POLYCOPIÉ IMMUNO

DOCUMENTS EXTRAITS DE

Cellular and molecular immunology, 4ème édition, Abbas HK et col., Saunders Ed.
Immunobiology, 5ème édition, C. Janeway and col, Garland Ed.
Immunology, 6ème édition, Roitt, and col., Mosby Ed.

LA RÉPONSE ANTICORPS [redacted] BMC 423

I-GÉNÉRALITÉS

II-ACTIVATION ET DIFFERENCIATION DES LB PAR ANTIGENES THYMODEPENDANTS

1- P remières étapes de l'activation B :
-1er signal
-Aprêtement de l'antigène
2-La réaction folliculaire, le rôle de CD40 :
-centre germinatif
-commutation isotypique
-maturation d'affinité

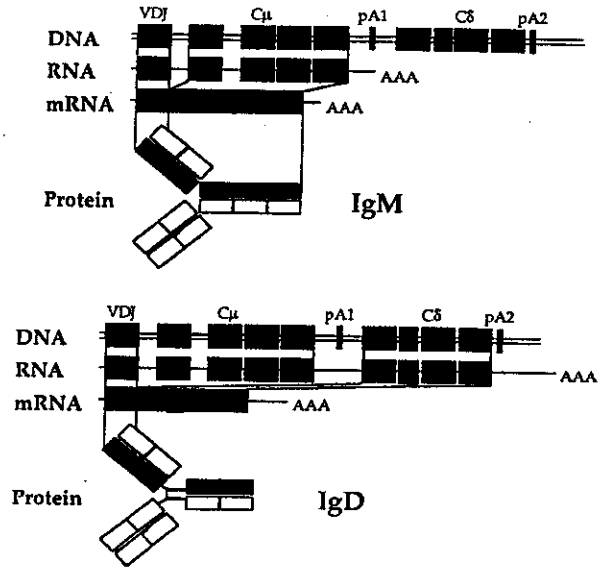
II-RÉPONSES VIS À VIS DES ANTIGÈNS THYMO-INDÉPENDANTS

1- Antigènes de Type 1, récepteurs Toll
2- Antigènes de Type 2
3-La réaction extrafolliculaire, le rôle de BLys et April

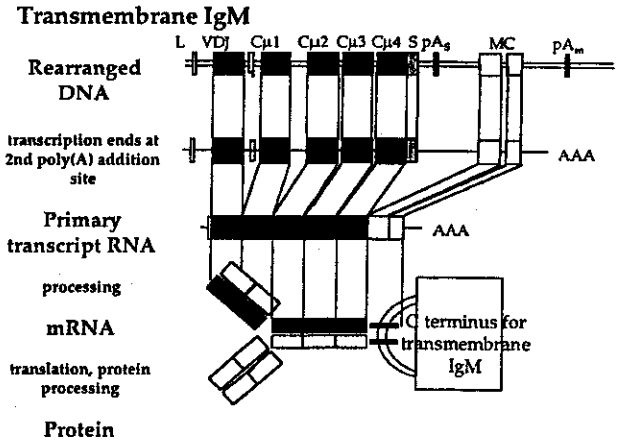
III-RÉGULATION DE L'ACTIVATION DES LB

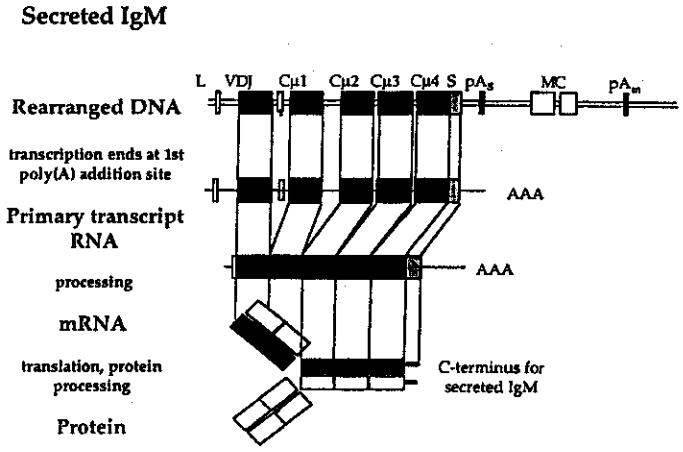
1- CD19
2- CD22
3- R écepteurs Fc gamma de type 2.

A common mRNA primary transcript for IgM and IgD.

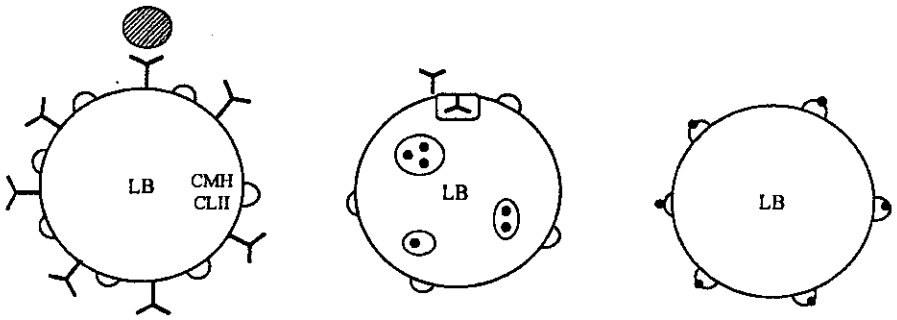


Transmembrane and secreted forms of Ig are derived from the same gene by alternative RNA processing.





APRETEMENT DE L 'ANTIGENE

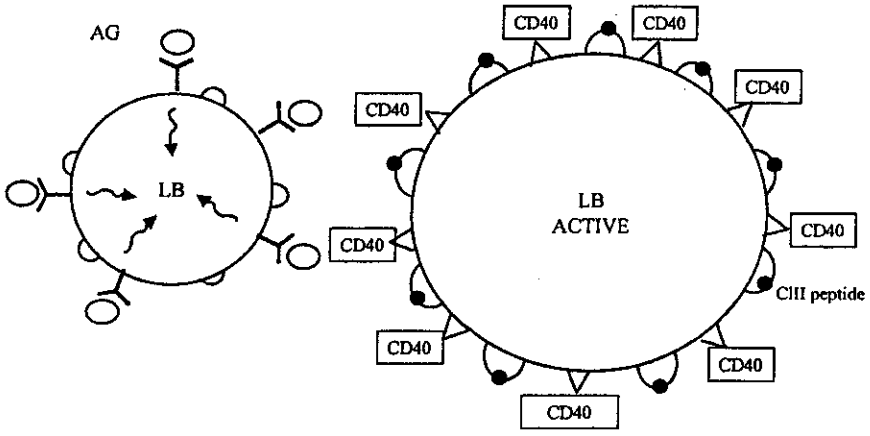


CONTACT AVEC
L 'ANTIGENE

INTERNALISATION
DEGRADATION
DE L'ANTIGENE
"APRETEMENT"

"PRESENTATION"
DES PEPTIDES
DERMES DE L'ANTIGENE
SUR LES MOLECULES
DE CLASSE II

AUGMENTATION DE L'EXPRESSION DE CD40, B7, ICAM1, SUR LES LB



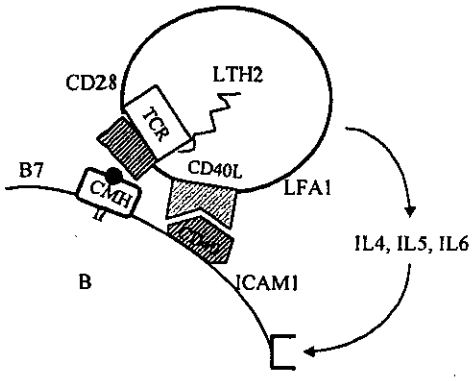
ACTIVATION DES
LB

EXPRESSION DE CD40

ACTIVATION DES LT PAR LB

- LTH2 (IL4, IL5, IL6)

- SONT ACTIVES PAR
2 SIGNAUX B : CMH/pep + CD40

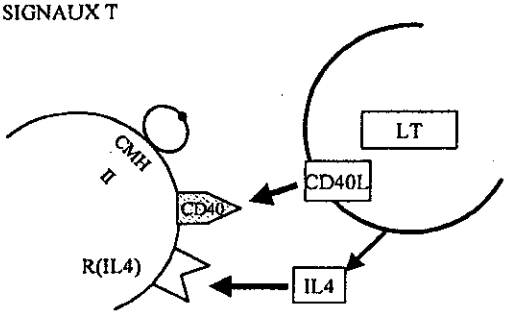


- PRODUISENT IL4, IL5, IL6 EN REPONSE A CETTE ACTIVATION

REPONSES DES LB A ACTIVATION LTh2

- PROLIFERENT EN REPONSE AUX DEUX SIGNAUX T

IL4 et CD40L



⟶ **PROLIFERATION B**

- SE DIFFERENCIENT EN REPONSE A IL5/IL6 PRODUITE PAR LES T

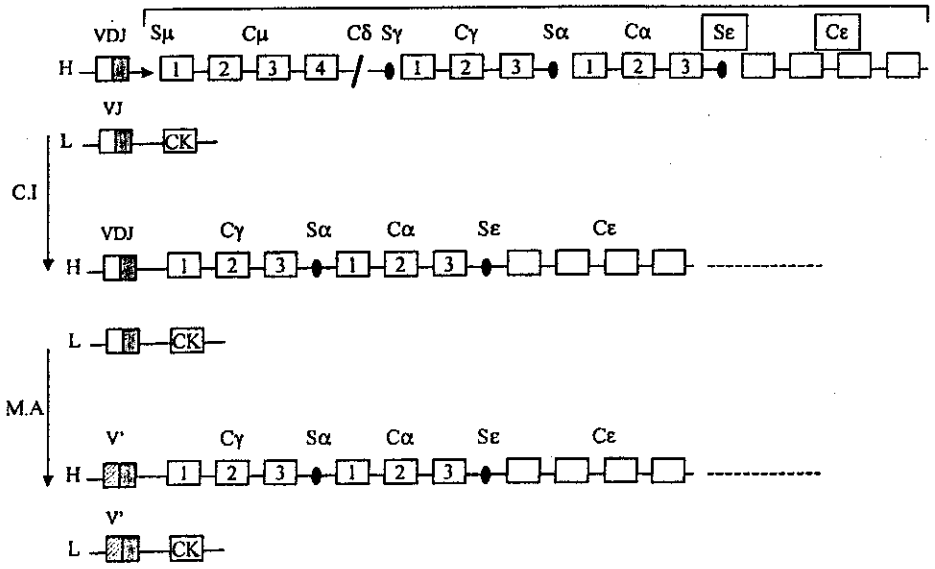
⟶ **DIFFERENCIATION EN PLASMOCYTES**

CARACTÉRISTIQUES DES PLASMOCYTES

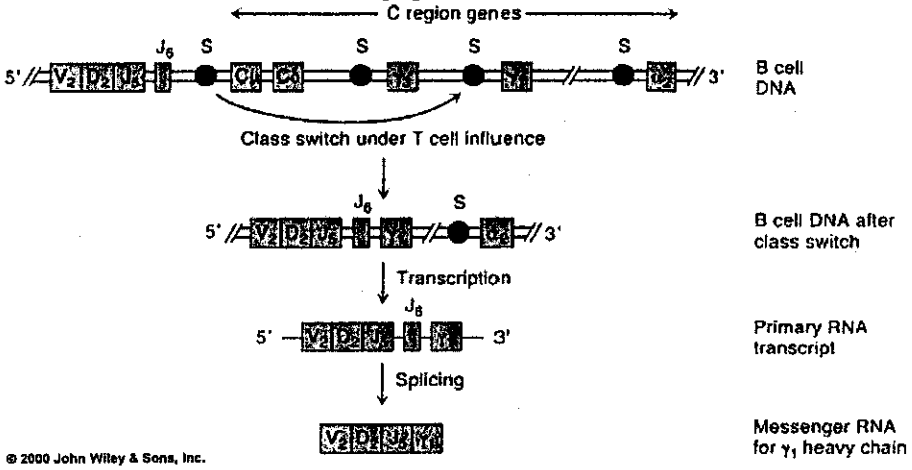
- SÉCRÈTENT LES ANTICORPS
- EXPRIMENT Ig MEMBRANE
- RICHES EN RÉTICULUM ENDOPLASMIQUE
- CMH NÉGATIFS
- CERTAINS ONT UNE TRÉS LONGUE DURÉE DE VIE

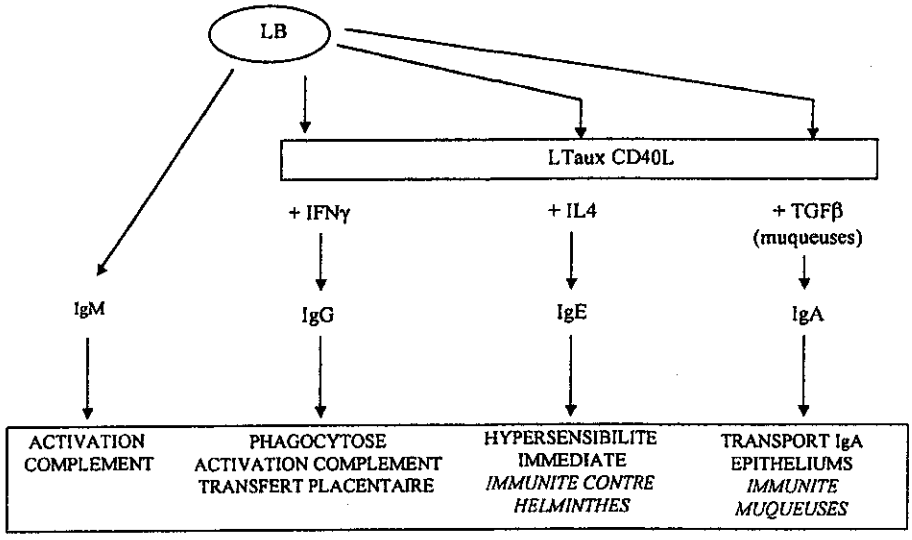
(6 MOIS / MOELLE OSSEUSE)

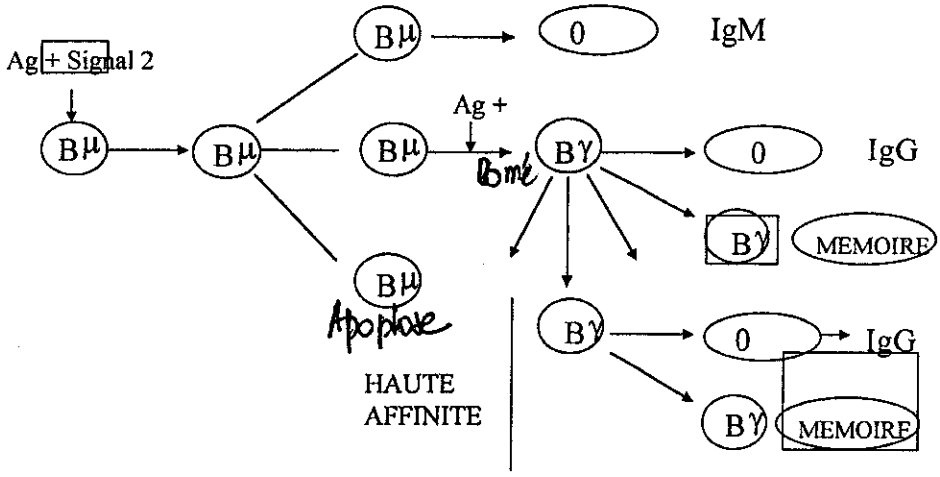
DANS LES CELLULES B MATURES :
COMMUTATION ISOTYPIQUE ET MATURATION D'AFFINITE



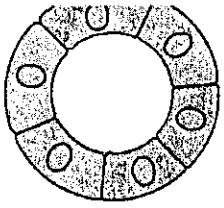
Isotypic switch



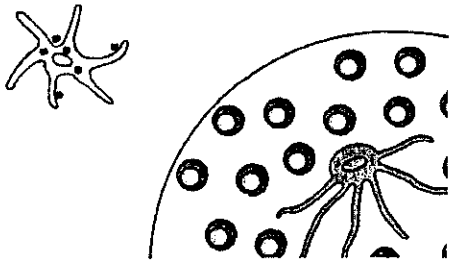




THE APC REACHES THE T CELL ZONE



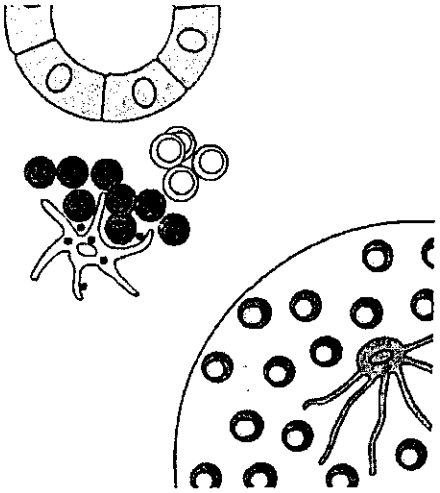
T cell zone



Follicular zone

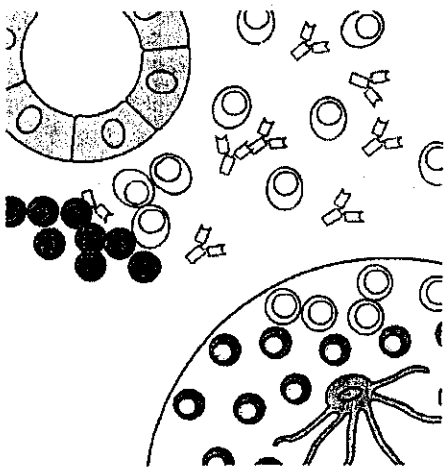
(from Janeway et al, « Immunobiology », 5th edition Garland ed »)

APC ACTIVATE TH2



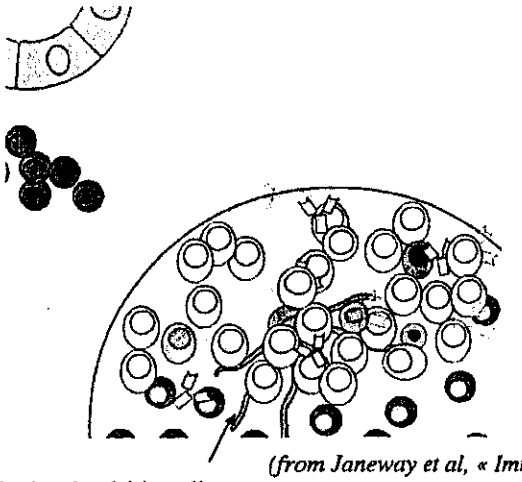
(from Janeway et al, « Immunobiology », 5th edition Garland ed »)

B CELLS RESPOND
AND SECRETE
LOW AFFINITY Ab
SOME REACH
THE FOLLICULE



(from Janeway et al, « Immunobiology », 5th edition Garland ed »)

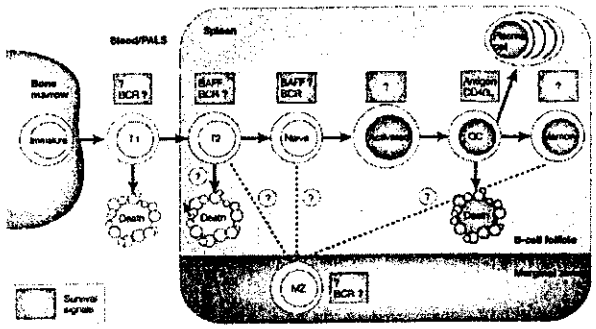
THEY PROLIFERATE, FORM A GERMINAL CENTER
WHERE SOMATIC MUTATION AND ISOTYPE SWITCH CAN OCCUR



Follicular dendritic cells

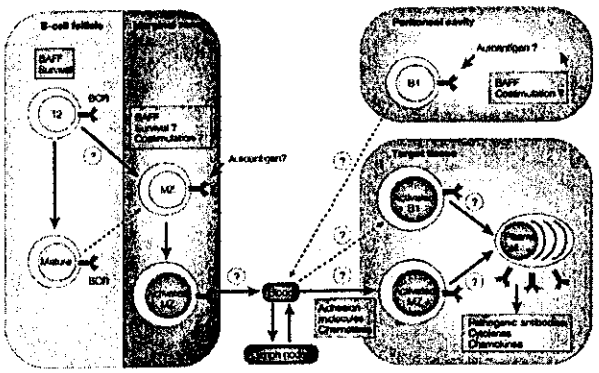
(from Janeway et al, « Immunobiology », 5th edition Garland ed »)

AG	EXEMPLE	REPONSE B			MECANISME	LIEU
		Type Cellule	AC	B mémoire		
TI1	LPS	B2	IgM IgG3 Anti Bactérien Faible Affinité	non	Pontage BCR/TLRs	ORGANES LYMPHOIDES
TI2	Polysaccharides	B1 CD5+ CR2+ IgM++	[IgM] [IgG3] [IgA] Anti Self Anti Bactérien Faible Affinité	non	Pontage BCR	PERITOINE MUQUEUSE LB ZONE MARGINALE RATE



Nature Reviews | Immunology

Figure 2 | **Survival signals during B-cell maturation.** During maturation, immature B cells that are formed in the bone marrow enter the spleen, where they pass through two intermediate stages of maturation, T1 and T2, before reaching maturity. Peripheral immature B cells (T1 and, potentially, T2 B cells) are vulnerable to strong antigenic signals through their B-cell receptor (BCR), which trigger cell death. In addition, newly formed B cells (T2 and, possibly, mature B cells) that are potentially self-reactive, such as B cells that bear two BCRs, might differentiate into marginal-zone (MZ) B cells, whereas non-self-reactive B cells might



Nature Reviews | Immunology

Figure 3 | **BAFF-mediated B-cell maturation: possible mechanisms.** a | T1 B cells do not

Kurosaki, Nature rev imm, 2, 354, 2002

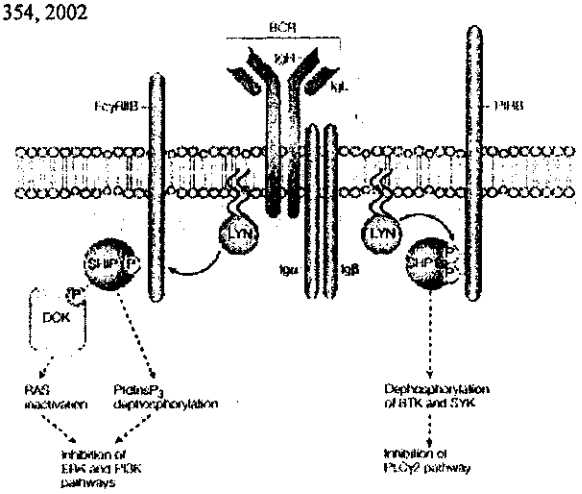
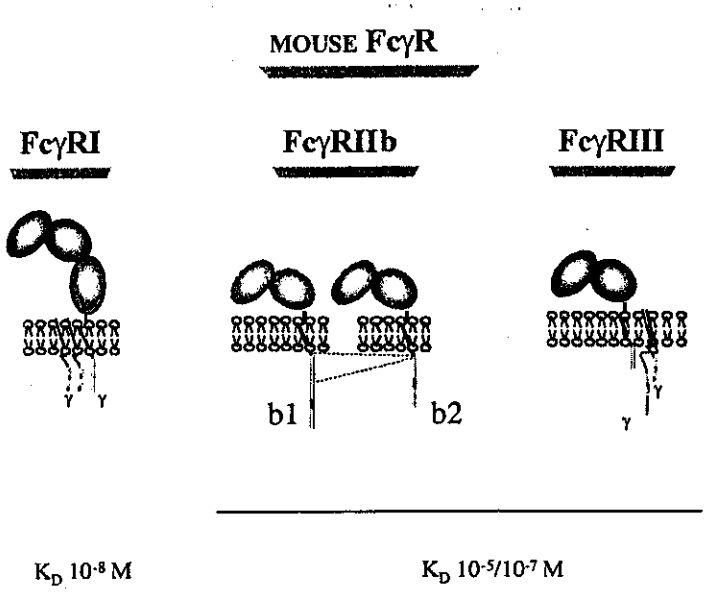


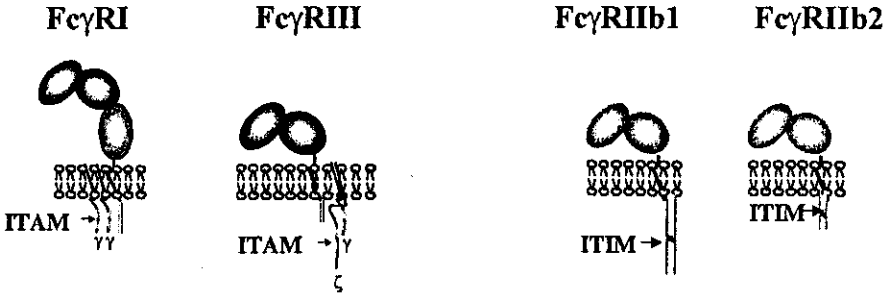
Figure 6 | **Negative-regulatory loops mediated by inhibitory receptors on B cells.** Once the immunoreceptor tyrosine-based inhibitory motif (ITIM) of FcγRIIB is phosphorylated, SH2 homology-2 (SH2)-domain-containing inositol 5-phosphatase (SHIP) and the associated docking protein (DOK) are recruited, which, in turn, have negative influences on phosphoinositide 3-kinase (PI3K) and extracellular signal regulated kinase (ERK; mitogen-activated protein kinase 1) pathways. By contrast, tyrosine phosphorylation of paired immunoglobulin-like receptor B (PIR-B) ITIMs recruits SH2-domain-containing protein tyrosine phosphatase 1 (SHP1), which, in turn, dephosphorylates various protein-tyrosine kinases, including SYK and Bruton's tyrosine kinase (BTK). BCR, B-cell receptor; IgH, immunoglobulin heavy chain; IgL, immunoglobulin light chain; PLCγ2, phospholipase Cγ2; PtdInsP_3, phosphatidylinositol-3,4,5-triphosphate.

BIOLOGICAL ACTIVITIES OF Ag-Ab (IgG) COMPLEXES

- **Internalization**
  - **Phagocytosis**
  - **Endocytosis**
- **Cell activation :**
  - **Release of mediators**
  - **Perforin and granzyme release (ADCC)**
  - **Cytokine secretion**
- **Inhibition of Cell activation**



ACTIVATING RECEPTORS INHIBITORY RECEPTORS



« Immunoreceptor tyrosine activation motif »

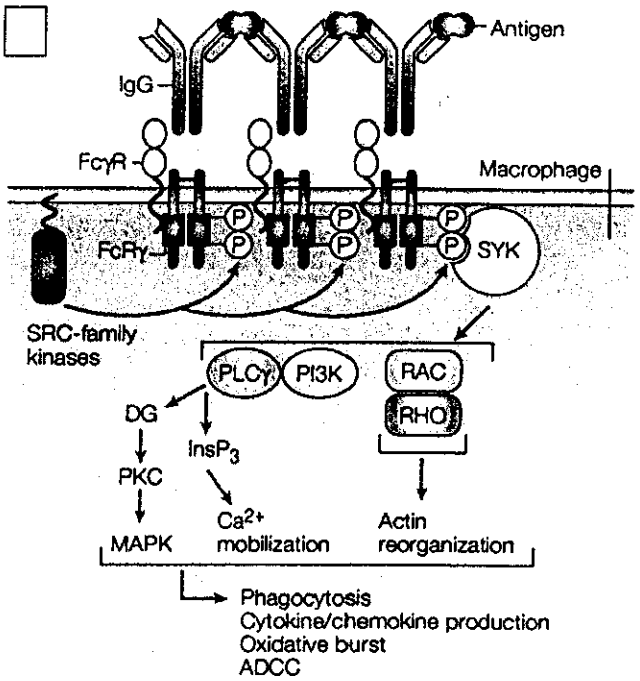
(YxxL)(X)n(YxxL)

« Immunoreceptor tyrosine inhibition motif »

ITYSLL

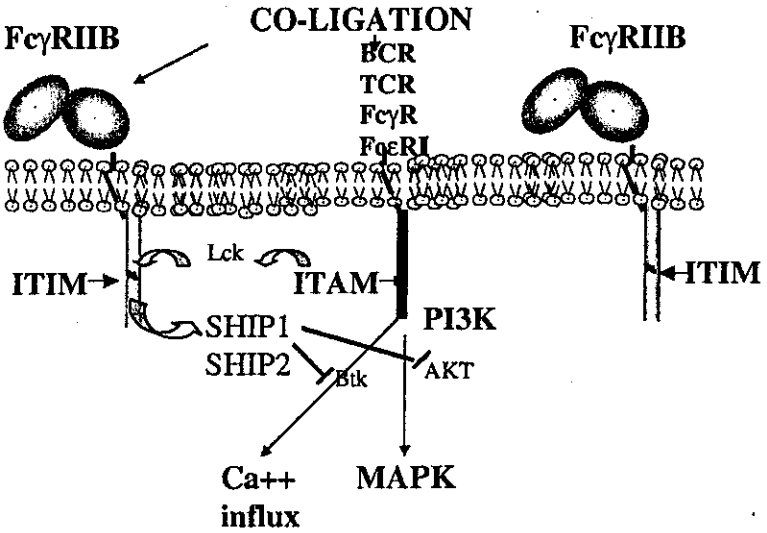
	ACTIVATING FcγR	INHIBITORY FcγR
Dendritic Cells	+	+
Macrophages	+	+
Neutrophils	+	+
Mast cells	+	+
NK cells	+	-
B cells	-	+

ACTIVATING RECEPTORS



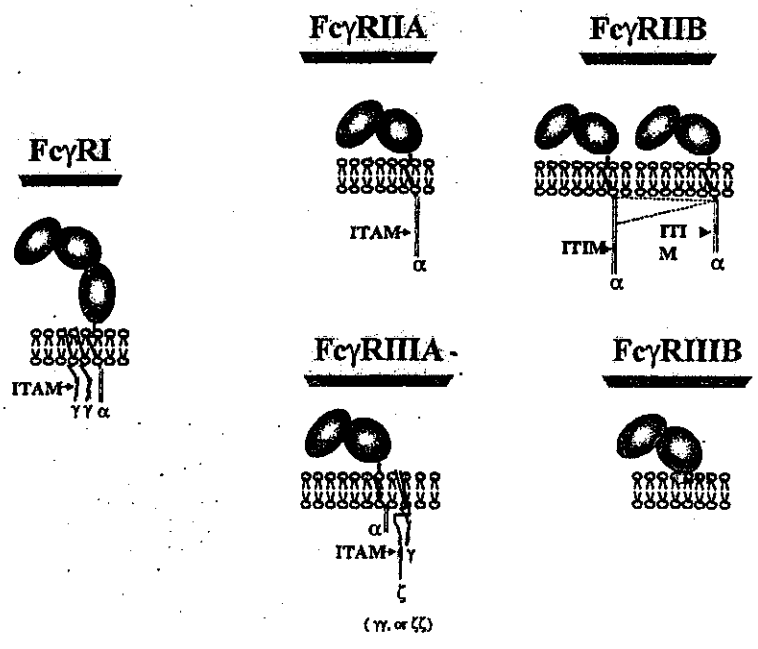
T. Takaï, Nature Rev 2002

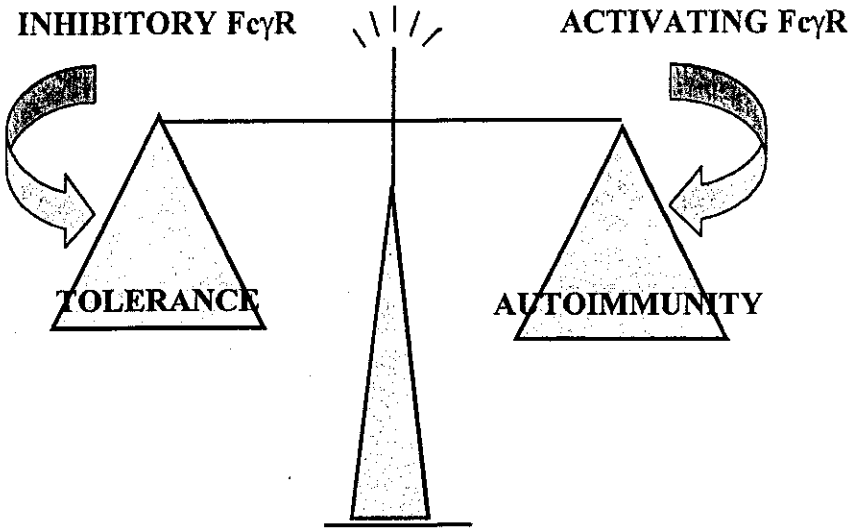
INHIBITORY FcγRECEPTORS DOWN REGULATE ITAM-DEPENDENT RESPONSES



MICE DEFICIENT IN	HYPERSENSITIVITY REACTIONS (II,III) ARTHUS REACTION	AUTOIMMUNE DISEASES (IgG DEPENDENT)
ACTIVATING FcγR	IMPAIRED	RESISTANT
INHIBITORY FcγR	ENHANCED	INCREASED SUSCEPTIBILITY

Human FcγR





FcγR POLYMORPHISMS IN HUMAN AUTOIMMUNE DISEASES

INCREASED SUSCEPTIBILITY TO	FcγRIIa	FcγRIIB	FcγRIIIA	FcγRIIIB
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	131 Arg	232 Thr*	158 Phe	NA2
RHUMATOID ARTHRITIS (RA)			158 Phe	
WEGENER GRANULOMATOSIS				NA1
GUILLAIN BARRE SYNDROME	131Arg			NA2
MULTIPLE SCLEROSIS	131 Arg			NA2

FcγR CONTROL AUTOIMMUNITY
VIA

1 - DENDRITIC CELLS =

FcγR REGULATE ANTIGEN PRESENTATION

2 - B CELLS =

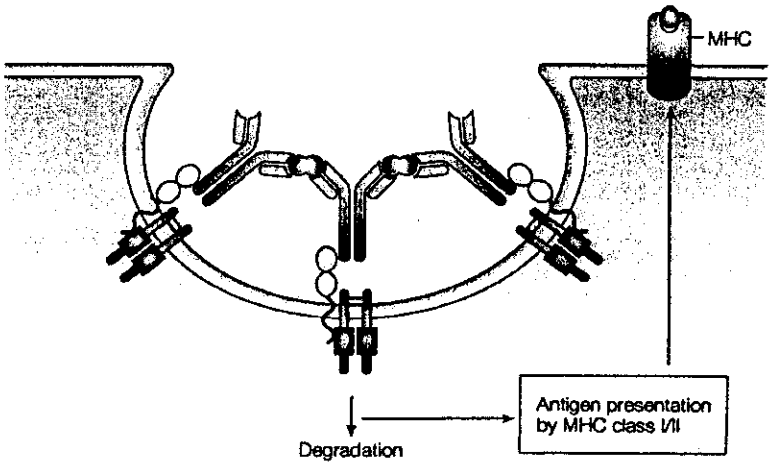
FcγR DOWN REGULATE AUTO ANTIBODY PRODUCTION

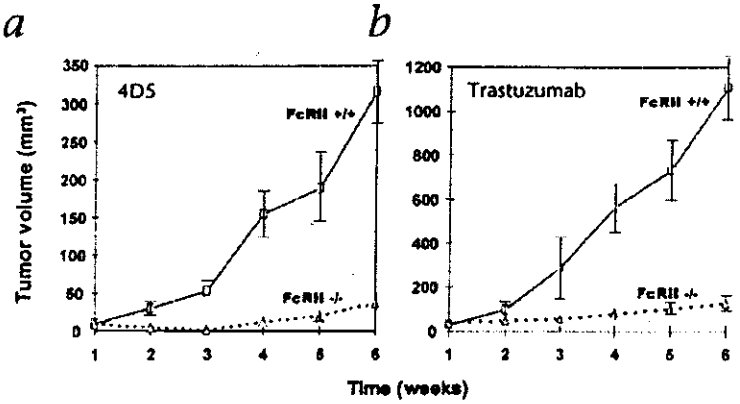
3 - MACROPHAGES =

FcγR CONTROL

PRODUCTION OF INFLAMMATORY CYTOKINES
CLEARANCE OF IMMUNE COMPLEXES (LIVER)

b Immune-complex clearance linked to antigen presentation





CONCLUSIONS

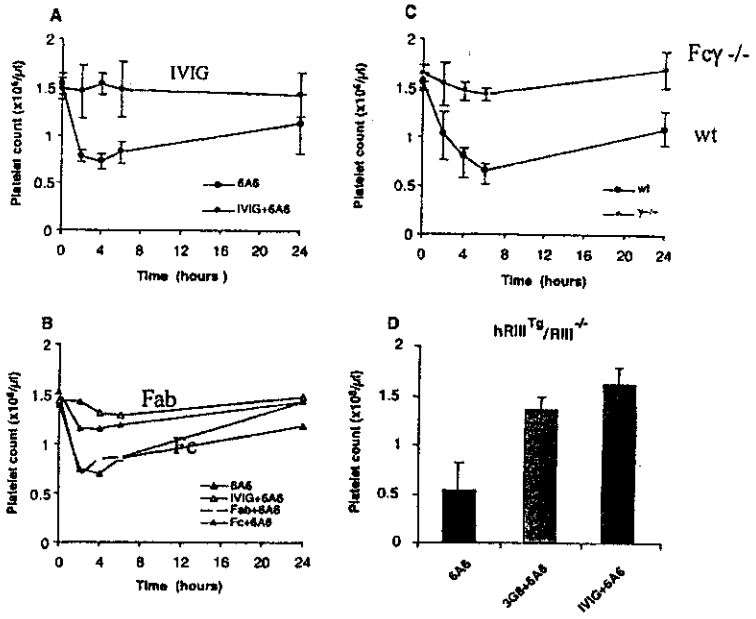
FcγR CONTROL

1-INFLAMMATION

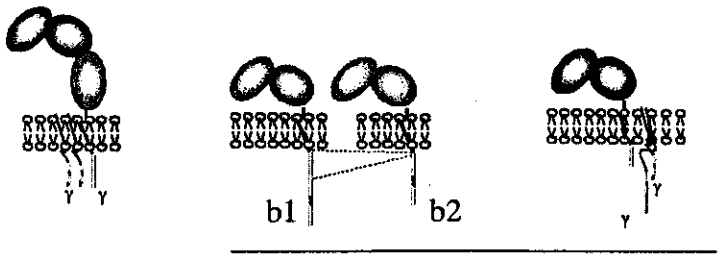
2-PERIPHERAL TOLERANCE

3-RESPONSE TO ANTIBODY-MEDIATED THERAPIES OF AUTOIMMUNE DISEASES AND CANCER

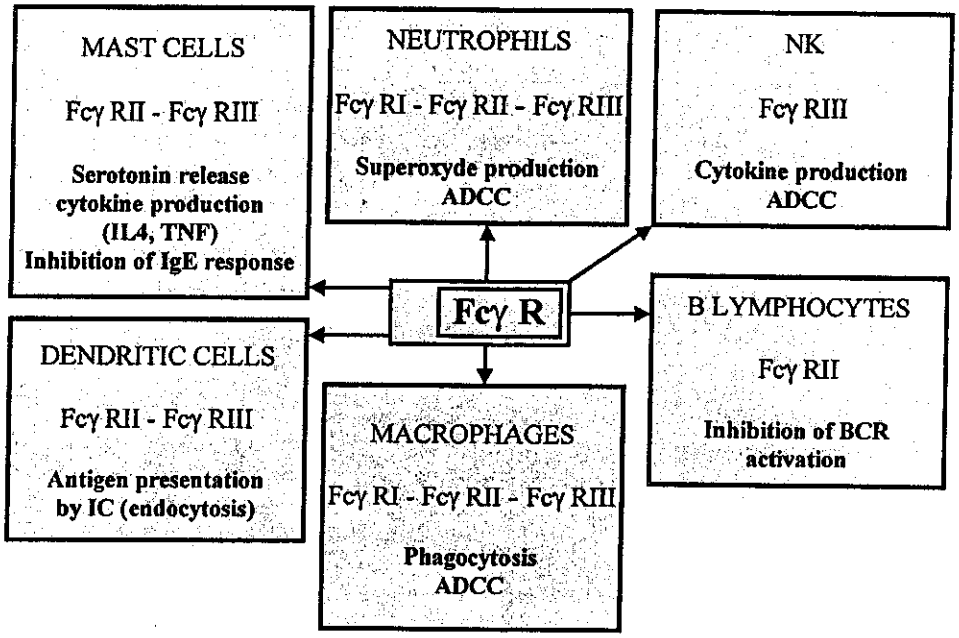
IVIG PROTECT MICE FROM Ab- INDUCED ITP

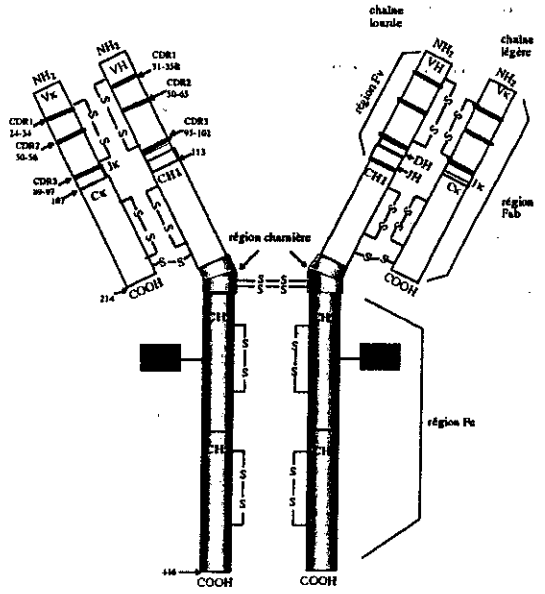


MOUSE FcγR



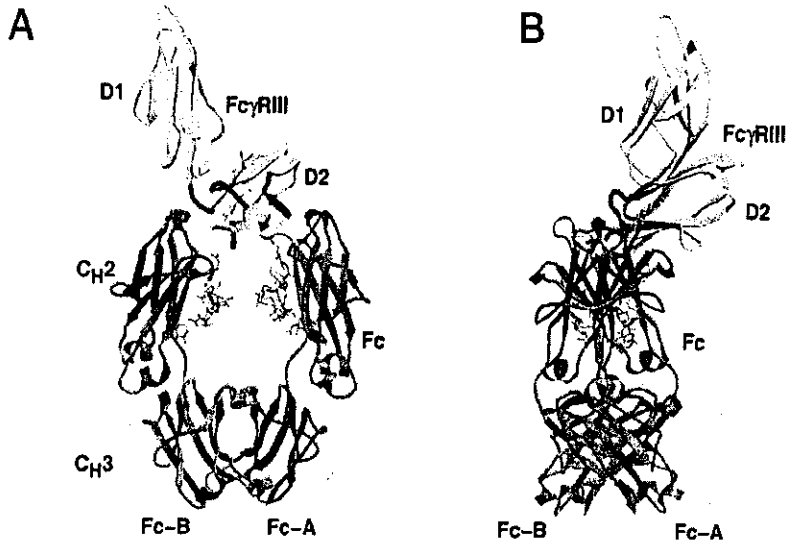
K_D 10^{-8} M		K_D $10^{-6}/10^{-7}$ M	
Macrophages	B cells	Macrophages	NK cells
Neutrophils	Mast cells	Dendritic cells	Monocytes
Dendritic cells			Dendritic cells
			Mast cells

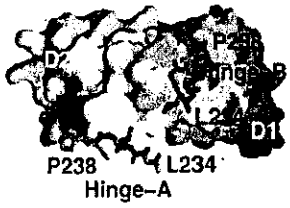

MAST CELLS
Fcγ RII - Fcγ RIII
Serotonin release
cytokine production
(IL4, TNF)
Inhibition of IgE response
NEUTROPHILS
Fcγ RI - Fcγ RII - Fcγ RIII
Superoxyde production
ADCC
NK
Fcγ RIII
Cytokine production
ADCC
Fcγ R
DENDRITIC CELLS
Fcγ RII - Fcγ RIII
Antigen presentation
by IC (endocytosis)
MACROPHAGES
Fcγ RI - Fcγ RII - Fcγ RIII
Phagocytosis
ADCC
B LYMPHOCYTES
Fcγ RII
Inhibition of BCR
activation

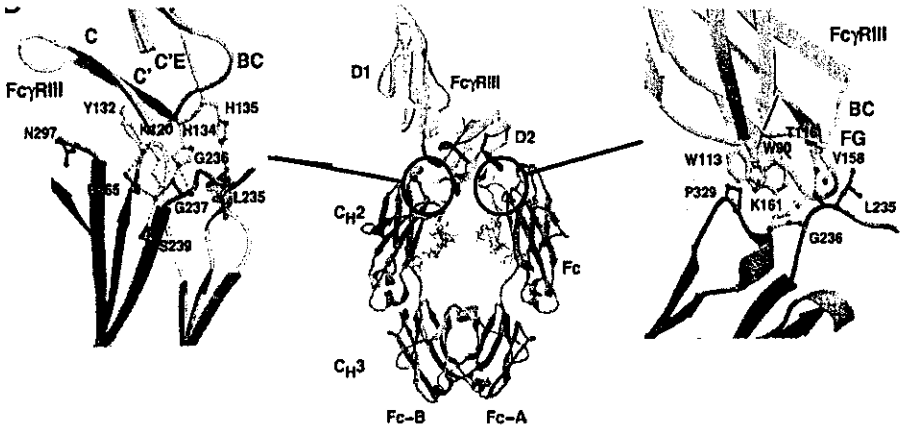

chaîne légère
chaîne lourde
région charnière
région Fc
région Fab
COOH

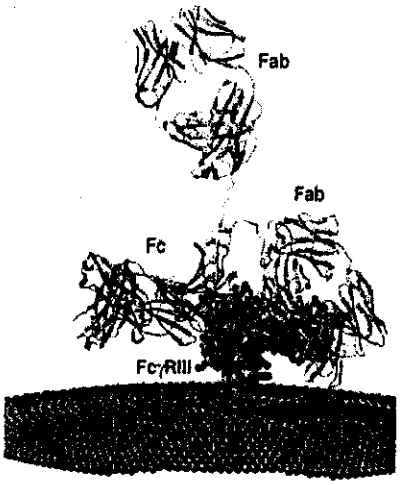
[redacted]

ONE IgG BINDS ONE FcγR
(Coll K. Kato et al, and P. Sun et al)









CONCLUSION 2

ONE FcγR MOLECULE BIND ONE IgG MOLECULE

THIS STOICHIOMETRY AVOIDS THE DELETERIOUS EFFECTS THAT IgG ANTIBODIES MAY EXERT VIA ACTIVATING FcγR