
MGA
GA
MAGA
VH1VH2
D region
Jα region
Cα
Cβ
Cγ2ACH1
Cγ3ACH1
3'LCR
HS3 HS1,2 HS4

FIG. 1

FIG. 2A

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

	WT	GA (~5 copies)	GA (single copy)	MAGA
BM	10.80 ± 2.09	5.94 ± 1.44	4.99 ± 1.79	6.08 ± 1.53
Spleen	41.80 ± 6.05	32.14 ± 9.46	28.70 ± 8.70	33.06 ± 3.24
Blood	43.72 ± 7.50	18.00 ± 5.68	18.01 ± 3.76	9.25 ± 3.74
Peritoneum	21.92 ± 9.90	*22.85 ± 6.71	*22.30 ± 7.29	21.21 ± 14.87

Mice were 14-20 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

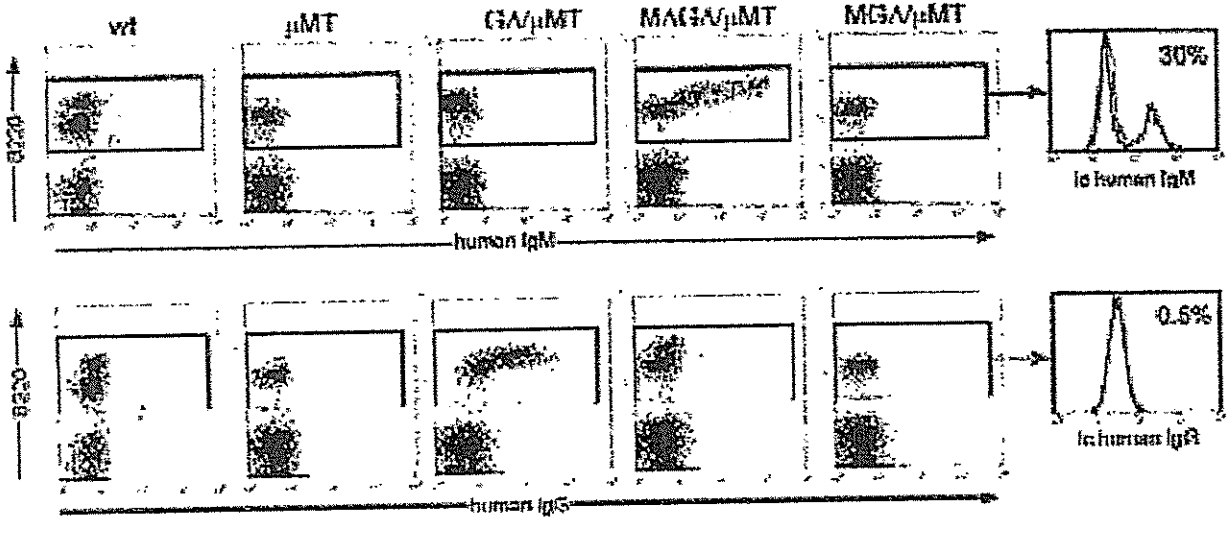


FIG. 2C

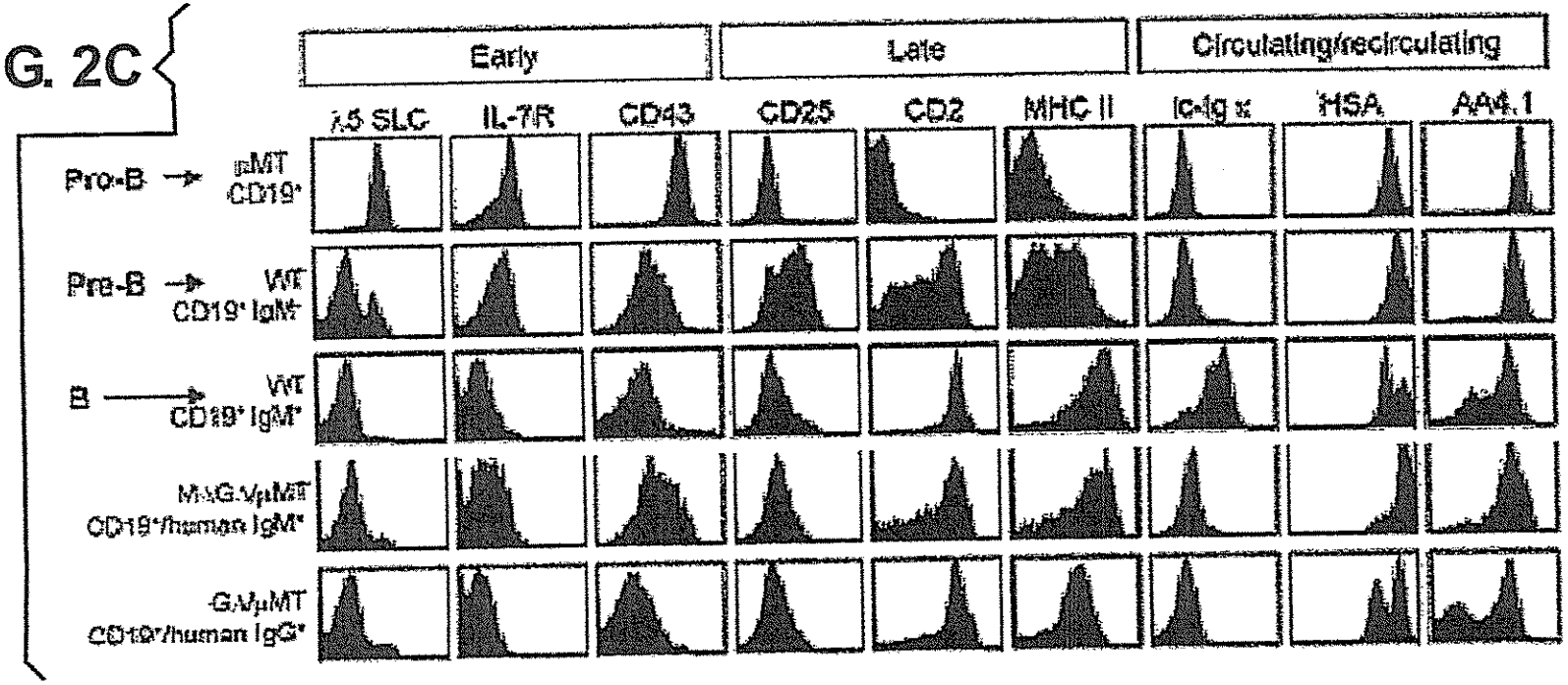

Early
Late
Circulating/recirculating
λ5 SLC
IL-7R
CD43
CD25
CD2
MHC II
Ic-Ig κ
HSA
AA4.1
Pro-B → μMT CD19+
Pre-B → WT CD19+ IgM+
B → WT CD19+ IgM+
M.G.V/μMT CD19+/human IgM+
G.V/μMT CD19+/human IgG+

FIG. 2D

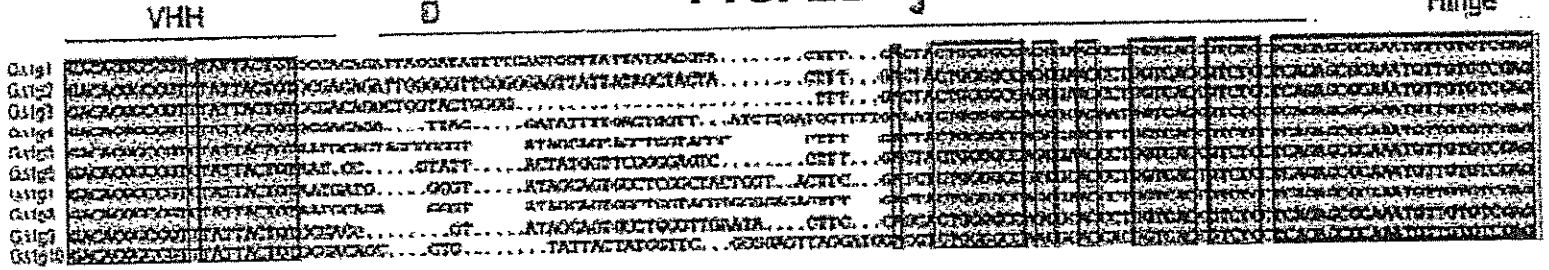
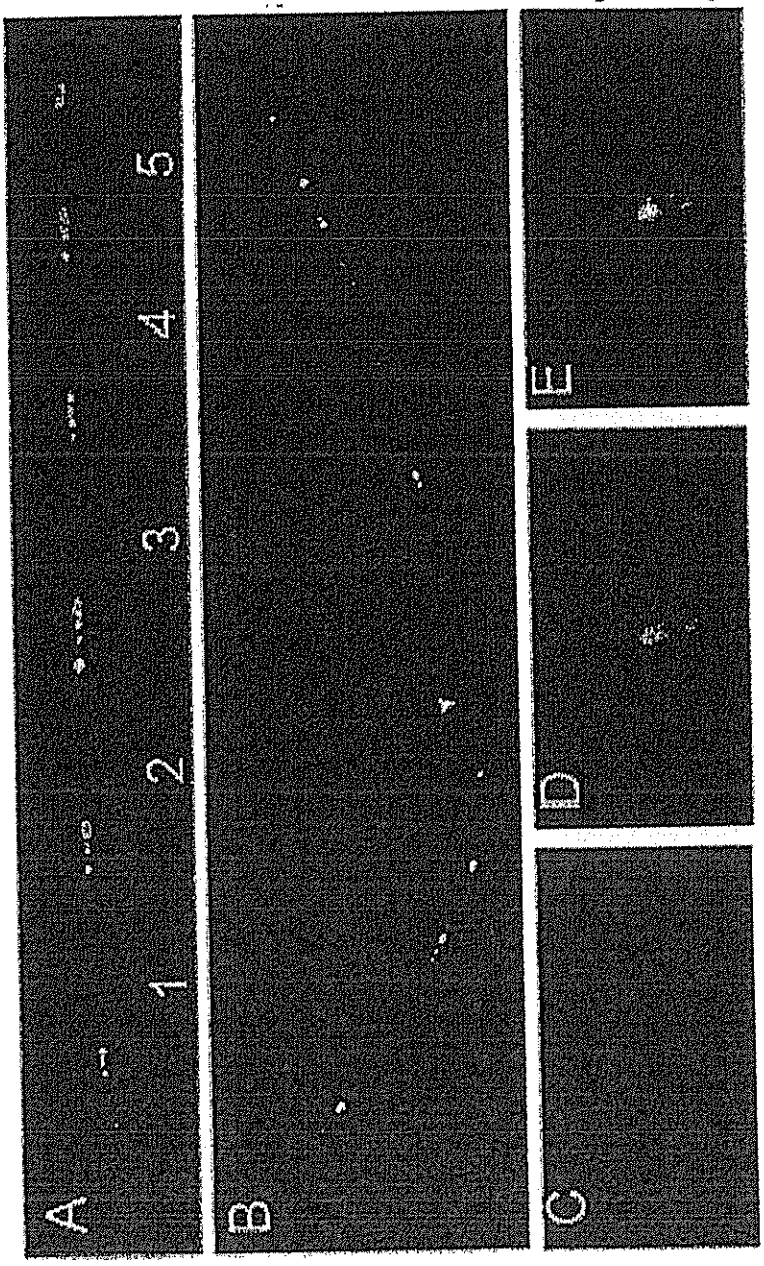

VHH
D
J
Hinge

FIG. 3



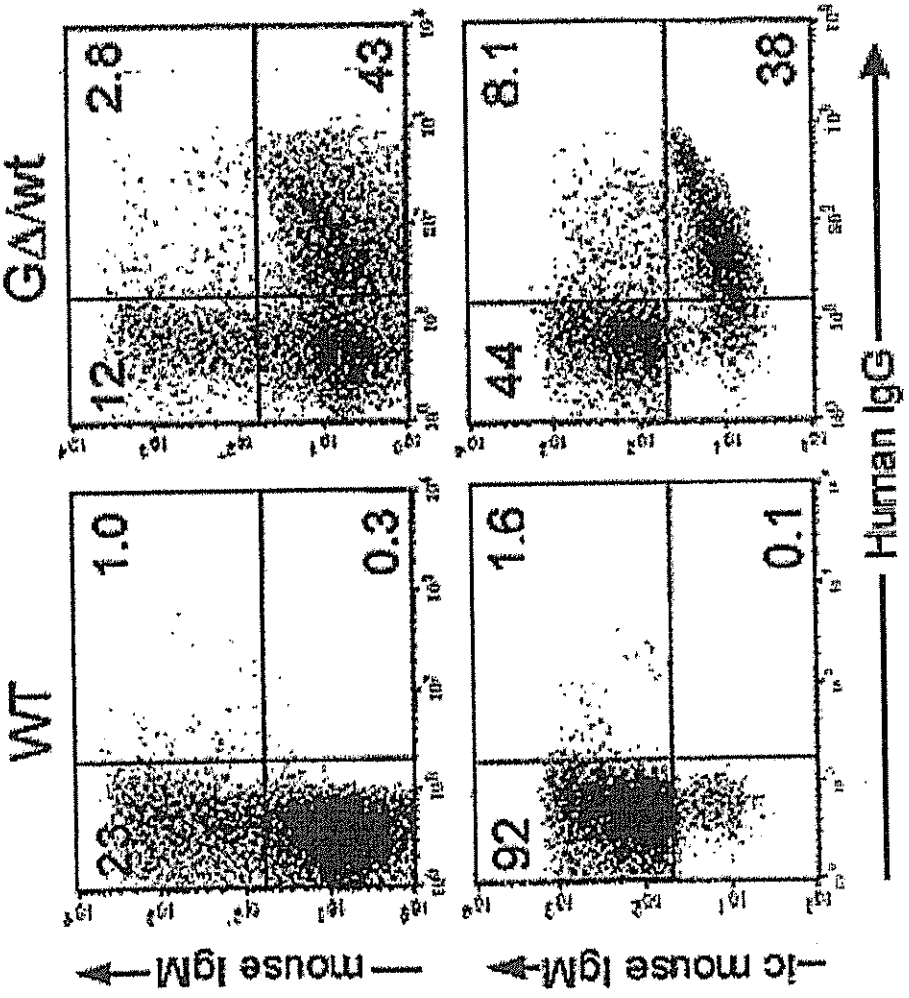

GΔ/wt
WT
2.8
43
12
8.1
38
44
1.0
0.3
23
1.6
0.1
92
Human IgG
mouse IgM
ic mouse IgM

FIG. 3F

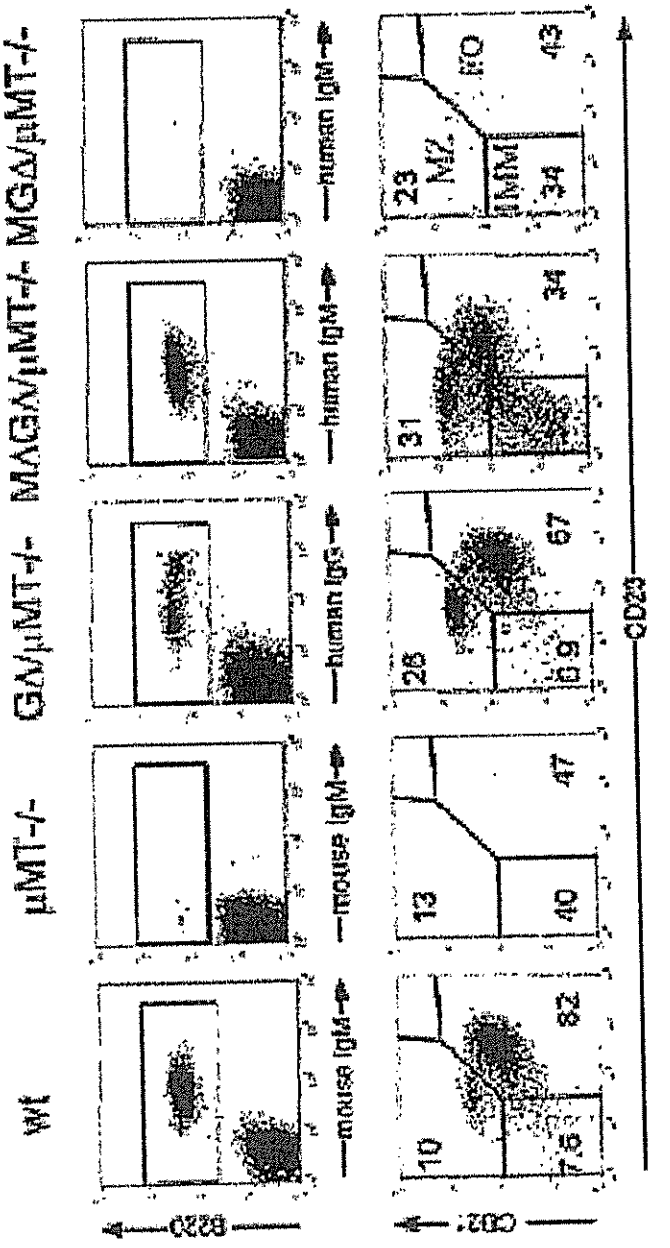

WT
μMT-/-
GAμMT-/-
MAGAμMT-/-
MGΔ/μMT-/-
B220
mouse IgM
CD21
human IgG
human IgM
CD23
10
82
15
13
47
40
28
67
9
31
34
23
MZ
FO
43
MM
34

FIG. 4A

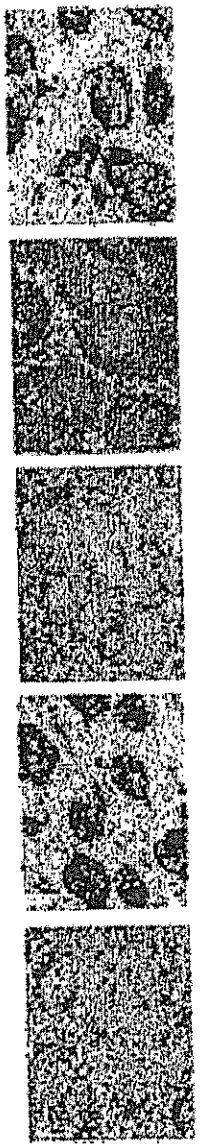
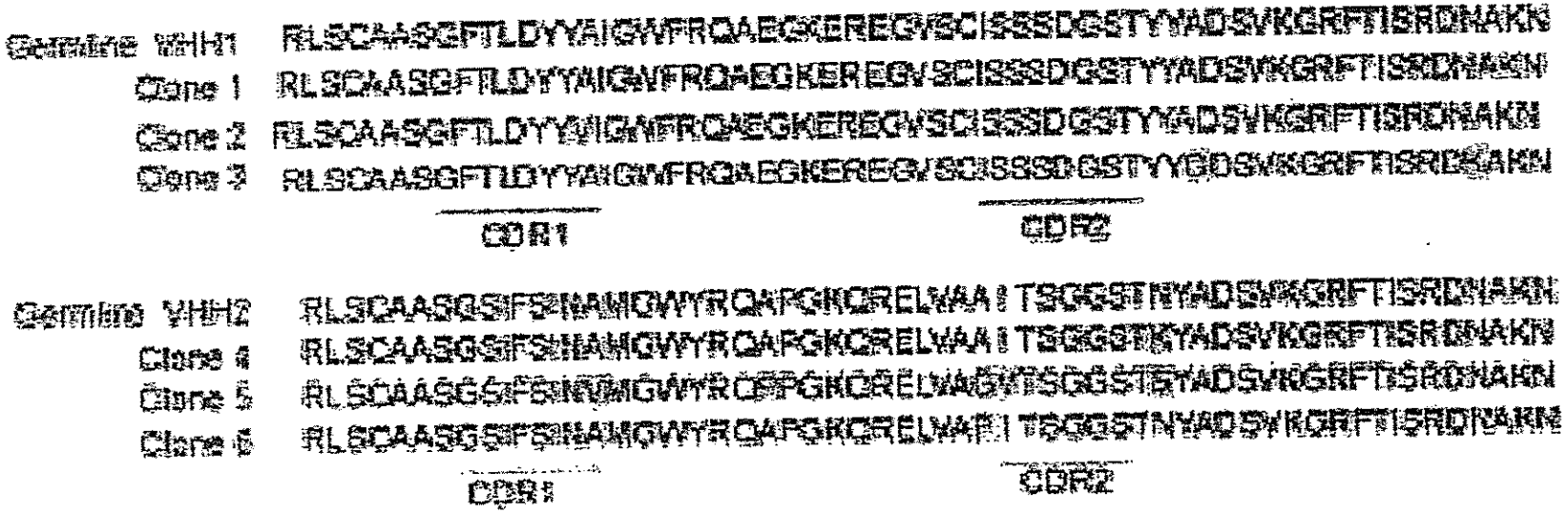


FIG. 4B

FIG. 4C


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

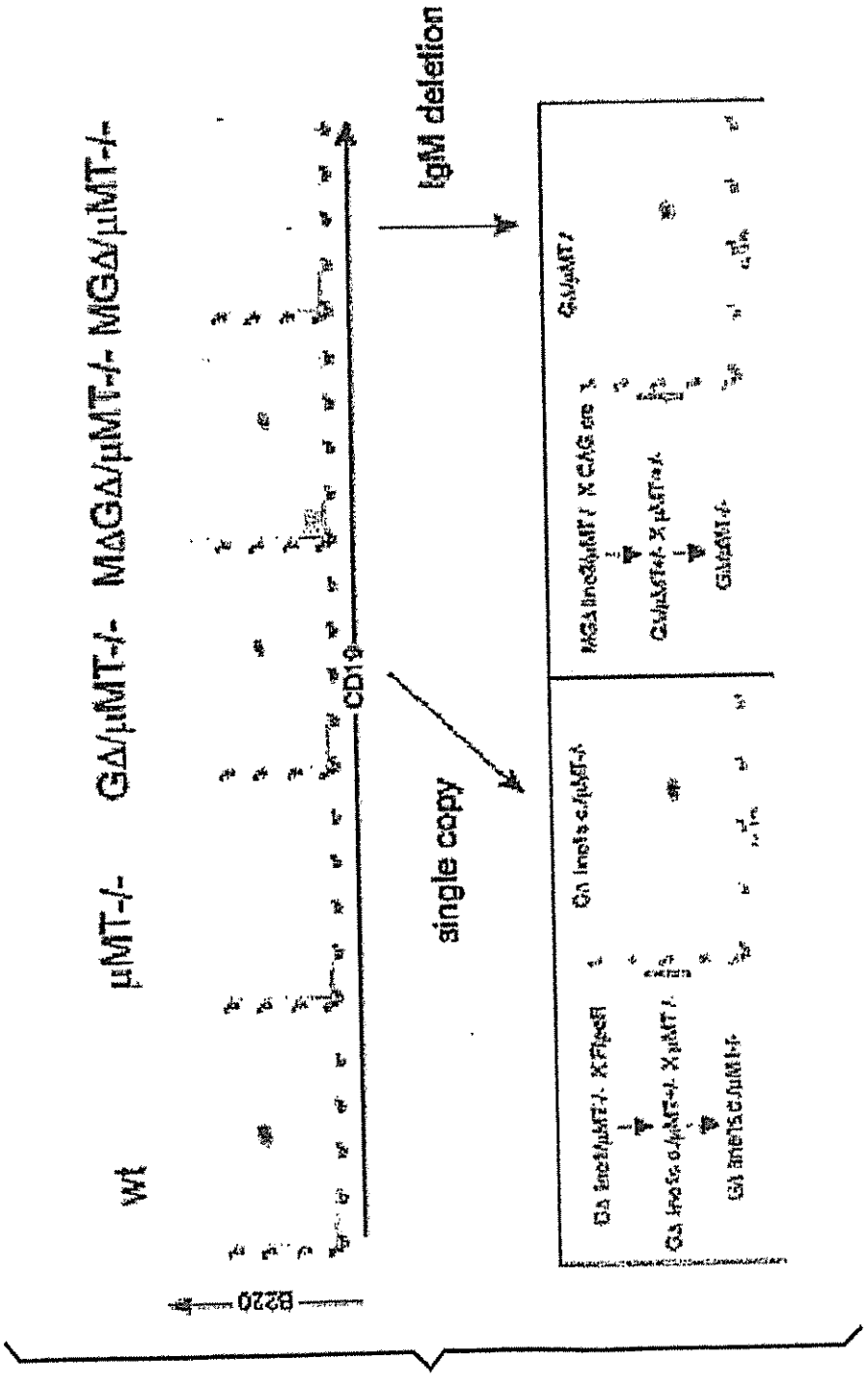

Wt
μMT-/-
GΔ/μMT-/-
MAGΔ/μMT-/-
MGΔ/μMT-/-
IgM deletion
single copy
B220
CD19

FIG. 4D

FIG. 5A

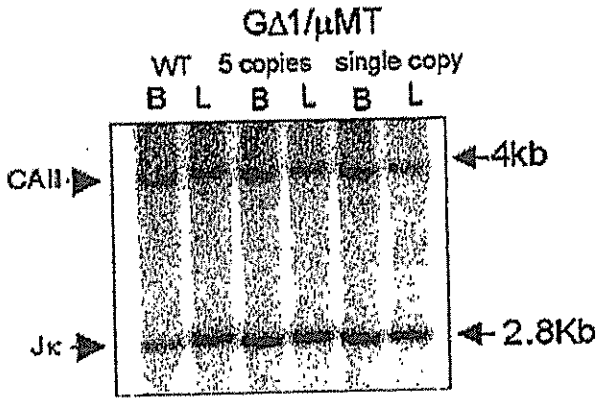

GΔ1/μMT
WT
5 copies
single copy
B L B L B L
CAII
Jκ
4kb
2.8Kb

FIG. 5B

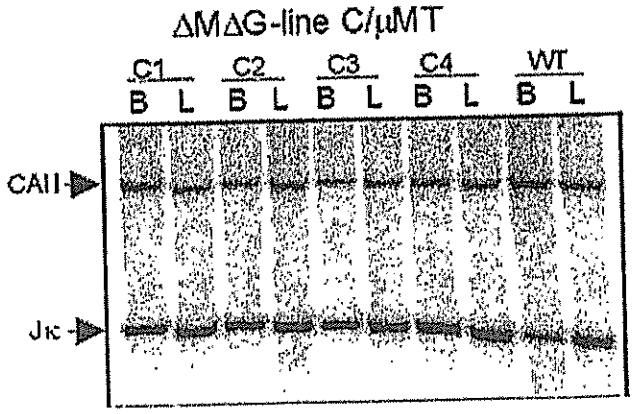

ΔMΔG-line C/μMT
C1
C2
C3
C4
WT
B L B L B L B L B L
CAII
Jκ

FIG. 6

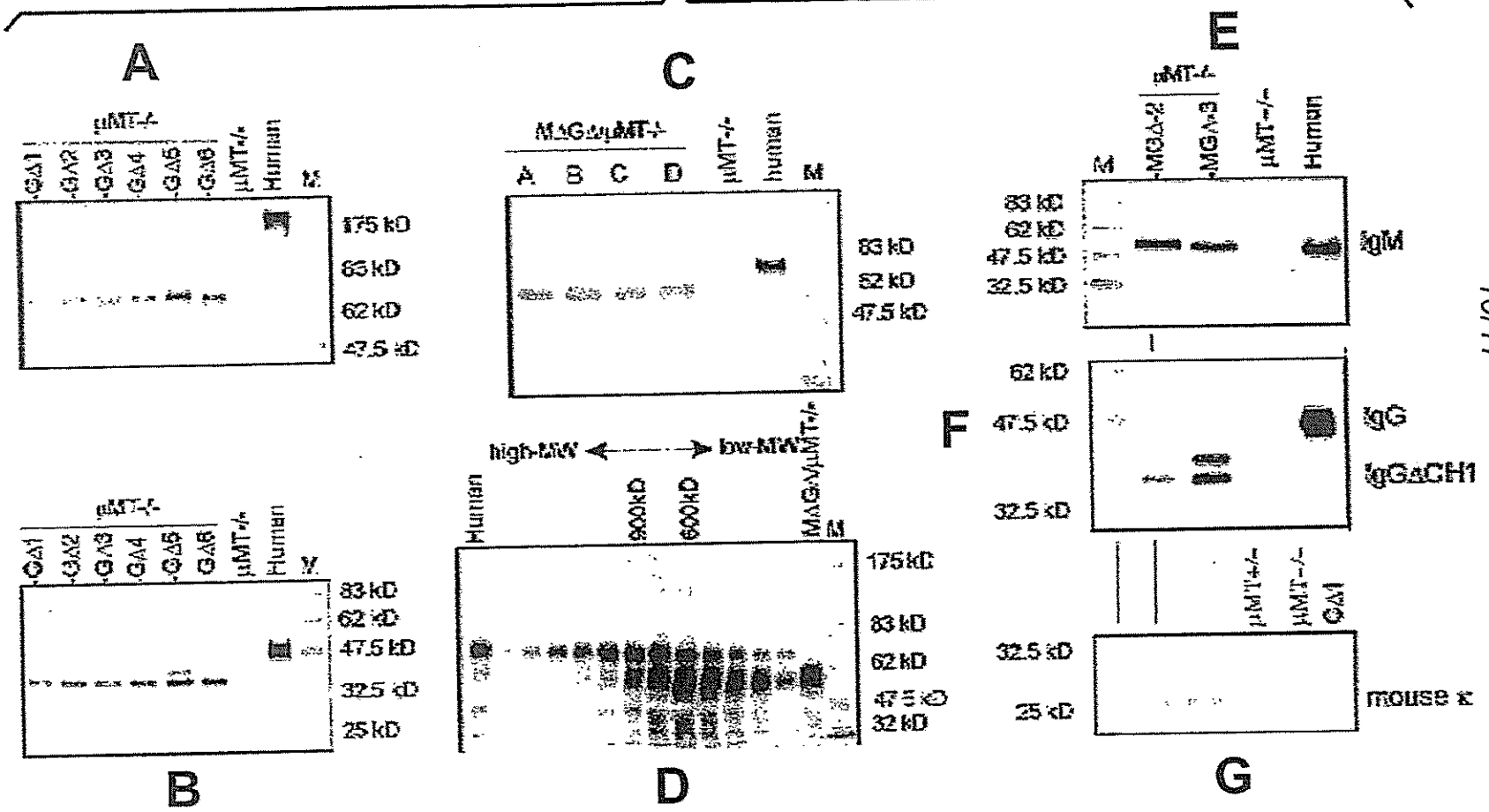

A
μMT-/-
GΔ1
GΔ2
GΔ3
GΔ4
GΔ5
GΔ6
μMT+/-
Human
M
175 kD
83 kD
62 kD
47.5 kD
B
μMT-/-
GΔ1
GΔ2
GΔ3
GΔ4
GΔ5
GΔ6
μMT+/-
Human
M
83 kD
62 kD
47.5 kD
32.5 kD
25 kD
C
MΔGΔμMT-/-
A
B
C
D
μMT-/-
Human
M
83 kD
62 kD
47.5 kD
D
high-MW
low-MW
Human
900kD
600kD
MΔGΔμMT+/-
M
175kD
83 kD
62 kD
47.5 kD
32 kD
E
μMT-/-
MGΔ2
MGΔ3
μMT-/-
Human
M
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-rtTA
α-hTNFα
α-B.Pertussis
Human IgG2 hinge
Human IgG3 hinge
Human IgM CH2

FIG. 3F

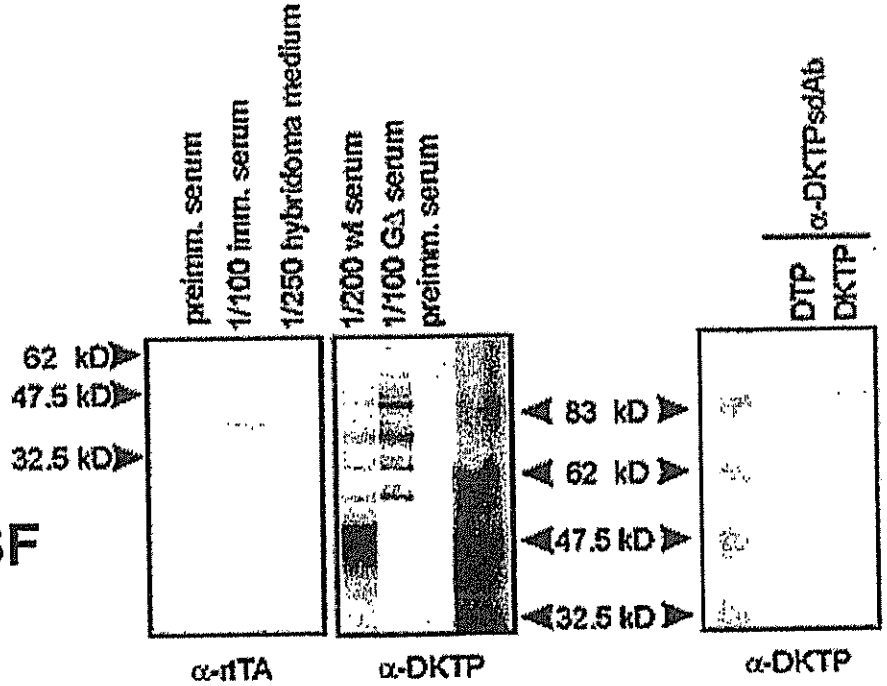


FIG. 7C

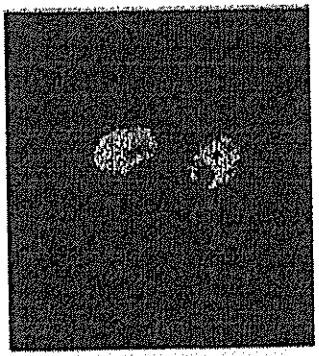


FIG. 7D

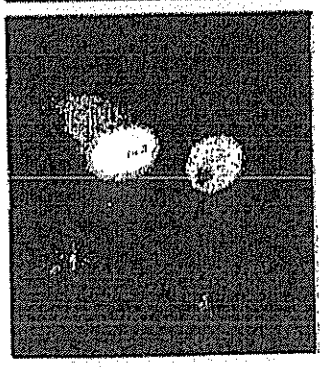


FIG. 7E

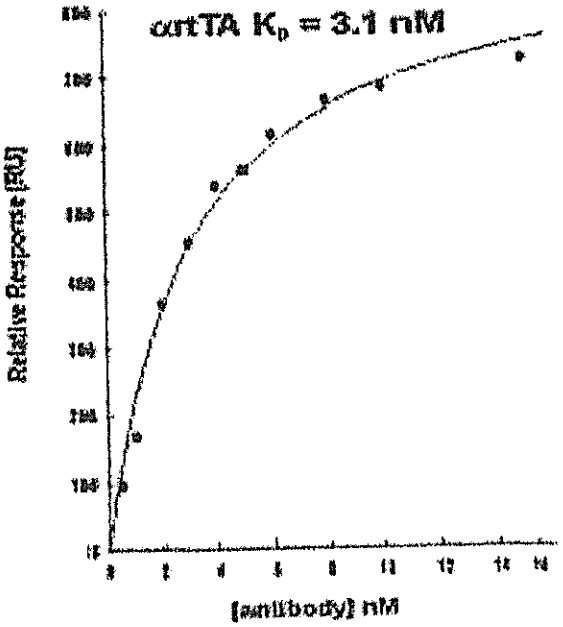


FIG. 8A

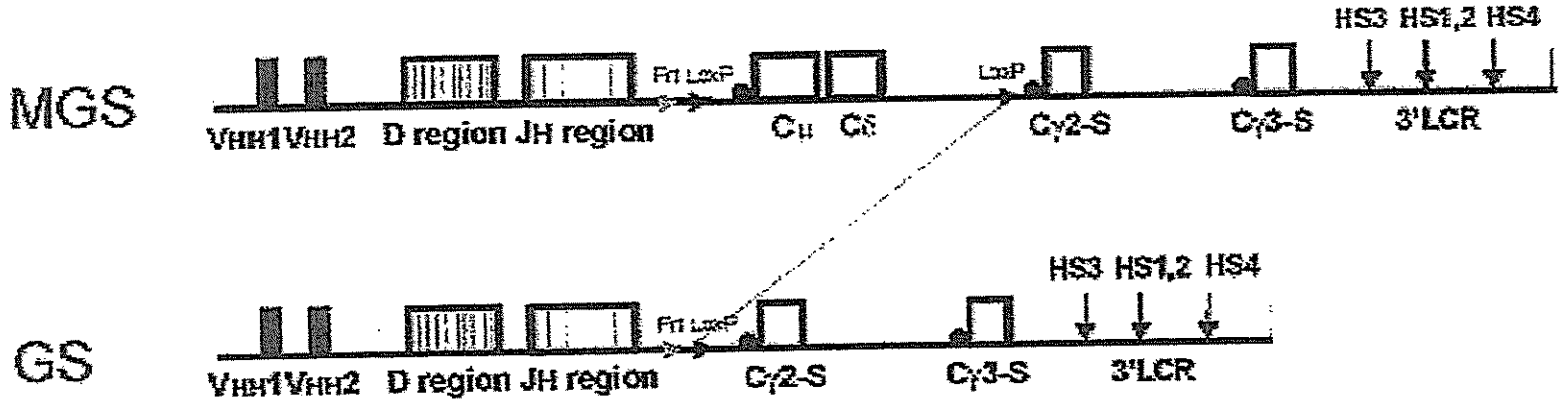
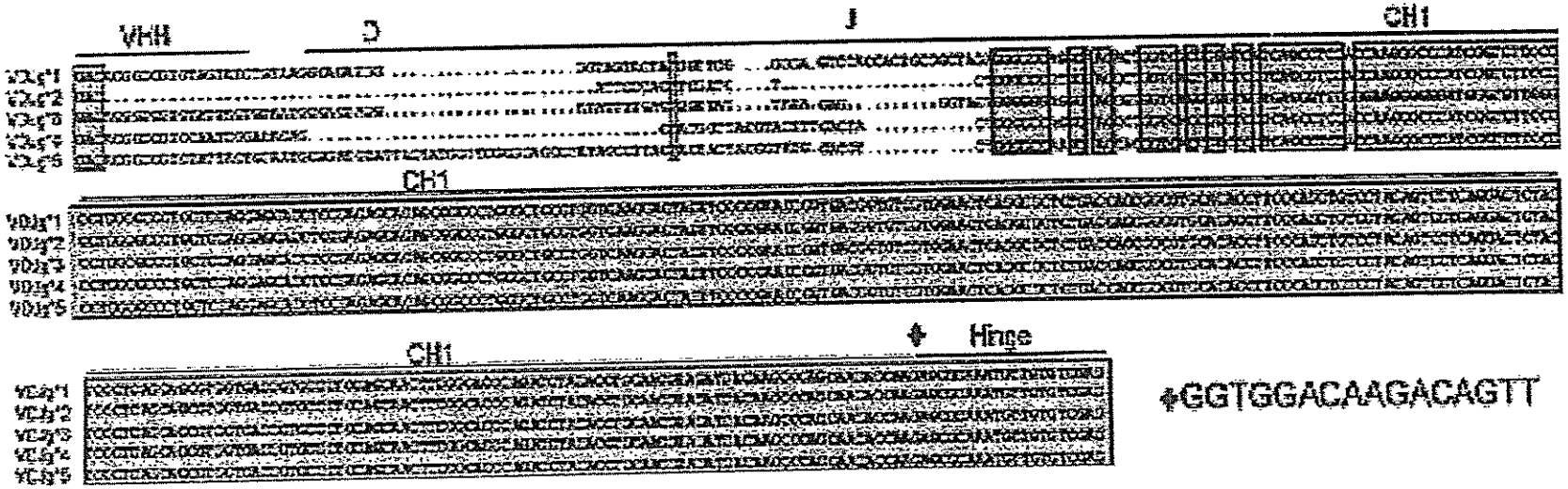

MGS
HS3 HS1,2 HS4
Frt LoxP
LoxP
VHH1VHH2 D region JH region
Cμ Cδ
Cγ2-S
Cγ3-S
3'LCR
GS
HS3 HS1,2 HS4
Frt LoxP
VHH1VHH2 D region JH region
Cγ2-S
Cγ3-S
3'LCR

FIG. 8B


VHH
D
J
CH1
CH1
Hinge
GGTGGACAAGACAGTT

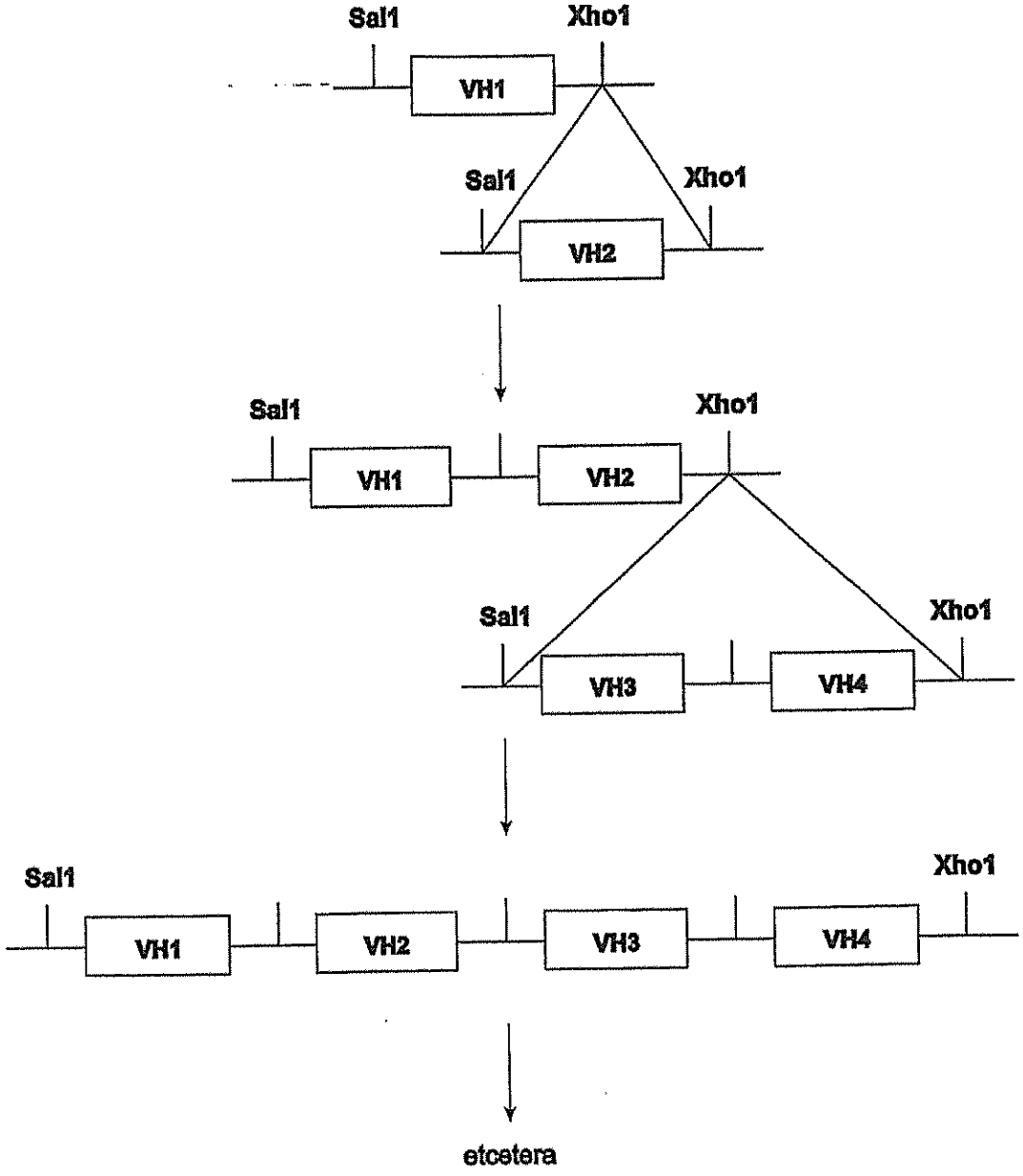

Sal1
Xho1
VH1
Sal1
Xho1
VH2
Sal1
Xho1
VH1
VH2
Sal1
Xho1
VH3
VH4
Sal1
Xho1
VH1
VH2
VH3
VH4
etcetera

FIG. 9

FIG. 10

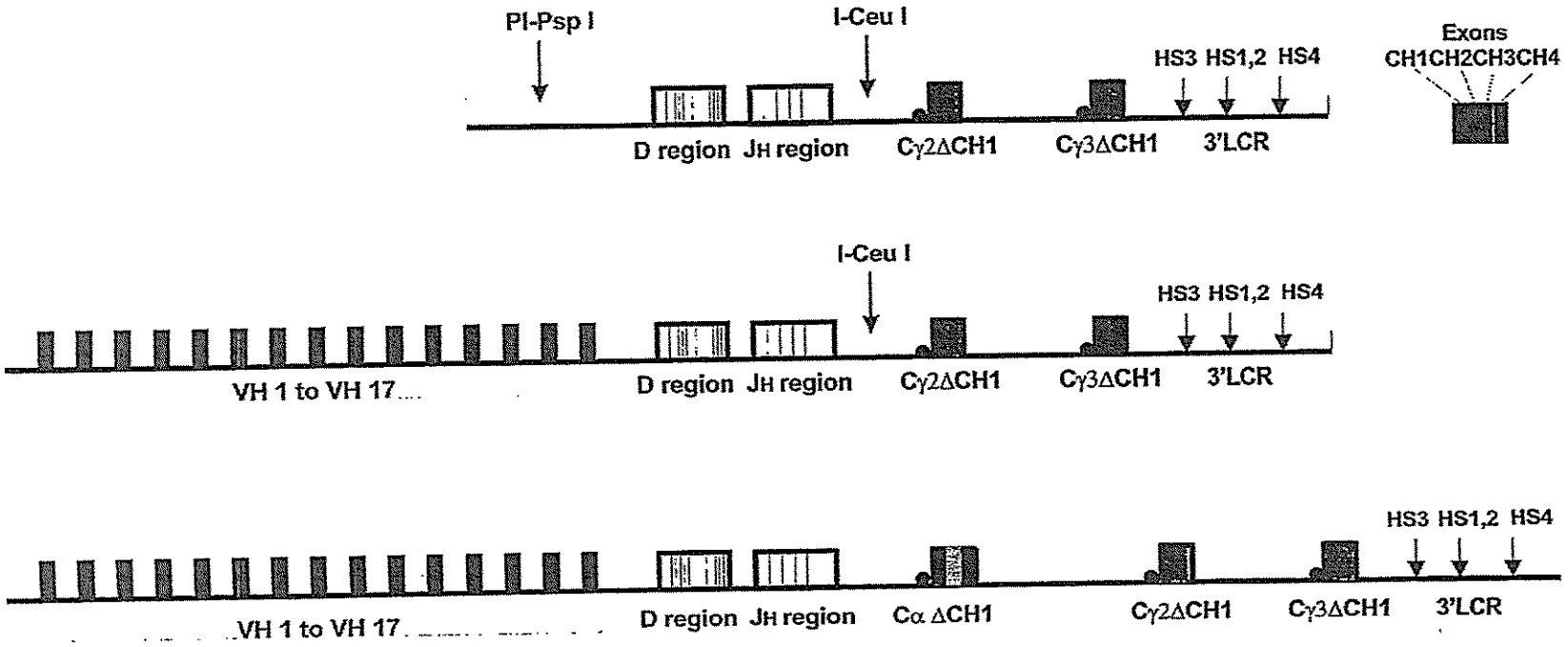

PI-Psp I
I-Ceu I
HS3 HS1,2 HS4
Exons
CH1CH2CH3CH4
D region JH region Cγ2ΔCH1 Cγ3ΔCH1 3'LCR
I-Ceu I
HS3 HS1,2 HS4
VH 1 to VH 17....
D region JH region Cγ2ΔCH1 Cγ3ΔCH1 3'LCR
HS3 HS1,2 HS4
VH 1 to VH 17.....
D region JH region Cα ΔCH1 Cγ2ΔCH1 Cγ3ΔCH1 3'LCR

FIG. 11

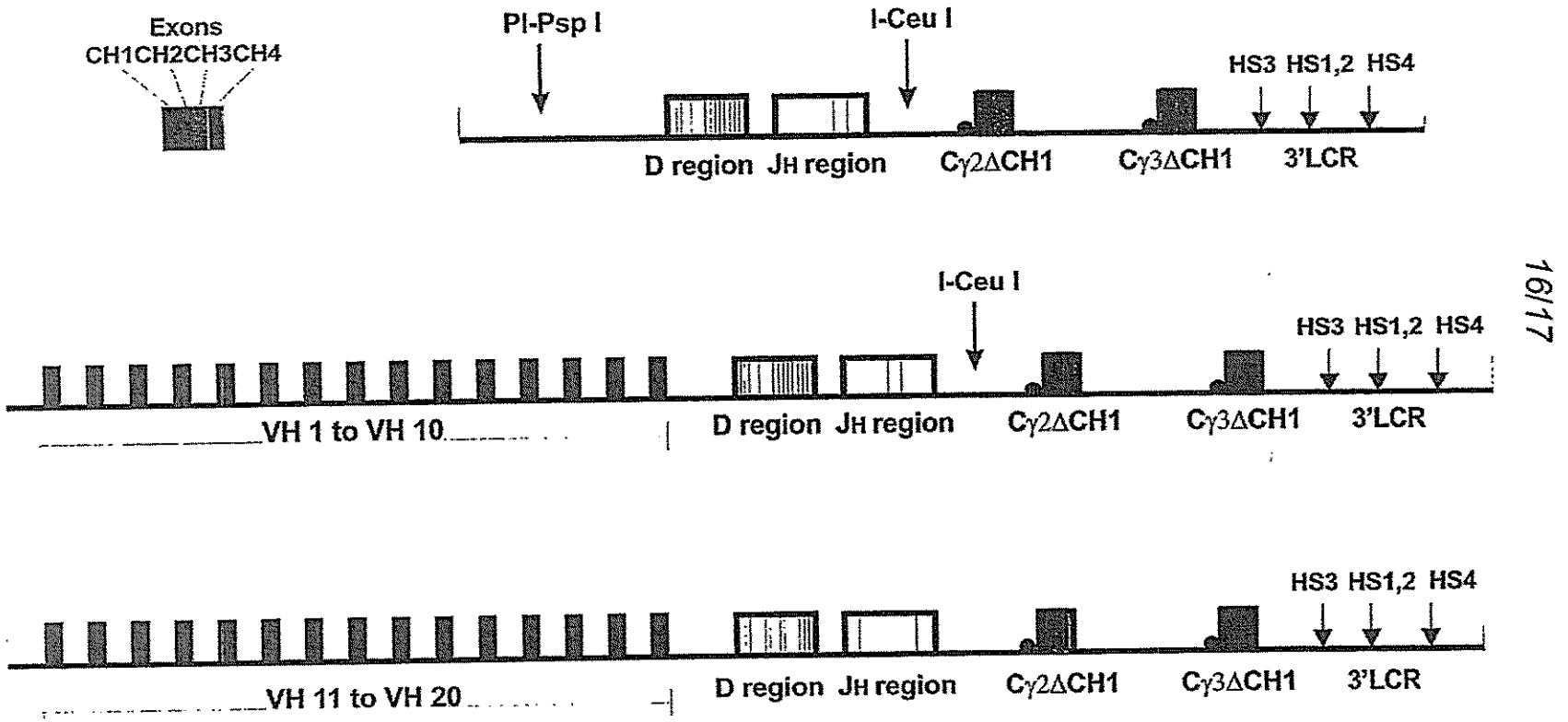

Exons
CH1CH2CH3CH4
PI-Psp I
I-Ceu I
HS3 HS1,2 HS4
D region JH region
Cγ2ΔCH1
Cγ3ΔCH1
3'LCR
I-Ceu I
HS3 HS1,2 HS4
VH 1 to VH 10
D region JH region
Cγ2ΔCH1
Cγ3ΔCH1
3'LCR
HS3 HS1,2 HS4
VH 11 to VH 20
D region JH region
Cγ2ΔCH1
Cγ3ΔCH1
3'LCR

FIG. 12

