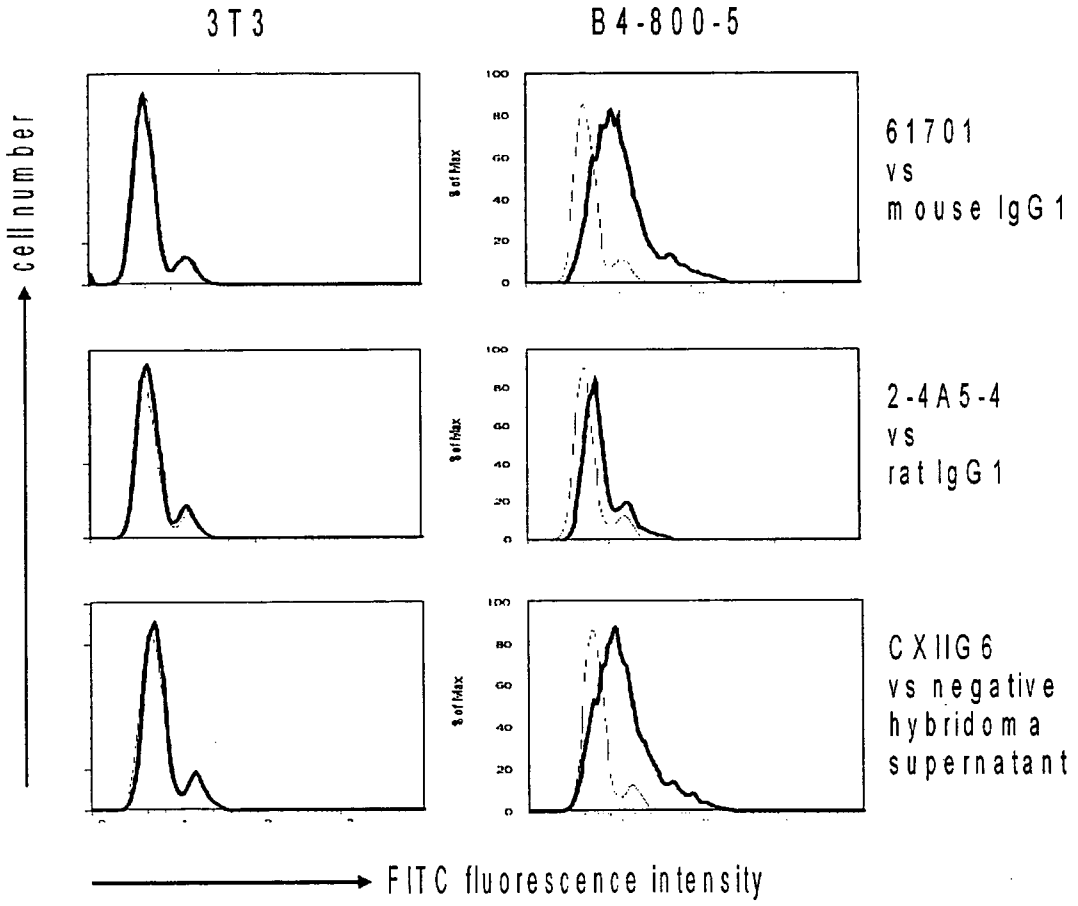

3T3
B4-800-5
cell number
% of Max
61701
vs
mouse IgG1
2-4A5-4
vs
rat IgG1
CXIIG6
vs negative
hybridoma
supernatant
FITC fluorescence intensity

Fig. 1

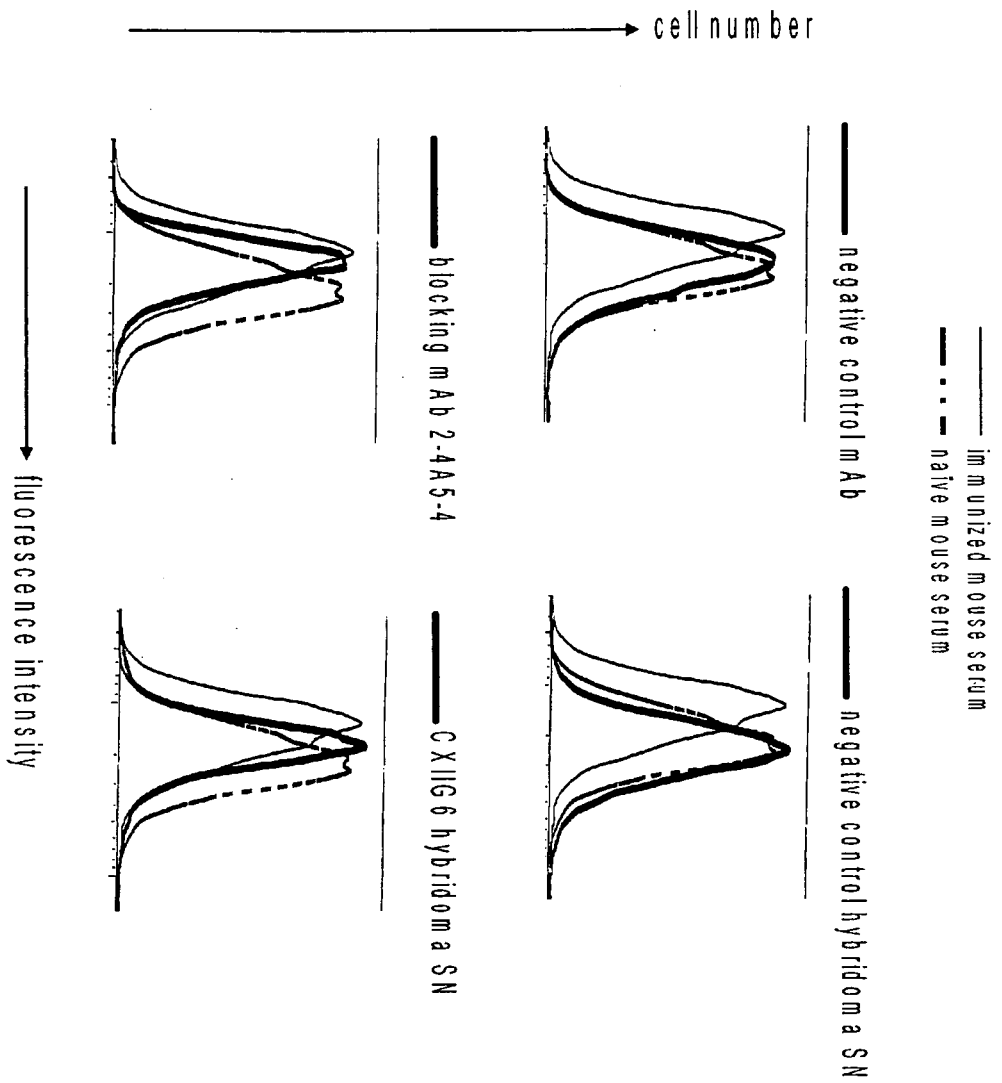

cell number
immunized mouse serum
naive mouse serum
negative control mAb
negative control hybridoma SN
blocking mAb 2-4A5-4
CXIIG6 hybridoma SN
fluorescence intensity

Fig. 2

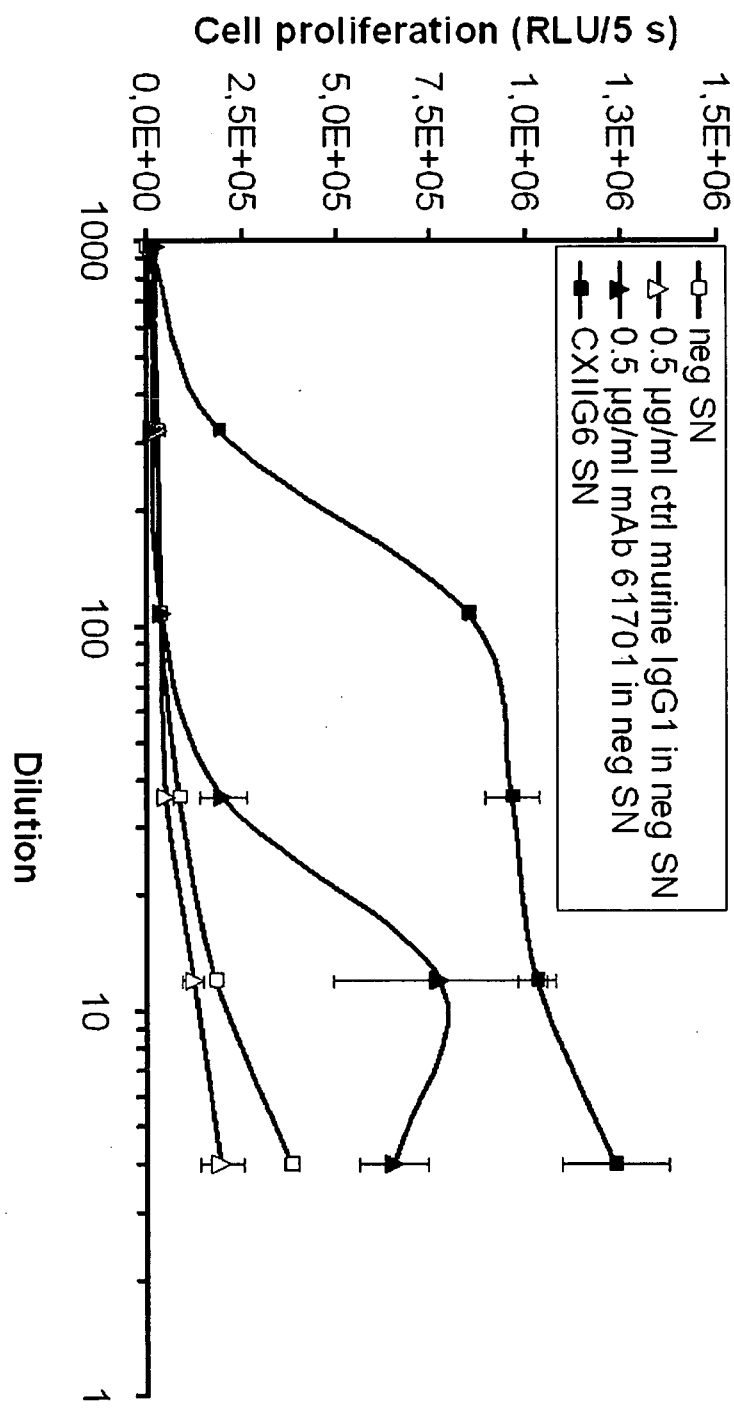

Cell proliferation (RLU/5 s)
0,0E+00
2,5E+05
5,0E+05
7,5E+05
1,0E+06
1,3E+06
1,5E+06
1000
100
10
1
Dilution
neg SN
0.5 µg/ml ctrl murine IgG1 in neg SN
0.5 µg/ml mAb 61701 in neg SN
CXIIG6 SN

Fig. 3

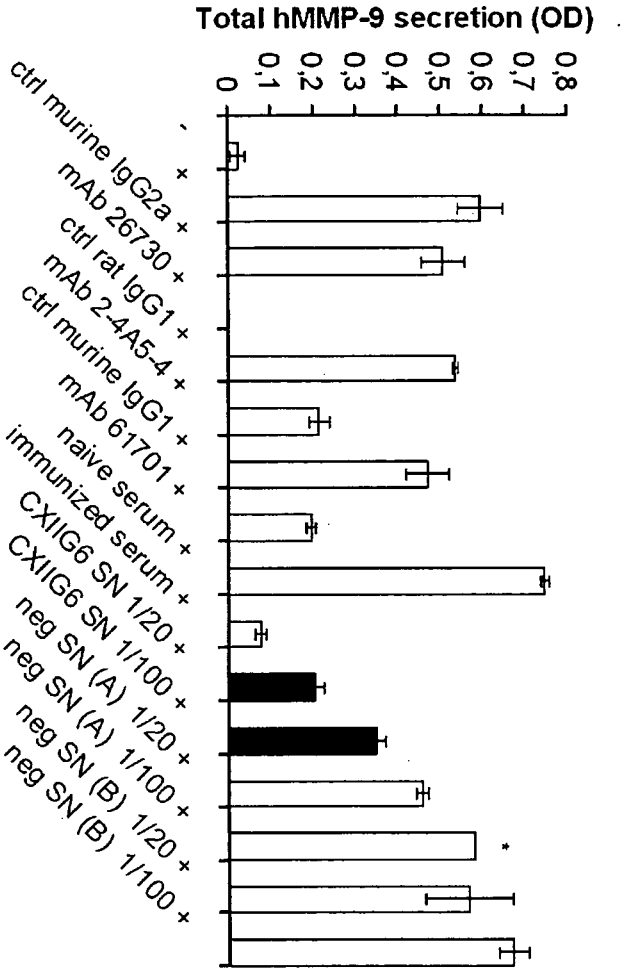

Total hMMP-9 secretion (OD)
0
0,1
0,2
0,3
0,4
0,5
0,6
0,7
0,8
-
ctrl murine IgG2a +
mAb 26730 +
ctrl rat IgG1 +
mAb 2-4A5-4 +
ctrl murine IgG1 +
mAb 61701 +
naive serum +
immunized serum +
CXIIG6 SN 1/20 +
CXIIG6 SN 1/100 +
neg SN (A) 1/20 +
neg SN (A) 1/100 +
neg SN (B) 1/20 +
neg SN (B) 1/100 +

Fig. 4

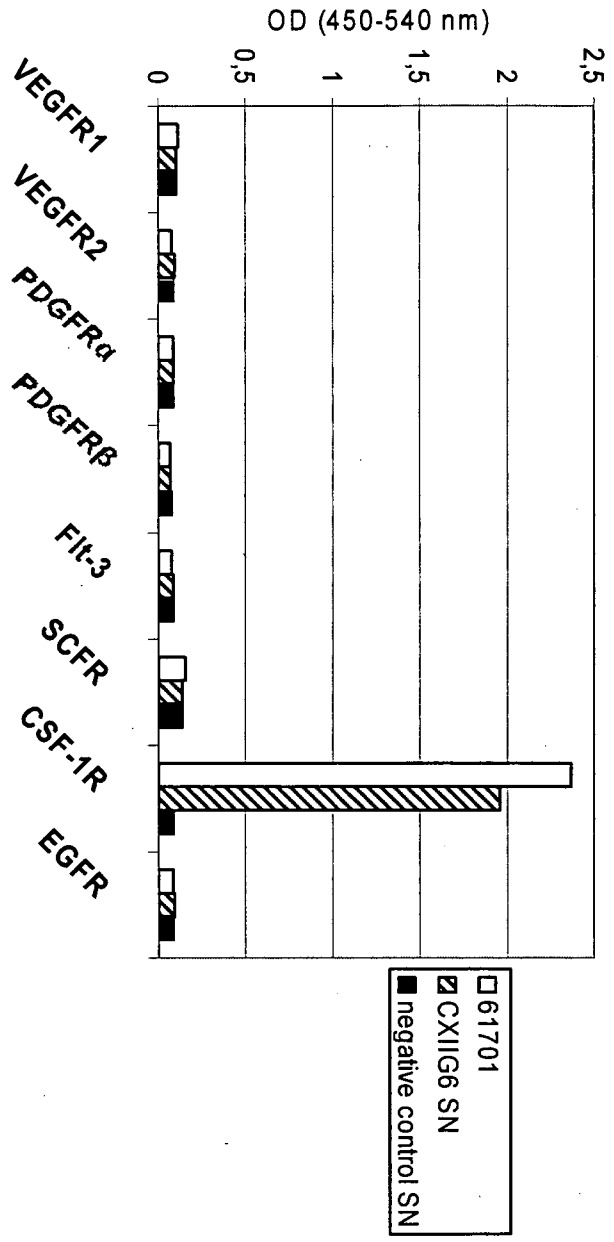

OD (450-540 nm)
0
0,5
1
1,5
2
2,5
VEGFR1
VEGFR2
PDGFRα
PDGFRβ
Flt-3
SCFR
CSF-1R
EGFR
61701
CXIIG6 SN
negative control SN

Fig. 5

```
     SfiI
GGCCCAGCCGGCCCAGTGACAGACACAGACATAGAACATTCACGATGTACTTGGGACTGA 60
                                                M  Y  L  G  L  N
ACTATGTATTCATAGTTTTTCTCCTAAATGGTGTCCAGAGTGAAGTGAAGCTTGAGGAGT 120
  Y  V  F  I  V  F  L  L  N  G  V  Q  S  E  V  K  L  E  E  S
CTGGAGGAGGCTTGGTGCAGCCTGGAGGATCCATGAAACTCTCTTGTGCTGCCTCTGGAT 180
  G  G  G  L  V  Q  P  G  G  S  M  K  L  S  C  A  A  S  G  F
TCACTTTTAGTGACGCCTGGATGGACTGGGTCCGCCAGTCTCCAGAGATGGGACTTGAGT 240
  T  F  S  D  A  W  M  D  W  V  R  Q  S  P  E  M  G  L  E  W
GGGTTGCTGAAATTAGAAGCAAAGCTAATAATCATGCAACATTCTATGCTGAGTCTGTGA 300
  V  A  E  I  R  S  K  A  N  N  N  H  A  T  F  Y  A  E  S  V  K
AAGGGAGGTTCACCATCTCAAGAGATGATTCCAAAAGTAGTGTCTACCTGCAAATGAACA 360
  G  R  F  T  I  S  R  D  D  S  K  S  S  V  Y  L  Q  M  N  S
GCTTAAGACCTGAAGACACTGGCATTTATTACTGTACCAGGGTAAAGGTAGGCTTTGACA 420
  L  R  P  E  D  T  G  I  Y  Y  C  T  R  V  K  V  G  F  D  N
ACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCAGCCAAAACAACAGCCCCATCGGTCT 480
  W  G  Q  G  T  T  L  T  V  S  S  A  K  T  T  A  P  S  V  Y
ATCCACTGGCCCCTGTGTGTGGAGATACAACTGGCTCCTCGGTGACTCTAGGATGCCTGG 540
  P  L  A  P  V  C  G  D  T  T  G  S  S  V  T  L  G  C  L  V
TCAAGGGTTATTTCCCTGAGCCAGTGACCTTGACCTGGAACTCTGGATCCCTGTCCAGTG 600
  K  G  Y  F  P  E  P  V  T  L  T  W  N  S  G  S  L  S  S  G
GTGTGCACACCTTCCCAGCTGTCCTGCAGTCTGACCTCTACACCCTCAGCAGCTCAGTGA 660
  V  H  T  F  P  A  V  L  Q  S  D  L  Y  T  L  S  S  S  V  T
       XhoI
CTGTAACCTCGAGCACCTGGCCCAGCCAGTCCATCACCTGCAATGTGGCCCACCCGGCAA 720
  V  T  S  S  T  W  P  S  Q  S  I  T  C  N  V  A  H  P  A  S
GCAGCACCAAGGTGGACAAGAAAATTGAGCCCAGAGGGCCCACAATCAAGCCCTGTCCTC 780
  S  T  K  V  D  K  K  I  E  P  R  G  P  T  I  K  P  C  P  P
CATGCAAATGCCCAGCACCTAACCTCTTGGGTGGACCATCCGTCTTCATCTTCCCTCCAA 840
  C  K  C  P  A  P  N  L  L  G  G  P  S  V  F  I  F  P  P  K
AGATCAAGGATGTACTCATGATCTCCCTGAGCCCCATAGTCACATGTGTGGTGGTGGATG 900
  I  K  D  V  L  M  I  S  L  S  P  I  V  T  C  V  V  V  D  V
TGAGCGAGGATGACCCAGATGTCCAGATCAGCTGGTTTGTGAACAACGTGGAAGTACACA 960
  S  E  D  D  P  D  V  Q  I  S  W  F  V  N  N  V  E  V  H  T
CAGCTCAGACACAAACCCATAGAGAGGATTACAACAGTACTCTCCGGGTGGTCAGTGCCC 1020
  A  Q  T  Q  T  H  R  E  D  Y  N  S  T  L  R  V  V  S  A  L
TCCCCATCCAGCACCAGGACTGGATGAGTGGCAAGGAGTTCAAATGCAAGGTCAACAACA 1080
  P  I  Q  H  Q  D  W  M  S  G  K  E  F  K  C  K  V  N  N  K
AAGACCTCCCAGCGCCCATCGAGAGAACCATCTCAAAACCCAAAGGGTCAGTAAGAGCTC 1140
  D  L  P  A  P  I  E  R  T  I  S  K  P  K  G  S  V  R  A  P
CACAGGTATATGTCTTGCCTCCACCAGAAGAAGAGATGACTAAGAAACAGGTCACTCTGA 1200
  Q  V  Y  V  L  P  P  P  E  E  E  M  T  K  K  Q  V  T  L  T
CCTGCATGGTCACAGACTTCATGCCTGAAGACATTTACGTGGAGTGGACCAACAACGGGA 1260
  C  M  V  T  D  F  M  P  E  D  I  Y  V  E  W  T  N  N  G  K
AAACAGAGCTAAACTACAAGAACACTGAACCAGTCCTGGACTCTGATGGTTCTTACTTCA 1320
  T  E  L  N  Y  K  N  T  E  P  V  L  D  S  D  G  S  Y  F  M
TGTACAGCAAGCTGAGAGTGGAAAAGAAGAACTGGGTGGAAAGAAATAGCTACTCCTGTT 1380
  Y  S  K  L  R  V  E  K  K  N  W  V  E  R  N  S  Y  S  C  S
CAGTGGTCCACGAGGGTCTGCACAATCACCACACGACTAAGAGCTTCTCCCGGACTCCGG 1440
  V  V  H  E  G  L  H  N  H  H  T  T  K  S  F  S  R  T  P  G
                                                    NotI
GTAAATGAGCTCAGCACCCACAAAACTCTCAGGTCCAAAGAGACACCCACGCGGCCGC 1498
  K  *
```

Fig. 6

SfiI
*GGCCCAGCCGGCC*GGAGTCAGCCTCACACTGATCACACACAGACATGAGTGTGCCCACTC 60
M S V P T Q

AGGTCCTGGGGTTGCTGCTGCTGTGGCTTACAGATGCCAGATGTGACATCCAGATGACTC 120
V L G L L L L W L T D A R C **D I Q M T Q**

AGTCTCCAGCCTCCCTATCTGTATCTGTGGGAGAAACTGTCACCATCACATGTCGAGCAA 180
S P A S L S V S V G E T V T I T C R A S

GTGAGAATATTTACAGTAATTTAGCATGGTATCAGCAGAAACAGGGAAAATCTCCTCAGC 240
E N I Y S N L A W Y Q Q K Q G K S P Q L

TCCTGGTCCATGCTGCAACAAACTTAGCAGATGGTGTGCCATCAAGGTTCAGTGGCAGTG 300
L V H A A T N L A D G V P S R F S G S G

GATCAGGCACACAGTATTCCCTCAAGATCAACAGCCTGCAGTCTGAAGATTTTGGGAGTT 360
S G T Q Y S L K I N S L Q S E D F G S Y

ATTACTGTCAACATTTTTGGGGTACTCCTCGGACGTTCGGTGGAGGCACCAAGTTGGAAA 420
Y C Q H F W G T P R T F G G G T K L E I

TCAAACGGGCTGATGCTGCACCAACTGTATCCATCTTCCCACCATCCAGTGAGCAGTTAA 480
K R A D A A P T V S I F P P S S E Q L T

CATCTGGAGGTGCCTCAGTCGTGTGCTTCTTGAACAACTTCTACCCCAAAGACATCAATG 540
S G G A S V V C F L N N F Y P K D I N V

TCAAGTGGAAGATTGATGGCAGTGAACGACAAAATGGCGTCCTGAACAGTTGGACTGATC 600
K W K I D G S E R Q N G V L N S W T D Q

AGGACAGCAAAGACAGCACCTACAGCATGAGCAGCACCCTCACGTTGACCAAGGACGAGT 660
D S K D S T Y S M S S T L T L T K D E Y

ATGAACGACATAACAGCTATACCTGTGAGGCCACTCACAAGACATCAACTTCACCCATTG 720
E R H N S Y T C E A T H K T S T S P I V

TCAAGAGCTTCAACAGGAATGAGTGTTAGAGACAAAGGTCCTGAGACGCCACCACCAGCT 788
K S F N R N E C *

NotI
GCGGCCGC 788

Fig. 7

pTG17753

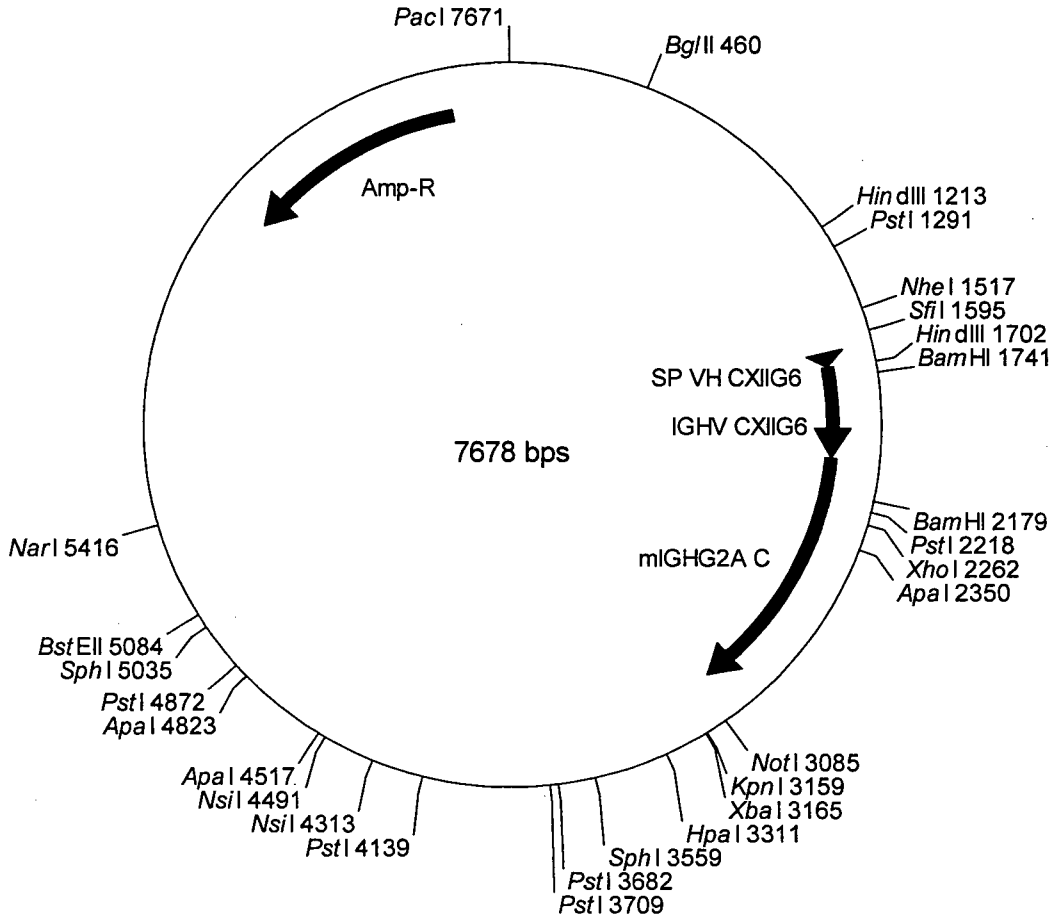


Fig. 8

pTG17727

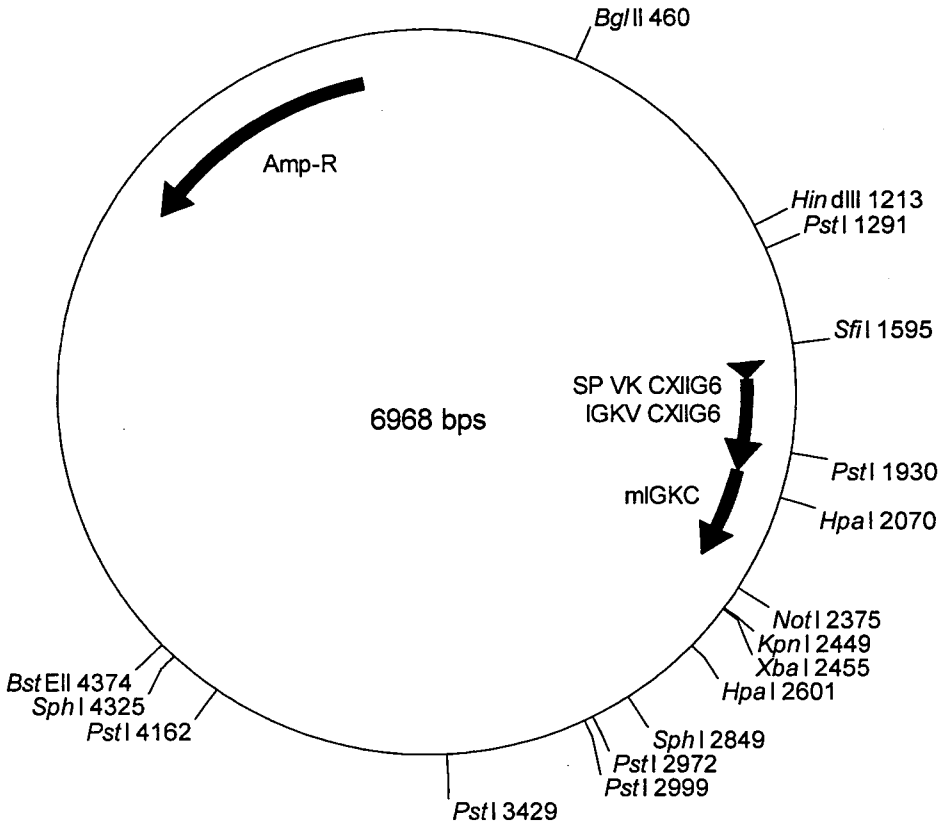


Fig. 9

pOptiVEC™

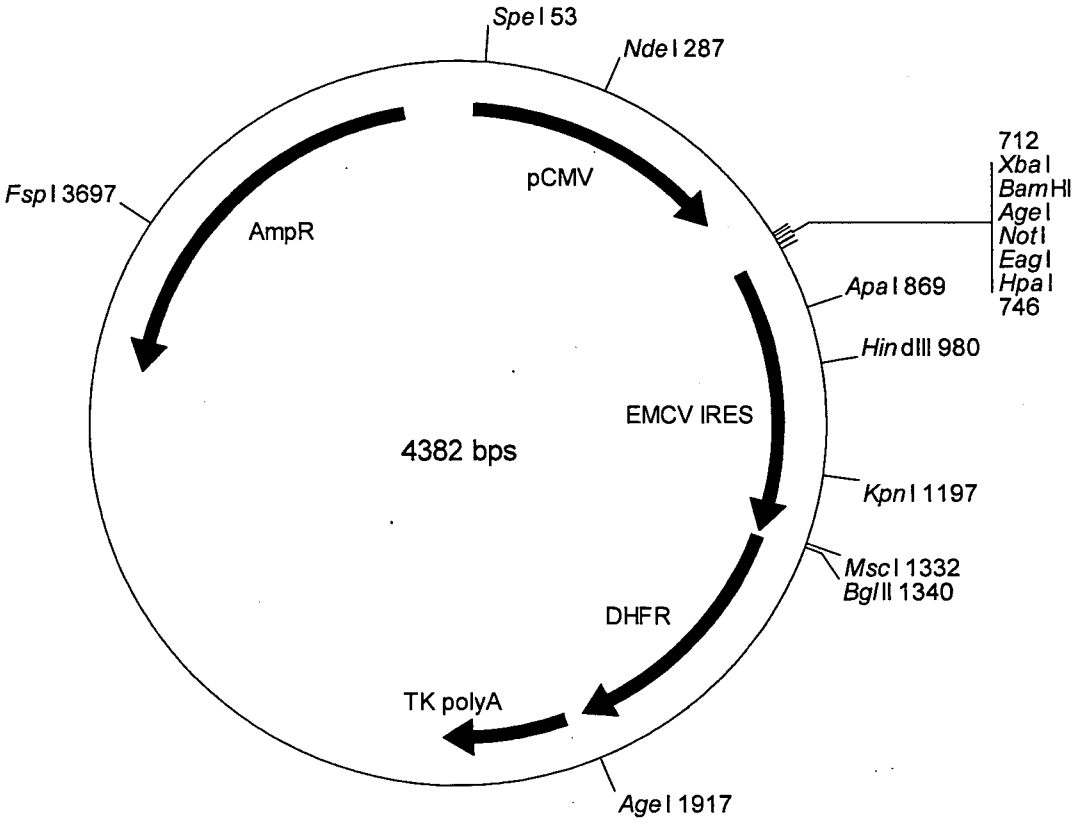


Fig. 10

pTG17895

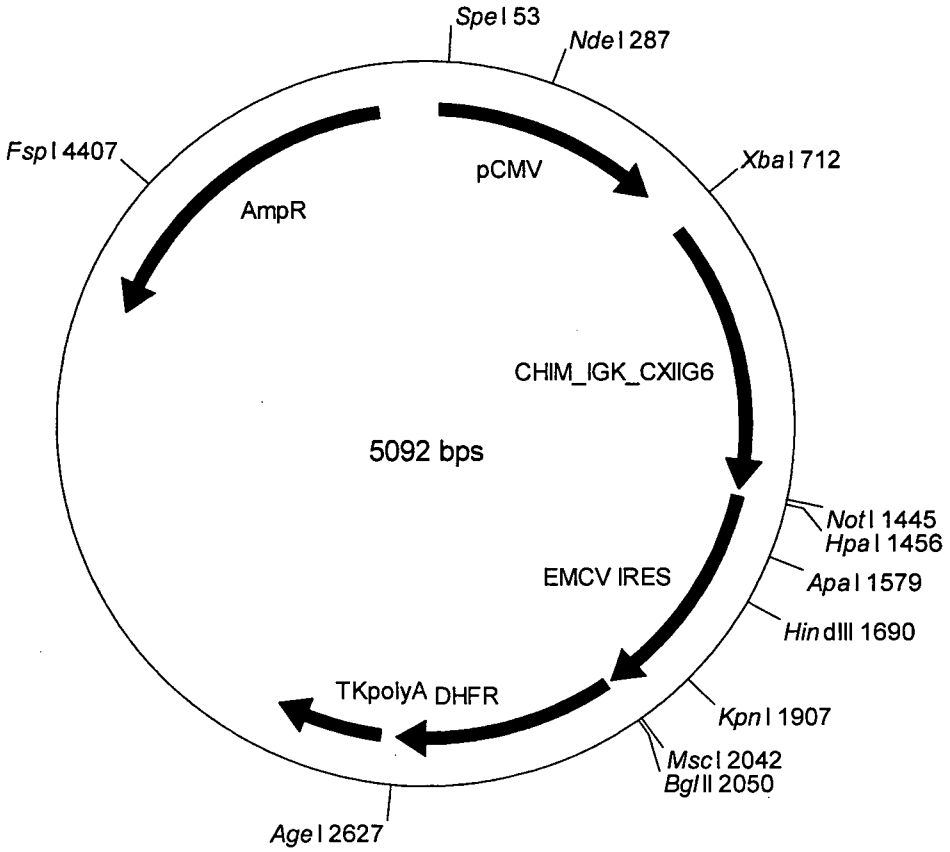


Fig. 11

pTG17812

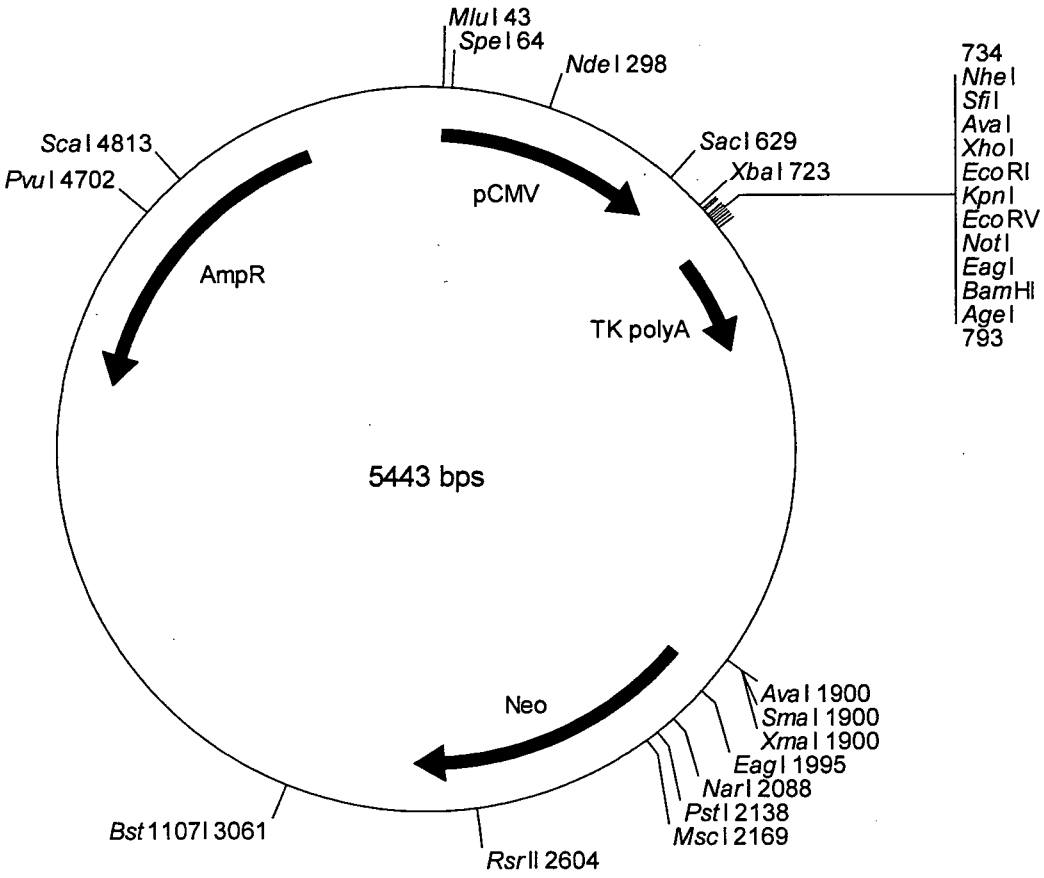


Fig. 12

pTG17868

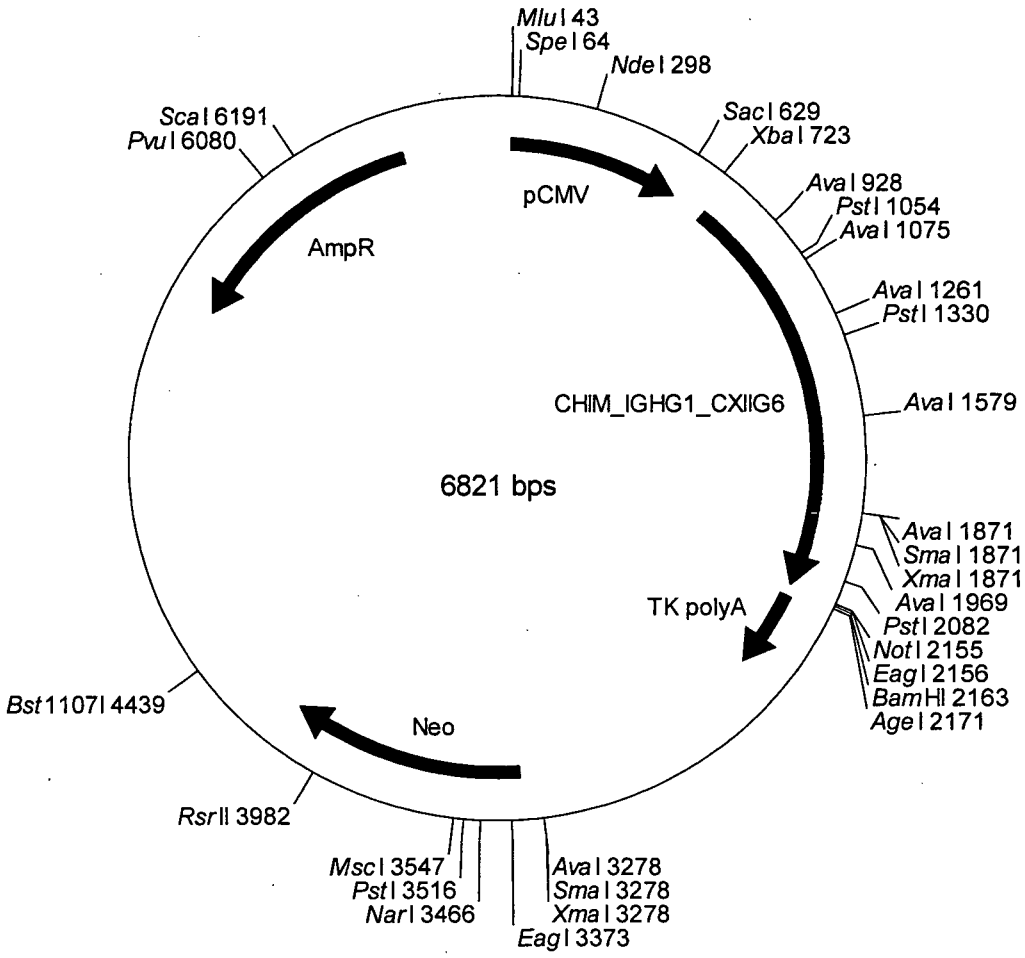


Fig. 13

pTG17869

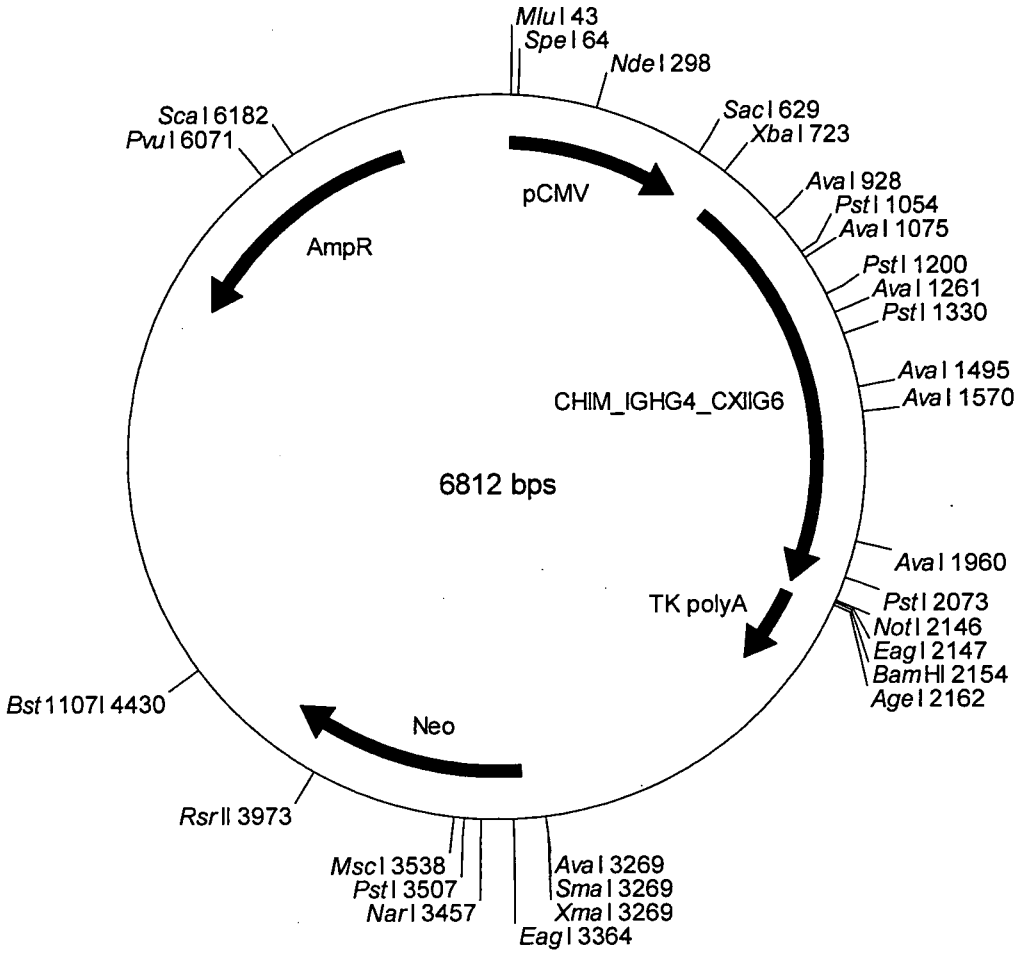


Fig. 14

		Substituted amino acids[a] in VL CXIIG																							
K1	pTG17896	A9S	V13A	E17D	T18R	Q40P	S43A	Q45K	V48L	H49Y	N53R	A55E	D56S	Q70D	S72T	K74T	N76S	S80P	G84A	S85T	G100Q
K2	pTG17897	A9S	V13A	E17D	T18R		S43A	Q45K	V48L	H49Y	N53R	A55E	D56S	Q70D	S72T	K74T	N76S		G84A	S85T	G100Q
K3	pTG17899	A9S	V13A	E17D	T18R		S43A	Q45K	V48L			A55E	D56S	Q70D	S72T	K74T	N76S		G84A	S85T	G100Q
K4	pTG17900	A9S		E17D	T18R		S43A	Q45K		H49Y	N53R	A55E	D56S	Q70D	S72T	K74T	N76S			S85T	G100Q
K5	pTG17901	A9S		E17D	T18R	Q40P	S43A	Q45K				A55E	D56S	Q70D	S72T	K74T	N76S	S80P		S85T	G100Q
K6	pTG17902	A9S		E17D	T18R		S43A	Q45K				A55E	D56S	Q70D	S72T	K74T	N76S			S85T	G100Q
K7	pTG17903	A9S		E17D	T18R		S43A	Q45K					D56S	Q70D			N76S				G100Q
K8	pTG17904			E17D												K74T	N76S	S80P			G100Q
K9	pTG17905	A9S	V13A	E17D	T18R		S43A	Q45K	V48L				D56S	Q70D	S72T	K74T	N76S		G84A	S85T	G100Q
K10	pTG17906	A9S		E17D	T18R	Q40P	S43A	Q45K					D56S	Q70D	S72T	K74T	N76S	S80P		S85T	G100Q
K11	pTG17907	A9S		E17D	T18R		S43A	Q45K					D56S	Q70D	S72T	K74T	N76S			S85T	G100Q
K12	pTG17947	A9S	V13A	E17D	T18R	Q40D										K74T	N76S	S80P			G100Q
K13	pTG17948	A9S	V13A	E17D	T18R	Q40D	S43A	Q45K	V48L				D56S	Q70D	S72T	K74T	N76S	S80P	G84A	S85T	G100Q
K14	pTG17949	A9S	V13A	E17D	T18R	Q40P										K74T	N76S	S80P			
K15	pTG17950	A9S	V13A	E17D	T18R	Q40P	S43A	Q45K	V48L				D56S	Q70D	S72T	K74T	N76S	S80P	G84A	S85T	G100Q

[a]amino acids in bold have a relative side-chain solvent-accessibility above 50 %, underlined above 25%

Fig. 15

		Substituted amino acids[a] in VH CXIIG6																					
H1	**pTG17870**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**	A49G	**E50R**	**F61E**	**E64A**	S79N	**V81L**	**R89K**	**P90T**	**G94A**	I95V	**T113L**	**L114V**
H2	**pTG17871**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**	A49G	**E50R**	**F61E**	**E64A**	S79N	**V81L**	**R89K**	**P90T**	**G94A**	I95V	**T113L**	
H3	**pTG17872**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**	A49G	**E50R**	**F61E**	**E64A**	S79N	**V81L**	**R89K**	**P90T**	**G94A**	I95V		**L114V**
H4	**pTG17873**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**	A49G	**E50R**		**E64A**	S79N	**V81L**	**R89K**		**G94A**	I95V	**T113L**	**L114V**
H5	**PTG17874**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**	A49G	**E50R**		**E64A**	S79N	**V81L**	**R89K**		**G94A**	I95V	**T113L**	
H6	**pTG17875**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**	A49G	**E50R**		**E64A**	S79N	**V81L**	**R89K**		**G94A**	I95V		**L114V**
H7	**pTG17883**	**K3Q**	**E5V**		**K19R**	S40A	**E42G**	**M43K**				**E64A**	S79N		**R89K**			I95V	**T113L**	**L114V**
H8	**pTG17884**	**K3Q**	**E5V**		**K19R**	S40A	**E42G**	**M43K**				**E64A**	S79N		**R89K**			I95V	**T113L**	
H9	**pTG17885**	**K3Q**	**E5V**		**K19R**	S40A	**E42G**	**M43K**				**E64A**	S79N		**R89K**			I95V		**L114V**
H10	**pTG17886**	**K3Q**	**E5V**		**K19R**		**E42G**	**M43K**				**E64A**			**R89K**				**T113L**	**L114V**
H11	**pTG17887**	**K3Q**	**E5V**		**K19R**		**E42G**	**M43K**				**E64A**			**R89K**				**T113L**	
H12	**pTG17888**	**K3Q**	**E5V**		**K19R**		**E42G**	**M43K**				**E64A**			**R89K**					**L114V**
H13	**pTG17889**				**K19R**										**R89K**				**T113L**	**L114V**
H14	**pTG17890**				**K19R**										**R89K**				**T113L**	
H15	**pTG17891**				**K19R**										**R89K**					**L114V**
H16	**pTG17892**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**	A49G			**E64A**	S79N	**V81L**	**R89K**		**G94A**	I95V	**T113L**	**L114V**
H17	**pTG17893**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**	A49G			**E64A**	S79N	**V81L**	**R89K**		**G94A**	I95V	**T113L**	
H18	**pTG17894**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**	A49G			**E64A**	S79N	**V81L**	**R89K**		**G94A**	I95V		**L114V**
H19	**pTG17943**	**K3Q**	**E5V**	**M18L**												**P90A**				
H20	**pTG17944**	**K3Q**	**E5V**	**M18L**	**K19R**		**E42G**	**M43K**				**E64A**			**R89K**				**T113L**	**L114V**
H21	**pTG17945**	**K3Q**	**E5V**	**M18L**	**K19R**		**E42G**	**M43K**				**E64A**			**R89K**	**P90A**			**T113L**	**L114V**
H22	**pTG17946**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**				**E64A**			**R89K**	**P90A**		I95V	**T113L**	**L114V**
H23	**pTG17968**	**K3Q**	**E5V**	**M18L**	**K19R**		**E42G**	**M43K**							**R89K**				**T113L**	**L114V**
H24	**pTG17969**	**K3Q**	**E5V**	**M18L**	**K19R**		**E42G**	**M43K**							**R89K**	**P90A**			**T113L**	**L114V**
H25	**pTG17970**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**							**R89K**	**P90A**		I95V	**T113L**	**L114V**
H26	**pTG17985**	**K3Q**	**E5V**	**M18L**	**K19R**		**E42G**	**M43K**							**R89K**	**P90T**			**T113L**	**L114V**
H27	**pTG17986**	**K3Q**	**E5V**	**M18L**	**K19R**	S40A	**E42G**	**M43K**							**R89K**	**P90T**		I95V	**T113L**	**L114V**

[a]amino acids in bold have a relative side-chain solvent-accessibility above 50 %, underlined above 25%

Fig. 16

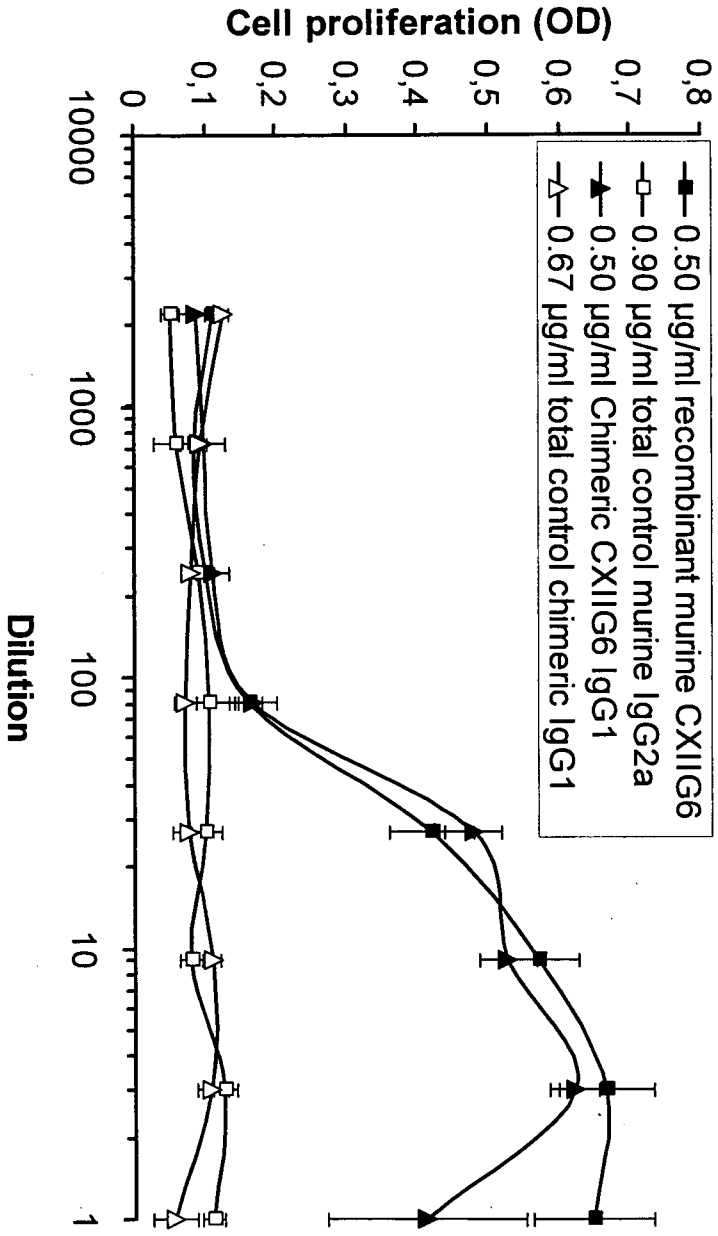

Cell proliferation (OD)
0
0,1
0,2
0,3
0,4
0,5
0,6
0,7
0,8
Dilution
10000
1000
100
10
1
0.50 µg/ml recombinant murine CXIIG6
0.90 µg/ml total control murine IgG2a
0.50 µg/ml Chimeric CXIIG6 IgG1
0.67 µg/ml total control chimeric IgG1

Fig. 17

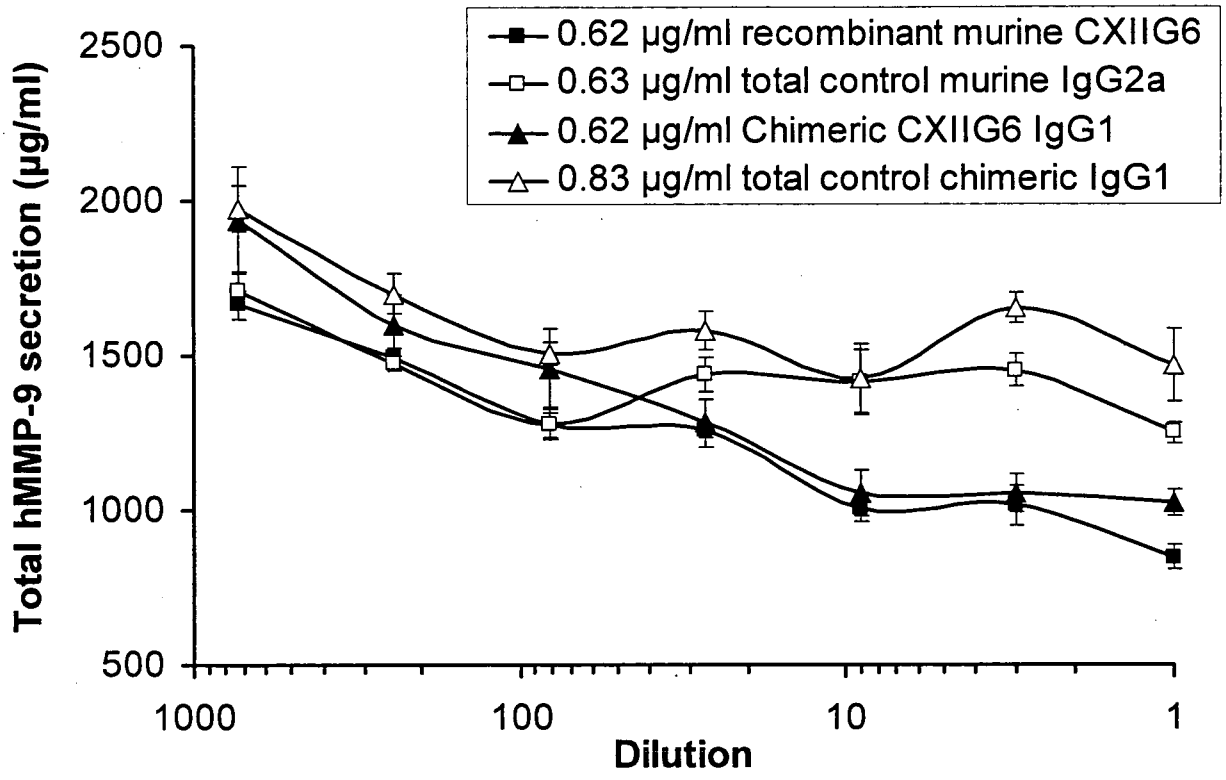

0.62 µg/ml recombinant murine CXIIG6
0.63 µg/ml total control murine IgG2a
0.62 µg/ml Chimeric CXIIG6 IgG1
0.83 µg/ml total control chimeric IgG1
Total hMMP-9 secretion (µg/ml)
2500
2000
1500
1000
500
1000
100
10
1
Dilution

Fig. 18