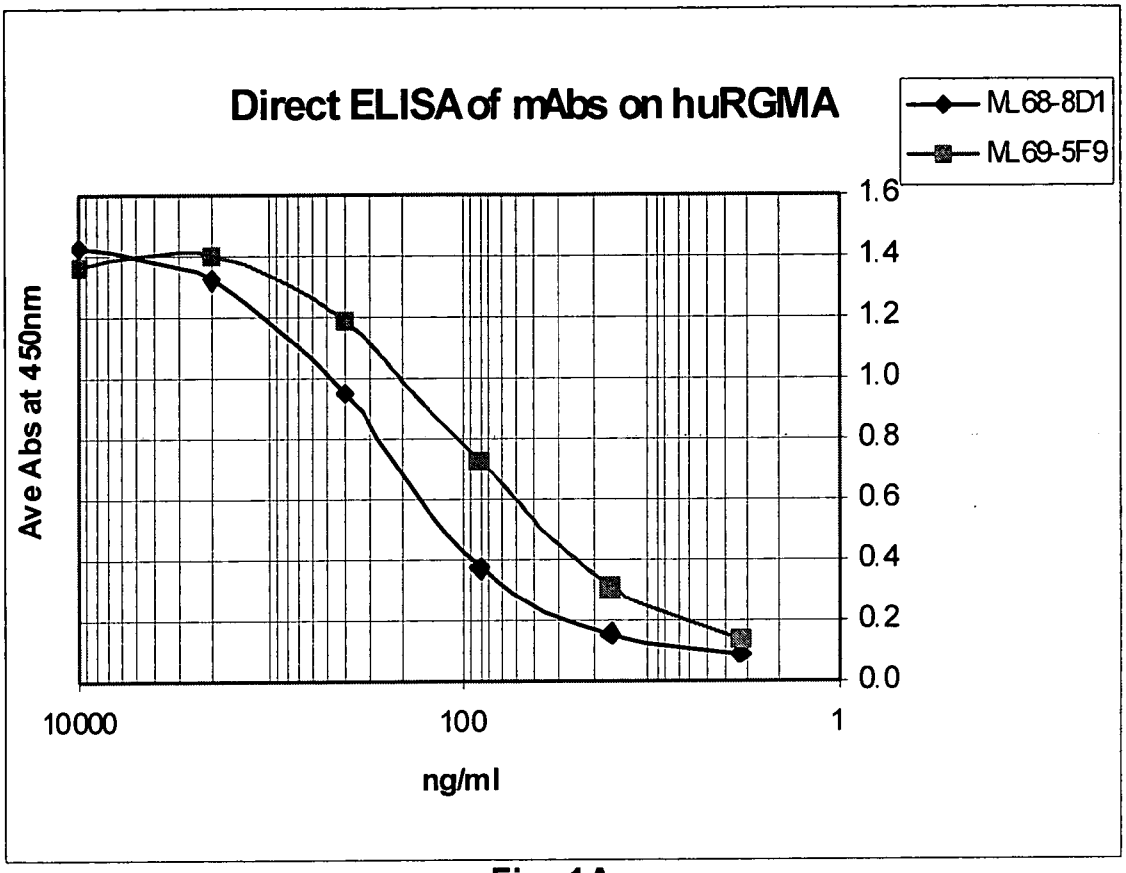

Direct ELISA of mAbs on huRGMA
ML68-8D1
ML69-5F9
Ave Abs at 450nm
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
10000
100
1
ng/ml

Fig. 1A

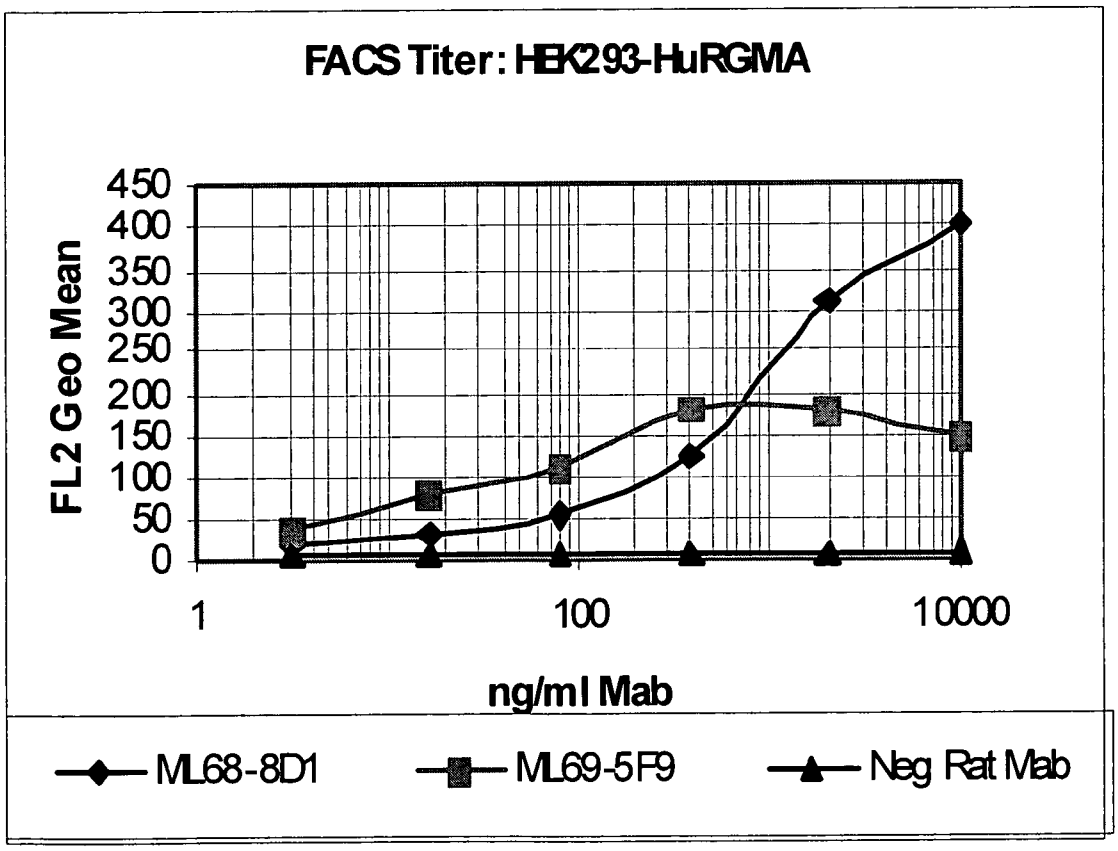

FACS Titer: HEK293-HuRGMA
FL2 Geo Mean
450
400
350
300
250
200
150
100
50
0
1
100
10000
ng/ml Mab
ML68-8D1
ML69-5F9
Neg Rat Mab

Fig. 1B

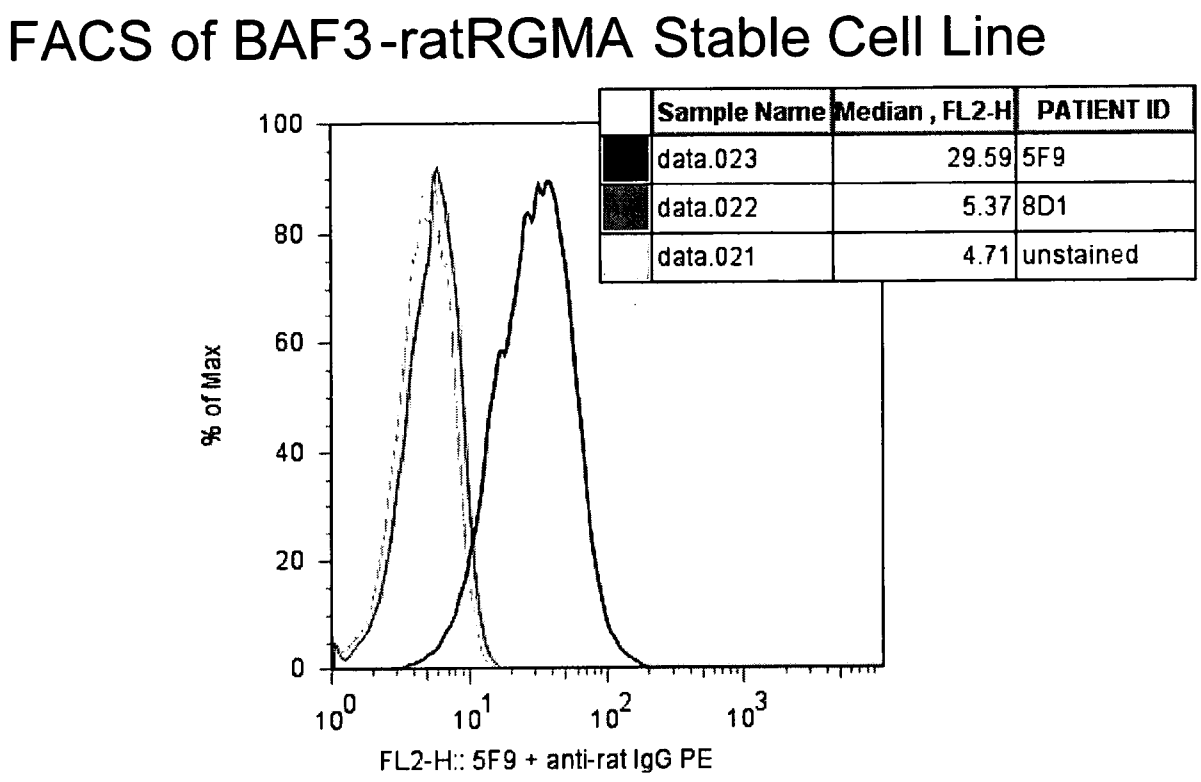

FACS of BAF3-ratRGMA Stable Cell Line
Sample Name
Median , FL2-H
PATIENT ID
data.023
29.59
5F9
data.022
5.37
8D1
data.021
4.71
unstained
% of Max
100
80
60
40
20
0
10^0
10^1
10^2
10^3
FL2-H:: 5F9 + anti-rat IgG PE

Fig. 1C

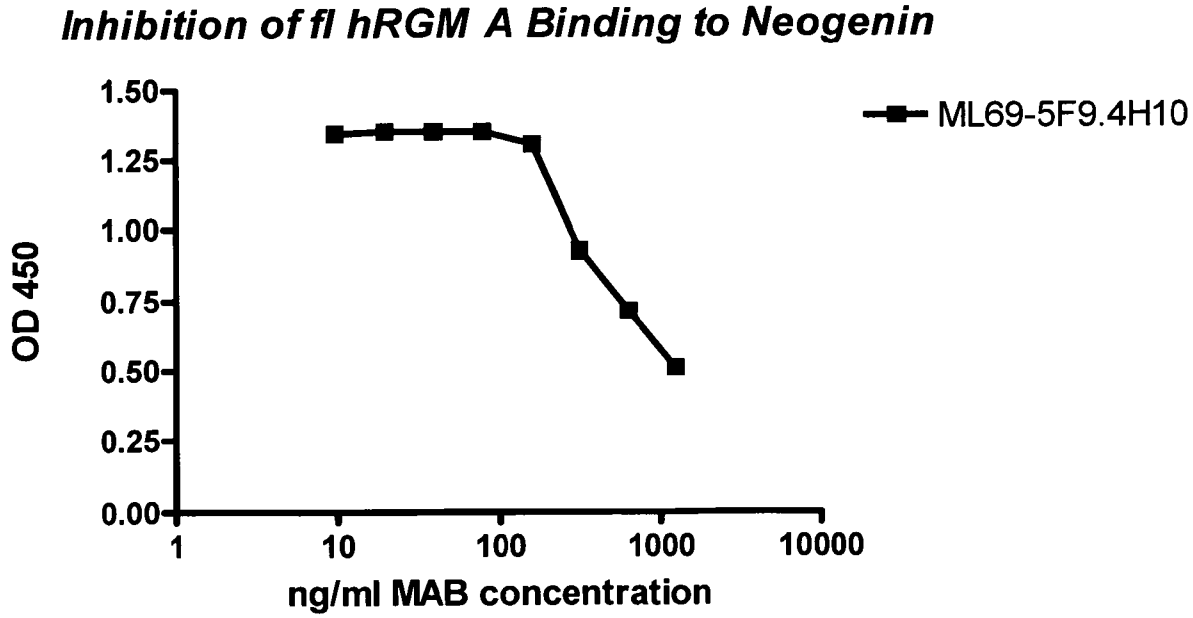

Inhibition of fl hRGM A Binding to Neogenin
ML69-5F9.4H10
OD 450
1.50
1.25
1.00
0.75
0.50
0.25
0.00
1
10
100
1000
10000
ng/ml MAB concentration

Fig. 2

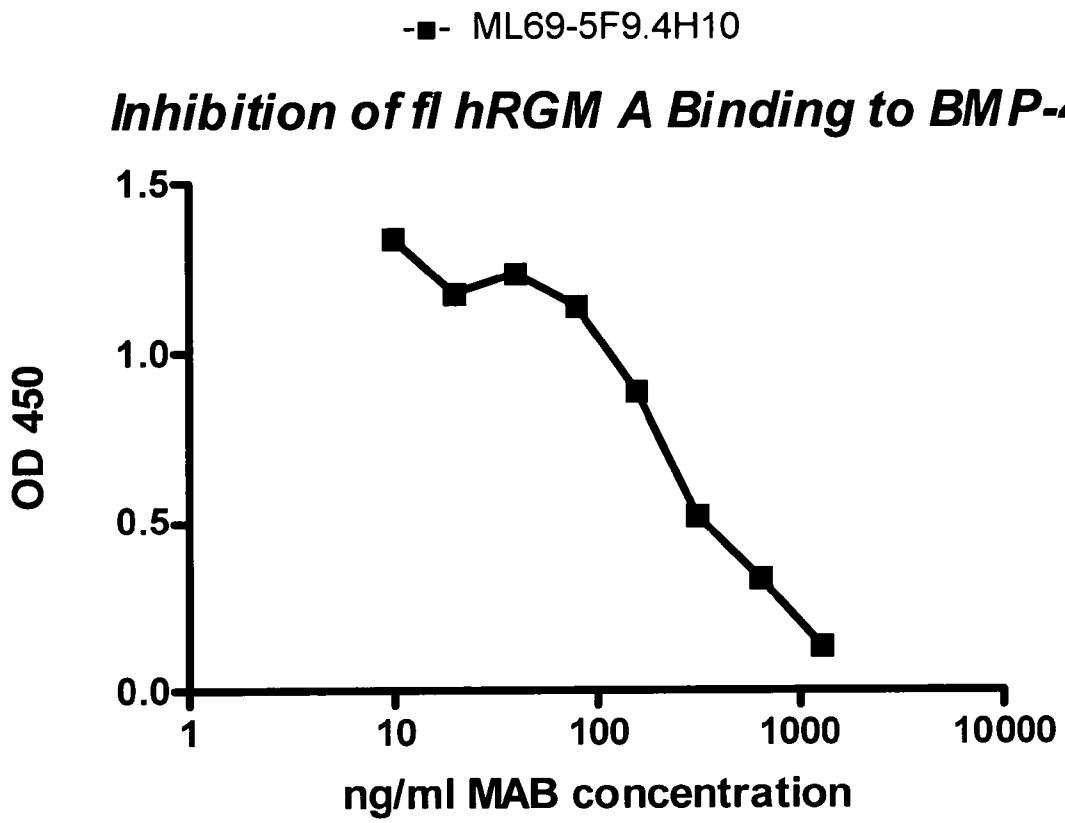

-■- ML69-5F9.4H10
Inhibition of fl hRGM A Binding to BMP-4
1.5
1.0
0.5
0.0
OD 450
1
10
100
1000
10000
ng/ml MAB concentration

Fig. 3

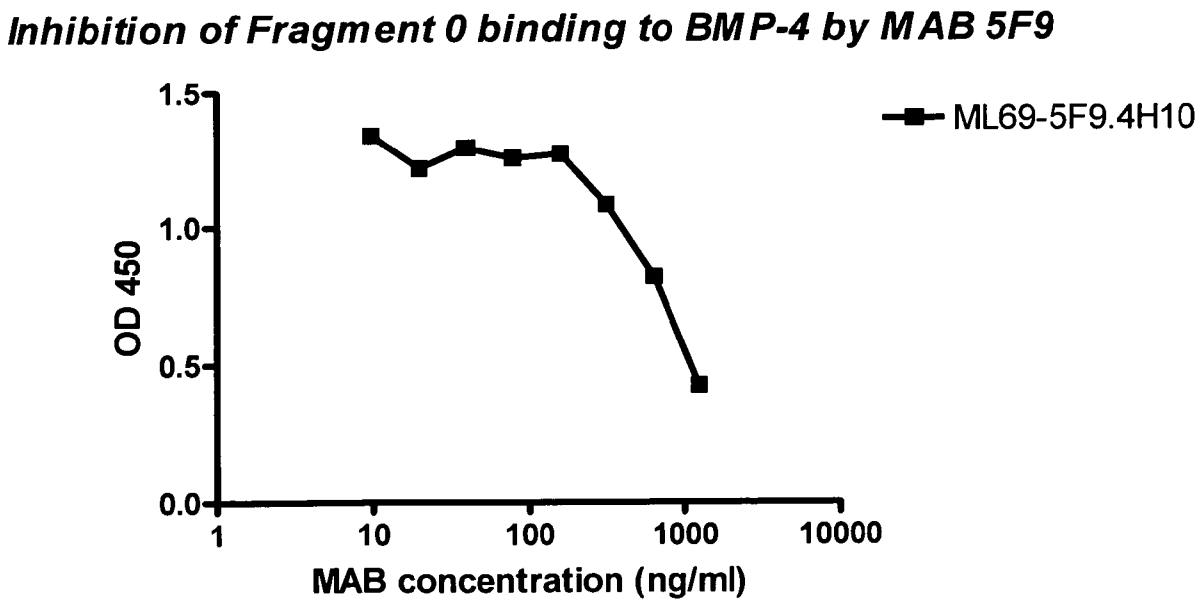

Inhibition of Fragment 0 binding to BMP-4 by MAB 5F9
ML69-5F9.4H10
1.5
1.0
0.5
0.0
OD 450
1
10
100
1000
10000
MAB concentration (ng/ml)

Fig. 4

Inhibition of binding of fc-conjugated, full length hRGM A to BMP-2

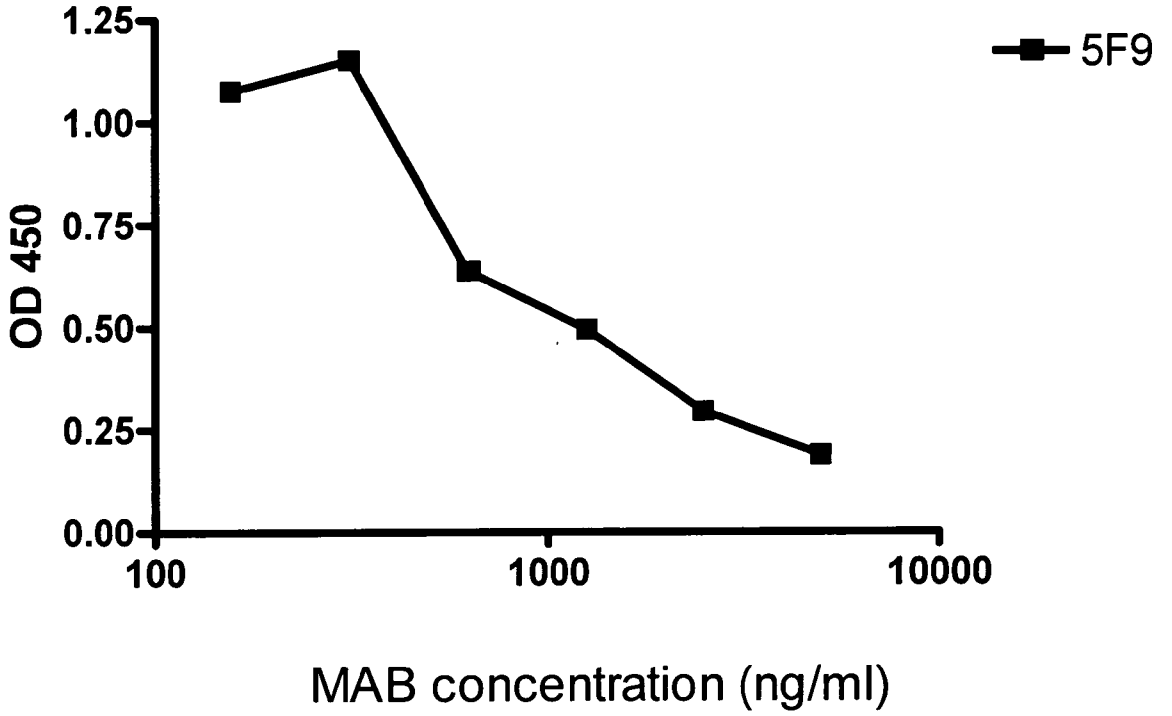


Fig. 5

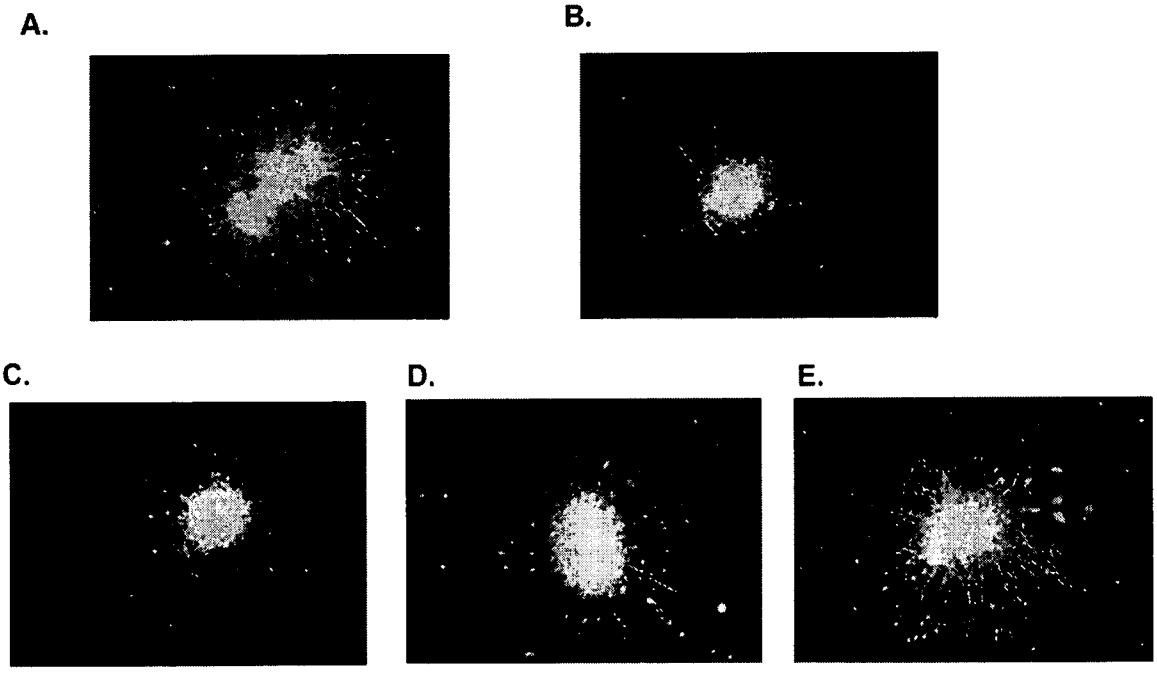


Fig. 6

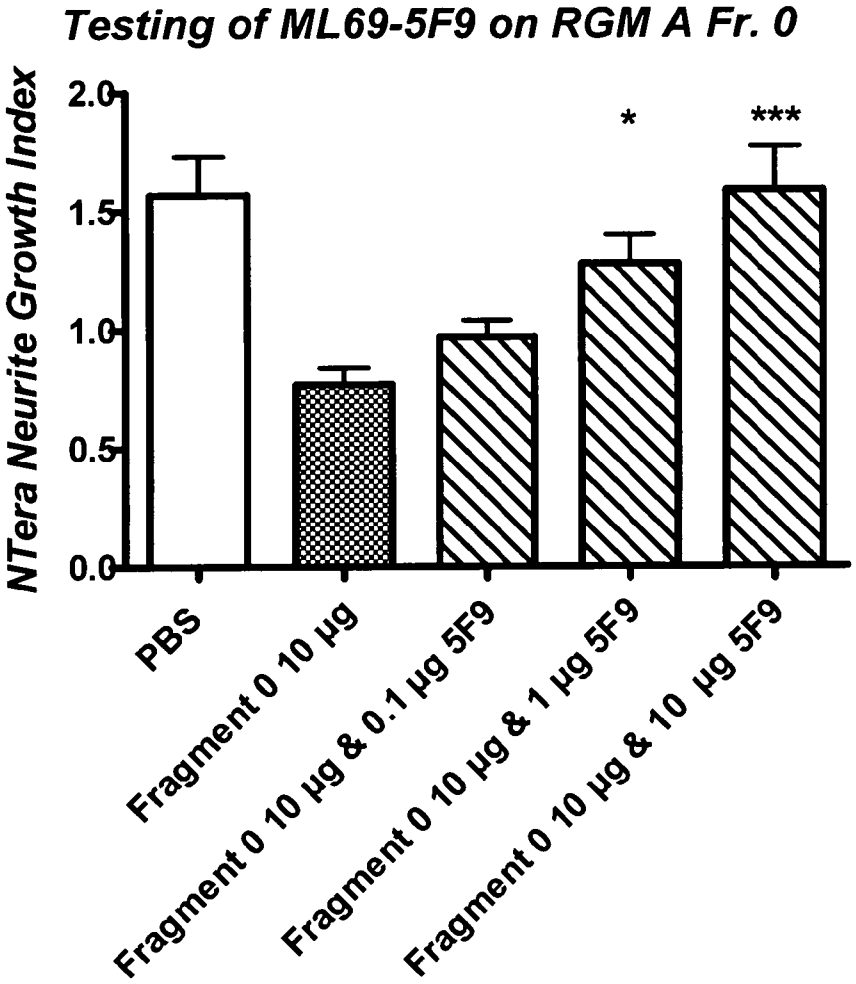

Testing of ML69-5F9 on RGM A Fr. 0
NTera Neurite Growth Index
2.0
1.5
1.0
0.5
0.0
*
***
PBS
Fragment 0 10 µg
Fragment 0 10 µg & 0.1 µg 5F9
Fragment 0 10 µg & 1 µg 5F9
Fragment 0 10 µg & 10 µg 5F9

Fig. 7

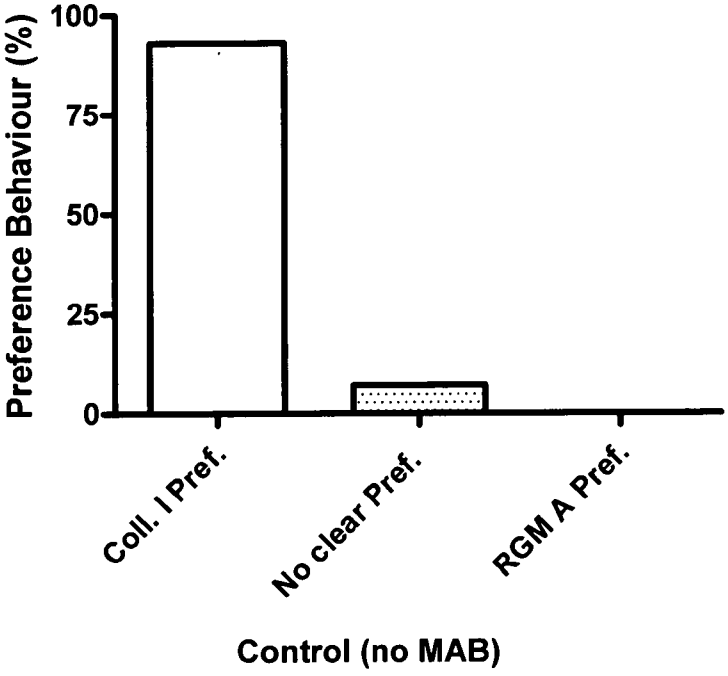

Preference Behaviour (%)
100
75
50
25
0
Coll. I Pref.
No clear Pref.
RGM A Pref.
Control (no MAB)

Fig. 8A

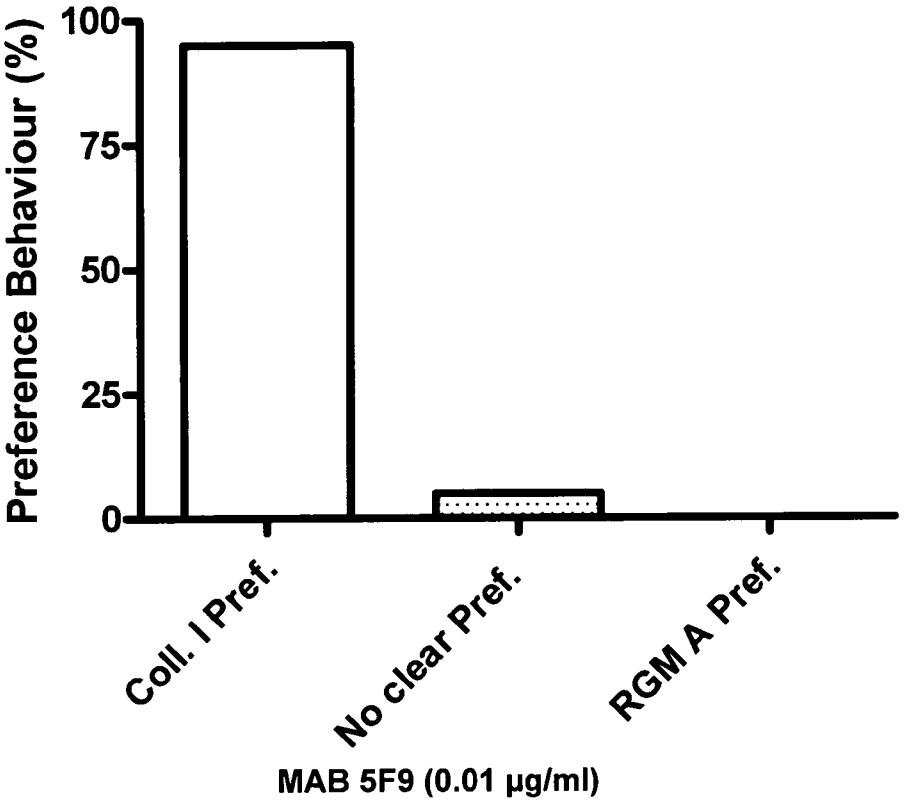

Preference Behaviour (%)
100
75
50
25
0
Coll. I Pref.
No clear Pref.
RGM A Pref.
MAB 5F9 (0.01 µg/ml)

Fig. 8B

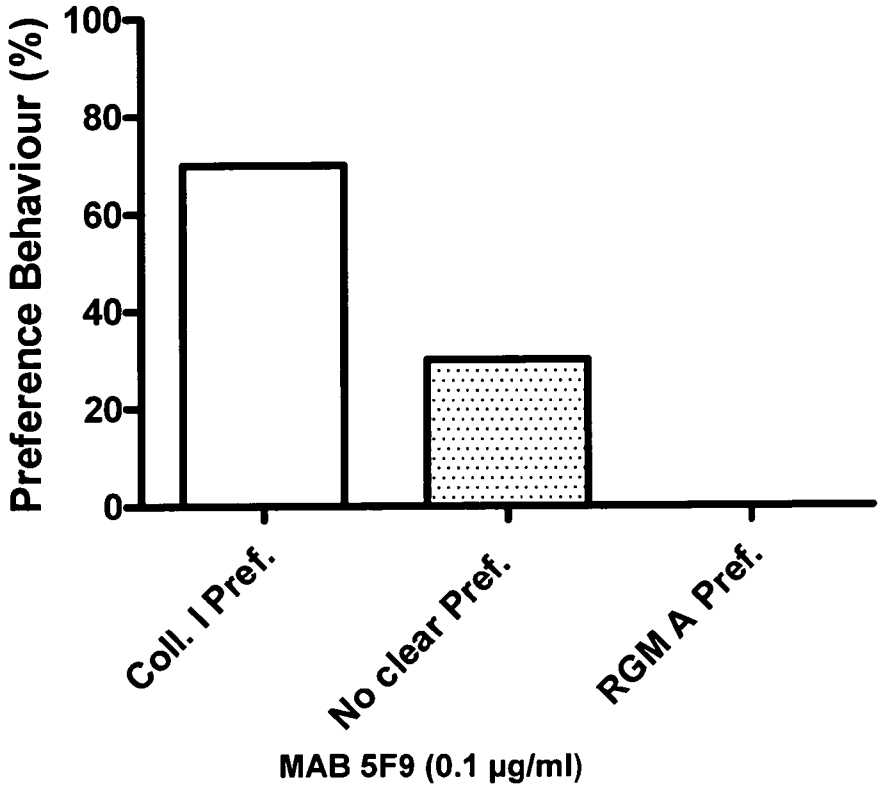

Preference Behaviour (%)
100
80
60
40
20
0
Coll. I Pref.
No clear Pref.
RGM A Pref.
MAB 5F9 (0.1 µg/ml)

Fig. 8C

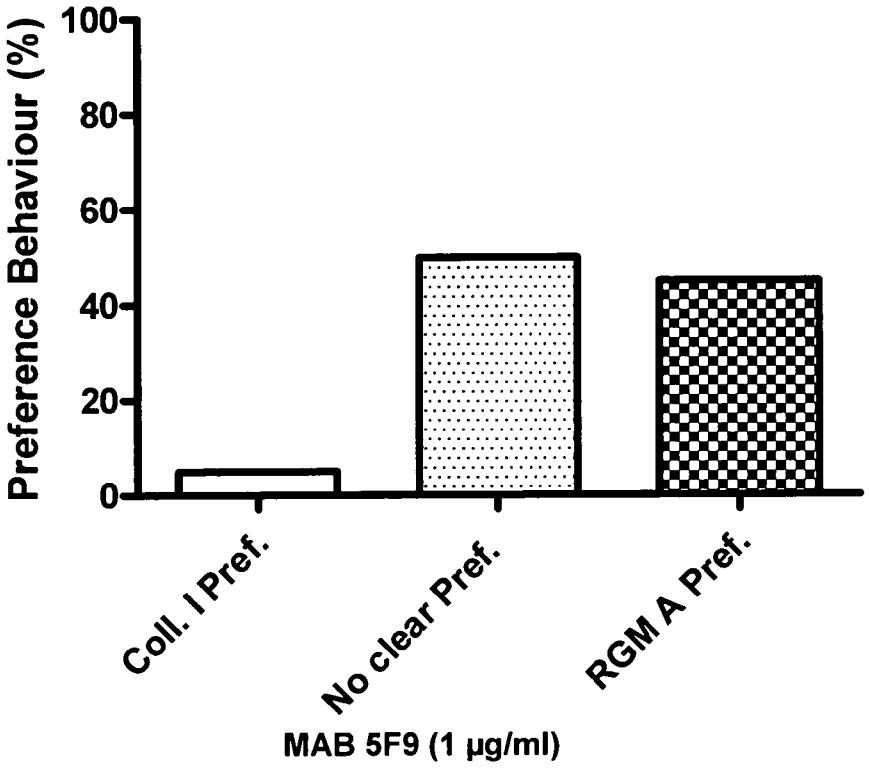

Preference Behaviour (%)
100
80
60
40
20
0
Coll. I Pref.
No clear Pref.
RGM A Pref.
MAB 5F9 (1 µg/ml)

Fig. 8D

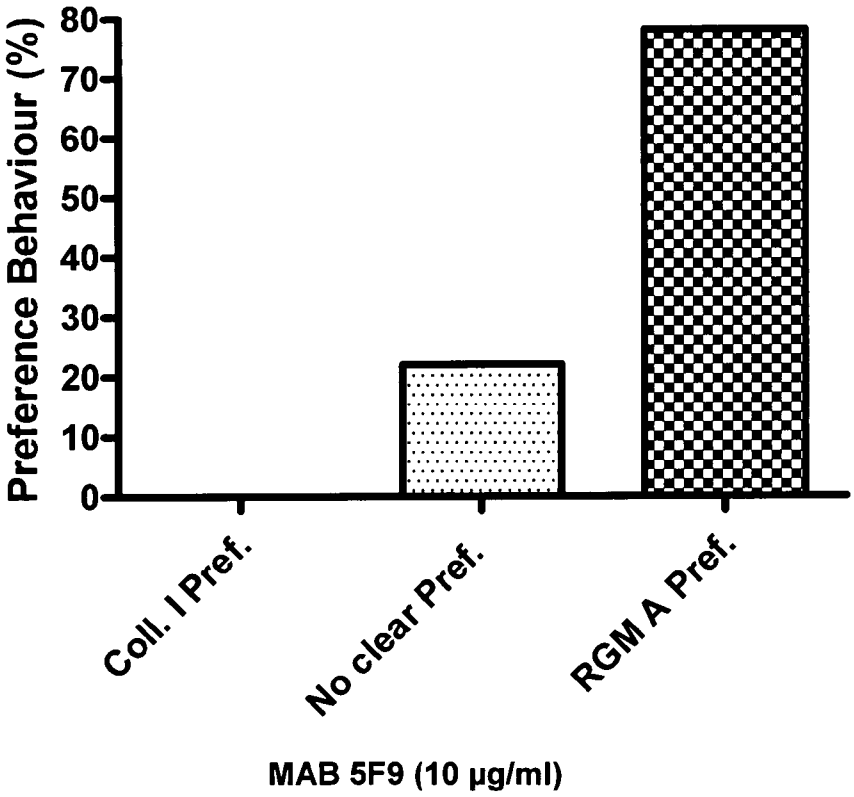

Preference Behaviour (%)
80
70
60
50
40
30
20
10
0
Coll. I Pref.
No clear Pref.
RGM A Pref.
MAB 5F9 (10 µg/ml)

Fig. 8E

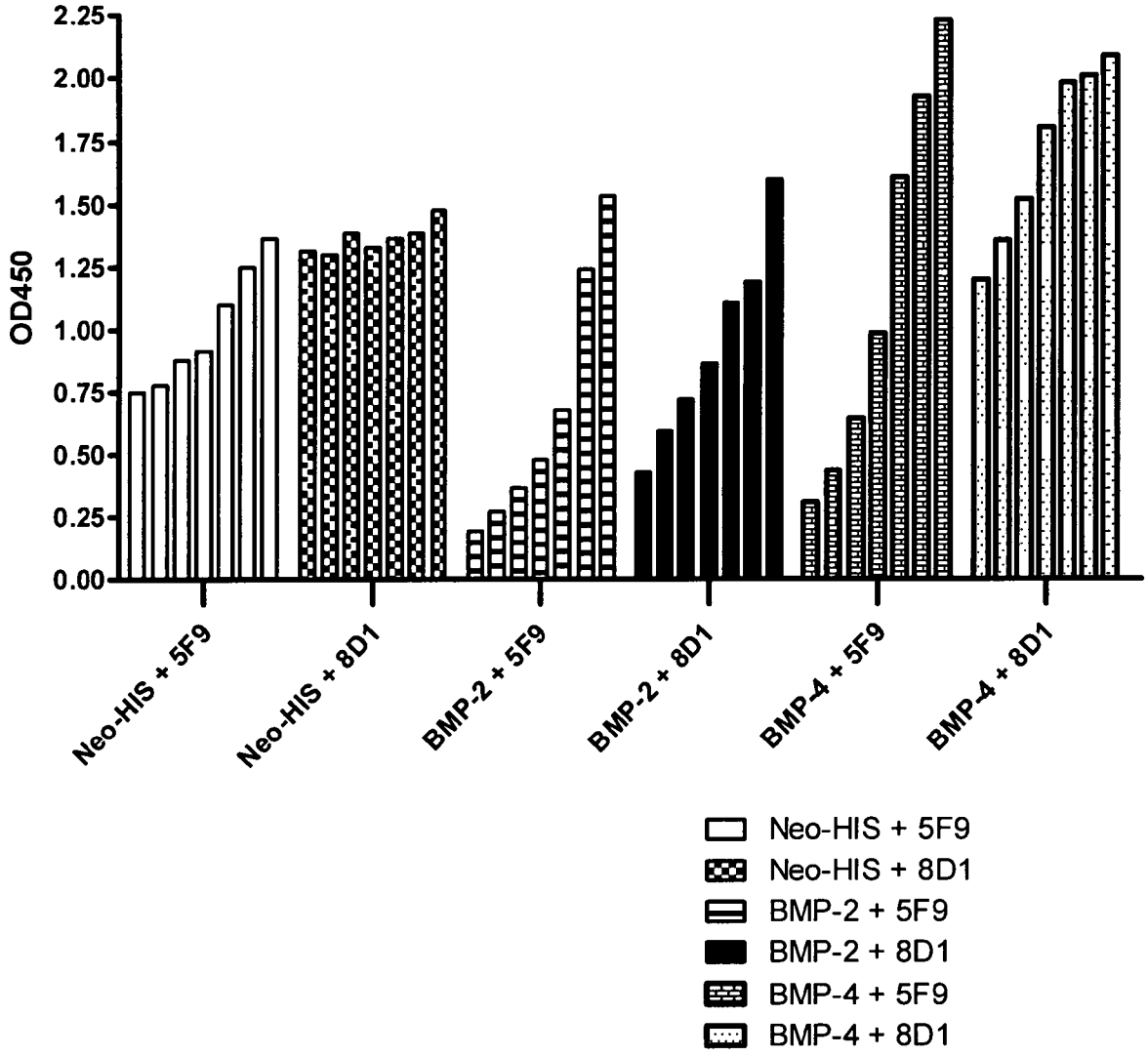
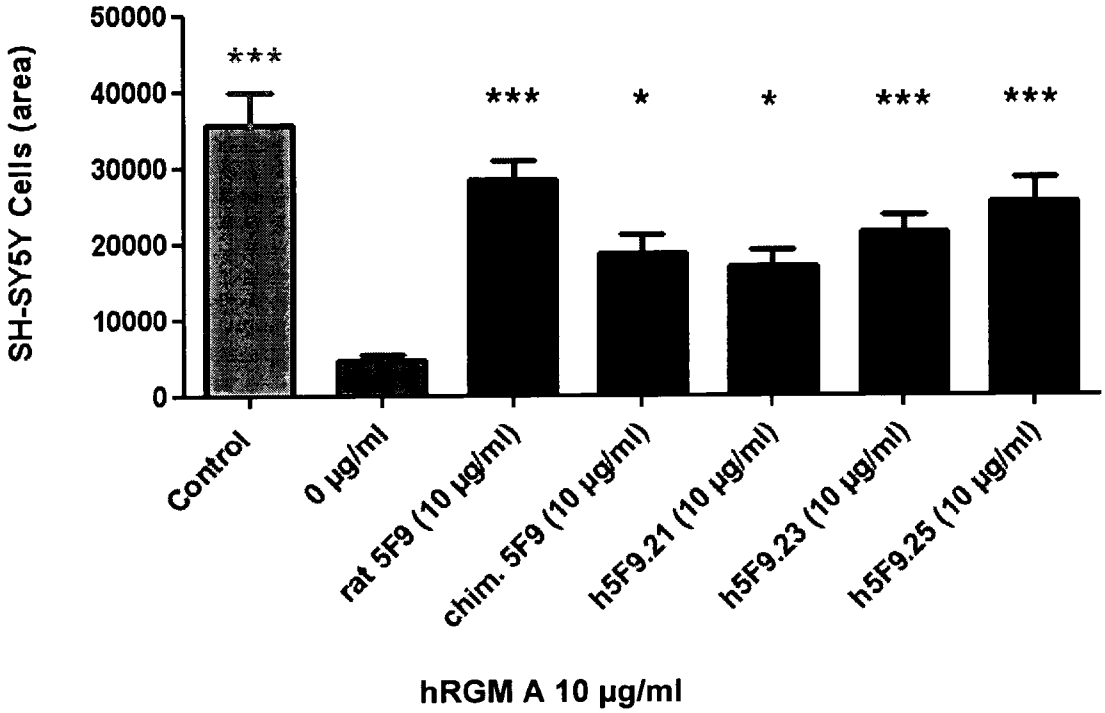

OD450
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
Neo-HIS + 5F9
Neo-HIS + 8D1
BMP-2 + 5F9
BMP-2 + 8D1
BMP-4 + 5F9
BMP-4 + 8D1
Neo-HIS + 5F9
Neo-HIS + 8D1
BMP-2 + 5F9
BMP-2 + 8D1
BMP-4 + 5F9
BMP-4 + 8D1

Fig. 9

Chemotaxis Assay (no EGF): Testing of rat, chimeric, humanized 5F9, n = 2



* p < 0.05: significance vs. 5F9 0 µg/ml
*** p < 0.001: significance vs. 5F9 0 µg/ml
*** p < 0.001: significance vs. 5F9 0 µg/ml

Fig. 10

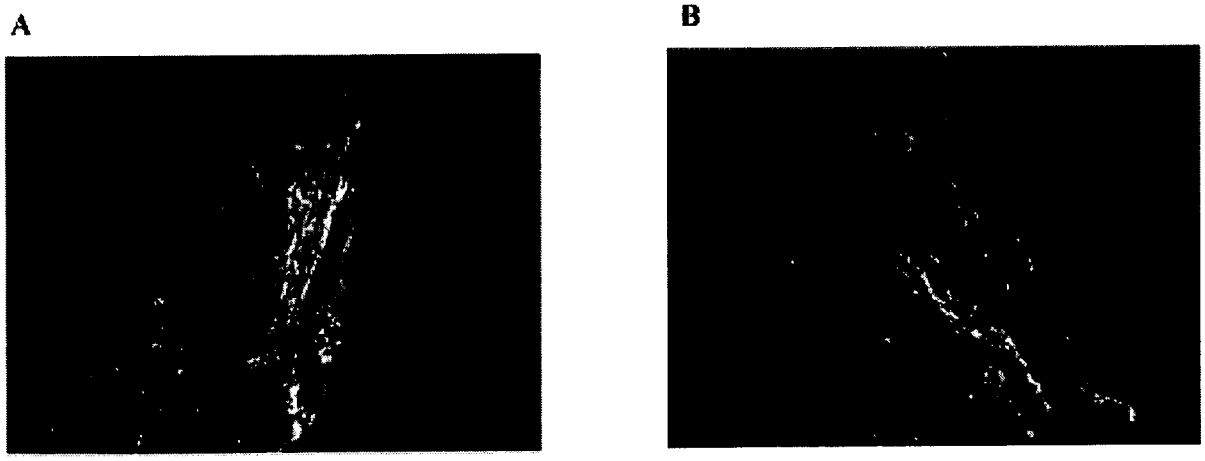
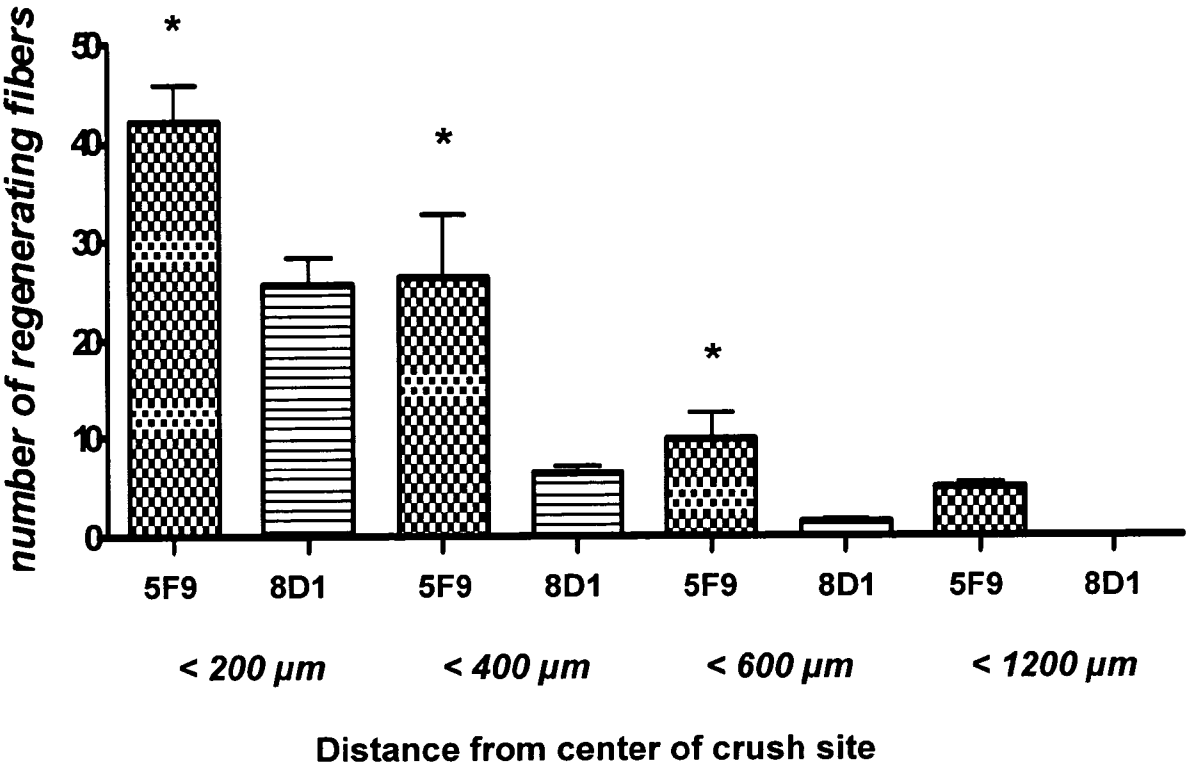


Fig. 11


number of regenerating fibers
50
40
30
20
10
0
*
*
*
5F9
8D1
5F9
8D1
5F9
8D1
5F9
8D1
< 200 µm
< 400 µm
< 600 µm
< 1200 µm
Distance from center of crush site

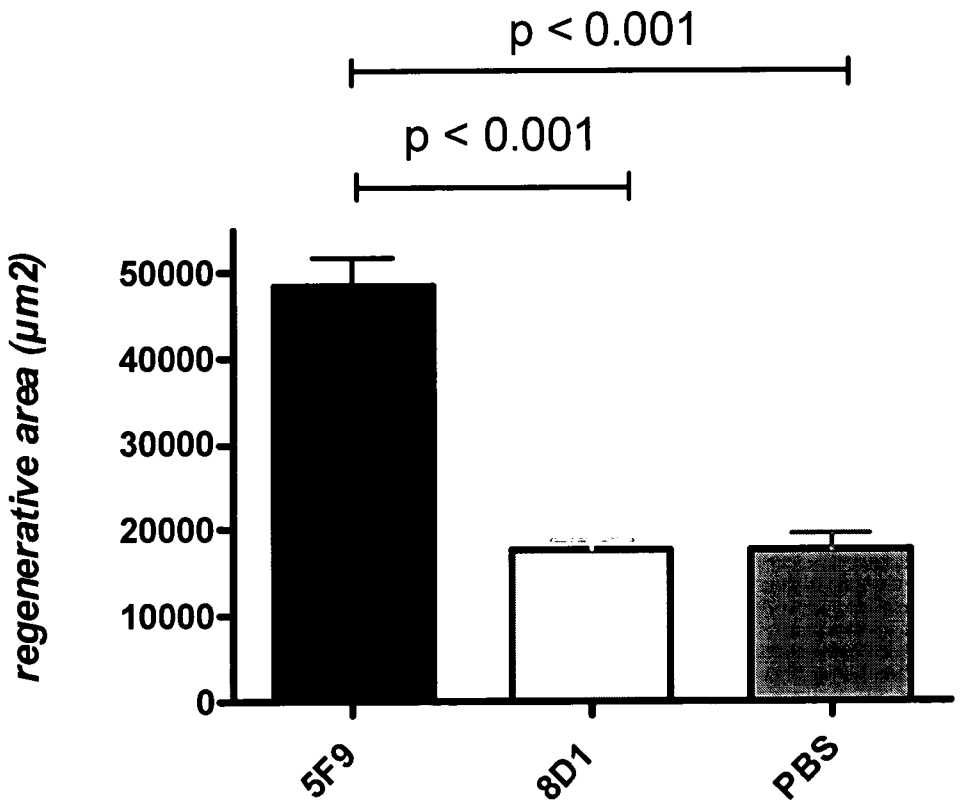

p < 0.001
p < 0.001
regenerative area (µm2)
50000
40000
30000
20000
10000
0
5F9
8D1
PBS

Fig. 12

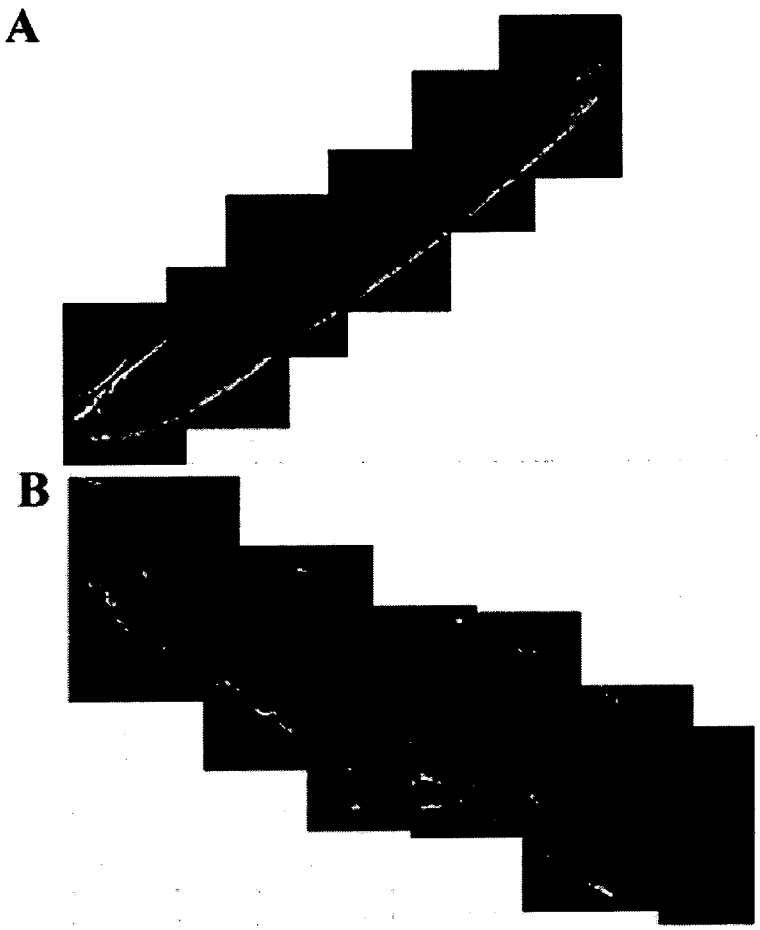


Fig. 13

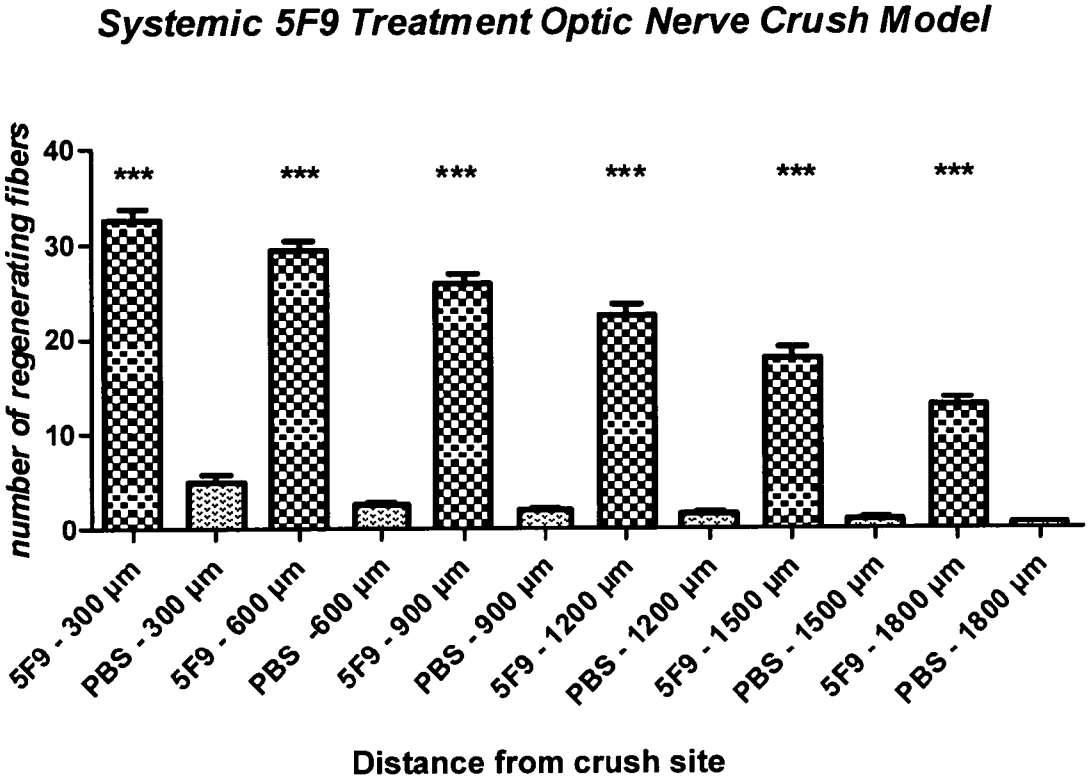


Fig. 14A

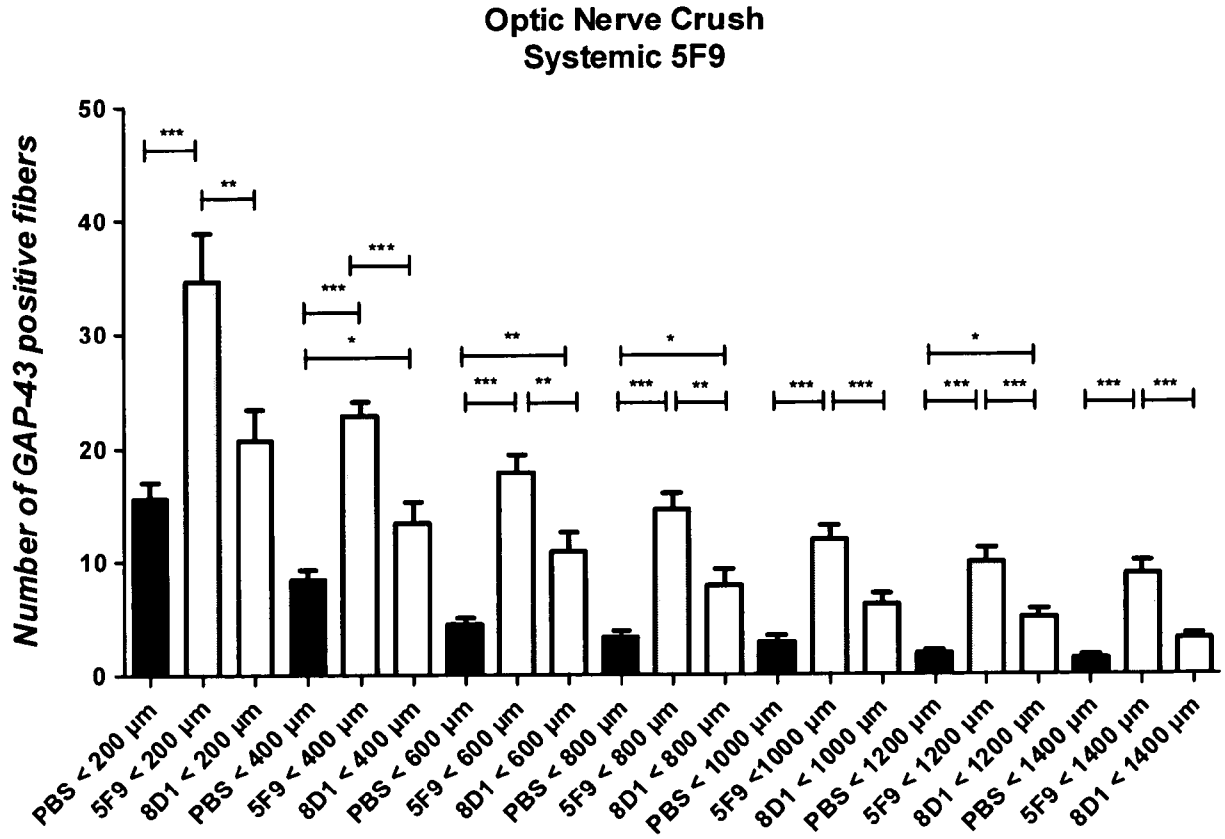


Fig. 14B

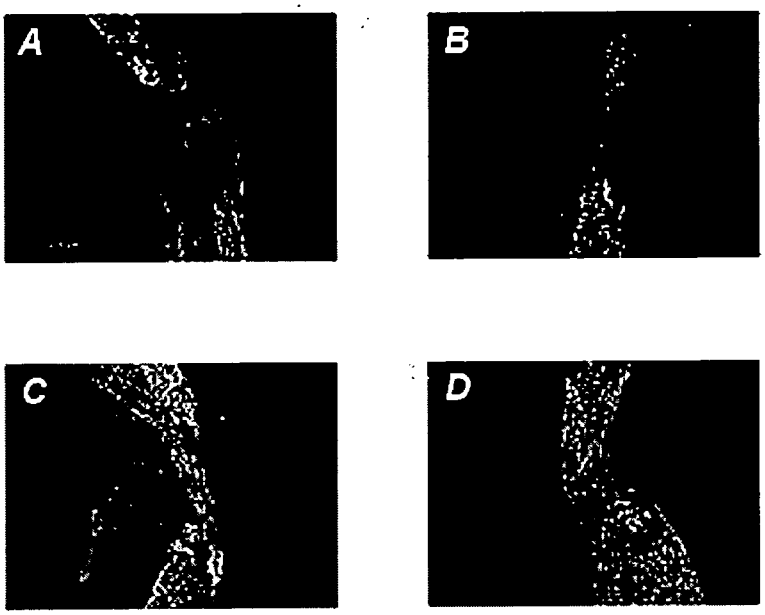

A
B
C
D

Fig. 15

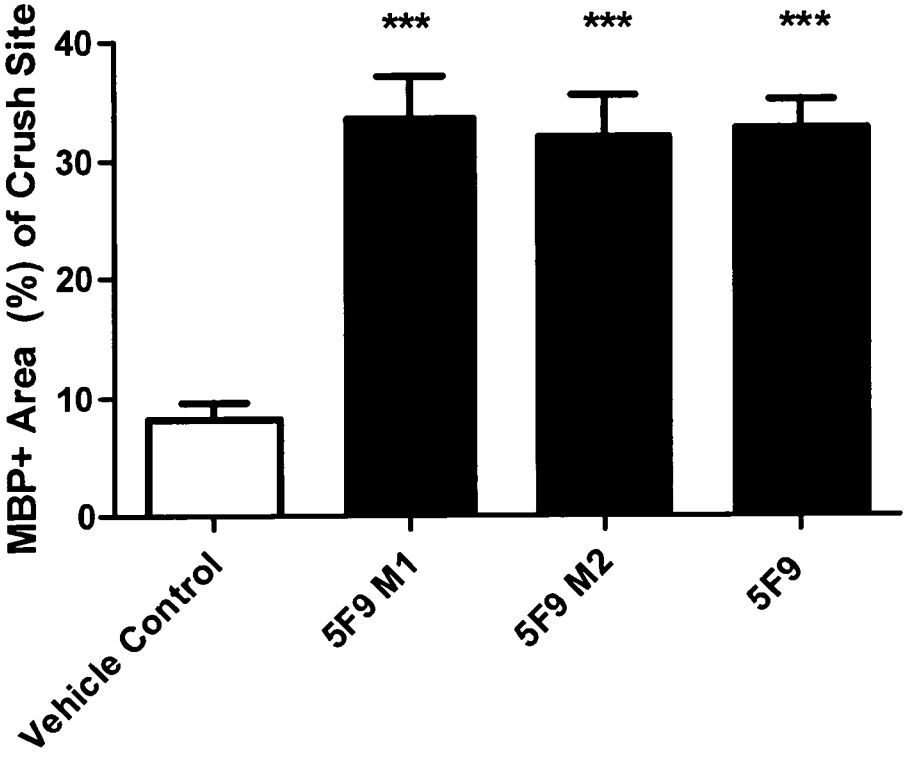

MBP+ Area (%) of Crush Site
40
30
20
10
0
***
***
***
Vehicle Control
5F9 M1
5F9 M2
5F9

Fig. 16

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/22 A61K39/395

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HATA KATSUHIKO ET AL: "RGMa inhibition promotes axonal growth and recovery after spinal cord injury." THE JOURNAL OF CELL BIOLOGY 10 APR 2006, vol. 173, no. 1, 10 April 2006 (2006-04-10), pages 47-58, XP002529131 ISSN: 0021-9525 the whole document	1-91
Y	KYOTO ET AL: "Synapse formation of the cortico-spinal axons is enhanced by RGMa inhibition after spinal cord injury" BRAIN RESEARCH, ELSEVIER, AMSTERDAM, NL, vol. 1186, 23 October 2007 (2007-10-23), pages 74-86, XP022374699 ISSN: 0006-8993 the whole document	1-91

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 June 2009	18/06/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Hix, Rebecca

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2007/062852 A (ABBOTT LAB [US]; ABBOTT GMBH & CO KG [DE]; BARGHORN STEFAN [DE]; EBERT) 7 June 2007 (2007-06-07) SEQ ID NO:40: 100% identity in 330aa overlap with SEQ ID NOS 11 & 12	1-91
A	RAJAGOPALAN SRIKANTH ET AL: "Neogenin mediates the action of repulsive guidance molecule" NATURE CELL BIOLOGY, NATURE PUBLISHING GROUP, GB, vol. 6, no. 8, 1 August 2004 (2004-08-01), pages 756-762, XP002424999 ISSN: 1465-7392 the whole document	
A	HAREL NOAM Y ET AL: "Can regenerating axons recapitulate developmental guidance during recovery from spinal cord injury?" NATURE REVIEWS NEUROSCIENCE, vol. 7, no. 8, August 2006 (2006-08), pages 603-616, XP002529132 ISSN: 1471-0048 the whole document	
A	LAURA MARIE CAMUS ET AL: "Molecular Evolution of Hemojuvelin and the Repulsive Guidance Molecule Family" JOURNAL OF MOLECULAR EVOLUTION, SPRINGER-VERLAG, NE, vol. 65, no. 1, 25 June 2007 (2007-06-25), pages 68-81, XP019538398 ISSN: 1432-1432 the whole document	
P,A	SCHAFFAR GREGOR ET AL: "LIM-only protein 4 interacts directly with the repulsive guidance molecule A receptor Neogenin" JOURNAL OF NEUROCHEMISTRY, vol. 107, no. 2, October 2008 (2008-10), pages 418-431, XP002529133 ISSN: 0022-3042 the whole document	
P,X	SUDA M ET AL: "Peptides derived from repulsive guidance molecule act as antagonists" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 371, no. 3, 4 July 2008 (2008-07-04), pages 501-504, XP022670730 ISSN: 0006-291X [retrieved on 2008-04-29] the whole document	1,2

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		CA 2628703 A1	07-06-2007
		EC SP088462 A	30-06-2008
		EP 1954718 A2	13-08-2008
		JP 2009517057 T	30-04-2009
		KR 20080090408 A	08-10-2008