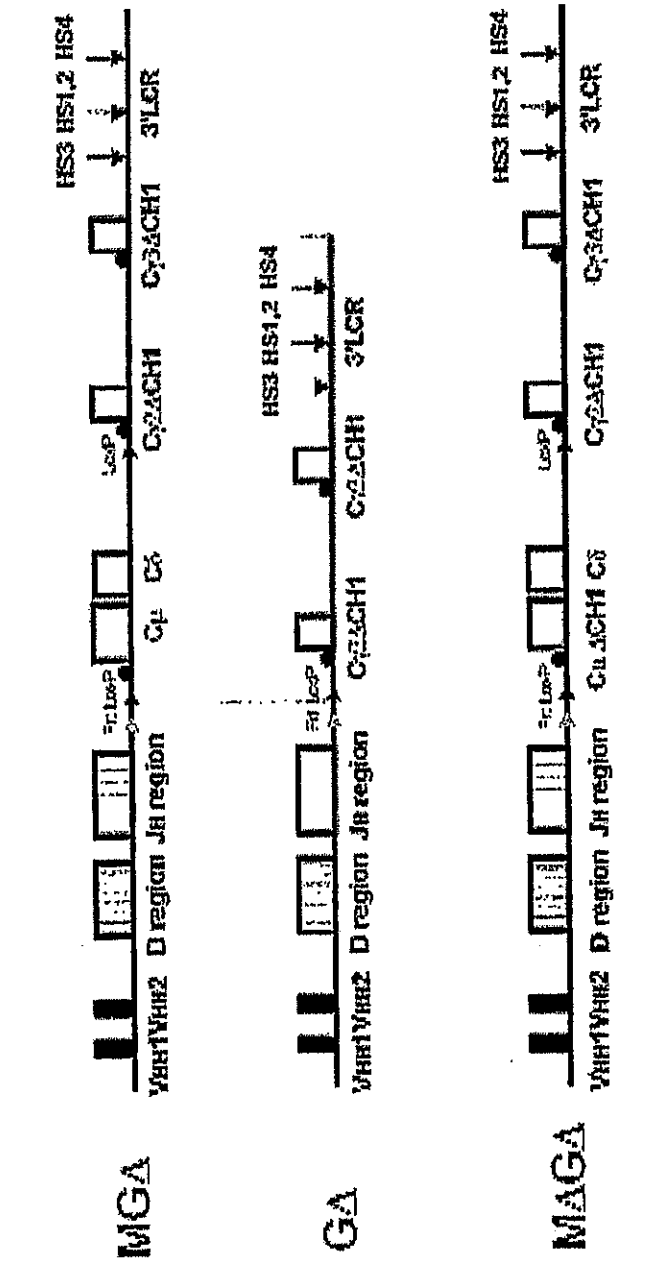

MGA
GA
MAGA
VHH1VHH2 D region JH region
Cμ Cδ
LoxP
Cγ2ΔCH1
Cγ3ΔCH1
HS3 HS1,2 HS4
3'LCR
Cα1CH1

FIG. 1

FIG. 2A

% of B220+/CD19+ cells in total population of nucleated cells

	WT	G1 (single copy)	M1/Sa
BM	10.80 ± 2.09	5.94 ± 1.44	4.98 ± 1.79	6.08 ± 1.50
Spleen	41.60 ± 5.05	32.11 ± 9.48	28.70 ± 8.70	33.05 ± 3.24
Blood	43.72 ± 7.50	18.09 ± 5.65	18.01 ± 3.76	9.25 ± 3.74
Peritoneum	21.82 ± 9.90	22.85 ± 6.71	22.38 ± 7.29	21.21 ± 14.49

Mice were 14-22 weeks old. Numbers of mice analyzed are 5-11 per mouse line with the exception of two peritoneal cells measurements, where calculations are based on two samples (marked by asterisks).

FIG. 2B

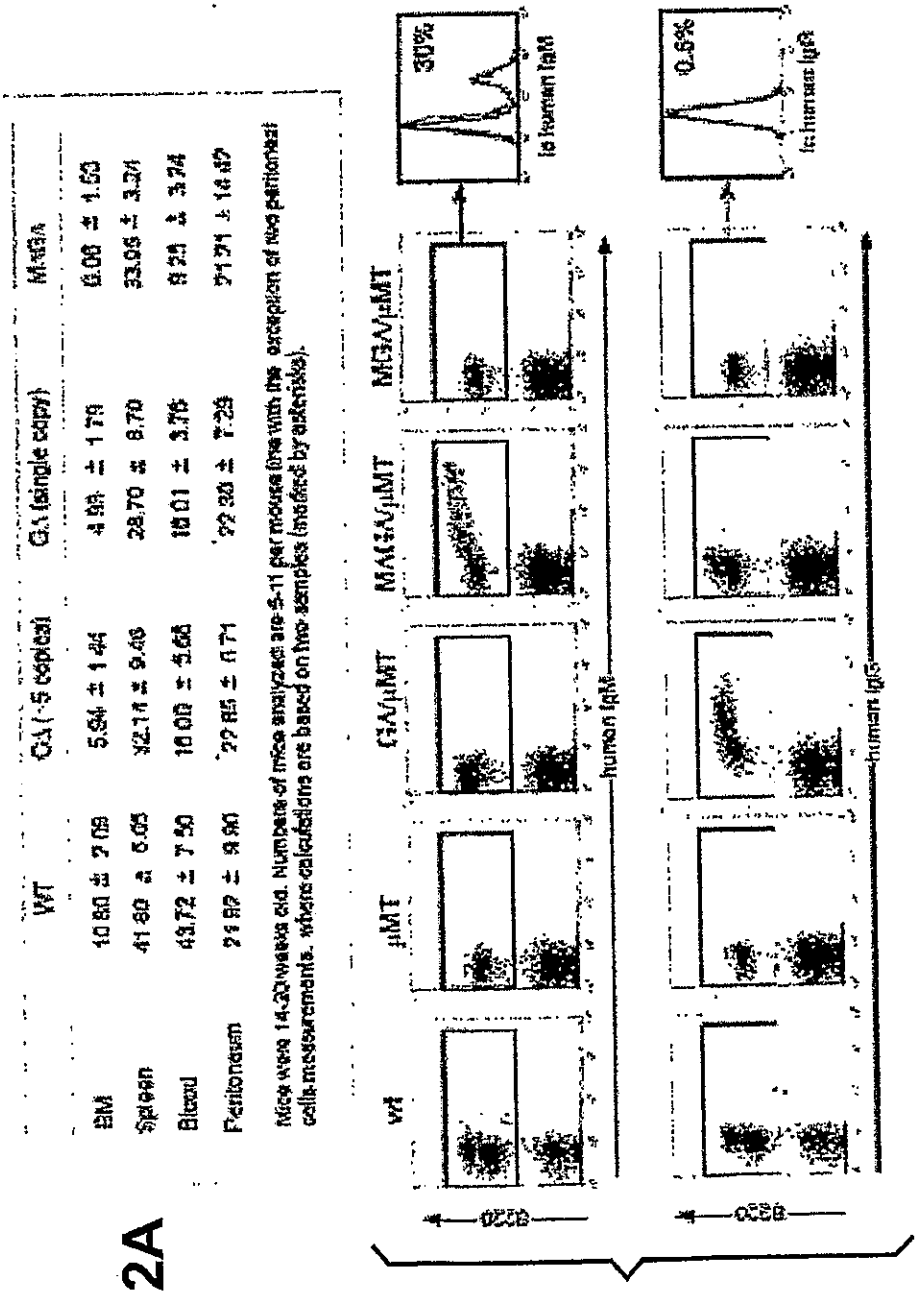


FIG. 2C

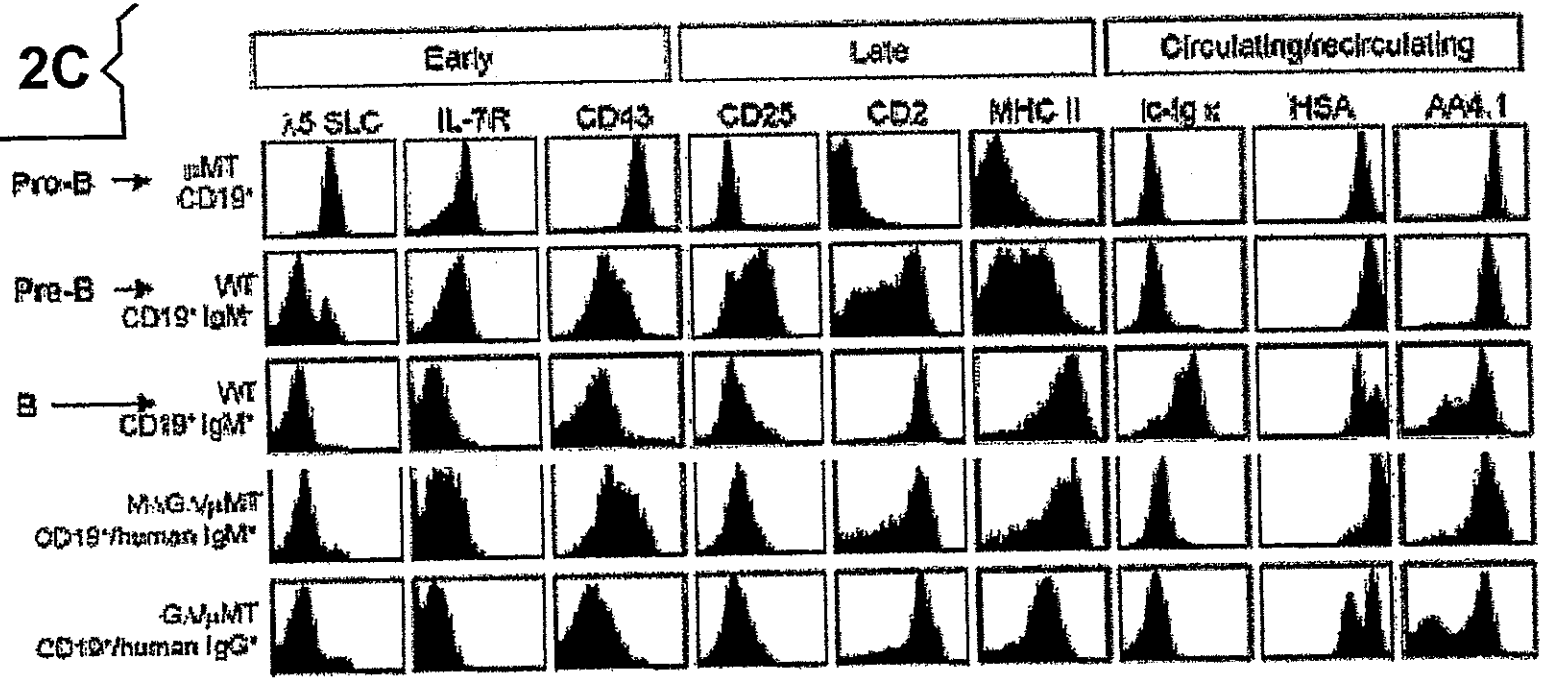

Early
Late
Circulating/recirculating
λ5 SLC
IL-7R
CD43
CD25
CD2
MHC II
Ic-Ig κ
HSA
AA4.1
Pro-B → μMT CD19+
Pre-B → WT CD19+ IgM-
B → WT CD19+ IgM+
M.G.V/μMT CD19+/human IgM+
G.V/μMT CD19+/human IgG+

FIG. 2D

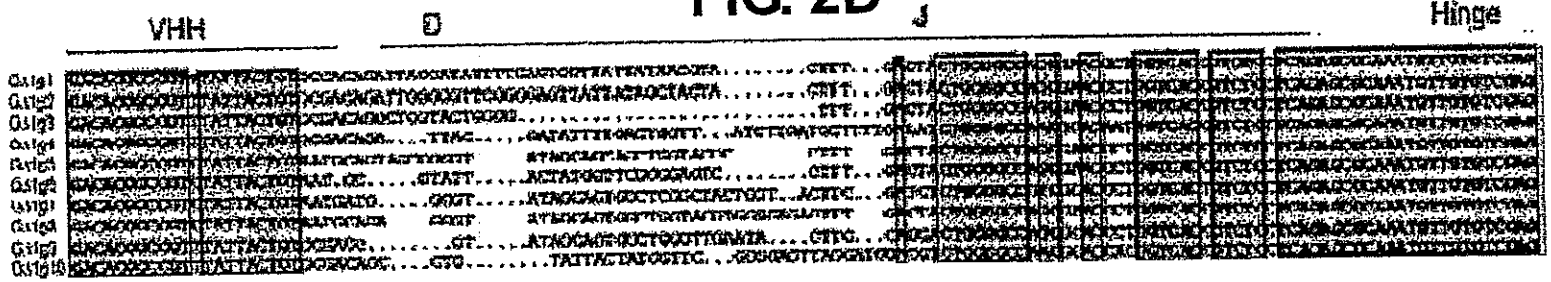
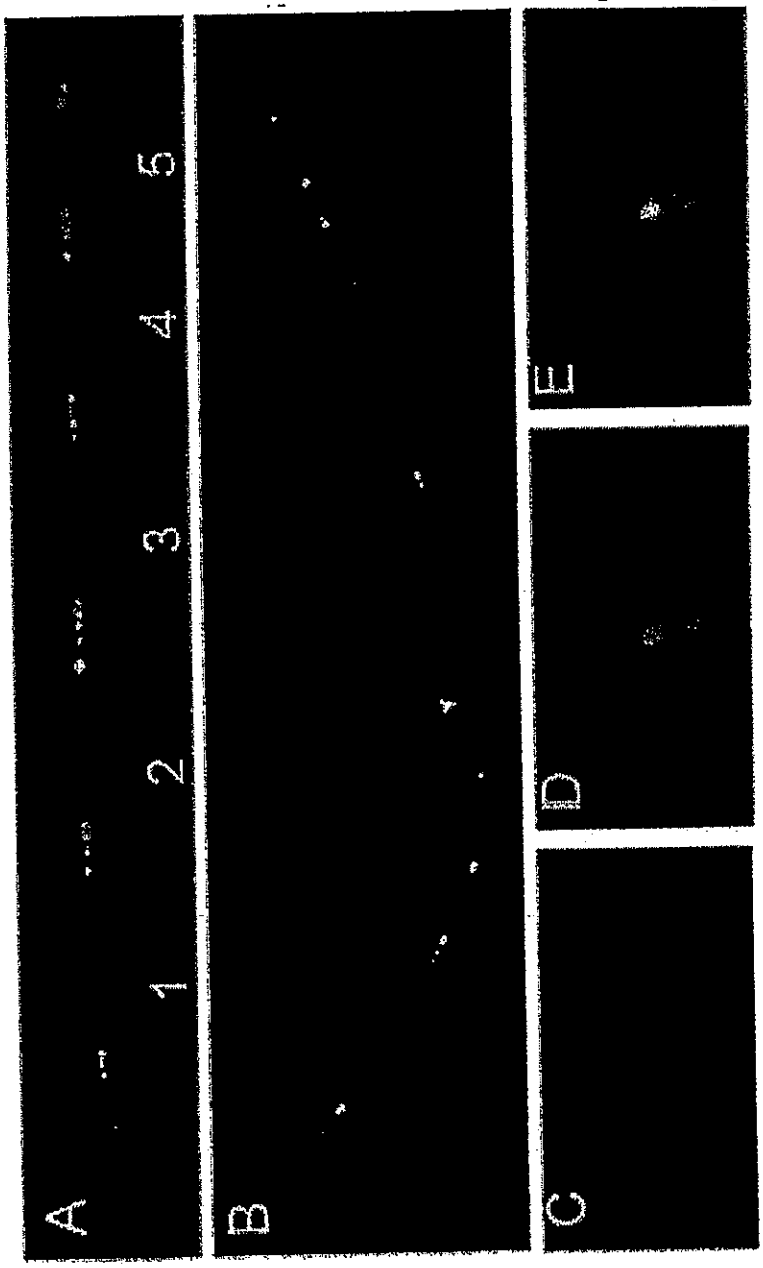

VHH
D
J
Hinge

FIG. 3



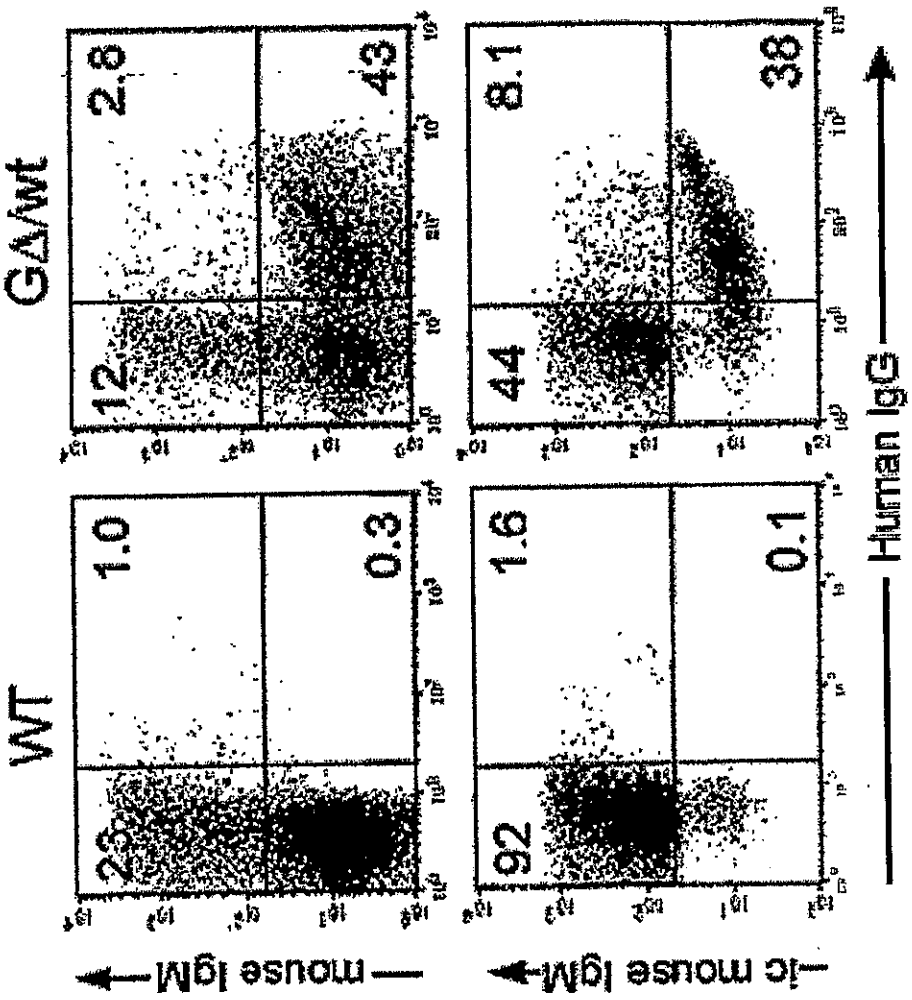

GΔ/wt
WT
2.8
43
12
8.1
38
44
1.0
0.3
23
1.6
0.1
92
mouse IgM
ic mouse IgM
Human IgG

FIG. 3F

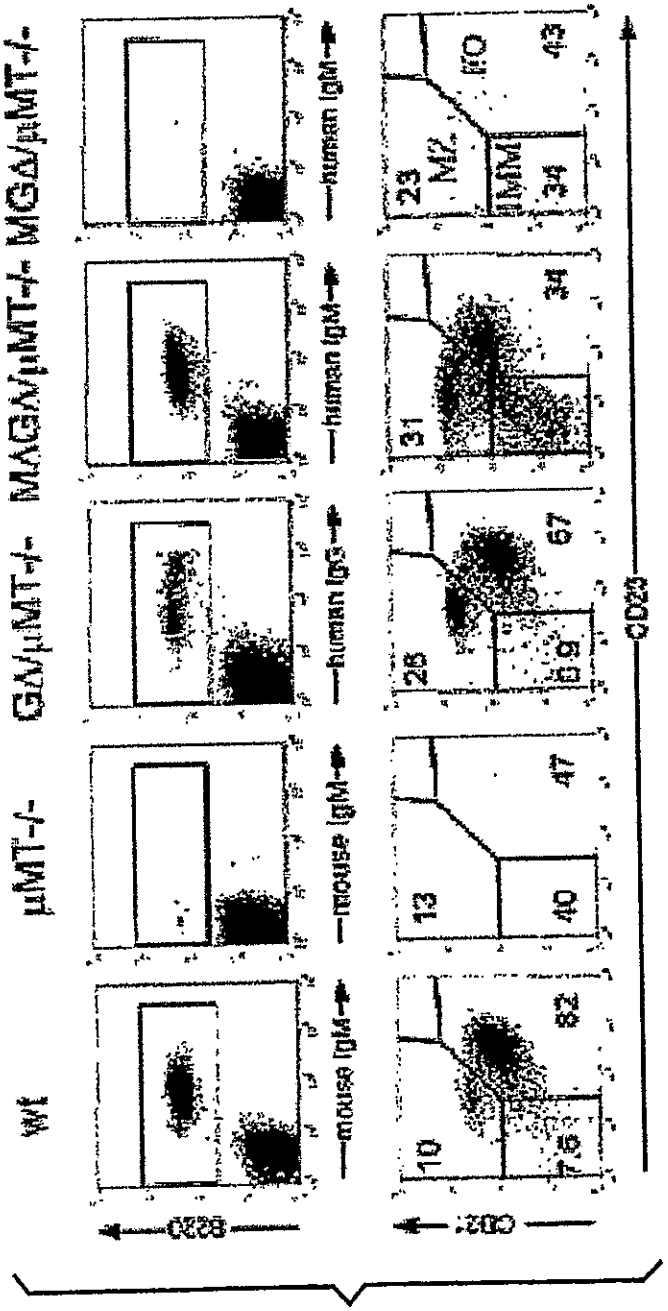

WT
μMT-/-
GAμMT-/-
MAGAμMT-/-
MGΔμMT-/-
B220
CD23
mouse IgM
human IgG
human IgM
10
82
13
47
40
28
67
9.9
31
34
23
MZ
MM
FO
43

FIG. 4A

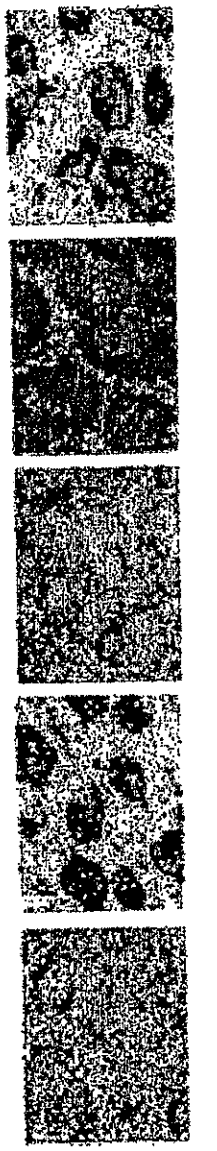
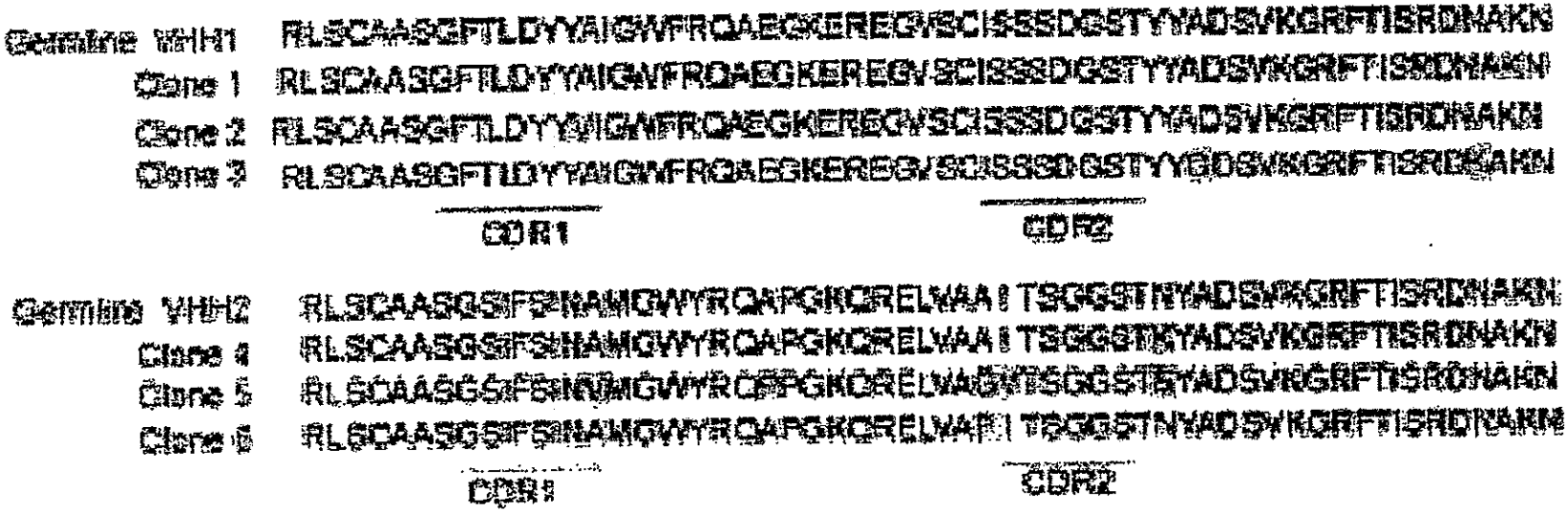


FIG. 4B

FIG. 4C


Camelid VHH1
Clone 1
Clone 2
Clone 3
CDR1
CDR2
Camelid VHH2
Clone 4
Clone 5
Clone 6
CDR1
CDR2

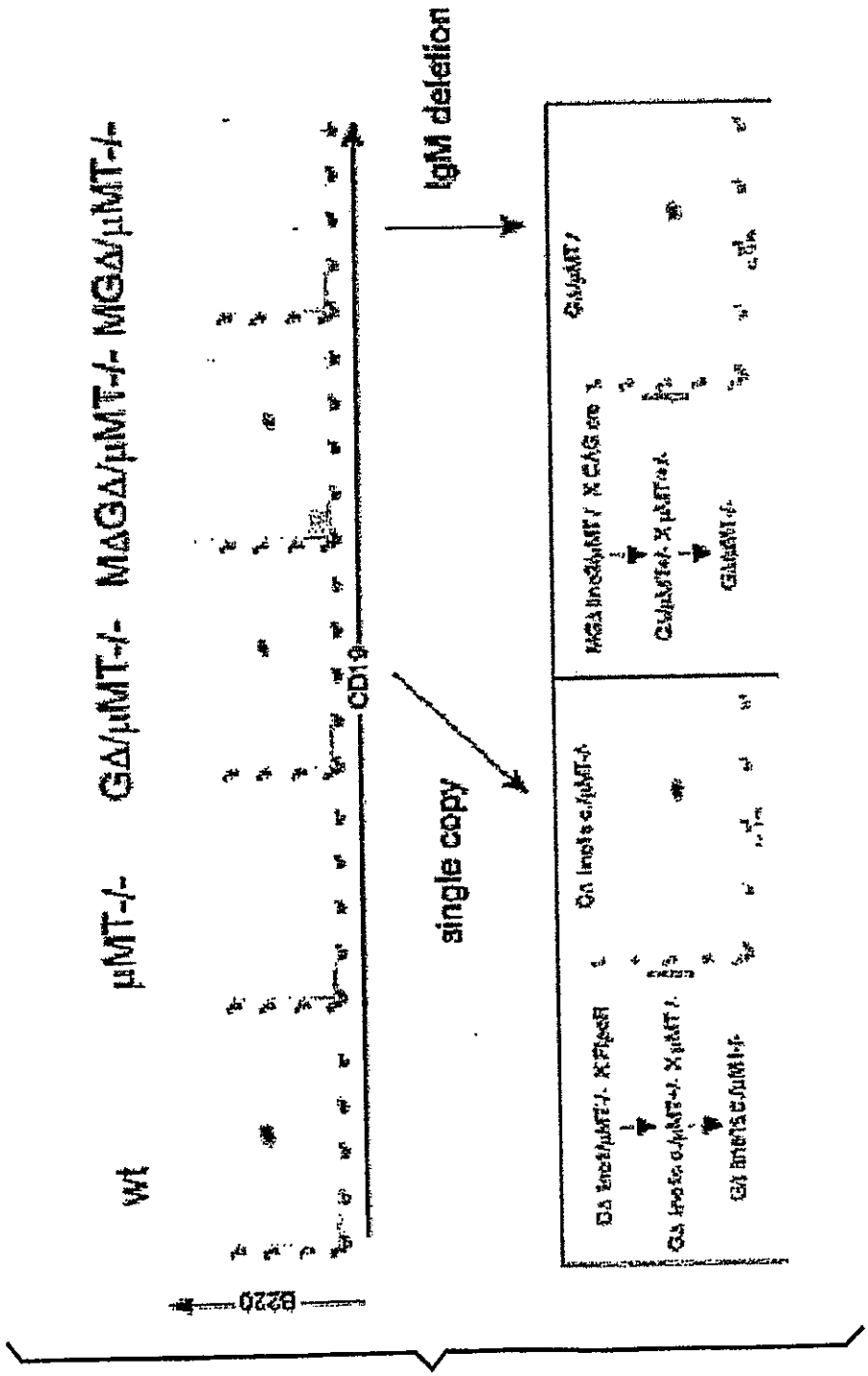

wt
μMT-/-
GΔ/μMT-/-
MΔGΔ/μMT-/-
MGΔ/μMT-/-
IgM deletion
single copy
B220
CD19

FIG. 4D

FIG. 5A

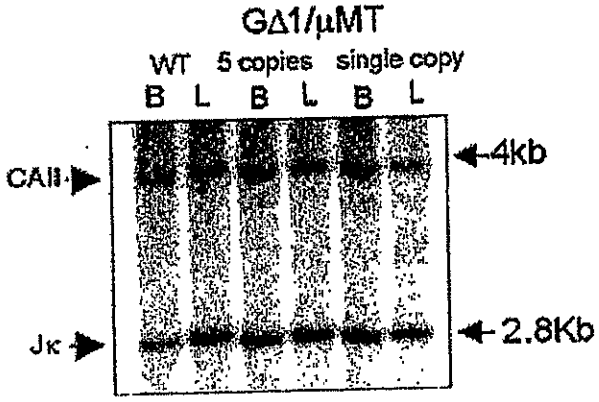

GΔ1/μMT
WT
5 copies
single copy
B L B L B L
CAII
Jκ
4kb
2.8Kb

FIG. 5B

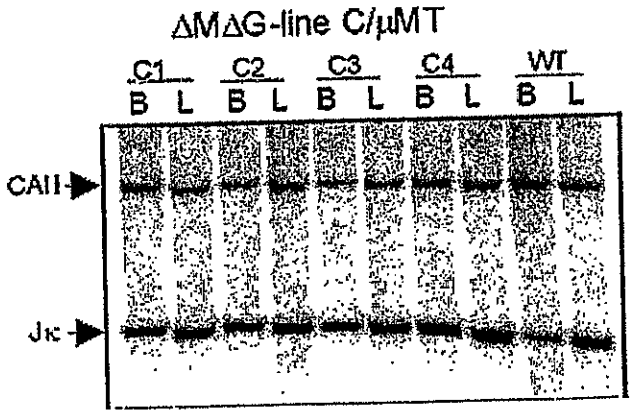

ΔMΔG-line C/μMT
C1
C2
C3
C4
WT
B L B L B L B L B L
CAII
Jκ

FIG. 6

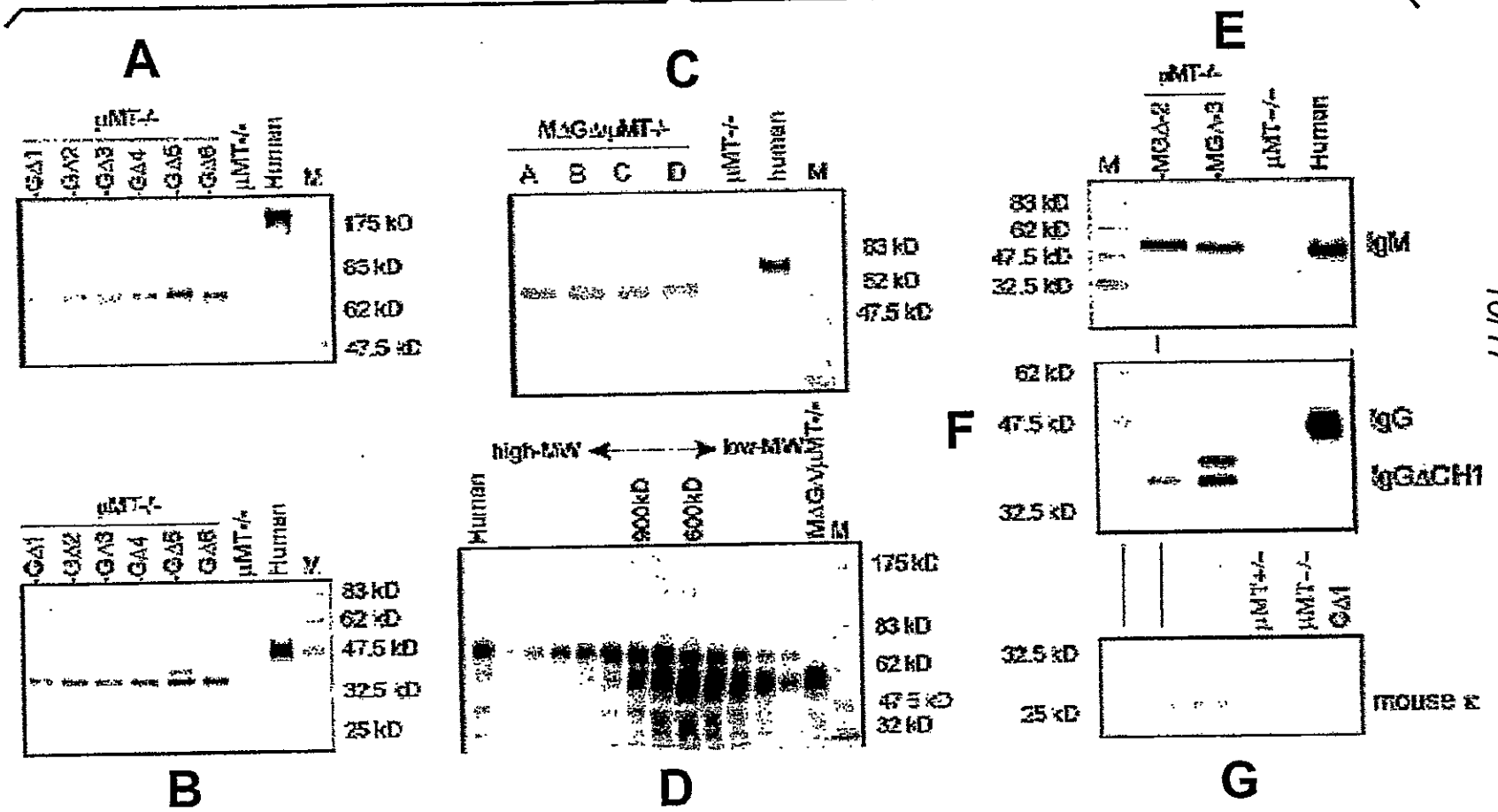

A
μMT-/-
GΔ1
GΔ2
GΔ3
GΔ4
GΔ5
GΔ6
μMT+/+
Human
M
175 kD
85 kD
62 kD
47.5 kD
B
μMT-/-
GΔ1
GΔ2
GΔ3
GΔ4
GΔ5
GΔ6
μMT+/+
Human
M
83 kD
62 kD
47.5 kD
32.5 kD
25 kD
C
MΔGΔμMT-/-
A
B
C
D
μMT-/-
human
M
83 kD
62 kD
47.5 kD
D
high-MW
low-MW
MΔGΔμMT+/+
Human
900kD
600kD
M
175 kD
83 kD
62 kD
47.5 kD
32 kD
E
μMT-/-
M
MGΔ-2
MGΔ-3
μMT-/-
Human
83 kD
62 kD
47.5 kD
32.5 kD
IgM
F
62 kD
47.5 kD
32.5 kD
IgG
IgGΔCH1
μMT+/+
μMT-/-
GΔ1
32.5 kD
25 kD
mouse κ
G

FIG. 7A

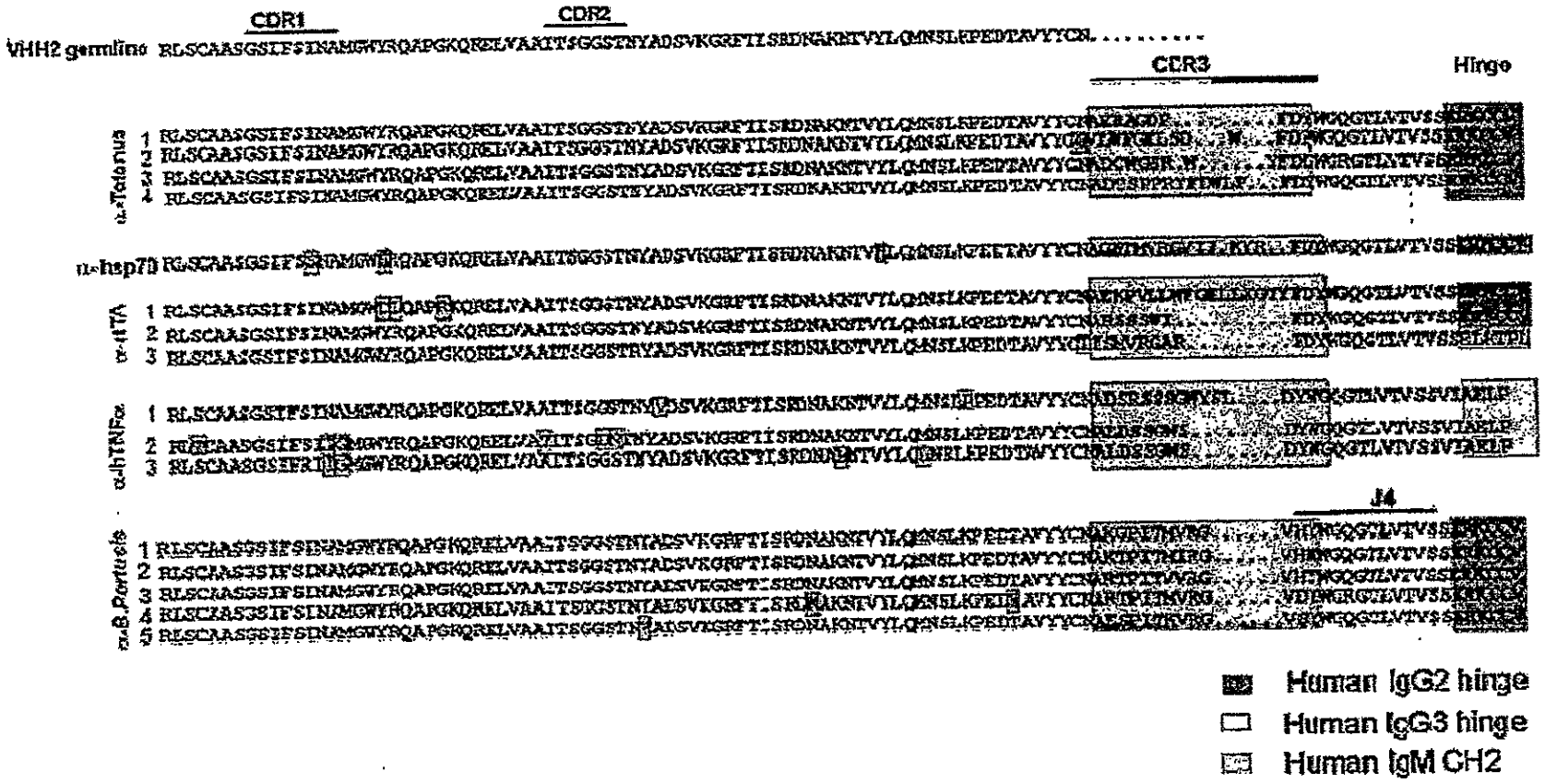

CDR1
CDR2
CDR3
Hinge
J4
VHH2 germline
α-Tetanus
α-hsp70
α-4TA
α-hTNFα
α-β.Portucalis
Human IgG2 hinge
Human IgG3 hinge
Human IgM CH2

FIG. 7B

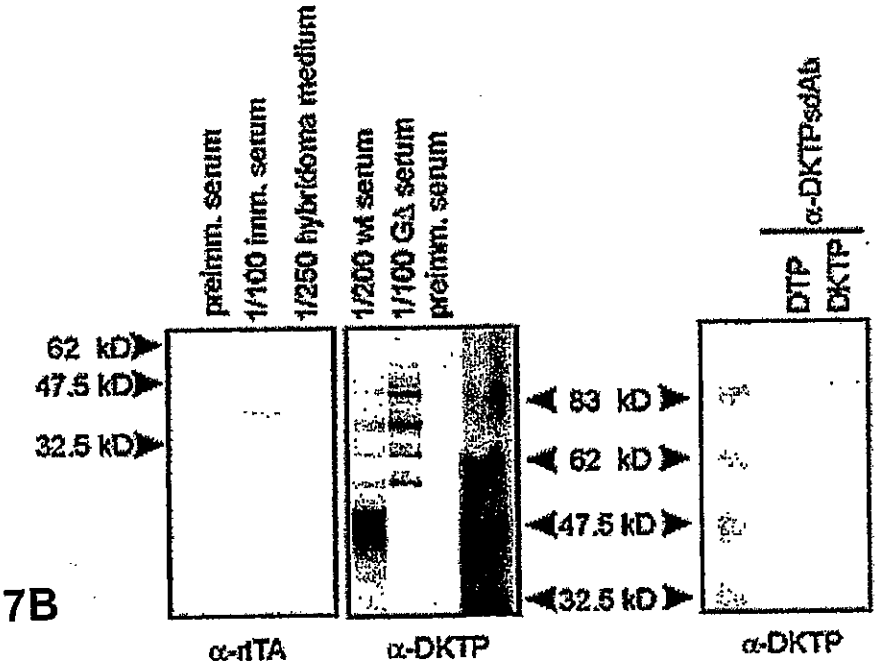


FIG. 7C

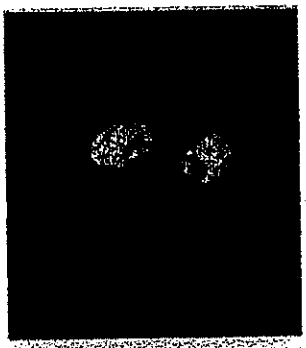


FIG. 7D



FIG. 7E

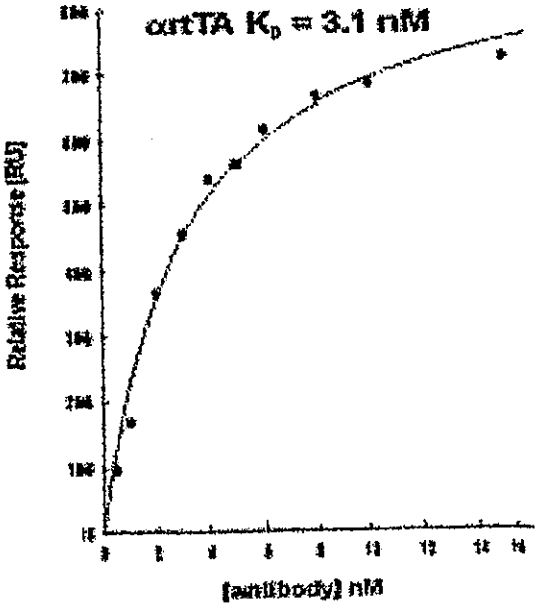


FIG. 8A

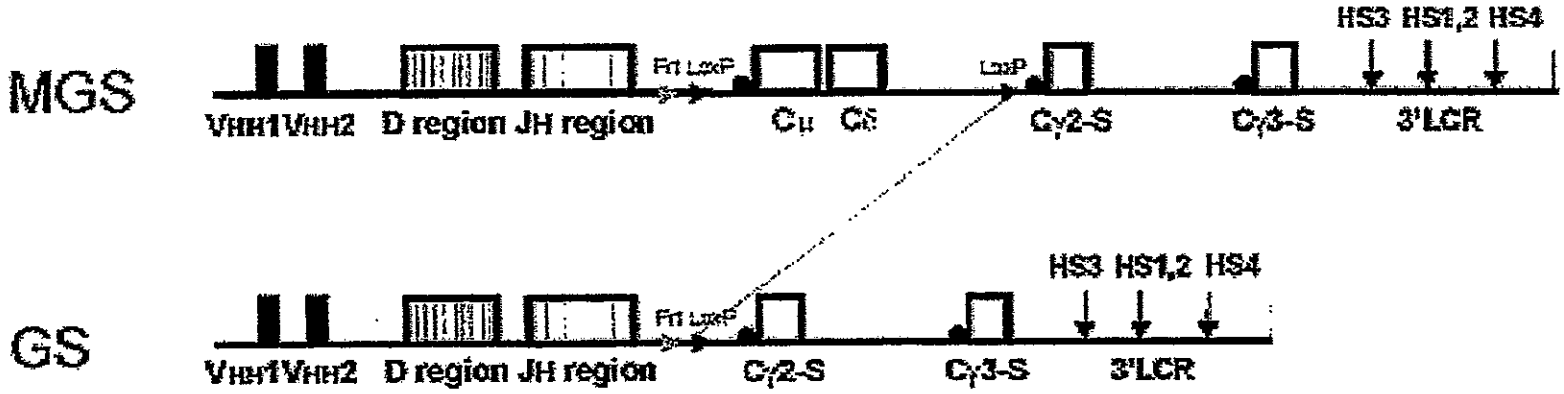
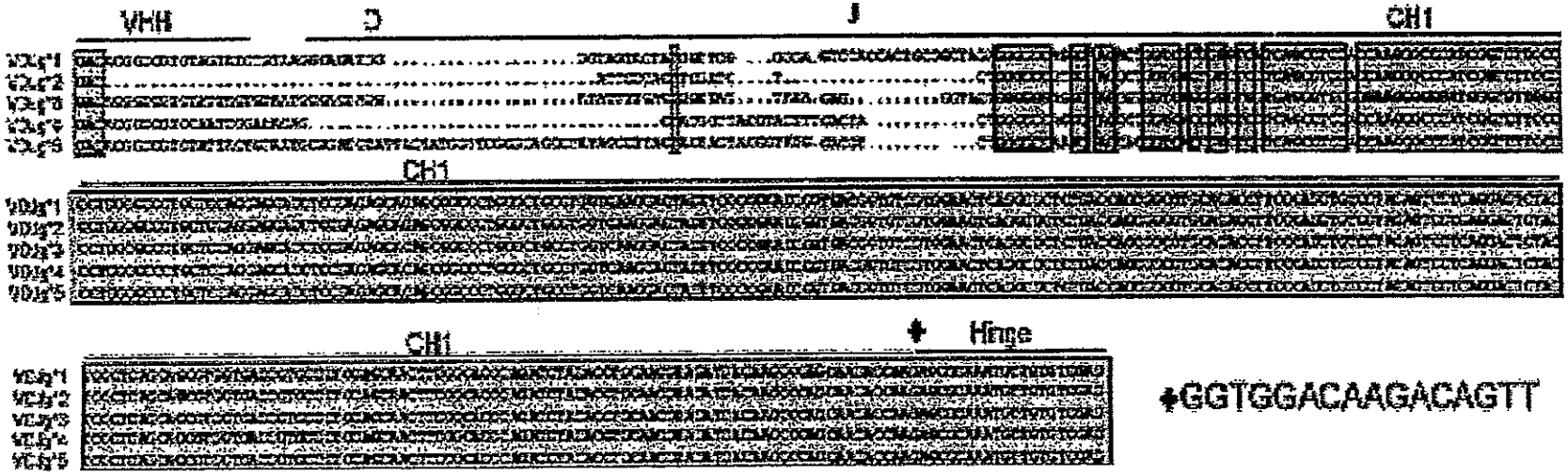

MGS
Frt LoxP
LoxP
HS3 HS1,2 HS4
VHH1VHH2 D region JH region
Cμ Cδ
Cγ2-S
Cγ3-S
3'LCR
GS
Frt LoxP
HS3 HS1,2 HS4
VHH1VHH2 D region JH region
Cγ2-S
Cγ3-S
3'LCR

FIG. 8B


VHH
D
J
CH1
CH1
CH1
Hinge
GGTGGACAAGACAGTT

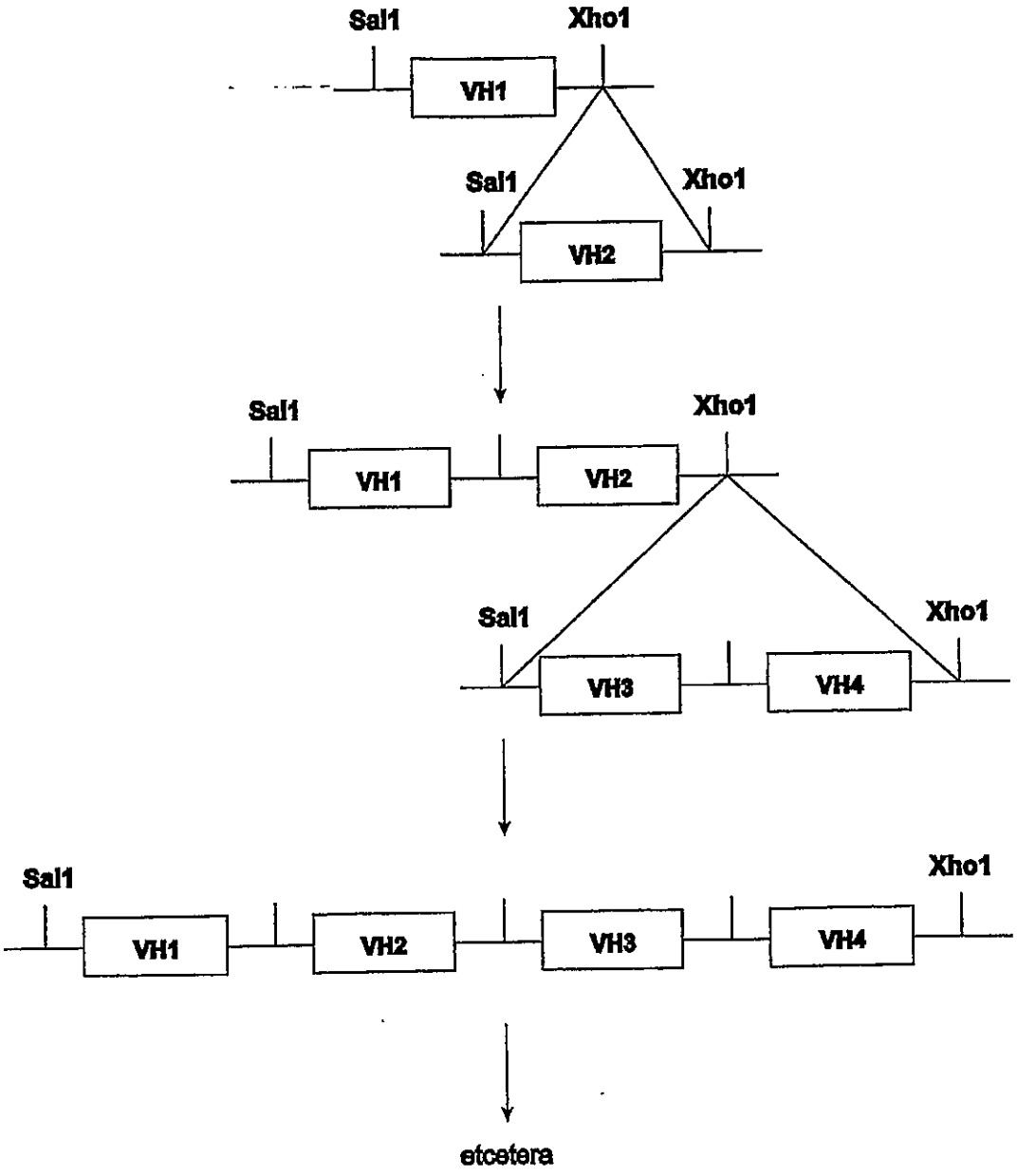

Sal1
Xho1
VH1
Sal1
Xho1
VH2
Sal1
Xho1
VH1
VH2
Sal1
Xho1
VH3
VH4
Sal1
Xho1
VH1
VH2
VH3
VH4
etcetera

FIG. 9

FIG. 10

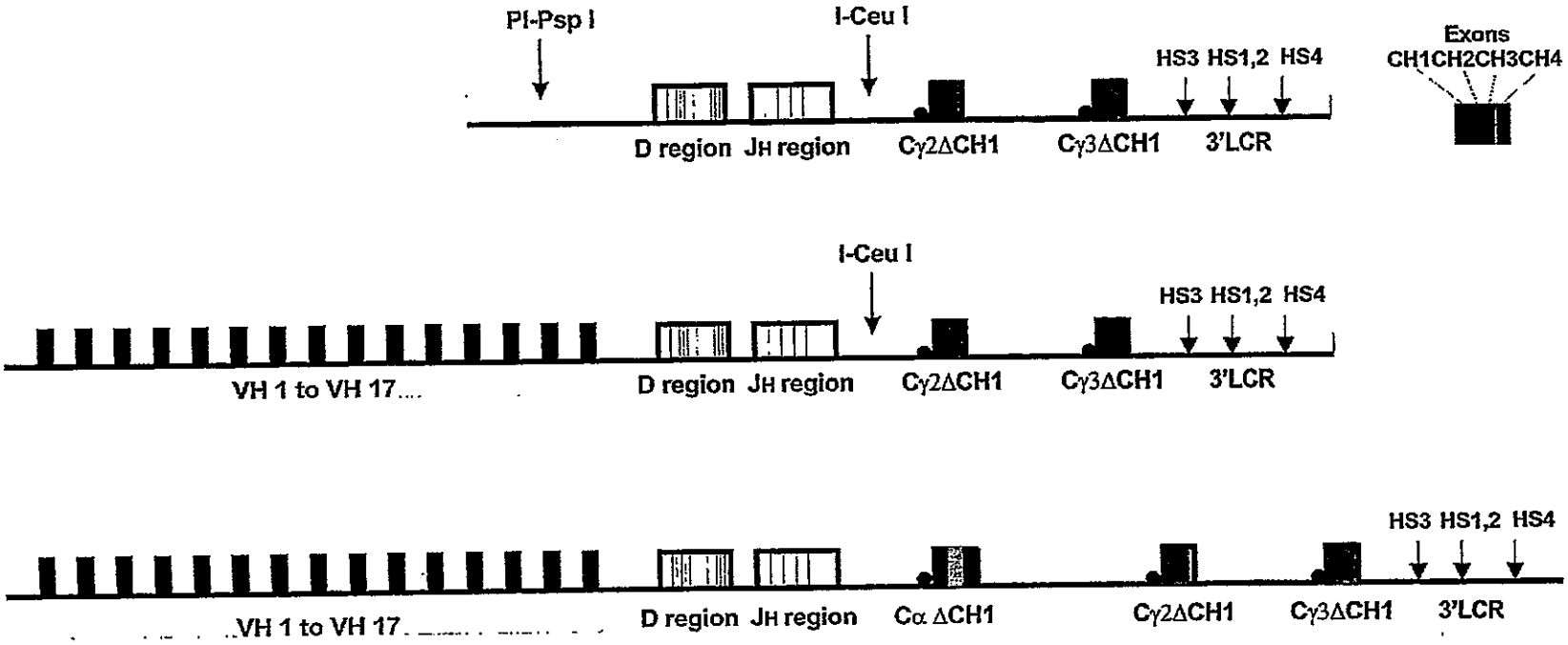

PI-Psp I
I-Ceu I
HS3 HS1,2 HS4
Exons
CH1CH2CH3CH4
D region JH region Cγ2ΔCH1 Cγ3ΔCH1 3'LCR
I-Ceu I
HS3 HS1,2 HS4
VH 1 to VH 17....
D region JH region Cγ2ΔCH1 Cγ3ΔCH1 3'LCR
HS3 HS1,2 HS4
VH 1 to VH 17.
D region JH region Cα ΔCH1 Cγ2ΔCH1 Cγ3ΔCH1 3'LCR

FIG. 11

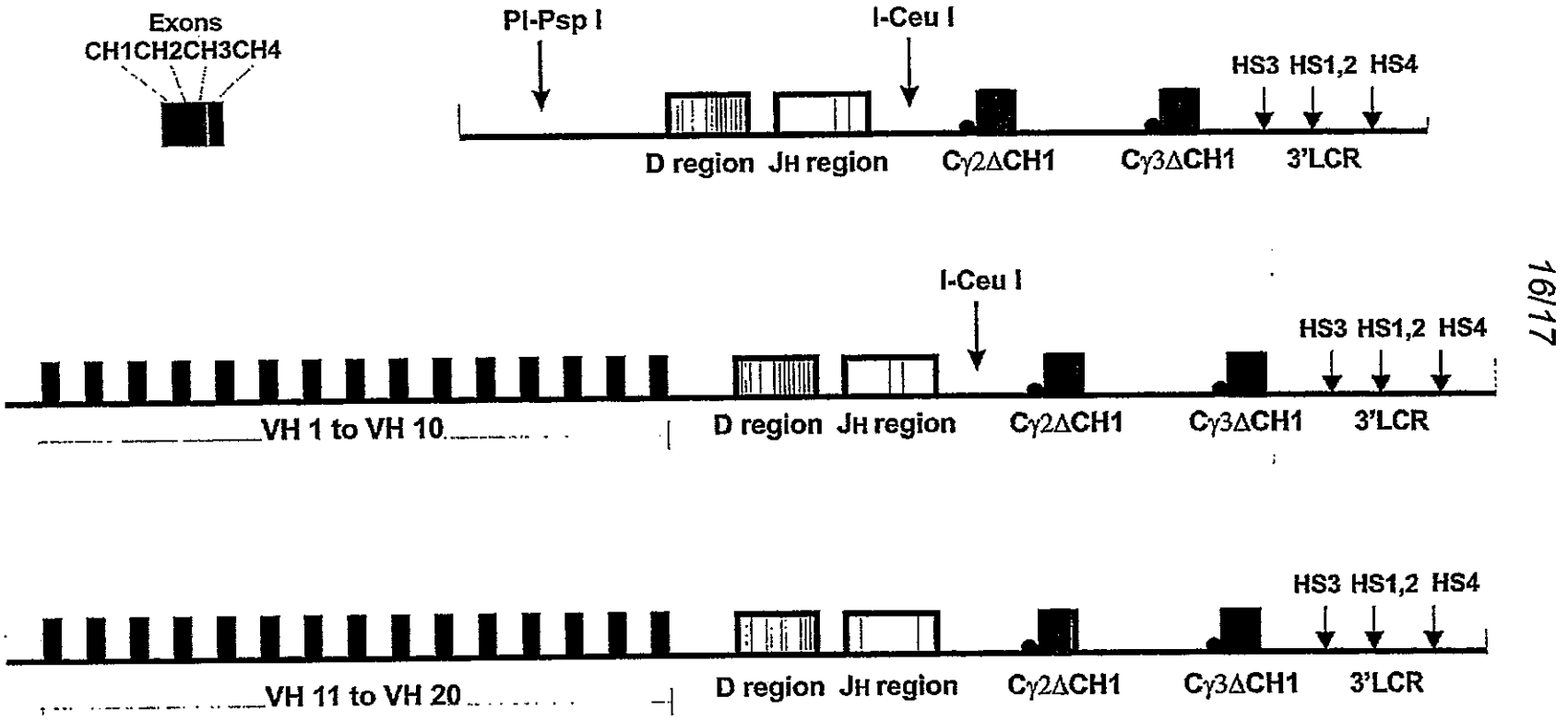

Exons
CH1CH2CH3CH4
PI-Psp I
I-Ceu I
HS3 HS1,2 HS4
D region JH region
Cγ2ΔCH1
Cγ3ΔCH1
3'LCR
I-Ceu I
HS3 HS1,2 HS4
VH 1 to VH 10
D region JH region
Cγ2ΔCH1
Cγ3ΔCH1
3'LCR
HS3 HS1,2 HS4
VH 11 to VH 20
D region JH region
Cγ2ΔCH1
Cγ3ΔCH1
3'LCR

FIG. 12

