctcaccat cacgggggcc 240

caggcagatg atgaatctga ttattactgt gtgctgtata tgggtagtgg catttcggtg 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 889
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 889

caggtgcagc tggtgcagtc tgggtctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaaga cttctggata catcttcacc gactactata tgcactgggt gcgacaggcc 120

cctggaaaag ggcttgagtg gatgggatgg attaacccta acagtggtgg cacatactat 180

gcacagaagt ttcacggcag ggtcaccatg accagtgaca cgtccatcag cacagcctac 240

atggagctga gcagtctgag atctgacgac acggccatat attactgtgc gagagaggat 300

tacgatattt tgactggttt ttatcccgcg tccggccacg gggactactg gggccaggga 360

accctggtca ccgtctcgag a 381

<210> SEQ ID NO 890
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 890

gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa 120

cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180

gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcactcac tttcggcgga 300

gggaccaagg tggagatcaa a 321

<210> SEQ ID NO 891
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 891

caggtgcagc tggtgcagtc tggagcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcggctgggt gcgccagatg 120

cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag caccgcctac 240

ctgcagtgga gcaccctgaa ggcctcggac accgccatgt attactgtgc gagacatggg 300

atgactagtg gctacgtcgc gcacaatgac tactggggcc agggaaccct ggtcaccgtc 360

tcgaga 366

<210> SEQ ID NO 892
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 892

cagactgtgg tgacccagga gccatcgttc tcagtgtccc ctggagggac agtcacactc 60

acttgtggct tgagctctgg ctcagtctct actagttact accccagctg gtaccagcag 120

accccaggcc aggctccacg cacgctcatc tacagcacaa acactcgctc ttctggggtc 180

cctgatcgct tctctggctc catccttggg aacaaagctg ccctcaccat cacgggggcc 240

caggcagatg atgaatctga ttattactgt gtgctgtata tgggtagtgg catttgggtg 300

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ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 893
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 893

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggggac cctgtccctc 60

acctgcgctg tctctggtgg ctccatcagc agtagtaact ggtggagttg ggtccgccag 120

cccccaggga aggggctgga gtggattggg gaaatctatc atagtgggag caccaactac 180

aacccgtccc tcaagagtcg agtcaccata tcagtagaca agtccaagaa ccagttctcc 240

ctgaagctga gctctgtgac cgccgcggac acggccgtgt attactgtgc gagaggtggg 300

agctactact ttgactactg gggccaggga accctggtca ccgtctcgag a 351

<210> SEQ ID NO 894
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 894

cagtctgccc tgactcagcc tgcctccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccatcag tgacgttggt ggttatgact ttgtctcctg gtaccaacac 120

caccccggca aagcccccaa actcctgatt tatgatgtca ataatcggcc ctctggggtt 180

tctcatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

caggctgagg acgaggctac ttattactgc agttcatatt caaacagaca ttctctcatc 300

gtcttcggat ctgggaccca ggtcgtcggc ctaggt 336

<210> SEQ ID NO 895
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 895

caggtgcagc tacagcagtg gggcgcagga ctgttgaagc cttcggagac cctgtccctc 60

acctgcgctg tctatggtgg gtccttcagt ggttactact ggagctggat ccgccagccc 120

ccagggaagg ggctggagtg gattggggaa atcaatcata gtggaagcac caactacaac 180

ccgtccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg 240

aagctgagct ctgtgaccgc cgcggacacg gctgtgtatt actgtgcgag aggcgggggg 300

gttgaggcgt tgaactacgg tatggacgtc tggggccaag ggaccacggt caccgtctcg 360

aga 363

<210> SEQ ID NO 896
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 896

cagtctgccc tgactcagcc tgcctccgtg tctgggtctc ctggacagac gatcaccatc 60

tcctgcactg gaaccatcag tgacgttggt ggttatgact ttgtctcctg gtaccaacac 120

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cacccggca aagcccccaa actcctgatt tatgatgtca ataatcggcc ctctggggtt 180

tctcatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

caggctgagg acgaggctac ttattactgc agttcatatt caaacagaca ttctctcatc 300

gtcttcggat ctgggaccca ggtcgtcggc ctaggt 336

<210> SEQ ID NO 897
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 897

caggtgcagc tacagcagtg gggcgcaggg ctgttgaagc cttcggaaac cctgtccctc 60

acctgcactg tccatggtgg gtccttcgat gattactact ggacctggat ccgccagccc 120

ccaggggggg ggctggaatg gattggggaa atgaattccg gtagaactta caactacaac 180

ccgttcctgg agagtcgagc ctccatagat gttgacacgt tcaagaagca gttctccctg 240

gcattgcgtt ctgtgaccgc cgcggacaca gctgtctatt actgtgcgcg gggcgcctat 300

gtcaactact actacataga cgtctggggc gacgggacca cggtcaccgt ctcgaga 357

<210> SEQ ID NO 898
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 898

cagtctgccc tgactcagcc tgcctccgtg tctgggtctc ctggacagac gatcaccatc 60

tcctgcactg gaaccatcag tgacgttggt ggttatgact ttgtctcctg gtaccaacac 120

cacccggca aagcccccaa actcctgatt tatgatgtca ataatcggcc ctctggggtt 180

tctcatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

caggctgagg acgaggctac ttattactgc agttcatatt caaacagaca ttctctcatc 300

gtcttcggat ctgggaccca ggtcgtcggc ctaggt 336

<210> SEQ ID NO 899
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 899

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagt agttactact ggagctggat ccggcagccc 120

gccgggaagg gactggagtg gattgggcgt atctatacca gtgggagcac caactacaac 180

ccctccctca agagtcgagt caccatgtca gtagacacgt ccaagaacca gttctccctg 240

aagctgagct ctgtgaccgc cgcggacacg gccgtgtatt actgtgcgag agagagggca 300

tattgtagta gtaccagctg ctatcgaaat gcttttgata tctggggcca agggaccacg 360

gtcaccgtct cgaga 375

<210> SEQ ID NO 900
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 900

cagtctgtgt tgacgcagcc gccctcagtg tctggggccc cagggcagag ggtcaacatc 60

tcctgcgctg ggagcagctc caacatcggg gcgggttatg atgttcactg gtaccagcag 120

attccaggaa cagccccaa actcctcatg tatggtaata gtaatcggcc ctcaggggtc 180

cctgaccgat tctctggctc caagtctggc gcctcagcct ccctggccat cactaggctc 240

caggctgagg atgaggctga ttattactgc cagtcctatg acagcagcct gagtggttcg 300

agggtcttcg gaactgggac caaggtcacc gtcctaggtc agtccaacgt cctaggt 357

<210> SEQ ID NO 901
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 901

gaggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60

tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120

ccaggcaagg ggctggagtg ggtgacagtt atatcatttg atggaagtaa taaatactat 180

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaagcgtat 300

accaacacct ggtggcctga tgcttttgat atctggggcc aagggaccac ggtcaccgtc 360

tcgaga 366

<210> SEQ ID NO 902
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 902

gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc aggcgagtca ggacattagc aactatttaa attggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctacgat gcatccaatt tggaaacagg ggtcccatca 180

aggttcagtg gaagtggatc tgggacagat tttactttca ccatcagcag cctgcagcct 240

gaagatattg caacatatta ctgtcaacag tatgataatc tccctcccac tttcggccct 300

gggaccaaag tggatatcaa a 321

<210> SEQ ID NO 903
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 903

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggtag ctccatcagt agttactact ggagctggat ccggcagccc 120

ccagggaagg gactggagtg gattgggtat atctattaca gtgggagcac caactacaac 180

ccctccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg 240

aagctgagct ctgtgaccgc tgcggacacg gccgtgtatt actgtgcgag agatctgtac 300

tggaacgacg cttttgatat ctggggccaa gggaccacgg tcaccgtctc gaga 354

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<210> SEQ ID NO 904
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 904

cagtctgccc tgactcagcc tctctcagcg tctgggaccc ccgggcagag ggtcaccatc 60

tcttgttctg gaagcagctc caacatcgga agtaatactg taaactggta ccagcagctc 120

ccaggaacgg cccccaaact cctcatctat agtaataatc agcggccctc aggggtccct 180

gaccgattct ctggctccaa gtctggcacc tcagcctccc tggccatcag tgggctccag 240

tctgaggatg aggctgatta ttactgcgca gcatgggatg acagcctgaa tggtccggta 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 905
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 905

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggtag ctccatcagt agttactact ggagctggat ccggcagccc 120

ccagggaagg gactggagtg gattgggtat atctattaca gtgggagcac caactacaac 180

ccctccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg 240

aagctgagct ctgtgaccgc tgcggacacg gccgtgtatt actgtgcgag agatctgtac 300

tggaacgacg cttttgatat ctggggccaa gggaccacgg tcaccgtctc gaga 354

<210> SEQ ID NO 906
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 906

cagtctgtgt tgacgcagcc gccctcagcg tctgggaccc ccgggcagag tgtcaccatc 60

tcttgttctg gaagcagctc caacatcgga agtaatactg taaactggta ccagcagctc 120

ccaggaacgg cccccaaact cctcatctat agtaataatc agcggccctc aggggtccct 180

gaccgattct ctggctccaa gtctggcacc tcagcctccc tggccatcag tgggctccag 240

tctgaggatg aggctgatta ttactgtgca gcatgggatg acagcctgaa tggtccggtg 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 907
<211> LENGTH: 378
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 907

caggtacagc tgcagcagtc aggtccagga ctggtgaagc cctcgcagac cctctcactc 60

acctgtgcca tctccgggga cagtgtctct agcaacagtg ctgcttggaa ctggatcagg 120

cagtccccat cgagaggcct tgagtggctg ggaaggacat actacaggtc caagtggtat 180

aatgattatg cagtatctgt gaaaagtcga ataaccatca acccagacac atccaagaac 240

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cagttctccc tgcagctgaa ctctgtgact cccgaggaca cggctgtgta ttactgtgca 300

agagaatcat ggctttgggg gattgggggg gatgcttttg atatctgggg ccaagggacc 360

acggtcaccg tctcgaga 378

<210> SEQ ID NO 908
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 908

cagtctgtgt tgacgcagcc gccctcggtg tctggggccc cccggcagac ggtcaccatc 60

tcctgctctg ggagcagctc caacatcgga caaaattctg ttacctggta ccagcgcctc 120

ccgggtgagg ctcccaaact cctcatctac tatgatgatc tcttgcactc aggagtctct 180

gaccgattct ctggctccaa gtctggcacc tcagcctcac tggccatcag tggactccag 240

tctgaggatg aggctgagta ctactgtgcg tcatgggatg acagcctgaa aggtccggta 300

ttcggcggag ggaccaaact gaccgtccta ggt 333

<210> SEQ ID NO 909
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 909

gaggtgcagc tggtggagtc tgggggaggc ttggtccagc ctgggggggtc cctgagactc 60

tcctgtgcag cctctggatt caccgtcagt agcaactaca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagtt atttatagcg gtggtagcac atactacgca 180

gactccgtga agggcagatt caccatctcc agagacaatt ccaagaacac gctgtatctt 240

caaatgaaca gcctgagagc cgaggacacg gctgtgtatt actgtgcgag ggagtttgac 300

tactggggcc agggaaccct ggtcaccgtc tcgaga 336

<210> SEQ ID NO 910
<211> LENGTH: 315
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 910

gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc aggcgagtca ggacattagc aactatttaa attggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctacgat gcatccaatt tggaaacagg ggtcccatca 180

aggttcagtg gaagtggatc tgggacagat tttactttca ccatcagcag cctgcagcct 240

gaagatatcg caacatatta ctgtcaacag tatgataatc ccgctttcgg cggagggacc 300

aaggtggaga tcaaa 315

<210> SEQ ID NO 911
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 911

caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60

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tcctgcaagg cttctggtta cacctttacc agctatggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagatcgt 300

tactatggtt cggggttcgg tatggacgtc tggggccaag ggacaatggt caccgtctcg 360

aga 363

<210> SEQ ID NO 912
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 912

tcttctgagc tgactcagga ccctgctatg tctgtggcct tgggacagac agtcaaaatc 60

acttgccaag gagacagcct cacaaactat tatccaagtt ggtatcagca gaagccagga 120

caggcccctg tccttgtcat gtatggaaaa gacagccggc cctcagggat ctcagaccga 180

ttctctggct ccagctcagg aatctcagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actactactg taactcccga gacggcagtg ctcaccgtct ggttttcggc 300

ggagggacca agttgaccgt cctgggt 327

<210> SEQ ID NO 913
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 913

caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggtta cacctttacc aactatggtc tcacctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcactt acaatagtaa cacaaactat 180

gcagagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagttga ggagcctgac atctgacgac acggccgtgt attactgtgc gagaggcccc 300

acatattcct ttgatagtag tggttatttt tttgactact ggggccaggg aaccctggtc 360

accgtctcga ga 372

<210> SEQ ID NO 914
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 914

tcttctgagc tgactcagga ccctgctgtg tctgtggcct tgggacagac agtcaggatc 60

acatgccaag gagacagcct cagaagctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctatggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacagcagtg gtaaccattg ggtgttcggc 300

ggagggacca agctgaccgt cctaggt 327

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<210> SEQ ID NO 915
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 915

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tcctgcaagg cttctggtta cacctttacc agctatggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagatacg 300

tatagcagtg gctggtactt tgactactgg ggccagggca ccctggtcac cgtctcgaga 360

<210> SEQ ID NO 916
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 916

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acatgccaag gagacagcct cagaaactat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctatggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccga gacagcagtg gtaaccatct ttatgtcttc 300

ggaactggga ccaaggtcac cgtcctaggt 330

<210> SEQ ID NO 917
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 917

caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggtta cacctttacc agctatggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc aacccttaac 300

attagtggga gctactactt tgactactgg ggccagggaa ccctggtcac cgtctcgaga 360

<210> SEQ ID NO 918
<211> LENGTH: 344
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 918

tcttctgagc tgactcagga ccctgctgtg tctgtggcct tgggacagac agtcaggatc 60

acatgccaag gagacagcct cagaagctat tatgcaacct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctctggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacagcagtg gttacccctc ttgggtgttc 300

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ggcggaggga ccaagctgac cggaccaagc tgaccgtcct aggt 344

<210> SEQ ID NO 919
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 919

caggtgcagc tggtgcagtc tgaagcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcggctgggt gcgccagatg 120

cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag caccgcctac 240

ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagaacgatc 300

gggcttggtg cttttgatat ctggggccaa gggaccacgg tcaccgtctc gaga 354

<210> SEQ ID NO 920
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 920

tcttctgagc tgactcagga ccctgctgtg tctgtggcct tgggacagac agtcaggatc 60

acatgccaag gagacagcct cagaagctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctatggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacagcagtg gtaaccatca ttatgtcttc 300

ggaactggga ccaaggtcac cgtcctaggt 330

<210> SEQ ID NO 921
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 921

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagc agtagtagtt actactgggg ctggatccgc 120

cagccccag ggaaggggct ggagtggatt gggagtatct attatagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gaccgccgca gacacggctg tgtattactg tgcgagacac 300

tggggaaact atgcttttga tatctggggc caagggacca cggtcaccgt ctcgaga 357

<210> SEQ ID NO 922
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 922

cagtctgtgt tgacgcagcc gccctcagcg tctgggaccc ccgggcagag ggtcaccatc 60

tcttgttctg gaagcagctc caacatcgga agtaattatg tatactggta ccaacagctc 120

ccaggaacgg cccccaaact cctcatctat agtaataatc agcggccctc aggggtccct 180

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gaccgattct ctggctccaa gtctggcacc tcagcctccc tggccatcag tgggctccgg 240

tccgaggatg aggctgatta ttactgtgca gcatgggatg acagcctgag tggtcaagtg 300

ttcggaggag gcacccagct gaccgtcctc ggt 333

<210> SEQ ID NO 923
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 923

gaggtgcagc tggtggagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggtta cacctttacc agctatggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagagaag 300

tatagcagtg gctggtactt tgactactgg ggccagggca ccctggtcac cgtctcgaga 360

<210> SEQ ID NO 924
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 924

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acatgccaag gagacagcct cagaagctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctatggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacagcagtg gtaaccatca ttatgtcttc 300

ggaactggga ccaaggtcac cgtcctaggt 330

<210> SEQ ID NO 925
<211> LENGTH: 345
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 925

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

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atagcagcgg actggggcca gggaaccctg gtcaccgtct cgaga 345

<210> SEQ ID NO 926
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 926

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acatgccaag gagacagcct cagaagctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctatggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacagcagtg gtaacgtggt attcggcgga 300

gggaccaagc tgaccgtcct aggt 324

<210> SEQ ID NO 927
<211> LENGTH: 345
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 927

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggGtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa ctcactgtat 240

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gctggggact actggggcca gggaaccctg gtcaccgtct cgaga 345

<210> SEQ ID NO 928
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 928

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tcttgttctg gaagcagctc caacatcgga agtaattatg tatactggta ccagcagctc 120

ccaggaacgg cccccaaact cctcatctat aggaataatc agcggccctc aggggtccct 180

gaccgattcg ctggctccaa gtctggcacg tcagccaccc tgggcatcac cggactccag 240

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ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 929
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 929

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cctggacaag ggcttgagtg gatgggaata atcaacccta gtggtggtag cacaagctac 180

gcacagaagt tccagggcag agtcaccatg accagggaca cgtccacgag cacagtctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagaattg 300

tcggctgcta ctgcttttga tatctggggc caagggacaa tggtcaccgt ctcgaga 357

<210> SEQ ID NO 930
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 930

gaaacgacac tcacgcagtc tccattttct gtgtctgcat ctgtaggaga cagagtcacc 60

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gggaaagccc ctaagctcct gatctatgct gcagccagtt tgcaaagtgg ggtcccatca 180

aggttcagcg gcagtggatc tgggacagat ttcactctca ctatcagcag cctgcaacct 240

gaagattttg caacttacta ttgccaacag gctaacagtt tccccgtcac cttcggccaa 300

gggacacgac tggagattaa a 321

<210> SEQ ID NO 931
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 931

caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggtta cacctttacc agctatggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagtaggt 300

tattactact actacggtat ggacgtctgg ggccaaggga ccacggtcac cgtctcgaga 360

<210> SEQ ID NO 932
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 932

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tcctgcactg gaaccagcag tgatgttggg agttataacc ttgtctcctg gtaccaacag 120

cacccaggca aagcccccaa actcatgatt tatgagggca gtaagcggcc ctcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

caggctgagg acgaggctga ttattactgc agctcatata caagcagcag cacttgggtg 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 933
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 933

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tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atgaacccta acagtggtaa cacaggctat 180

gcacagaagt tccagggcag agtcaccatg accaggaaca cctccataag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagacgtt 300

gggattgggg tctttgacta ctggggccag ggaaccctgg tcaccgtctc gaga 354

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<210> SEQ ID NO 934
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 934

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acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcat ctattatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

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ggagggacca agctgaccgt cctaggt 327

<210> SEQ ID NO 935
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 935

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggGTC cctgagactc 60

tcctgtgcag cctctggatt cacctttagc gactatgcca tgaactgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct actagtggta gtggaggcag cacattctac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagag tacgttgtat 240

ctgcaaatga acagcctgag agacgaggac acggccgtgt attactgtgc gaaagggacc 300

ttaccgcatt actatgatag tagtggtata gggggccagg gcaccctggt caccgtctcg 360

agc 363

<210> SEQ ID NO 936
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 936

caggctgtgc tcactcagcc gtcttccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtaccaacag 120

cacccaggca aagcccccaa actcatgatt tatgatgtcg gtaagcggcc ctcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

cgggctgagg acgaggctaa ttattactgc agctcatata caagcagcag cacttggttt 300

gtggtattcg gcggagggac caagctgacc gtcctaggt 339

<210> SEQ ID NO 937
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 937

caggtacagc tgcagcagtc aggggctgag gtgaagaagc ctggggcctc agtgaaggtt 60

tcctgcaagg catctggata caccttcacc acctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaata atcaatccta gtggtgaaaa tacaaactac 180

gcacagaagt tccagggcag agtcaccatg accagggaca catccacgac cacagtctac 240

-continued

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagatctttc 300

ataggaactc gtgggggcgg tttggacgtc tggggccaag ggaccacggt caccgtctcg 360

aga 363

<210> SEQ ID NO 938
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 938

cagtctgtgt tgacgcagcc gccctcagtg tctggggccc cagggcagag ggtcaacatc 60

tcctgcgctg ggagcagctc caacatcggg gcgggttatg atgttcactg gtaccagcag 120

attccaggaa cagccccaa actcctcatg tatggtaata gtaatcggcc ctcaggggtc 180

cctgaccgat tctctggctc caagtctggc gcctcagcct ccctggccat cactaggctc 240

caggctgagg atgaggctga ttattactgc cagtcctatg acagcagcct gagtggttcg 300

agggtcttcg gaactgggac caaggtcacc gtcctaggt 339

<210> SEQ ID NO 939
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 939

gaggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120

ccggggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag cataggctat 180

gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240

ctgcaaatga acagtctgag agctgaggac acggctgtgt attactgtgc gacggaagaa 300

tggtggcgct tcgatctctg gggccgtggc accctggtca ccgtctcgag a 351

<210> SEQ ID NO 940
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 940

cagtctgccc tgactcagcc tccctccgcg tccgggtctc ctggacagtc agtcaccatc 60

tcctgcactg gaaccagcag tgacgttgat gattacaact atgtctcctg gtaccaacag 120

cacccaggca aagcccccaa actcatgatt tatgaggtca ctaagcggcc ctcaggggtc 180

cctgatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

caggctgagg atgaggctga ttattactgc agctcatatg tgggcagcga caatagagtc 300

ttcggaactg ggaccaaggt caccgtccca ggt 333

<210> SEQ ID NO 941
<211> LENGTH: 1897
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 941

Met Val Pro Leu Val Pro Ala Leu Val Met Leu Gly Leu Val Ala Gly

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1               5                   10                  15

Ala His Gly Asp Ser Lys Pro Val Phe Ile Lys Val Pro Glu Asp Gln
            20                  25                  30

Thr Gly Leu Ser Gly Gly Val Ala Ser Phe Val Cys Gln Ala Thr Gly
        35                  40                  45

Glu Pro Lys Pro Arg Ile Thr Trp Met Lys Lys Gly Lys Lys Val Ser
    50                  55                  60

Ser Gln Arg Phe Glu Val Ile Glu Phe Asp Asp Gly Ala Gly Ser Val
65                  70                  75                  80

Leu Arg Ile Gln Pro Leu Arg Val Gln Arg Asp Glu Ala Ile Tyr Glu
                85                  90                  95

Cys Thr Ala Thr Asn Ser Leu Gly Glu Ile Asn Thr Ser Ala Lys Leu
            100                 105                 110

Ser Val Leu Glu Glu Glu Gln Leu Pro Pro Gly Phe Pro Ser Ile Asp
        115                 120                 125

Met Gly Pro Gln Leu Lys Val Val Glu Lys Ala Arg Thr Ala Thr Met
    130                 135                 140

Leu Cys Ala Ala Gly Gly Asn Pro Asp Pro Glu Ile Ser Trp Phe Lys
145                 150                 155                 160

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

Leu Arg Ser Gly Ala Leu Gln Ile Glu Ser Ser Glu Glu Ser Asp Gln
            180                 185                 190

Gly Lys Tyr Glu Cys Val Ala Thr Asn Ser Ala Gly Thr Arg Tyr Ser
        195                 200                 205

Ala Pro Ala Asn Leu Tyr Val Arg Val Arg Arg Val Ala Pro Arg Phe
    210                 215                 220

Ser Ile Pro Pro Ser Ser Gln Glu Val Met Pro Gly Gly Ser Val Asn
225                 230                 235                 240

Leu Thr Cys Val Ala Val Gly Ala Pro Met Pro Tyr Val Lys Trp Met
                245                 250                 255

Met Gly Ala Glu Glu Leu Thr Lys Glu Asp Glu Met Pro Val Gly Arg
            260                 265                 270

Asn Val Leu Glu Leu Ser Asn Val Val Arg Ser Ala Asn Tyr Thr Cys
        275                 280                 285

Val Ala Ile Ser Ser Leu Gly Met Ile Glu Ala Thr Ala Gln Val Thr
    290                 295                 300

Val Lys Ala Leu Pro Lys Pro Pro Ile Asp Leu Val Val Thr Glu Thr
305                 310                 315                 320

Thr Ala Thr Ser Val Thr Leu Thr Trp Asp Ser Gly Asn Ser Glu Pro
                325                 330                 335

Val Thr Tyr Tyr Gly Ile Gln Tyr Arg Ala Ala Gly Thr Glu Gly Pro
            340                 345                 350

Phe Gln Glu Val Asp Gly Val Ala Thr Thr Arg Tyr Ser Ile Gly Gly
        355                 360                 365

Leu Ser Pro Phe Ser Glu Tyr Ala Phe Arg Val Leu Ala Val Asn Ser
    370                 375                 380

Ile Gly Arg Gly Pro Pro Ser Glu Ala Val Arg Ala Arg Thr Gly Glu
385                 390                 395                 400

Gln Ala Pro Ser Ser Pro Pro Arg Arg Val Gln Ala Arg Met Leu Ser
                405                 410                 415
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Ala Ser Thr Met Leu Val Gln Trp Glu Pro Pro Glu Glu Pro Asn Gly
            420                 425                 430

Leu Val Arg Gly Tyr Arg Val Tyr Tyr Thr Pro Asp Ser Arg Arg Pro
        435                 440                 445

Pro Asn Ala Trp His Lys His Asn Thr Asp Ala Gly Leu Leu Thr Thr
    450                 455                 460

Val Gly Ser Leu Leu Pro Gly Ile Thr Tyr Ser Leu Arg Val Leu Ala
465                 470                 475                 480

Phe Thr Ala Val Gly Asp Gly Pro Pro Ser Pro Thr Ile Gln Val Lys
                485                 490                 495

Thr Gln Gln Gly Val Pro Ala Gln Pro Ala Asp Phe Gln Ala Glu Val
            500                 505                 510

Glu Ser Asp Thr Arg Ile Gln Leu Ser Trp Leu Leu Pro Pro Gln Glu
        515                 520                 525

Arg Ile Ile Met Tyr Glu Leu Val Tyr Trp Ala Ala Glu Asp Glu Asp
    530                 535                 540

Gln Gln His Lys Val Thr Phe Asp Pro Thr Ser Ser Tyr Thr Leu Glu
545                 550                 555                 560

Asp Leu Lys Pro Asp Thr Leu Tyr Arg Phe Gln Leu Ala Ala Arg Ser
                565                 570                 575

Asp Met Gly Val Gly Val Phe Thr Pro Thr Ile Glu Ala Arg Thr Ala
            580                 585                 590

Gln Ser Thr Pro Ser Ala Pro Pro Gln Lys Val Met Cys Val Ser Met
        595                 600                 605

Gly Ser Thr Thr Val Arg Val Ser Trp Val Pro Pro Pro Ala Asp Ser
    610                 615                 620

Arg Asn Gly Val Ile Thr Gln Tyr Ser Val Ala His Glu Ala Val Asp
625                 630                 635                 640

Gly Glu Asp Arg Gly Arg His Val Val Asp Gly Ile Ser Arg Glu His
                645                 650                 655

Ser Ser Trp Asp Leu Val Gly Leu Glu Lys Trp Thr Glu Tyr Arg Val
            660                 665                 670

Trp Val Arg Ala His Thr Asp Val Gly Pro Gly Pro Glu Ser Ser Pro
        675                 680                 685

Val Leu Val Arg Thr Asp Glu Asp Val Pro Ser Gly Pro Pro Arg Lys
    690                 695                 700

Val Glu Val Glu Pro Leu Asn Ser Thr Ala Val His Val Tyr Trp Lys
705                 710                 715                 720

Leu Pro Val Pro Ser Lys Gln His Gly Gln Ile Arg Gly Tyr Gln Val
                725                 730                 735

Thr Tyr Val Arg Leu Glu Asn Gly Glu Pro Arg Gly Leu Pro Ile Ile
            740                 745                 750

Gln Asp Val Met Leu Ala Glu Ala Gln Trp Arg Pro Glu Glu Ser Glu
        755                 760                 765

Asp Tyr Glu Thr Thr Ile Ser Gly Leu Thr Pro Glu Thr Thr Tyr Ser
    770                 775                 780

Val Thr Val Ala Ala Tyr Thr Thr Lys Gly Asp Gly Ala Arg Ser Lys
785                 790                 795                 800

Pro Lys Ile Val Thr Thr Thr Gly Ala Val Pro Gly Arg Pro Thr Met
                805                 810                 815
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Met Ile Ser Thr Thr Ala Met Asn Thr Ala Leu Leu Gln Trp His Pro
            820                 825                 830

Pro Lys Glu Leu Pro Gly Glu Leu Leu Gly Tyr Arg Leu Gln Tyr Cys
        835                 840                 845

Arg Ala Asp Glu Ala Arg Pro Asn Thr Ile Asp Phe Gly Lys Asp Asp
    850                 855                 860

Gln His Phe Thr Val Thr Gly Leu His Lys Gly Thr Thr Tyr Ile Phe
865                 870                 875                 880

Arg Leu Ala Ala Lys Asn Arg Ala Gly Leu Gly Glu Glu Phe Glu Lys
                885                 890                 895

Glu Ile Arg Thr Pro Glu Asp Leu Pro Ser Gly Phe Pro Gln Asn Leu
            900                 905                 910

His Val Thr Gly Leu Thr Thr Ser Thr Thr Glu Leu Ala Trp Asp Pro
        915                 920                 925

Pro Val Leu Ala Glu Arg Asn Gly Arg Ile Ile Ser Tyr Thr Val Val
    930                 935                 940

Phe Arg Asp Ile Asn Ser Gln Gln Glu Leu Gln Asn Ile Thr Thr Asp
945                 950                 955                 960

Thr Arg Phe Thr Leu Thr Gly Leu Lys Pro Asp Thr Thr Tyr Asp Ile
                965                 970                 975

Lys Val Arg Ala Trp Thr Ser Lys Gly Ser Gly Pro Leu Ser Pro Ser
            980                 985                 990

Ile Gln Ser Arg Thr Met Pro Val  Glu Gln Val Phe Ala  Lys Asn Phe
        995                 1000                1005

Arg Val  Ala Ala Ala Met Lys  Thr Ser Val Leu Leu  Ser Trp Glu
    1010                1015                1020

Val Pro  Asp Ser Tyr Lys Ser  Ala Val Pro Phe Lys  Ile Leu Tyr
    1025                1030                1035

Asn Gly  Gln Ser Val Glu Val  Asp Gly His Ser Met  Arg Lys Leu
    1040                1045                1050

Ile Ala  Asp Leu Gln Pro Asn  Thr Glu Tyr Ser Phe  Val Leu Met
    1055                1060                1065

Asn Arg  Gly Ser Ser Ala Gly  Gly Leu Gln His Leu  Val Ser Ile
    1070                1075                1080

Arg Thr  Ala Pro Asp Leu Leu  Pro His Lys Pro Leu  Pro Ala Ser
    1085                1090                1095

Ala Tyr  Ile Glu Asp Gly Arg  Phe Asp Leu Ser Met  Pro His Val
    1100                1105                1110

Gln Asp  Pro Ser Leu Val Arg  Trp Phe Tyr Ile Val  Val Val Pro
    1115                1120                1125

Ile Asp  Arg Val Gly Gly Ser  Met Leu Thr Pro Arg  Trp Ser Thr
    1130                1135                1140

Pro Glu  Glu Leu Glu Leu Asp  Glu Leu Leu Glu Ala  Ile Glu Gln
    1145                1150                1155

Gly Gly  Glu Glu Gln Arg Arg  Arg Arg Arg Gln Ala  Glu Arg Leu
    1160                1165                1170

Lys Pro  Tyr Val Ala Ala Gln  Leu Asp Val Leu Pro  Glu Thr Phe
    1175                1180                1185

Thr Leu  Gly Asp Lys Lys Asn  Tyr Arg Gly Phe Tyr  Asn Arg Pro
    1190                1195                1200

Leu Ser  Pro Asp Leu Ser Tyr  Gln Cys Phe Val Leu  Ala Ser Leu
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    1205                1210                1215

Lys Glu  Pro Met Asp Gln Lys  Arg Tyr Ala Ser Ser  Pro Tyr Ser
    1220                1225                1230

Asp Glu  Ile Val Val Gln Val  Thr Pro Ala Gln Gln  Gln Glu Glu
    1235                1240                1245

Pro Glu  Met Leu Trp Val Thr  Gly Pro Val Leu Ala  Val Ile Leu
    1250                1255                1260

Ile Ile  Leu Ile Val Ile Ala  Ile Leu Leu Phe Lys  Arg Lys Arg
    1265                1270                1275

Thr His  Ser Pro Ser Ser Lys  Asp Glu Gln Ser Ile  Gly Leu Lys
    1280                1285                1290

Asp Ser  Leu Leu Ala His Ser  Ser Asp Pro Val Glu  Met Arg Arg
    1295                1300                1305

Leu Asn  Tyr Gln Thr Pro Gly  Met Arg Asp His Pro  Pro Ile Pro
    1310                1315                1320

Ile Thr  Asp Leu Ala Asp Asn  Ile Glu Arg Leu Lys  Ala Asn Asp
    1325                1330                1335

Gly Leu  Lys Phe Ser Gln Glu  Tyr Glu Ser Ile Asp  Pro Gly Gln
    1340                1345                1350

Gln Phe  Thr Trp Glu Asn Ser  Asn Leu Glu Val Asn  Lys Pro Lys
    1355                1360                1365

Asn Arg  Tyr Ala Asn Val Ile  Ala Tyr Asp His Ser  Arg Val Ile
    1370                1375                1380

Leu Thr  Ser Ile Asp Gly Val  Pro Gly Ser Asp Tyr  Ile Asn Ala
    1385                1390                1395

Asn Tyr  Ile Asp Gly Tyr Arg  Lys Gln Asn Ala Tyr  Ile Ala Thr
    1400                1405                1410

Gln Gly  Pro Leu Pro Glu Thr  Met Gly Asp Phe Trp  Arg Met Val
    1415                1420                1425

Trp Glu  Gln Arg Thr Ala Thr  Val Val Met Met Thr  Arg Leu Glu
    1430                1435                1440

Glu Lys  Ser Arg Val Lys Cys  Asp Gln Tyr Trp Pro  Ala Arg Gly
    1445                1450                1455

Thr Glu  Thr Cys Gly Leu Ile  Gln Val Thr Leu Leu  Asp Thr Val
    1460                1465                1470

Glu Leu  Ala Thr Tyr Thr Val  Arg Thr Phe Ala Leu  His Lys Ser
    1475                1480                1485

Gly Ser  Ser Glu Lys Arg Glu  Leu Arg Gln Phe Gln  Phe Met Ala
    1490                1495                1500

Trp Pro  Asp His Gly Val Pro  Glu Tyr Pro Thr Pro  Ile Leu Ala
    1505                1510                1515

Phe Leu  Arg Arg Val Lys Ala  Cys Asn Pro Leu Asp  Ala Gly Pro
    1520                1525                1530

Met Val  Val His Cys Ser Ala  Gly Val Gly Arg Thr  Gly Cys Phe
    1535                1540                1545

Ile Val  Ile Asp Ala Met Leu  Glu Arg Met Lys His  Glu Lys Thr
    1550                1555                1560

Val Asp  Ile Tyr Gly His Val  Thr Cys Met Arg Ser  Gln Arg Asn
    1565                1570                1575

Tyr Met  Val Gln Thr Glu Asp  Gln Tyr Val Phe Ile  His Glu Ala
    1580                1585                1590
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Leu Leu  Glu Ala Ala Thr Cys  Gly His Thr Glu Val  Pro Ala Arg
    1595                 1600                 1605

Asn Leu  Tyr Ala His Ile Gln  Lys Leu Gly Gln Val  Pro Pro Gly
    1610                 1615                 1620

Glu Ser  Val Thr Ala Met Glu  Leu Glu Phe Lys Leu  Leu Ala Ser
    1625                 1630                 1635

Ser Lys  Ala His Thr Ser Arg  Phe Ile Ser Ala Asn  Leu Pro Cys
    1640                 1645                 1650

Asn Lys  Phe Lys Asn Arg Leu  Val Asn Ile Met Pro  Tyr Glu Leu
    1655                 1660                 1665

Thr Arg  Val Cys Leu Gln Pro  Ile Arg Gly Val Glu  Gly Ser Asp
    1670                 1675                 1680

Tyr Ile  Asn Ala Ser Phe Leu  Asp Gly Tyr Arg Gln  Gln Lys Ala
    1685                 1690                 1695

Tyr Ile  Ala Thr Gln Gly Pro  Leu Ala Glu Ser Thr  Glu Asp Phe
    1700                 1705                 1710

Trp Arg  Met Leu Trp Glu His  Asn Ser Thr Ile Ile  Val Met Leu
    1715                 1720                 1725

Thr Lys  Leu Arg Glu Met Gly  Arg Glu Lys Cys His  Gln Tyr Trp
    1730                 1735                 1740

Pro Ala  Glu Arg Ser Ala Arg  Tyr Gln Tyr Phe Val  Val Asp Pro
    1745                 1750                 1755

Met Ala  Glu Tyr Asn Met Pro  Gln Tyr Ile Leu Arg  Glu Phe Lys
    1760                 1765                 1770

Val Thr  Asp Ala Arg Asp Gly  Gln Ser Arg Thr Ile  Arg Gln Phe
    1775                 1780                 1785

Gln Phe  Thr Asp Trp Pro Glu  Gln Gly Val Pro Lys  Thr Gly Glu
    1790                 1795                 1800

Gly Phe  Ile Asp Phe Ile Gly  Gln Val His Lys Thr  Lys Glu Gln
    1805                 1810                 1815

Phe Gly  Gln Asp Gly Pro Ile  Thr Val His Cys Ser  Ala Gly Val
    1820                 1825                 1830

Gly Arg  Thr Gly Val Phe Ile  Thr Leu Ser Ile Val  Leu Glu Arg
    1835                 1840                 1845

Met Arg  Tyr Glu Gly Val Val  Asp Met Phe Gln Thr  Val Lys Thr
    1850                 1855                 1860

Leu Arg  Thr Gln Arg Pro Ala  Met Val Gln Thr Glu  Asp Gln Tyr
    1865                 1870                 1875

Gln Leu  Cys Tyr Arg Ala Ala  Leu Glu Tyr Leu Gly  Ser Phe Asp
    1880                 1885                 1890

His Tyr  Ala Thr
    1895
```

<210> SEQ ID NO 942
<211> LENGTH: 628
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 942

```
Met Glu Pro Pro Asp Ala Pro Ala Gln Ala Arg Gly Ala Pro Arg Leu
1               5                  10                  15

Leu Leu Leu Ala Val Leu Leu Ala Ala His Pro Asp Ala Gln Ala Glu
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            20                  25                  30

Val Arg Leu Ser Val Pro Pro Leu Val Glu Val Met Arg Gly Lys Ser
        35                  40                  45

Val Ile Leu Asp Cys Thr Pro Thr Gly Thr His Asp His Tyr Met Leu
    50                  55                  60

Glu Trp Phe Leu Thr Asp Arg Ser Gly Ala Arg Pro Arg Leu Ala Ser
65                  70                  75                  80

Ala Glu Met Gln Gly Ser Glu Leu Gln Val Thr Met His Asp Thr Arg
                85                  90                  95

Gly Arg Ser Pro Pro Tyr Gln Leu Asp Ser Gln Gly Arg Leu Val Leu
            100                 105                 110

Ala Glu Ala Gln Val Gly Asp Glu Arg Asp Tyr Val Cys Val Val Arg
        115                 120                 125

Ala Gly Ala Ala Gly Thr Ala Glu Ala Thr Ala Arg Leu Asn Val Phe
    130                 135                 140

Ala Lys Pro Glu Ala Thr Glu Val Ser Pro Asn Lys Gly Thr Leu Ser
145                 150                 155                 160

Val Met Glu Asp Ser Ala Gln Glu Ile Ala Thr Cys Asn Ser Arg Asn
                165                 170                 175

Gly Asn Pro Ala Pro Lys Ile Thr Trp Tyr Arg Asn Gly Gln Arg Leu
            180                 185                 190

Glu Val Pro Val Glu Met Asn Pro Glu Gly Tyr Met Thr Ser Arg Thr
        195                 200                 205

Val Arg Glu Ala Ser Gly Leu Leu Ser Leu Thr Ser Thr Leu Tyr Leu
    210                 215                 220

Arg Leu Arg Lys Asp Asp Arg Asp Ala Ser Phe His Cys Ala Ala His
225                 230                 235                 240

Tyr Ser Leu Pro Glu Gly Arg His Gly Arg Leu Asp Ser Pro Thr Phe
                245                 250                 255

His Leu Thr Leu His Tyr Pro Thr Glu His Val Gln Phe Trp Val Gly
            260                 265                 270

Ser Pro Ser Thr Pro Ala Gly Trp Val Arg Glu Gly Asp Thr Val Gln
        275                 280                 285

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

Arg Leu Gln Asp Glu Gln Glu Glu Val Leu Asn Val Asn Leu Glu Gly
305                 310                 315                 320

Asn Leu Thr Leu Glu Gly Val Thr Arg Gly Gln Ser Gly Thr Tyr Gly
                325                 330                 335

Cys Arg Val Glu Asp Tyr Asp Ala Ala Asp Asp Val Gln Leu Ser Lys
            340                 345                 350

Thr Leu Glu Leu Arg Val Ala Tyr Leu Asp Pro Leu Glu Leu Ser Glu
        355                 360                 365

Gly Lys Val Leu Ser Leu Pro Leu Asn Ser Ser Ala Val Val Asn Cys
    370                 375                 380

Ser Val His Gly Leu Pro Thr Pro Ala Leu Arg Trp Thr Lys Asp Ser
385                 390                 395                 400

Thr Pro Leu Gly Asp Gly Pro Met Leu Ser Leu Ser Ser Ile Thr Phe
                405                 410                 415

Asp Ser Asn Gly Thr Tyr Val Cys Glu Ala Ser Leu Pro Thr Val Pro
            420                 425                 430
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```
Val Leu Ser Arg Thr Gln Asn Phe Thr Leu Leu Val Gln Gly Ser Pro
        435                 440                 445

Glu Leu Lys Thr Ala Glu Ile Glu Pro Lys Ala Asp Gly Ser Trp Arg
    450                 455                 460

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

Pro Lys Leu Ser Trp Ser Gln Leu Gly Gly Ser Pro Ala Glu Pro Ile
                485                 490                 495

Pro Gly Arg Gln Gly Trp Val Ser Ser Ser Leu Thr Leu Lys Val Thr
            500                 505                 510

Ser Ala Leu Ser Arg Asp Gly Ile Ser Cys Glu Ala Ser Asn Pro His
        515                 520                 525

Gly Asn Lys Arg His Val Phe His Phe Gly Thr Val Ser Pro Gln Thr
    530                 535                 540

Ser Gln Ala Gly Val Ala Val Met Ala Val Ala Val Ser Val Gly Leu
545                 550                 555                 560

Leu Leu Leu Val Val Ala Val Phe Tyr Cys Val Arg Arg Lys Gly Gly
                565                 570                 575

Pro Cys Cys Arg Gln Arg Arg Glu Lys Gly Ala Pro Pro Pro Gly Glu
            580                 585                 590

Pro Gly Leu Ser His Ser Gly Ser Glu Gln Pro Glu Gln Thr Gly Leu
        595                 600                 605

Leu Met Gly Gly Ala Ser Gly Gly Ala Arg Gly Gly Ser Gly Gly Phe
    610                 615                 620

Gly Asp Glu Cys
625


<210> SEQ ID NO 943
<211> LENGTH: 621
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 943

Leu Glu Glu Lys Lys Val Cys Gln Gly Thr Ser Asn Lys Leu Thr Gln
1               5                   10                  15

Leu Gly Thr Phe Glu Asp His Phe Leu Ser Leu Gln Arg Met Phe Asn
            20                  25                  30

Asn Cys Glu Val Val Leu Gly Asn Leu Glu Ile Thr Tyr Val Gln Arg
        35                  40                  45

Asn Tyr Asp Leu Ser Phe Leu Lys Thr Ile Gln Glu Val Ala Gly Tyr
    50                  55                  60

Val Leu Ile Ala Leu Asn Thr Val Glu Arg Ile Pro Leu Glu Asn Leu
65                  70                  75                  80

Gln Ile Ile Arg Gly Asn Met Tyr Tyr Glu Asn Ser Tyr Ala Leu Ala
                85                  90                  95

Val Leu Ser Asn Tyr Asp Ala Asn Lys Thr Gly Leu Lys Glu Leu Pro
            100                 105                 110

Met Arg Asn Leu Gln Glu Ile Leu His Gly Ala Val Arg Phe Ser Asn
        115                 120                 125

Asn Pro Ala Leu Cys Asn Val Glu Ser Ile Gln Trp Arg Asp Ile Val
    130                 135                 140

Ser Ser Asp Phe Leu Ser Asn Met Ser Met Asp Phe Gln Asn His Leu
```

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```
145                 150                 155                 160

Gly Ser Cys Gln Lys Cys Asp Pro Ser Cys Pro Asn Gly Ser Cys Trp
                165                 170                 175

Gly Ala Gly Glu Glu Asn Cys Gln Lys Leu Thr Lys Ile Ile Cys Ala
            180                 185                 190

Gln Gln Cys Ser Gly Arg Cys Arg Gly Lys Ser Pro Ser Asp Cys Cys
        195                 200                 205

His Asn Gln Cys Ala Ala Gly Cys Thr Gly Pro Arg Glu Ser Asp Cys
    210                 215                 220

Leu Val Cys Arg Lys Phe Arg Asp Glu Ala Thr Cys Lys Asp Thr Cys
225                 230                 235                 240

Pro Pro Leu Met Leu Tyr Asn Pro Thr Thr Tyr Gln Met Asp Val Asn
                245                 250                 255

Pro Glu Gly Lys Tyr Ser Phe Gly Ala Thr Cys Val Lys Lys Cys Pro
            260                 265                 270

Arg Asn Tyr Val Val Thr Asp His Gly Ser Cys Val Arg Ala Cys Gly
        275                 280                 285

Ala Asp Ser Tyr Glu Met Glu Glu Asp Gly Val Arg Lys Cys Lys Lys
    290                 295                 300

Cys Glu Gly Pro Cys Arg Lys Val Cys Asn Gly Ile Gly Ile Gly Glu
305                 310                 315                 320

Phe Lys Asp Ser Leu Ser Ile Asn Ala Thr Asn Ile Lys His Phe Lys
                325                 330                 335

Asn Cys Thr Ser Ile Ser Gly Asp Leu His Ile Leu Pro Val Ala Phe
            340                 345                 350

Arg Gly Asp Ser Phe Thr His Thr Pro Pro Leu Asp Pro Gln Glu Leu
        355                 360                 365

Asp Ile Leu Lys Thr Val Lys Glu Ile Thr Gly Phe Leu Leu Ile Gln
    370                 375                 380

Ala Trp Pro Glu Asn Arg Thr Asp Leu His Ala Phe Glu Asn Leu Glu
385                 390                 395                 400

Ile Ile Arg Gly Arg Thr Lys Gln His Gly Gln Phe Ser Leu Ala Val
                405                 410                 415

Val Ser Leu Asn Ile Thr Ser Leu Gly Leu Arg Ser Leu Lys Glu Ile
            420                 425                 430

Ser Asp Gly Asp Val Ile Ile Ser Gly Asn Lys Asn Leu Cys Tyr Ala
        435                 440                 445

Asn Thr Ile Asn Trp Lys Lys Leu Phe Gly Thr Ser Gly Gln Lys Thr
    450                 455                 460

Lys Ile Ile Ser Asn Arg Gly Glu Asn Ser Cys Lys Ala Thr Gly Gln
465                 470                 475                 480

Val Cys His Ala Leu Cys Ser Pro Glu Gly Cys Trp Gly Pro Glu Pro
                485                 490                 495

Arg Asp Cys Val Ser Cys Arg Asn Val Ser Arg Gly Arg Glu Cys Val
            500                 505                 510

Asp Lys Cys Asn Leu Leu Glu Gly Glu Pro Arg Glu Phe Val Glu Asn
        515                 520                 525

Ser Glu Cys Ile Gln Cys His Pro Glu Cys Leu Pro Gln Ala Met Asn
    530                 535                 540

Ile Thr Cys Thr Gly Arg Gly Pro Asp Asn Cys Ile Gln Cys Ala His
545                 550                 555                 560
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Tyr Ile Asp Gly Pro His Cys Val Lys Thr Cys Pro Ala Gly Val Met
                565                 570                 575

Gly Glu Asn Asn Thr Leu Val Trp Lys Tyr Ala Asp Ala Gly His Val
            580                 585                 590

Cys His Leu Cys His Pro Asn Cys Thr Tyr Gly Cys Thr Gly Pro Gly
        595                 600                 605

Leu Glu Gly Cys Pro Thr Asn Gly Pro Lys Ile Pro Ser
    610                 615                 620


<210> SEQ ID NO 944
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 944

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Val Ser Gly Tyr Thr Leu Thr Glu Leu
            20                  25                  30

Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Gly Phe Asp Pro Glu Asp Gly Glu Thr Ile Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Glu Asp Thr Ser Thr Asp Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Thr Asp Leu Asp Tyr Tyr Gly Ser Gly Ser Tyr Ala Phe Asp Ile
            100                 105                 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Arg
        115                 120


<210> SEQ ID NO 945
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 945

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1               5                   10                  15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ser Tyr
20                  25                  30

Asn Leu Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35                  40                  45

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
                85                  90                  95

Ser Thr Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 946
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<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 946

Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ala Tyr Gly Gly Ser Phe Ser Gly Tyr
            20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35 40 45

Gly Glu Ile Asn His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
    50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85 90 95

Arg Thr Tyr Tyr Gly Ser Gly Ser Tyr Gln Tyr Asn Trp Phe Asp Pro
            100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg
        115 120

<210> SEQ ID NO 947
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 947

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
            20 25 30

Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
        35 40 45

Leu Ile Tyr Gly Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
    50 55 60

Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
                85 90 95

Leu Ser Gly Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100 105 110

<210> SEQ ID NO 948
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 948

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35 40 45

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Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Asn Leu Glu Gly Leu Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Arg
        115


<210> SEQ ID NO 949
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 949

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Lys
1               5                   10                  15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45

Tyr Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
    50                  55                  60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
                85                  90                  95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105


<210> SEQ ID NO 950
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 950

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Asp Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Gly Thr Gly Asp Leu Glu Trp Phe Asp Pro Trp Gly Gln
        100                 105                 110

Gly Thr Leu Val Thr Val Ser Arg
    115                 120
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<210> SEQ ID NO 951
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 951

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Arg Gln
1 5 10 15

Thr Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Gln Asn
20 25 30

Ser Val Thr Trp Tyr Gln Arg Leu Pro Gly Glu Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Tyr Asp Asp Leu Leu His Ser Gly Val Ser Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Ser Trp Asp Asp Ser Leu
85 90 95

Lys Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 952
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 952

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Pro Arg Gly Ser Tyr Tyr Tyr Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 953
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 953

Asn Phe Met Leu Thr Gln Pro His Ser Val Ser Glu Ser Pro Gly Lys
1 5 10 15

Thr Val Thr Ile Ser Cys Thr Arg Ser Ser Gly Ser Ile Ala Ser Asn
20 25 30

Tyr Val Gln Trp Tyr Gln Gln Arg Pro Gly Ser Ala Pro Thr Thr Val

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        35                  40                  45

Ile Tyr Glu Asp Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Ile Asp Ser Ser Ser Asn Ser Ala Ser Leu Thr Ile Ser Gly
65                  70                  75                  80

Leu Lys Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser
                85                  90                  95

Ser Asn Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110


<210> SEQ ID NO 954
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 954

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ala Lys Arg Arg Gly Ser Ala Phe Asp Ile Trp Gly Gln Gly
            100                 105                 110

Thr Thr Val Thr Val Ser Arg
        115


<210> SEQ ID NO 955
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 955

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1               5                   10                  15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
            20                  25                  30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
    50                  55                  60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
                85                  90                  95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105
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<210> SEQ ID NO 956
<211> LENGTH: 369
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 956

caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg tttccggata caccctcact gaattatcca tgcactgggt gcgacaggct 120

cctggaaaag ggcttgagtg gatgggaggt tttgatcctg aagatggtga aacaatctac 180

gcacagaagt tccagggcag agtcaccatg accgaggaca catctacaga cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc aacagatctc 300

gattactatg gttcggggag ttatgctttt gatatctggg gccaagggac cacggtcacc 360

gtctcgaga 369

<210> SEQ ID NO 957
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 957

cagtctgccc tgactcagcc tgcctccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgatgttggg agttataacc ttgtctcctg gtaccaacag 120

cacccaggca aagcccccaa actcatgatt tatgagggca gtaagcggcc tcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

caggctgagg acgaggctga ttattactgc agctcatata caagcagcag cacttgggtg 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 958
<211> LENGTH: 369
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 958

caggtgcagc tacagcagtg gggcgcagga ctgttgaagc cttcggagac cctgtccctc 60

acctgcgctg cctatggtgg gtccttcagt ggttactact ggagctggat ccgccagccc 120

ccagggaagg ggctggagtg gattggggaa atcaatcata gtggaagcac caactacaac 180

ccgtccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg 240

aagctgagct ctgtgaccgc cgcggacacg gctgtgtatt actgtgcgag gacttactat 300

ggttcgggga gttatcagta caactggttc gacccctggg gccagggaac cctggtcacc 360

gtctcgaga 369

<210> SEQ ID NO 959
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 959

cagtctgtgt tgacgcagcc gccctcagtg tctggggccc agggcagag ggtcaccatc 60

tcctgcactg ggagcagctc caacatcggg gcaggttatg atgtacactg gtaccagcag 120

cttccaggaa cagccccaa actcctcatc tatggtaaca gcaatcggcc ctcaggggtc 180

-continued

cctgaccgat tctctggctc caagtctggc acctcagcct ccttggccat cactgggctc 240

caggctgagg atgaggctga ttattactgc cagtcctatg acagcagcct gagtggtgtg 300

gtattcggcg gagggaccaa gctgaccgtc ctaggt 336

<210> SEQ ID NO 960
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 960

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggGTC cctgagactc 60

tcctgtgcag cctctggatt caccttcagt agctatagca tgaactgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtttcatat attagtagta gtagtagtac catatactac 180

gcagactctg tgaagggccg attcaccatc tccagagaca atgccaagaa ctcactgtat 240

ctgcaaatga acagcctgag agacgaggac acggctgtgt attactgtgc gagagataat 300

cttgaaggcc tggactactg gggccaggga accctggtca ccgtctcgag a 351

<210> SEQ ID NO 961
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 961

tcctatgtgc tgactcagcc accctcagtg tcagtggccc caggaaagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcat ctattatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgt ggtattcggc 300

ggagggacca agctgaccgt cctaggt 327

<210> SEQ ID NO 962
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 962

caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcacagac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagc agtggtgatt actactggag ttggatccgc 120

cagcccccag ggaagggcct ggagtggatt gggtacatct attacagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagttacc atatcagtag acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gactgccgca gacacggccg tgtattactg tgccagaggg 300

actggggatc ttgagtggtt cgacccctgg ggccagggca ccctggtcac cgtctcgaga 360

<210> SEQ ID NO 963
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 963

cagtctgtgt tgacgcagcc gccctcggtg tctggggccc cccggcagac ggtcaccatc 60

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tcctgctctg ggagcagctc caacatcgga caaaattctg ttacctggta ccagcgcctc 120

ccgggtgagg ctcccaaact cctcatctac tatgatgatc tcttgcactc aggagtctct 180

gaccgattct ctggctccaa gtctggcacc tcagcctcac tggccatcag tggactccag 240

tctgaggatg aggctgagta ctactgtgcg tcatgggatg acagcctgaa aggtccggta 300

ttcggcggag ggaccaaact gaccgtccta ggt 333

<210> SEQ ID NO 964
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 964

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt caccttcagt agctatagca tgaactgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtttcatac attagtagta gtagtagtac catatactac 180

gcagactctg tgaagggccg attcaccatc tccagagaca atgccaagaa ctcactgtat 240

ctgcaaatga acagcctgag agacgaggac acggctgtgt attactgtgc gagagagggc 300

ccaaggggga gctactacta ctttgactac tggggccagg gaaccctggt caccgtctcg 360

aga 363

<210> SEQ ID NO 965
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 965

aattttatgc tgactcagcc gcactctgtg tcggagtctc cggggaagac ggtaaccatc 60

tcctgcaccc gcagcagtgg cagcattgcc agcaactatg tgcagtggta ccagcagcgc 120

ccgggcagtg cccccaccac tgtgatctat gaggataacc aaagaccctc tggggtccct 180

gatcggttct ctggctccat cgacagctcc tccaactctg cctccctcac catctctgga 240

ctgaagactg aggacgaggc tgactactac tgtcagtctt atgatagcag caattgggtg 300

ttcggcggag ggaccaagct gaccgtccta ggt 333

<210> SEQ ID NO 966
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 966

caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtt 60

tcctgcaagg catctggata caccttcacc agctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaata atcaacccta gtggtggtag cacaagctac 180

gcacagaagt tccagggcag agtcaccatg accagggaca cgtccacgag cacagtctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagcgaag 300

agaaggggat ctgcttttga tatctggggc caagggacca cggtcaccgt ctcgaga 357

<210> SEQ ID NO 967
<211> LENGTH: 327

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<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 967

tcttctgagc tgactcagga ccctgctgtg tctgtggcct tgggacagac agtcaggatc 60

acatgccaag gagacagcct cagaagctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctatggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacagcagtg gtaaccatgt ggtattcggc 300

ggagggacca agctgaccgt cctaggt 327

<210> SEQ ID NO 968
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 968

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Arg Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Gly Asp Ile Ser Arg Gly Ser Ser Trp Tyr Gly Tyr Tyr Phe Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg
115 120

<210> SEQ ID NO 969
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 969

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ala Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Ser Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys

-continued

100 105

<210> SEQ ID NO 970
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 970

caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaggg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttggtac agcaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggaca aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gggagatatc 300

agccgaggca gcagctggta cgggtactac tttgactact ggggccaggg aaccctggtc 360

accgtctcga ga 372

<210> SEQ ID NO 971
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 971

gacatccaga tgacccagtc tccttccacc ctggctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca 180

aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct 240

gatgattttg caacttatta ctgccaacag tataatagtt attccacttt tggccagggg 300

accaagctgg agatcaaa 318

1. A method of classifying antibody including the following steps:

(1) preparing a plurality of antibodies recognizing cell surface antigen;

(2) bringing each of the antibodies into contact with cells of the same kinds;

(3) analyzing each cell after step (2) by flow cytometry so as to obtain data showing reactivity between the antibody and the cell surface; and

(4) comparing the obtained data and classifying antibodies based on the similarity of the data.

2. The method of classifying antibody according to claim **1**, wherein the cell surface antigen is an intact cell surface antigen.

3. The classifying method according to claim **1**, wherein the cell surface antigen is a cell surface antigen of a cancer cell.

4. The classifying method according to claim **1**, wherein the plurality of antibodies recognize cell surface antigen are composed of an assembly of antibodies derived from antibody clones selected as being capable of recognizing a cell surface antigen, from an antibody library.

5. The classifying method according to claim **4**, wherein the antibody library is a phage antibody library.

6. The classifying method according to claim **1**, wherein the antibody is an antibody to which a label material is bound or fused.

7. The classifying method according to claim **1**, wherein the antibody does not include a label material and the method includes a step of labeling the antibody bound to the cell after step (2).

8. The classifying method according to claim **1**, wherein the cell is an established cell line.

9. The classifying method according to claim **1**, wherein the cell is an established cancer cell line.

10. The classifying method according to claim **1**, wherein the data are shown in a histogram showing a relationship between a binding amount of antibodies and a number of cells, and the similarity of the data is determined by comparing the shapes of the histograms.

11. The classifying method according to claim **1**, wherein the data are shown in a histogram showing a relationship between a binding amount of antibodies and a number of cells, and the similarity of the data is determined based on one or more values selected from the group consisting of a median value, a mode, a maximum value, a range, a standard deviation, a kurtosis and a skewness of the histogram.

12. The classifying method according to claim **11**, wherein the similarity of the data is determined based on the values of the median value, the mode, and the kurtosis and a skewness of the histogram.

13. The classifying method according to claim **10**, wherein the binding amount of antibody is shown by a fluorescence intensity.

14. The classifying method according to claim **1**, wherein in step (4), a plurality of antibodies having the identical or high similar data are classified into one antibody group.

15. The classifying method according to claim **1**, wherein two or more kinds of cells are prepared and each kind of cell is subjected to steps (2) to (4).

16. The classifying method according to claim **15**, wherein a plurality of antibodies having the identical or high similar data with respect to two or more kinds of cells in the cells are classified into one antibody group.

17. The classifying method according to claim **1**, wherein an antibody that has been determined to have a low reactivity with respect to the cell surface antigen during classification or after classification is excluded.

18. The classifying method according to claim **1**, wherein classification results of antibodies are displayed as a panel.

19. The classifying method according to claim **1**, wherein after step (4), the following steps are carried out:

(i) associating the classified antibodies to a combination of n pieces of parameters including a first parameter, a second parameter, . . . , and an n-th parameter (wherein, n represents an integer of 2 or more, each parameter has two or more parameter values and the same parameter value is given to two or more antibodies in each parameter);

(ii) with respect to each parameter, preparing antibody mixtures of the antibodies having the same parameter value;

(iii) examining a reactivity of each of the antibody mixtures with a target antigen by an enzyme linked immunosorbent assay (ELISA) so as to specify the antibody mixture which shows reactivity;

(iv) specifying a combination of a parameter name and a parameter value that are common to the antibody group contained in the specified antibody mixture;

(v) selecting an antibody corresponding to the combination specified in the step (iv) in terms of all parameters among the antibodies subjected to step (i); and

(vi) classifying the selected antibodies into one antibody group.

20. The classifying method according to claim **19**, wherein the steps (i) to (v) are repeated several times under the conditions in which the combination of parameters is different in each trial; an antibody in which results of all trials are not contradictory is selected; and the antibody is subjected to the step (vi).

21. The classifying method according to claim **19**, further including the following steps between the step (v) and the step (vi);

(v-1) newly associating the classified antibodies selected in step (v) with a combination of n pieces of parameters in a same manner as in the step (i);

(v-2) with respect to each parameter, preparing the antibody mixture of antibodies having the same parameter value for each parameter;

(v-3) examining a reactivity of each of the antibody mixtures with a target antigen by an enzyme linked immunosorbent assay (ELISA) so as to specify the antibody mixture showing the reactivity;

(v-4) determining a combination of a parameter name and a parameter value that are common to the antibody group contained in the specified antibody mixture; and

(v-5) selecting an antibody having the combination specified in the step (v-4) in terms of all parameters among the antibodies subjected to the step (v-1).

22. The classifying method according to claim **21**, wherein the steps (v-1) to (v-4) are repeated twice or more.

23. The classifying method according to claim **19**, wherein n is 3.

24. The classifying method according to claim **19**, wherein two or more kinds of target antigens are prepared and the steps (iii) to (vi) are carried out by using each target antigen.

25. The classifying method according to claim **19**, wherein the target antigen is an antigen selected from the group consisting of HER1, HER2, CD46, ITGA3, ICAM1, ALCAM, CD147, IgSF4, BCAM, C1qR, CD44, CD73, LAR, EpCAM and HGFR.

26. An identifying method of an antigen including the following steps:

(1) preparing a plurality of antibodies recognizing cell surface antigen;

(2) bringing each of the antibodies into contact with cells of the same kind;

(3) analyzing each cell after step (2) by flow cytometry so as to obtain data showing the reactivity between the antibody and the cell surface;

(4) comparing the obtained data and classifying antibodies based on the similarity of the data;

(5) selecting one or several antibodies from each antibody group formed in the step (4) and identifying an antigen thereof; and

(6) associating the antigens identified in the step (5) with an antibody group, based on the estimation that antigens to antibodies belonging to the same antibody group are identical or have high relationship.

27. The identification method according to claim **26**, wherein in the step (5), one antibody is selected from each antibody group.

28. The identification method according to claim **26**, wherein in the step (5), from the results of a flow cytometry analysis, an antibody that is determined to have a high reactivity with respect to an antigen is selected.

29. The identification method according to claim **26**, wherein in the step (5), the identification of an antigen is carried out by one or more methods selected from the group consisting of an immunoprecipitation test, Western blotting, affinity chromatography, proteomics techniques (electrophoresis, mass spectrometry, genome data base retrieve, and analysis by bioinformatics), and an expression analysis of corresponding gene.

30. The identification method according to claim **26**, further including a step of examining a reactivity between an antigen identified in the step (5) and an antibody belonging to an antibody group with which the antigen is associated in the step (6) so as to confirm that the estimation is correct.

31. The identification method according to claim **26**, wherein an identification result of antigen is displayed as a panel.

32. The identification method according to claim **31**, wherein the panel is any of the following (a) to (c):

(a) a panel displaying a plurality of antibodies showing identical or high similar data in the flow cytometry analysis in the step (3) as one antibody group in which each antibody group is associated with its antigen;

(b) a panel displaying a plurality of antibodies showing identical or high similar data in the flow cytometry analysis in the step (3) as one antibody group in which each antibody group is associated with a cell expressing a cell surface antigen recognized by the each antibody group; and

(c) a panel displaying a plurality of antibodies showing identical or high similar data in the flow cytometry analysis in the step (3) as one antibody group in which each antibody group, its antigen and a cell expressing a cell surface antigen recognized by the antibody group are associated with each other.

33. A method of obtaining an antibody having a relationship with respect to a certain disease, the method comprising the following steps:

(1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to claim **1**;

(2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

(3) selecting an antibody in the antibody group, to which an antibody having a specific reactivity to any of diseases belongs, as a useful antibody.

34. A method of obtaining an antibody having a relationship with respect to a certain disease, the method comprising the following steps:

(1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to claim **19**;

(2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

(3) selecting an antibody in the antibody group, to which an antibody having a specific reactivity to any of diseases belongs, as a useful antibody.

35. A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

(1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to claim **1**;

(2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

(3') selecting a disease to which two or more antibodies show a specific reactivity, then selecting antibodies from the antibody group, to which the antibody having a specific reactivity to the disease belongs, and combining the selected antibodies.

36. A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

(1) selecting two or more antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to claim **1**;

(2) with respect to two kinds or more diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

(3) selecting antibodies from the antibody group, to which the antibody having a specific reactivity to any of disease belongs, and combining the selected antibodies.

37. A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

(1) selecting two or more antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to claim **1**;

(2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

(3) selecting an antibody from the antibody group to which the antibody having a specific reactivity to any of diseases belongs, and an antibody belonging to other antibody group whose antigen is common to that of the antibody group, and combining the selected antibodies.

38. A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

(1) selecting two or more antibody groups recognizing the common antigen from the plurality of antibody groups classified by the classifying method according to claim **1**;

(2) with respect to one kind or two or more kinds of pathologic conditions, examining a reactivity between an antibody in each of the selected antibody groups and a pathologic condition; and

(3) connecting information about the reactivity and then combining the antibodies in the antibody groups.

39. A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

(1) selecting one or two or more antibody groups from the plurality of antibody groups classified by the classifying method according to claim **19**;

(2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

(3') selecting a disease to which two or more antibodies show a specific reactivity, then selecting antibodies from an antibody group which the antibodies showing a specific reactivity to the disease belong to, and combining the selected antibodies.

40. A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

(1) selecting two or more antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to claim **19**;

(2) with respect to two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease in two or more kinds of diseases; and

(3) selecting antibodies from the antibody group to which the antibody having a specific reactivity to any of diseases belong, and combining the selected antibodies.

41. A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

(1) selecting two or more antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to claim **19**;

(2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

(3) selecting an antibody from the antibody group to which the antibody having a specific reactivity to any of disease belongs, and an antibody belonging to other antibody group whose antigen is common to that of the antibody group, and combining the selected antibodies.

42. A method of obtaining an antibody set having a relationship with respect to a certain disease, the method comprising the following steps:

(1) selecting two or more antibody groups recognizing the common antigen from the plurality of antibody groups classified by the classifying method according to claim **19**;

(2) with respect to one kind or two or more kinds of pathologic conditions, examining a reactivity between an antibody in each of the selected antibody groups and a pathologic condition; and

(3) associating information about the reactivity and then combining the antibodies in the antibody groups.

43. The obtaining method according to claim **33**, wherein the disease is selected from the group consisting of: kidney cancer, hepatic cell carcinoma, gallbladder and liver cancer, alveolar cell carcinoma, lung squamous cell cancer, pulmonary adenocarcinoma, pancreas cancer, adenocarcinoma, and ovarian cancer.

44. The obtaining method according to claim **33**, wherein in the step (2), the reactivity is examined by one or more methods selected from the group consisting of an immunostaining procedure, an immunoprecipitation method, a flow cytometry analysis, cell ELISA, an intermolecular interactive analysis between a disease-related molecule (disease causative gene product and the like) and an antibody, and application test to a disease model cell (or animal).

45. An isolated antibody obtained by the method according to claim **33**.

46. An antibody set obtained by the method described in claim **35**.

47. A production method of a panel displaying a relationship between an antibody and a disease, the method comprising the following steps:

(1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to claim **1**;

(2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

(3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

48. A production method of a panel displaying a relationship between an antibody and a disease, the method comprising the following steps:

(1) selecting two or more of antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to claim **1**;

(2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

(3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

49. A production method of a panel displaying a relationship between an antibody and a pathologic condition, the method comprising the following steps:

(1) selecting two or more of antibody groups recognizing a common antigen from the plurality of antibody groups classified by the classifying method according to claim **1**;

(2) with respect to one kind or two or more kinds of pathologic condition, examining a reactivity between an antibody in each of the selected antibody groups and a certain pathologic condition of disease; and

(3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

50. A production method of a panel displaying a relationship between an antibody and a disease, the method comprising the following steps:

(1) selecting one or two or more of antibody groups from the plurality of antibody groups classified by the classifying method according to claim **19**;

(2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

(3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

51. A production method of a panel displaying a relationship between an antibody and a disease, the method comprising the following steps:

(1) selecting two or more of antibody groups recognizing different antigens from the plurality of antibody groups classified by the classifying method according to claim **19**;

(2) with respect to one kind or two or more kinds of diseases, examining a reactivity between an antibody in each of the selected antibody groups and a certain disease; and

(3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

52. A production method of a panel displaying a relationship between an antibody and a pathologic condition, the method comprising the following steps:

(1) selecting two or more of antibody groups recognizing a common antigen from the plurality of antibody groups classified by the classifying method according to claim **19**;

(2) with respect to one kind or two or more kinds of pathologic condition, examining a reactivity between an antibody in each of the selected antibody groups and a certain pathologic condition of disease; and

(3) associating the results of the step (2) with each antibody and displaying by using a drawing or a tabular format.

53. A panel produced by the method according to claim **47**.

54. (canceled)

55. A method of testing a disease in which a cell surface antigen is an indicator, the method comprising the following steps:

(1) preparing a cell or a tissue separated from a subject;

(2) examining a reactivity between the cell or the tissue and each antibody displayed on the panel according to claim **53**; and

(3) collating the results in the step (2) with the panel.

56. A method of selecting an optimum treatment method for a certain disease, the method comprising the following steps:

(1) preparing a cell or a tissue separated from a subject;

(2) examining a reactivity between the cell or the tissue and each antibody displayed on the panel according to claim **53**;

(3) collating the results in the step (2) with the panel, and

(4) selecting an effective antibody according to the results of collating.

57. The method according to claim **56**, wherein the effective antibody is an antibody showing a specific reactivity in the step (2) or an antibody equivalent thereto.

58. The method according to claim **56**, wherein the certain disease is a disease in which a cell surface antigen selected from the group consisting of HER1, HER2, CD46, ITGA3, ICAM1, ALCAM, CD147, IgSF4, BCAM, C1qR, CD44, CD73, LAR, EpCAM and HGFR is an indicator.

59. The method according to claim **56**, wherein the panel displays two or more antibodies selected from the group consisting of 048-006 antibody, 057-091 antibody, 059-152 antibody, 048-040 antibody, 054-101 antibody, 055-147 antibody, 059-173 antibody, 067-149 antibody, 067-176 antibody, 015-126 antibody, 015-044 antibody, 015-102 antibody, 015-136 antibody, 015-143 antibody, 015-209 antibody, 039-016 antibody, 053-216 antibody, 075-024 antibody, 075-110 antibody, 086-032 antibody, 086-035 antibody, 086-036 antibody, 086-061 antibody, 086-138 antibody, 086-182 antibody, 035-224 antibody, 045-011 antibody, 051-144 antibody, 052-053 antibody, 052-073 antibody, 053-049 antibody, 3172-120 antibody, 066-069 antibody, 015-003 antibody, 064-002 antibody, 064-006 antibody, 064-012a antibody, 064-012b antibody, 064-014 antibody, 064-054 antibody, 064-085 antibody, 064-093 antibody, 064-116 antibody, 065-183 antibody, 067-142 antibody, 068-007 antibody, 052-033 antibody, 053-042 antibody, 053-051 antibody, 053-059 antibody, 053-085 antibody, 035-234 antibody, 040-107 antibody, 041-118 antibody, 066-174 antibody, 083-040 antibody, 029-143 antibody, 045-134 antibody, 062-101 antibody, 062-109 antibody, 084-103 antibody, 052-274 antibody, 029-067 antibody, 083-131 antibody, 059-053 antibody, 064-003 antibody, 067-213 antibody, 067-153 antibody, 067-126 antibody, 067-133 antibody, 067-287 antibody, 064-044 antibody, 065-030 antibody, 065-358 antibody, 066-019 antibody, 079-085 antibody, 067-024 antibody and 076-048 antibody.

60. A method of selecting an optimum treatment method of a certain disease, the method comprising the following steps:

(1) preparing a panel displaying a reactivity between one or more antibodies selected from the group consisting of 048-006 antibody, 015-126 antibody, 067-133 antibody, 064-044 antibody, 076-048 antibody and 059-053 antibody, and a clinical cancer tissue of one or more diseases selected from the group consisting of squamous carcinoma, adenosquamous carcinoma, alveolar adenocarcinoma, adenocarcinoma, and large cell carcinoma, and a cell or tissue separated from a subject;

(2) examining a reactivity between the cell or the tissue and each antibody displayed on the panel;

(3) collating the results in the step (2) with the panel, and

(4) selecting an effective antibody according to the results of collating.

61. The method according to claim **60**, wherein the effective antibody is an antibody showing a specific reactivity in the step (2) or an antibody equivalent thereto.

62. The method according to claim **60**, wherein the certain disease is a disease selected from the group consisting of squamous carcinoma, adenosquamous carcinoma, alveolar adenocarcinoma, adenocarcinoma, and large cell carcinoma.

63-85. (canceled)

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