



INMUNOLOGÍA CLÍNICA 2010

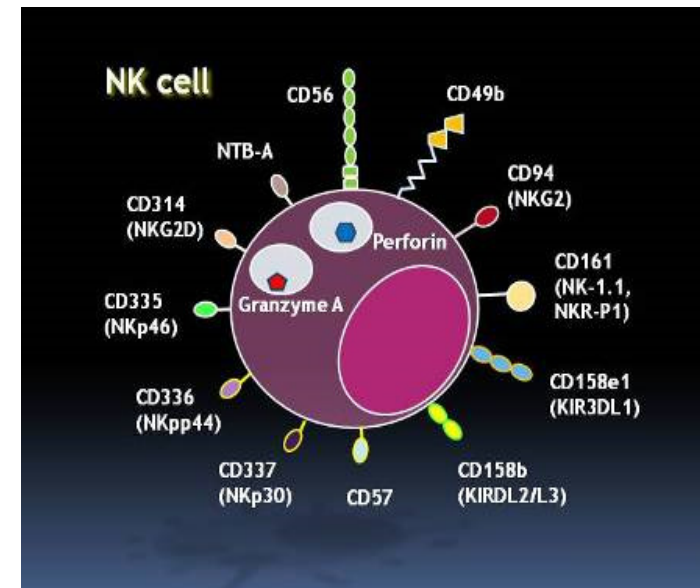
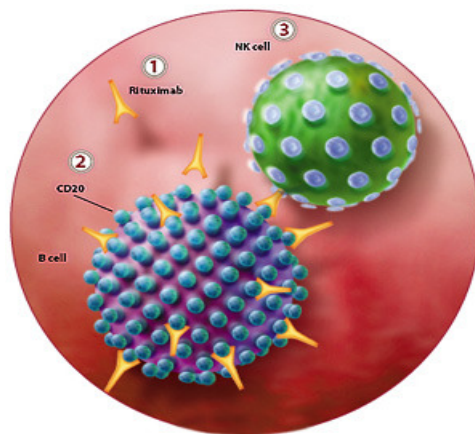


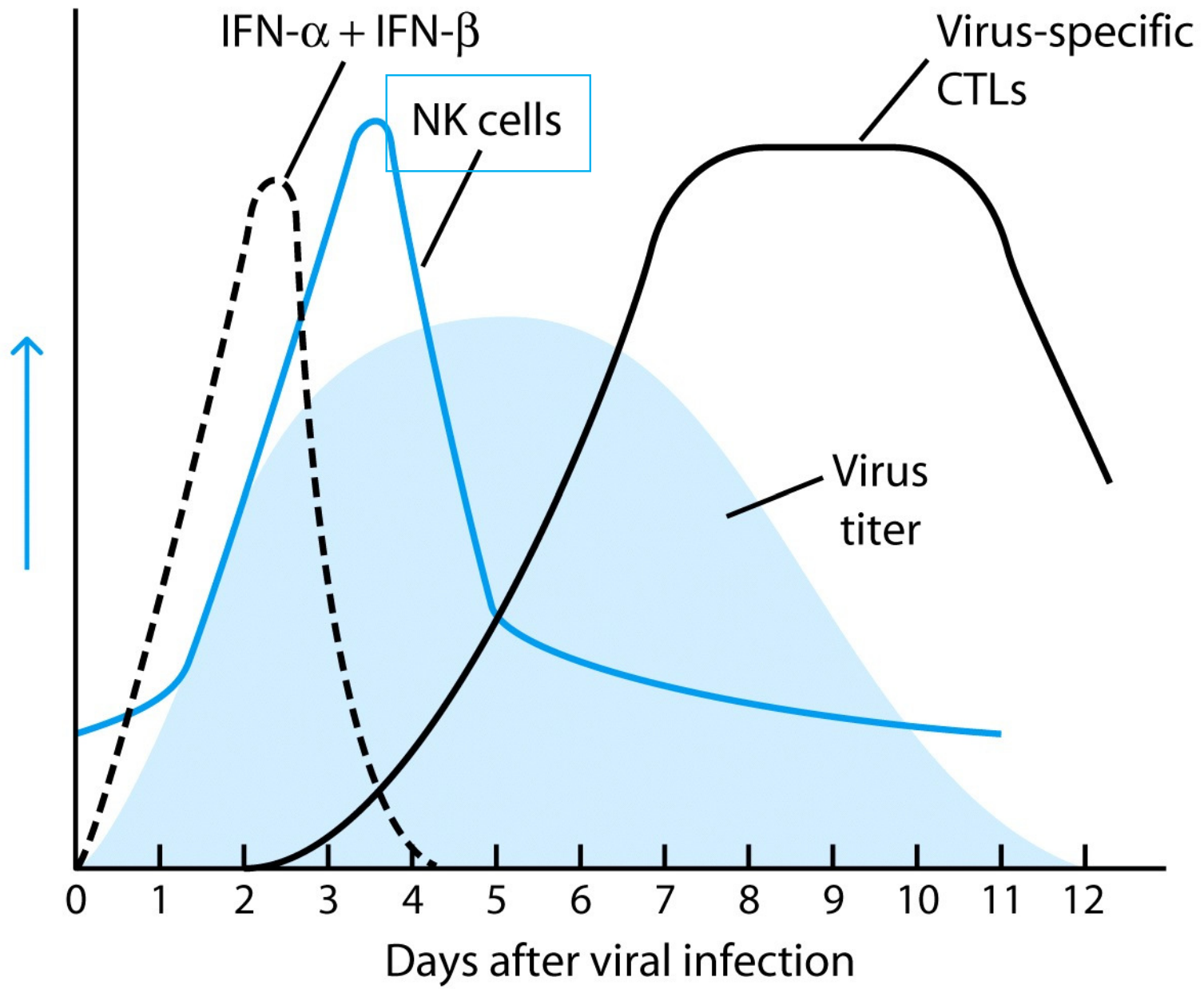
BIOQ GRACIELA SVIBEL



CÉLULAS “NATURAL KILLER”

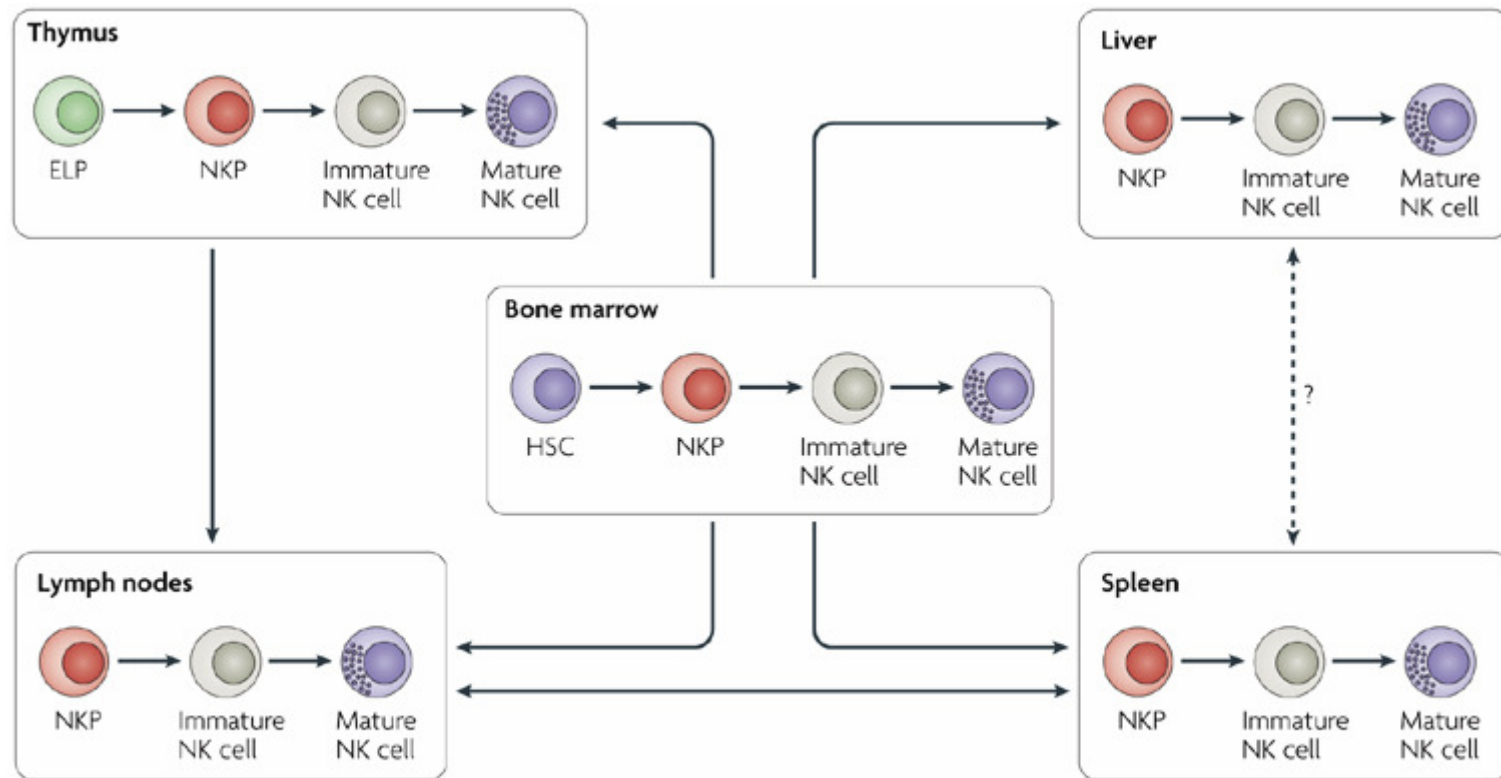
LINOCITOS GRANDES GRANULARES
CAPACES DE PRODUCIR CITOQUINAS
INFLAMATORIAS Y DESTRUIR CÉLULAS
TUMORALES, ESTRESADAS O
INFECTADAS.....

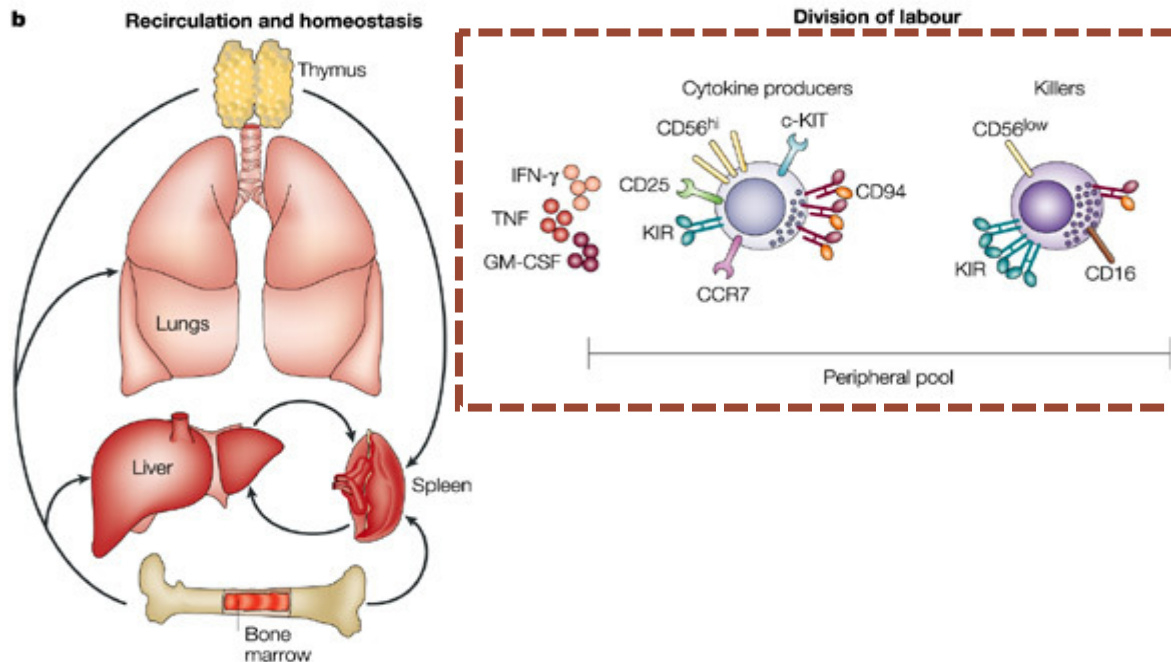
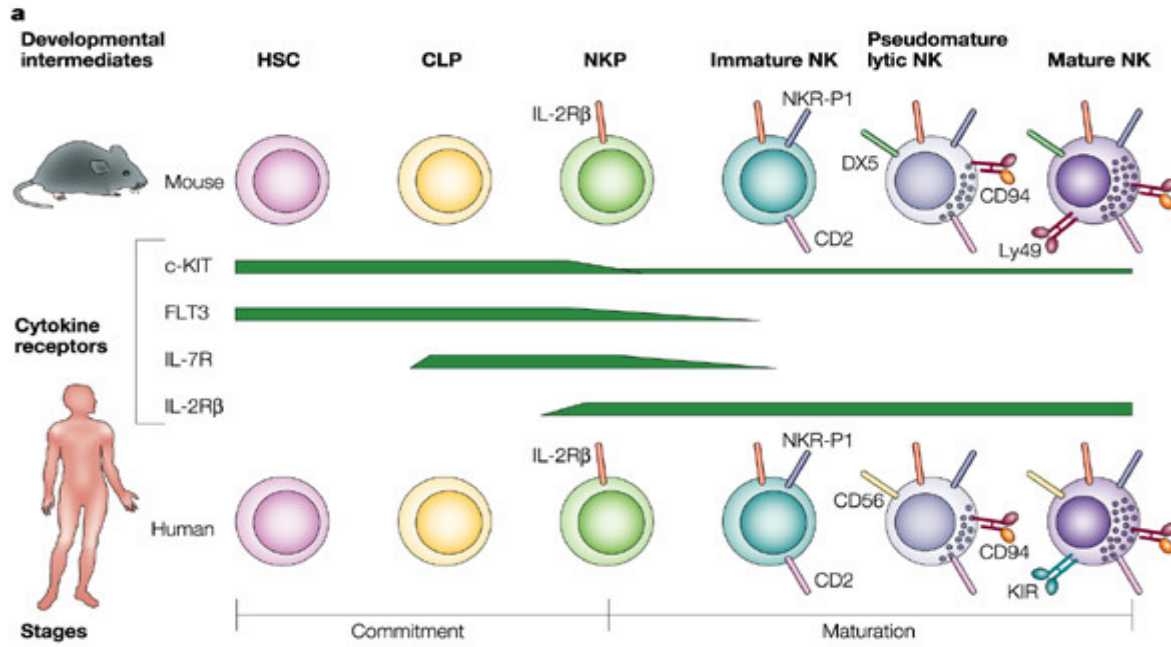




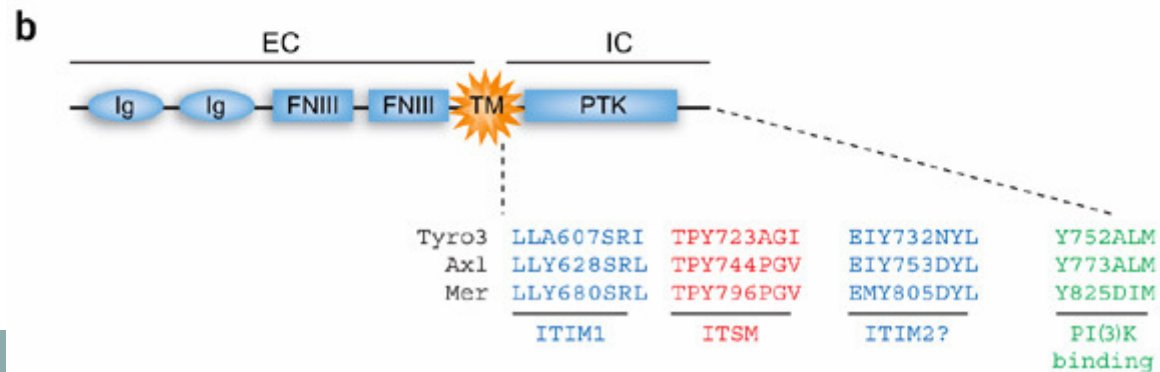
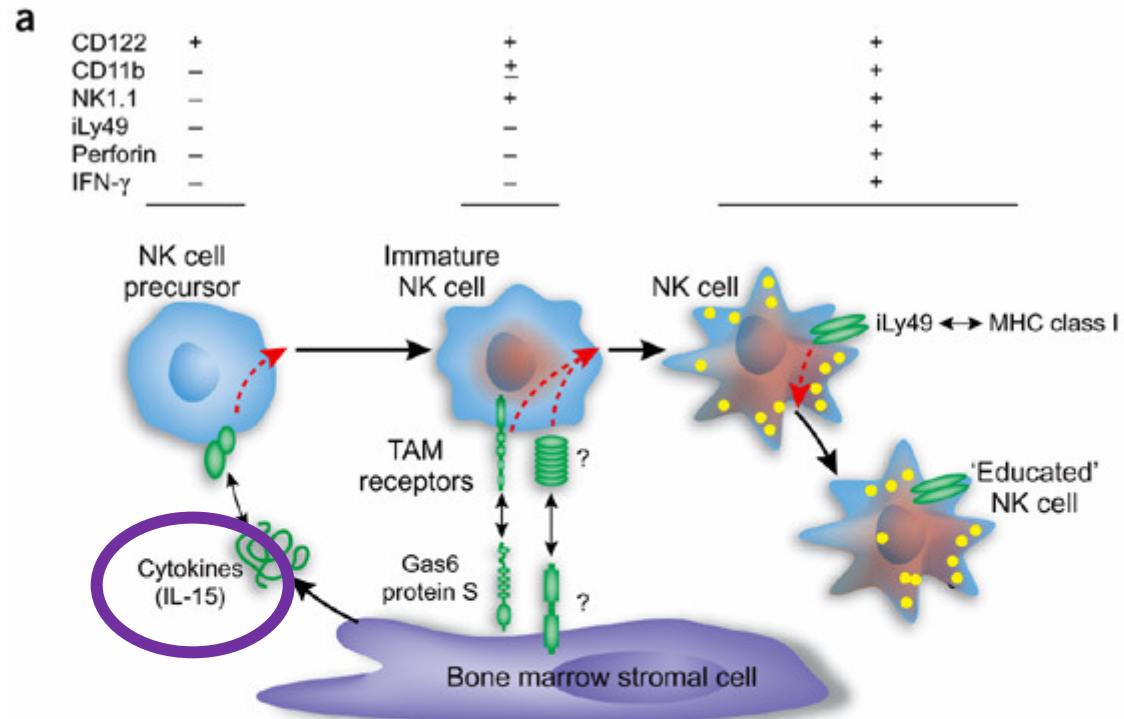
ONTOGENIA DE CÉLULAS NK

early lymphoid precursors (ELPs).

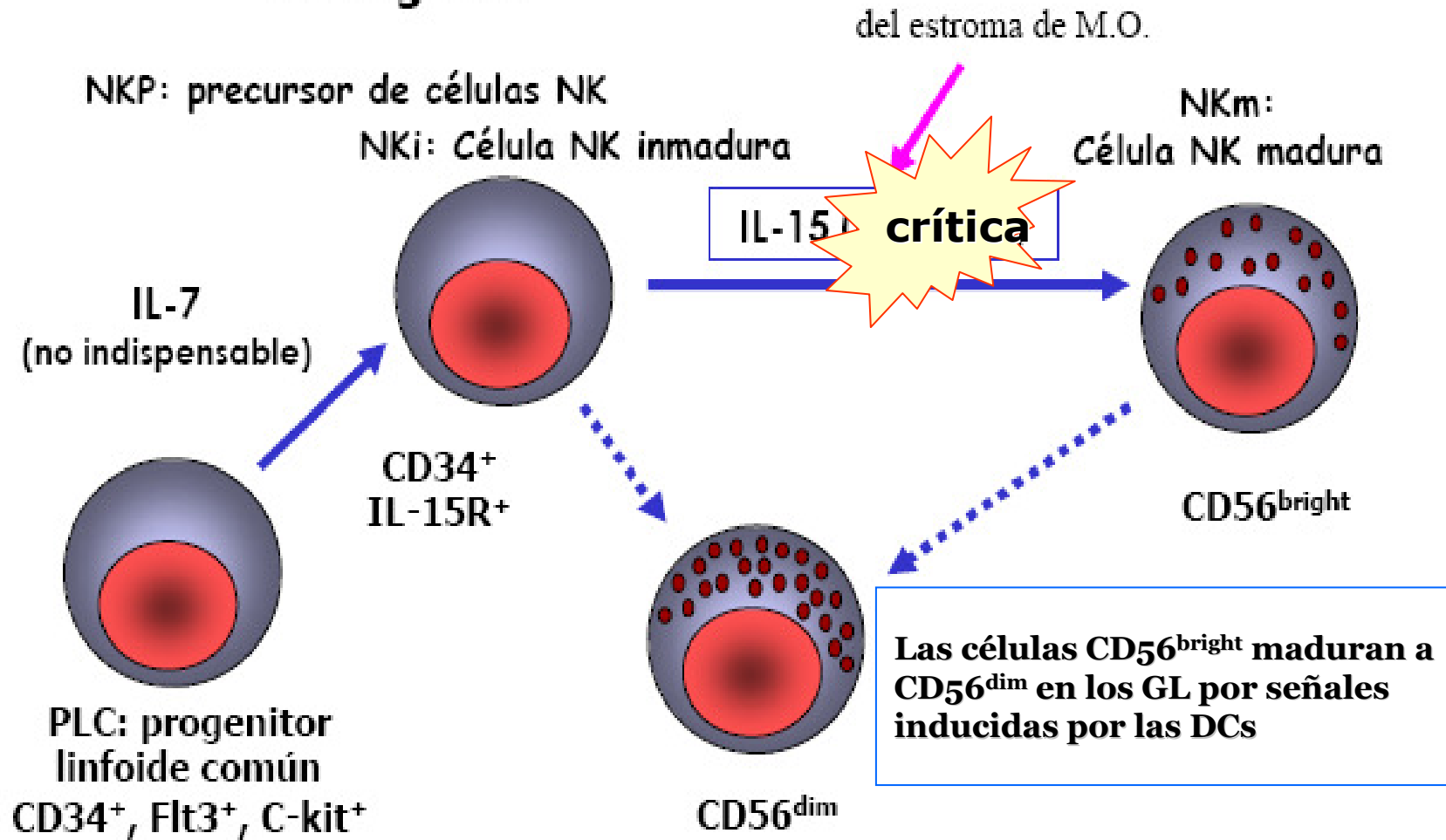




EL DESARROLLO DE CÉLULAS NK DEPENDE DE **IL-15**



Ontogenia



Localización de las células NK

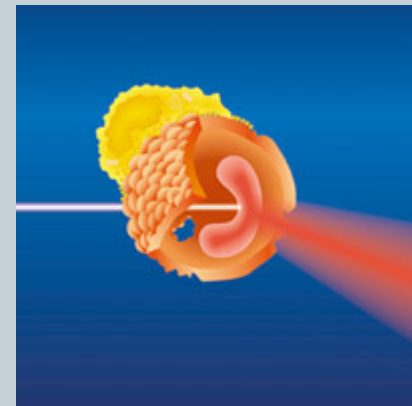


- **~5-20% de los linfocitos de sangre periférica**
- **~5% linfocitos en el bazo**
- **Abundantes en el hígado**
- **Baja frecuencia en el timo, médula ósea, nódulos linfáticos y linfáticos no infectados**
- **>90% de los linfocitos en el tejido decidual**

¿Qué papel cumplen las células NK?



- **Defensa frente a bacterias y parásitos intracelulares**
- **Control de infecciones virales**
- **Eliminación de células tumorales**
- **Determinación del perfil de respuesta adaptativa que se montará contra un determinado patógeno**





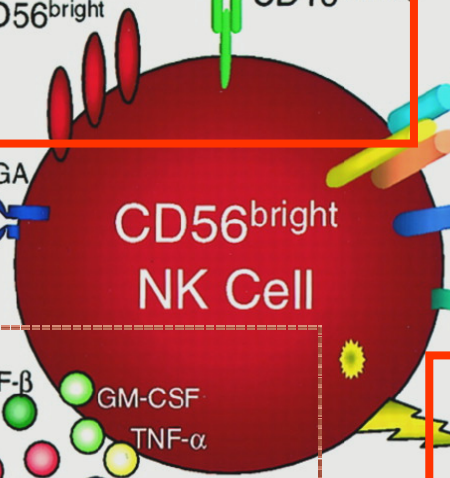
Una población heterogénea!!!!!!

FENOTIPOS

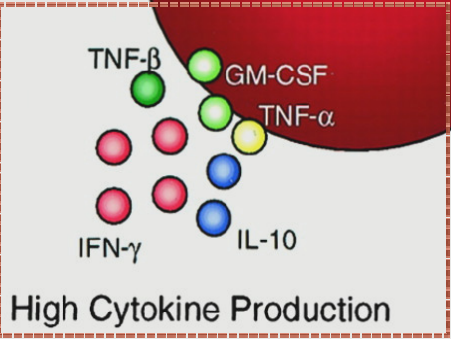
**CD56^{bright}
CD16^{dim}**

CD56^{bright} CD16^{dim/neo}

NKRs
+ KIR
+++ CD94/NKG2A



Effector Functions
+ADCC
+++LAK
+Natural Cytotoxicity

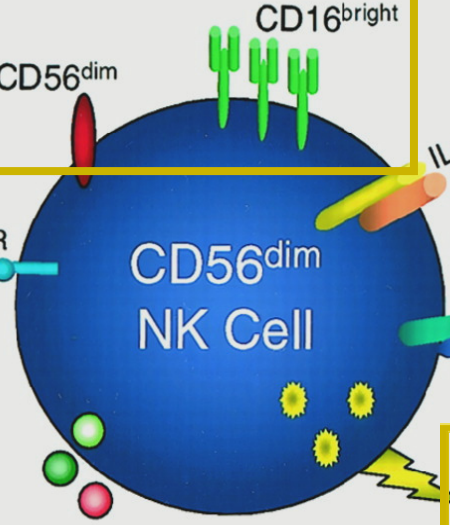


High Cytokine Production

**CD56^{dim}
CD16^{bright}**

CD56^{dim} CD16^{bright}

NKRs
+++ KIR
+ CD94/NKG2A



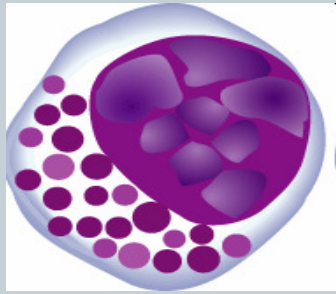
Effector Functions
+++ADCC
+++LAK
+++Natural Cytotoxicity

Low Cytokine Production

TRÁFICO Y MIGRACIÓN



**CD56^{bright}
CD16^{dim}**



**CD56^{dim}
CD16^{bright}**

CD62L+, CCR7+: TRÁFICO A OLS
CROSS TALK CON LINFOCITOS T Y CD
SECRECIÓN DE INF- γ : ¿SHIFT A Th1?

CD62L-, CCR7-: NO INGRESAN A OLS
REPRESENTA EL 90% DE CÉLULAS NK EN
SANGRE PERIFERICA

Citoquinas que regulan la actividad de las células NK

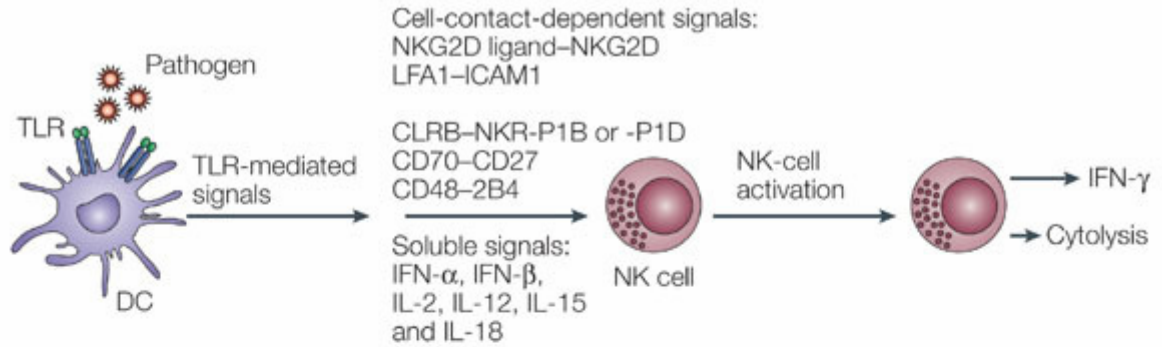
IL-2	Estimula citotoxicidad, proliferación y producción de citoquinas
IL-12	Estimula citotoxicidad, proliferación y producción de citoquinas
IL-15	Estimula citotoxicidad, proliferación y producción de citoquinas
IFN-γ	Estimula citotoxicidad
IFN-α/β	Estimula citotoxicidad
IL-10	Inhibe producción de citoquinas

Citoquinas secretadas por células NK

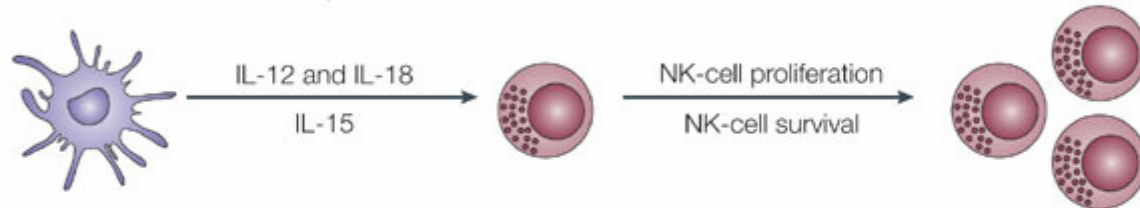
IFN-γ	Inducción respuesta Th1. Activación de monocitos y macrófagos
TNF	Mediador de la respuesta inflamatoria. Activa monocito y LT. Acción lítica
GM-CSF	Factor estimulante de colonias de granulocitos/macrófagos
TGF-β	Inmunosupresión
IL-3	Induce proliferación y diferenciación de precursores hematopoyéticos
IL-10	Inmunosupresión



a DC-mediated NK-cell activation



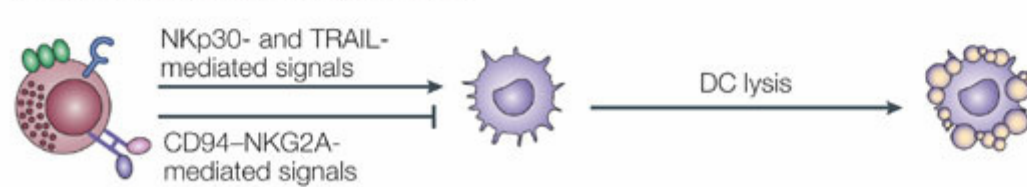
b DC-mediated NK-cell proliferation



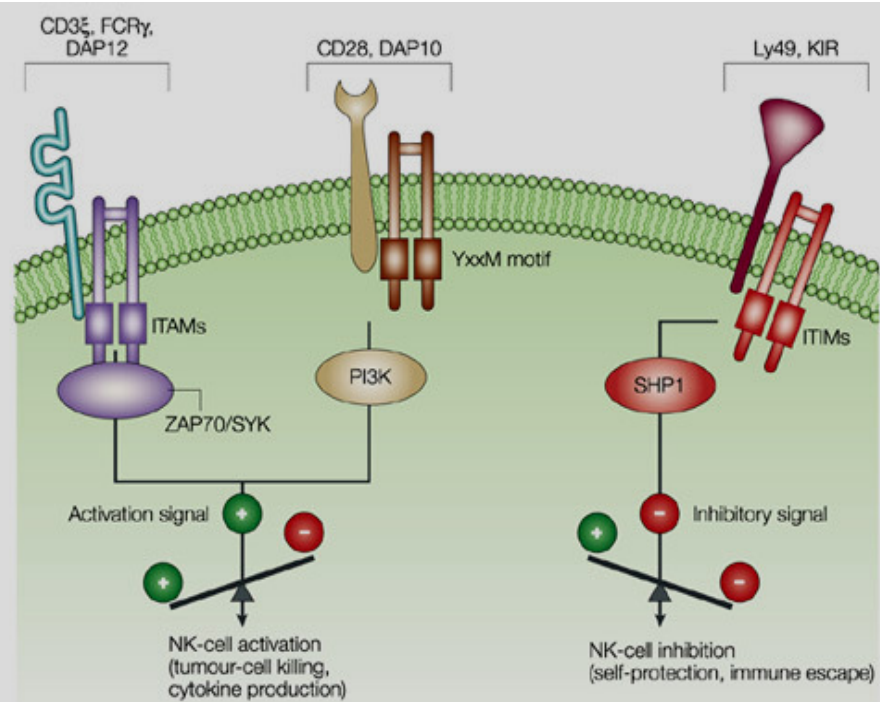
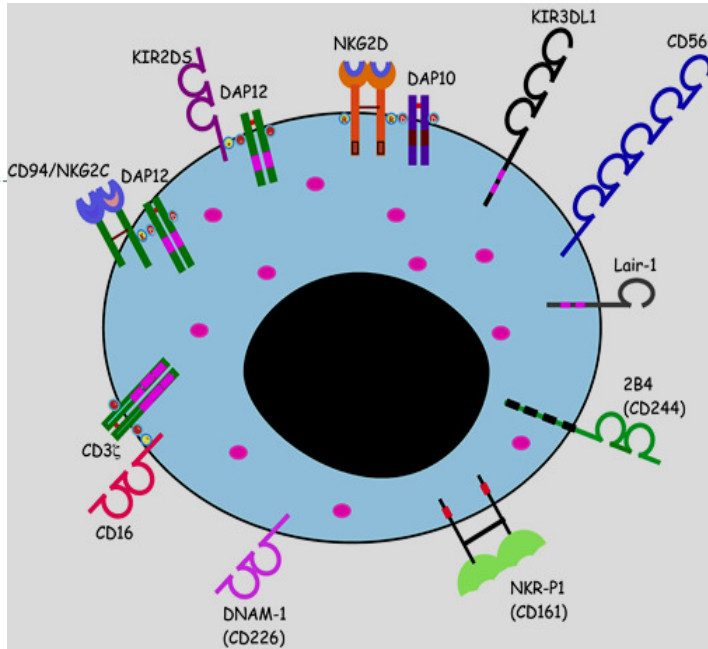
c NK-cell-mediated DC activation



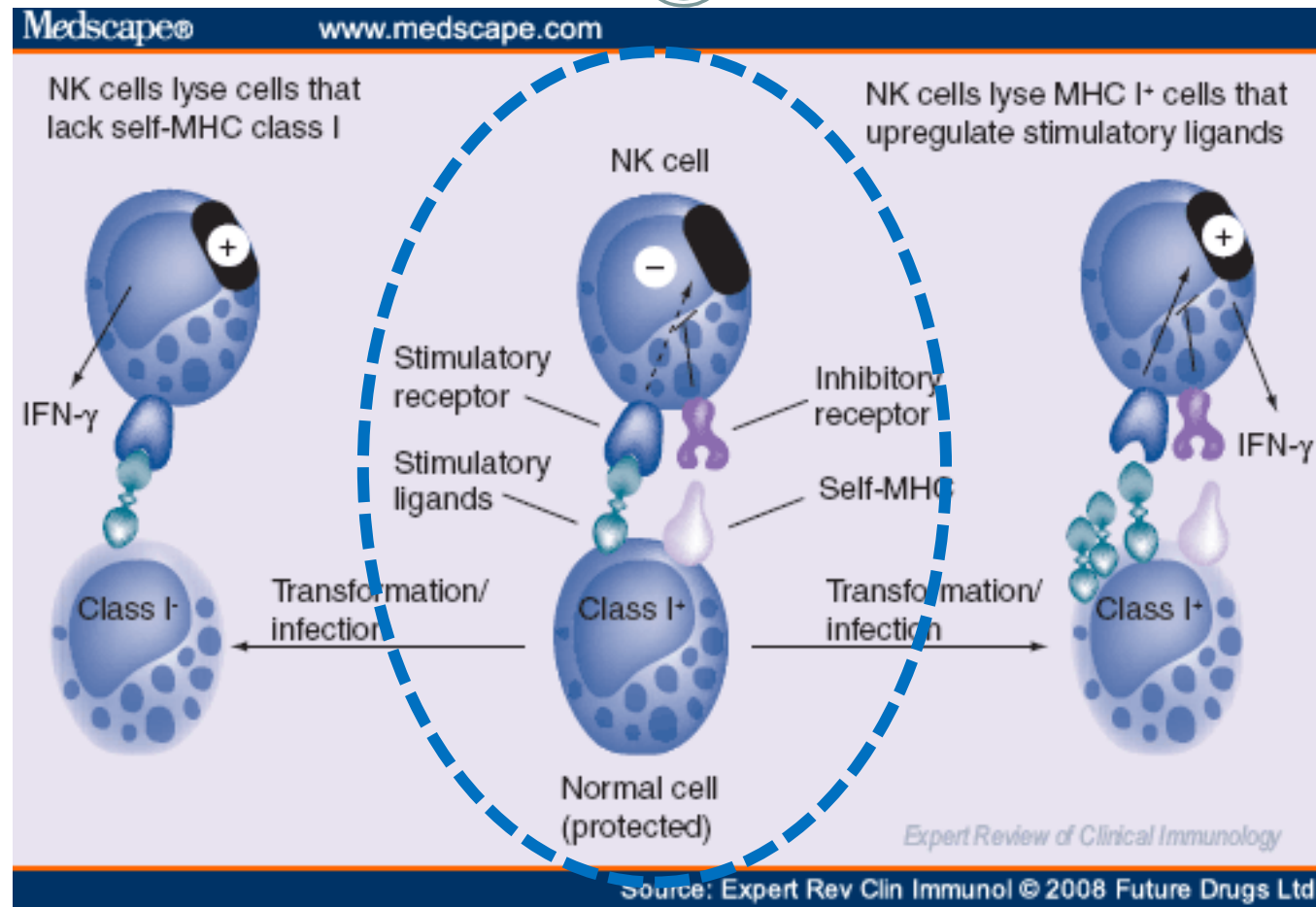
d NK-cell-mediated DC elimination



RECEPTORES DE CÉLULAS NK



EN CONDICIONES NORMALES, EXISTE EQUILIBRIO ENTRE RECEPTORES ACTIVADORES E INHIBIDORES.....



LA INDUCCIÓN DE LA MAYORÍA DE LAS FUNCIONES EFECTORAS DE LA CÉLULA NK REQUIEREN EL CONTACTO CÉLULA-CÉLULA....

RECEPTORES INHIBIDORES EXPRESADOS POR CÉLULAS NK



Receptor	Ligand	
KIR2DL1 (CD158a)	HLA-C group 2	MHC
KIR2DL2/3 (CD158b)	HLA-C group 1	
KIR3DL1	HLA-B alleles	
KIR3DL2	HLA-A alleles	
LIR-1/ILT2 (CD85j)	Multiple HLA class I	
ITIM <u>NKG2A</u> (<u>CD94</u> / <u>CD159a</u>)	HLA-E	Non-MHC
KLRG1	E/N/P-cadherin	
NKR-P1 (CD161)	LLT1	
Siglec-7 (CD328)	sialic acid	
Siglec-9 (CD329)	sialic acid	
IRp60 (CD300a)	?	



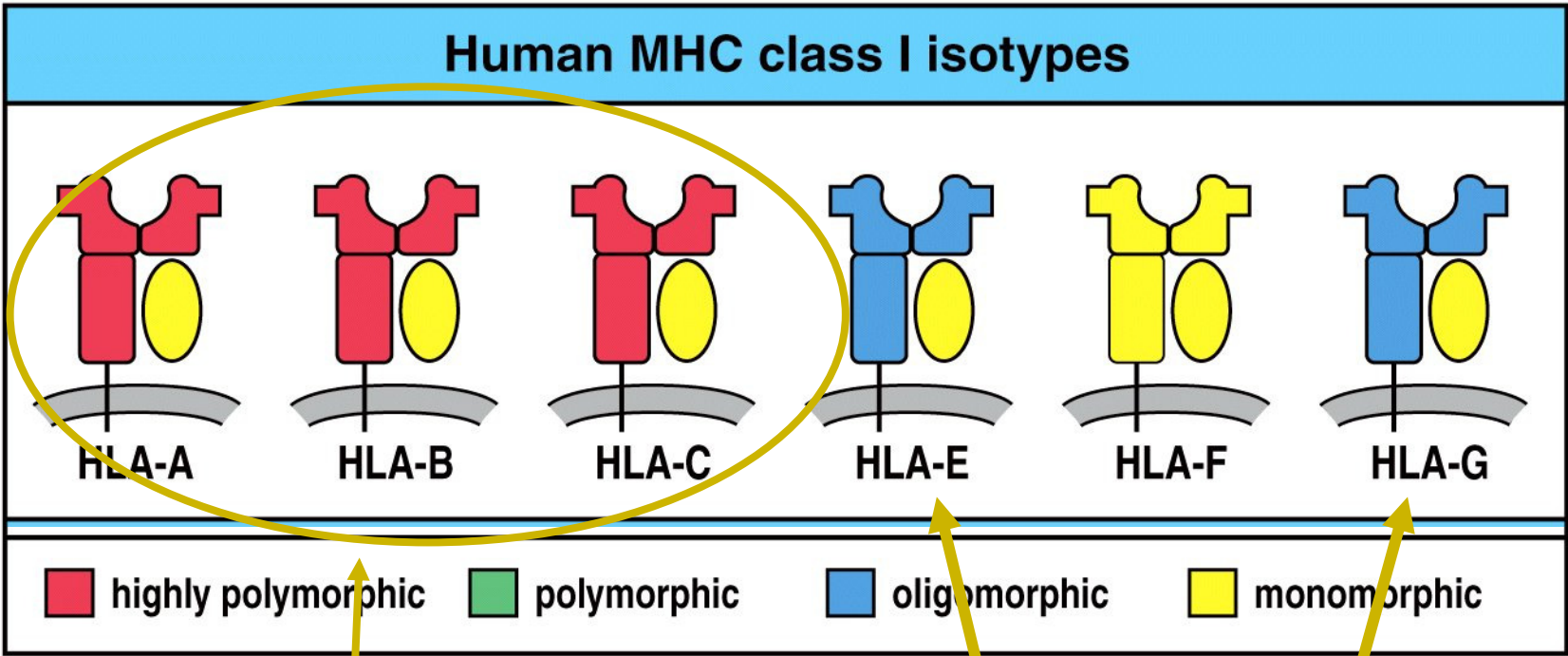
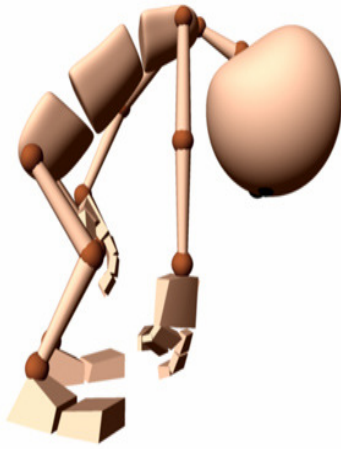


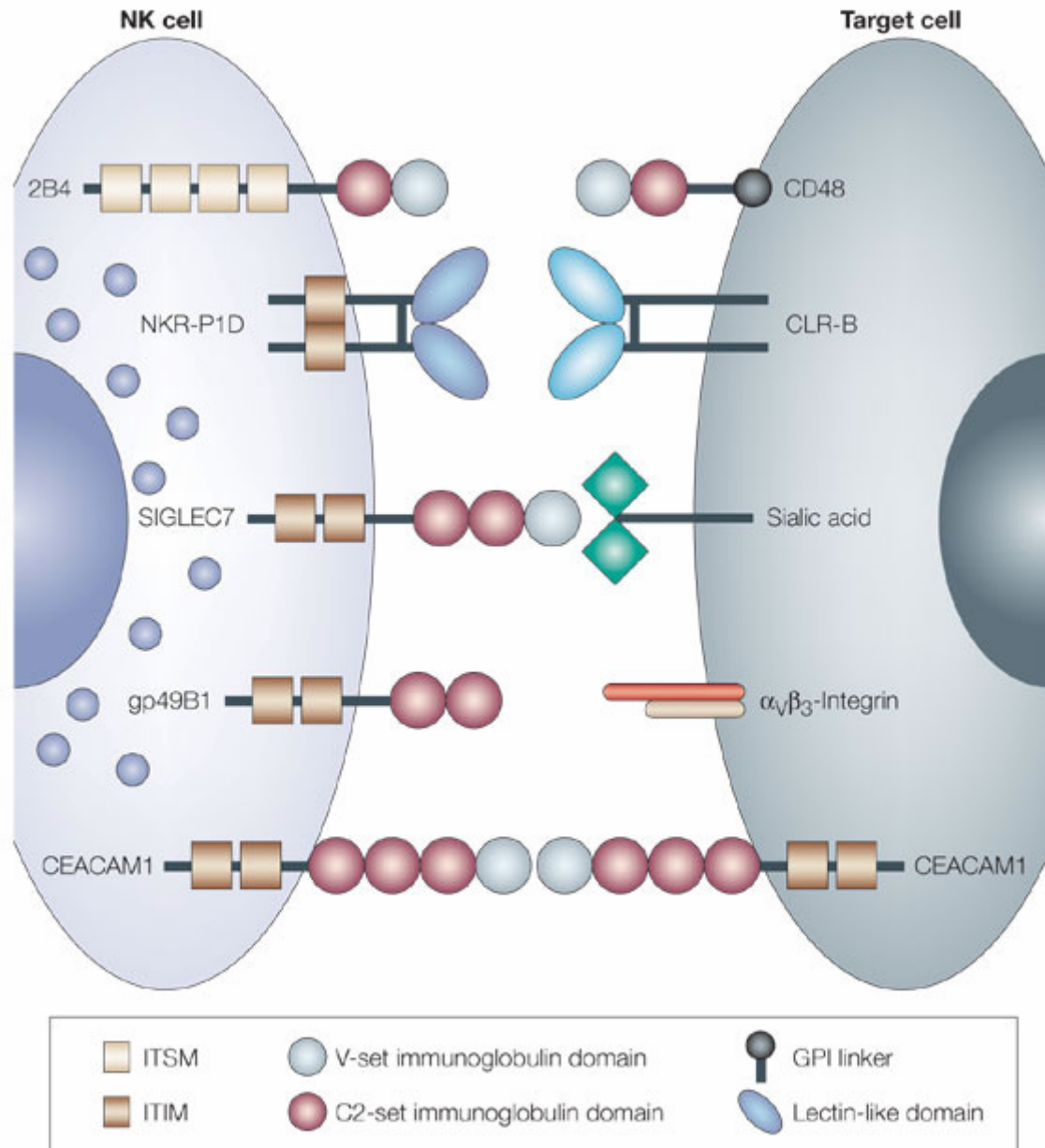
Figure 3-23 The Immune System, 2/e (© Garland Science 2005)

Estas moléculas son importantes en la presentación de antígenos a linfocitos TCD8⁺

Estas moléculas son importantes ligandos inhibidores de células NK

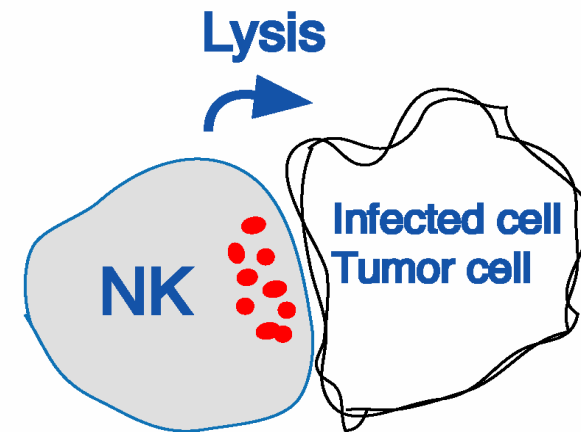


INHIBICIÓN DE LA FUNCIÓN NK...



RECEPTORES ACTIVADORES EXPRESADOS POR CÉLULAS NK

	Receptor	Ligand
ITAM	CD16 (FcγRIIIA)	IgG
	NKp30 (CD337)	?
	NKp46 (CD335)	Viral hemagglutinin
	KIR2DS1–2	HLA-C (low affinity)
	KIR2DS3–6	?
	KIR3DS1	?
	NKG2C (CD94/159c)	HLA-E
Non-ITAM	NKG2D (CD314)	ULBPs, MICA, MICB
	2B4 (CD244)	CD48
	CD2	LFA-3 (CD58)
	CRACC (CD319)	CRACC (CD319)
	NTB-A	NTB-A
	DNAM-1 (CD226)	PVR (CD155), CD112
	CD7	SECTM1, Galectin
	CD59	C8, C9
	BY55 (CD160)	HLA-C
	KIR2DL4 (CD158d)	HLA-G (soluble)
CD44	Hyaluronan	
Integrin	LFA-1 (αLβ2, CD11a/18)	ICAM-1–5
	MAC-1 (αMβ2, CD11b/18)	ICAM-1, iC3b, Fibrinogen
	CD11c/18	ICAM-1, iC3b
	VLA-4 (α4β1, CD49d/29)	VCAM-1, Fibronectin
	VLA-5 (α5β1, CD49e/29)	Fibronectin



Funciones citotóxicas



Actividad NK (Natural Killer)

- Citotoxicidad espontánea. Se mide frente a células diana sensibles que carecen de expresión de moléculas de histocompatibilidad

Actividad LAK (Lymphokine Activated Killer)

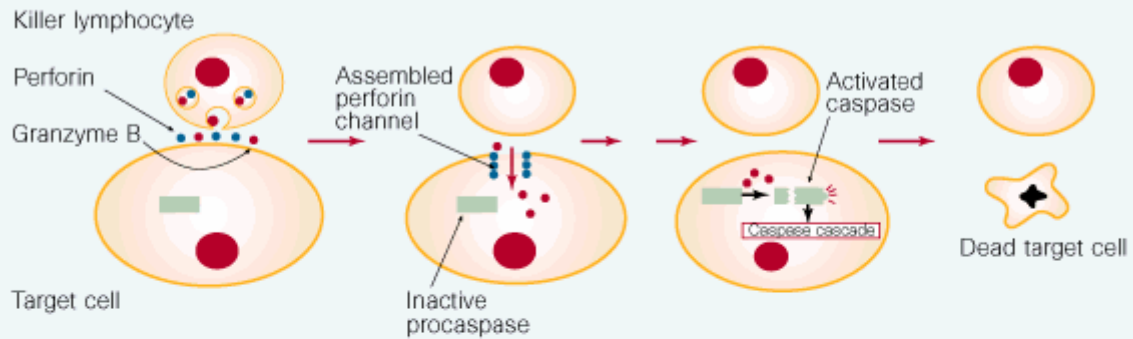
- Citotoxicidad inducida por citocinas (IL-2, IFN α) frente a células diana NK resistentes

Actividad ADCC (Antibody dependent cell cytotoxicity)

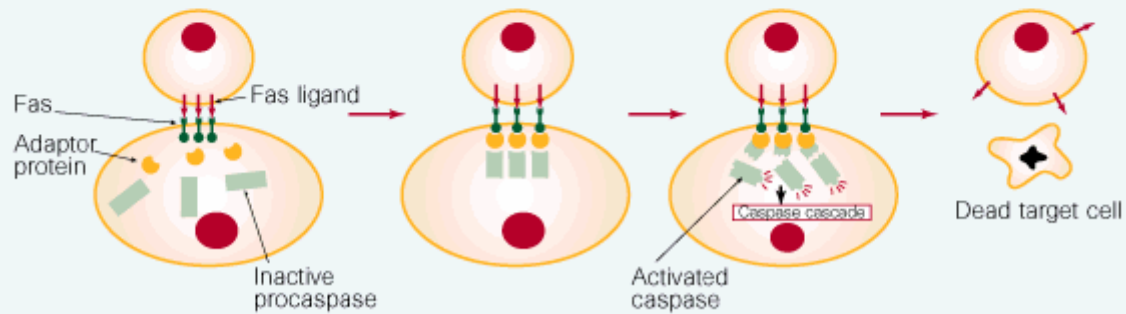
- Citotoxicidad dependiente de anticuerpos mediada por receptor Fc γ IIIb (CD16) Se mide en presencia de anticuerpos unidos a un antígeno en la superficie de la célula diana

CITOTOXICIDAD NATURAL

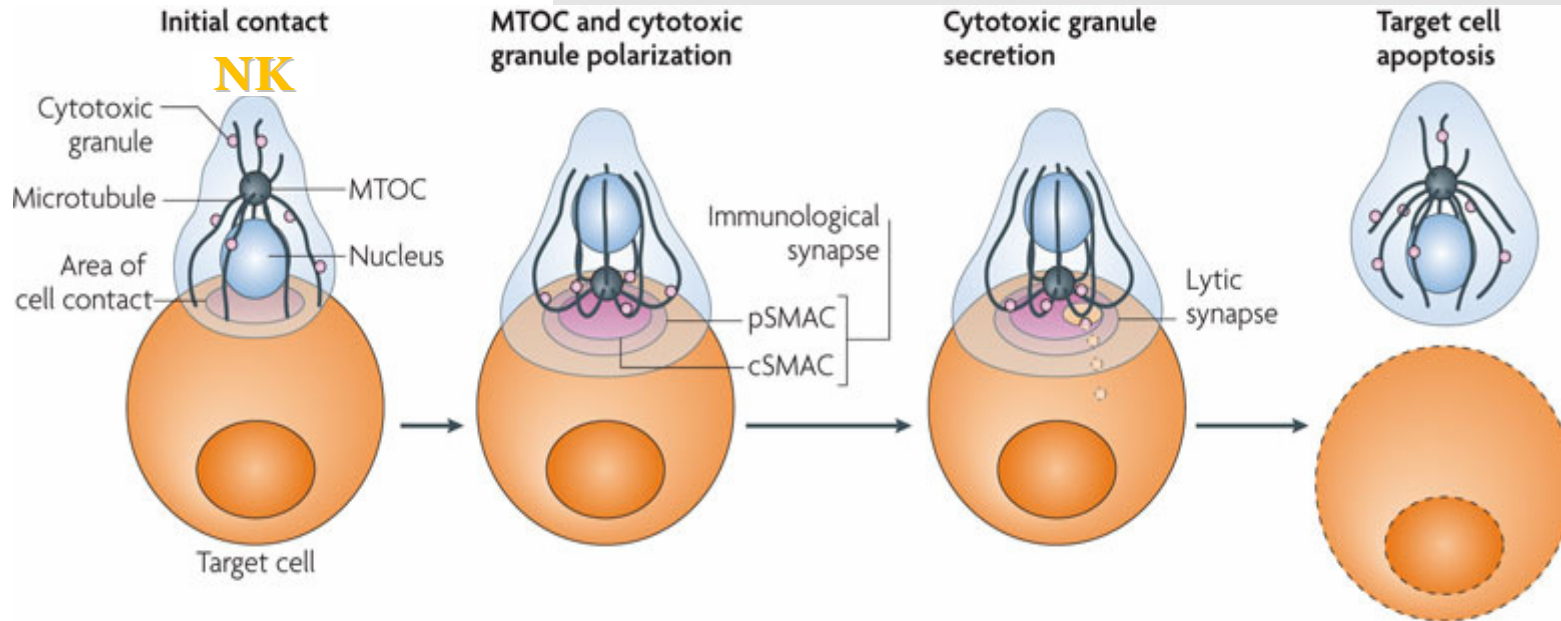
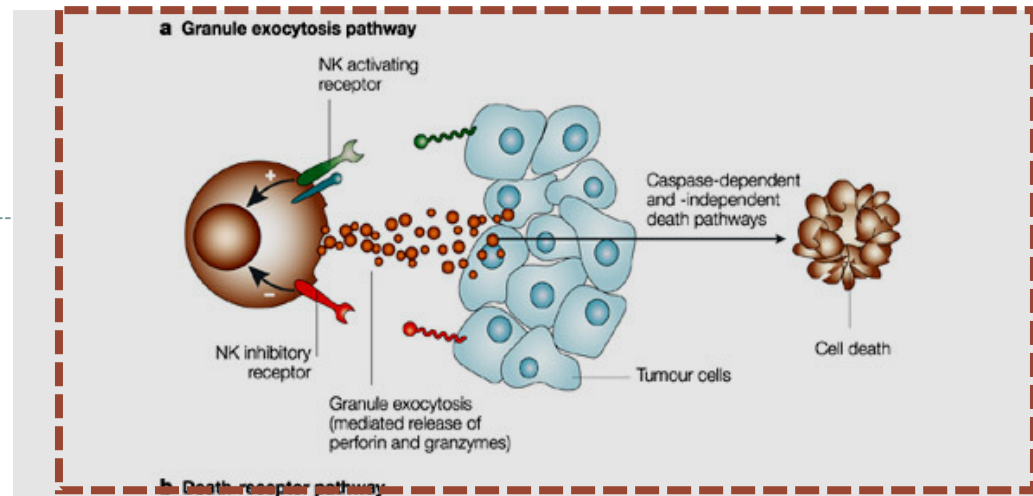
a Perforin-granzyme B pathway

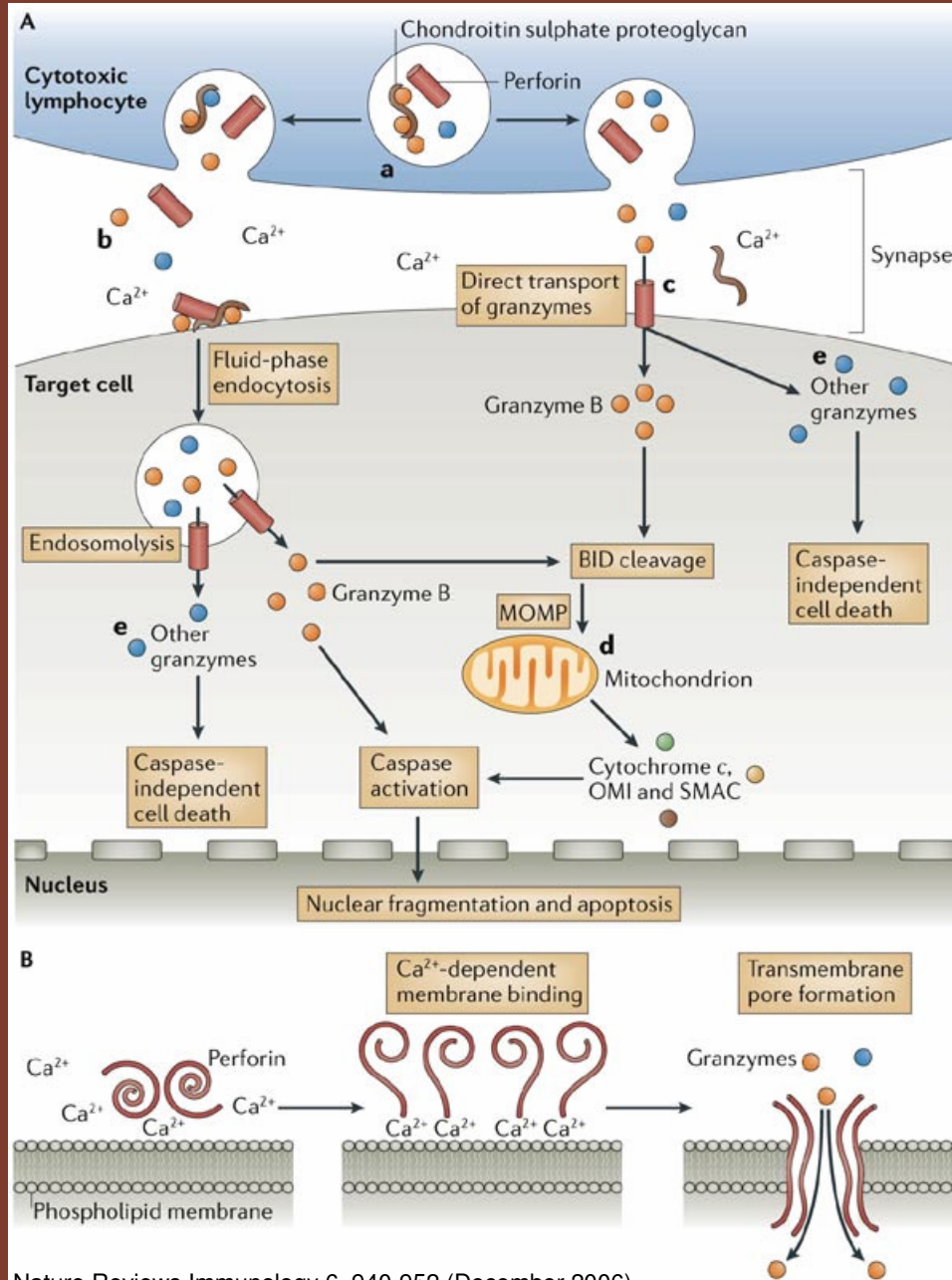


b Fas pathway



NK CD16^{BRIGHT} CD56^{LOW} EN ACCIÓN..



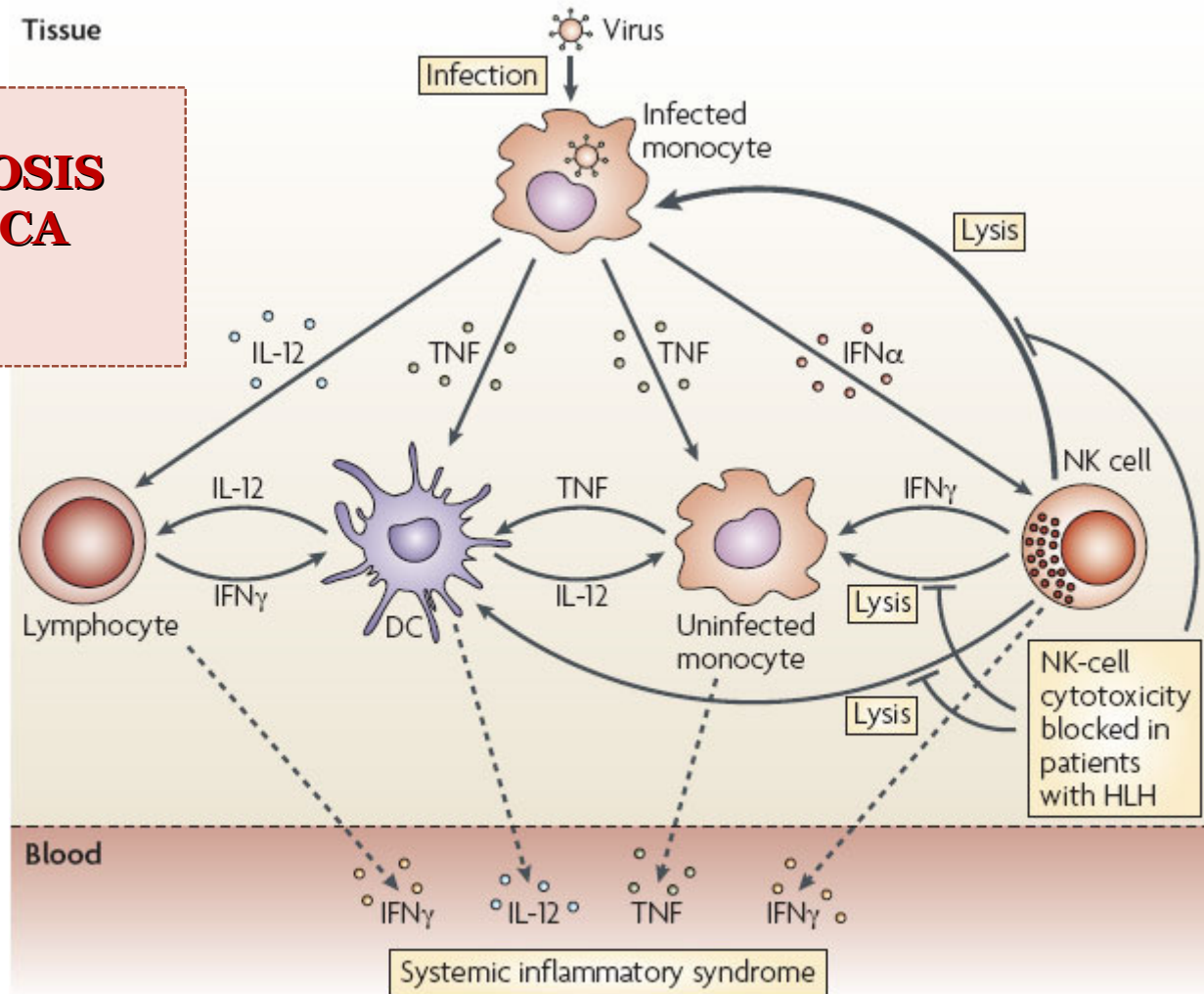


**CITOTOXICIDAD
NATURAL: VÍA
PERFORINA-
GRANZIMA B**

Nature Reviews Immunology 6, 940-952 (December 2006)

¿QUÉ OCURRE SI LA SINAPSIS INMUNOLÓGICA LÍTICA ENTRE LA CÉLULA NK Y EL TARGET NO ES ADECUADA.....

LINFOHISTIOCITOSIS HEMOFAGOCÍTICA (HLH)...

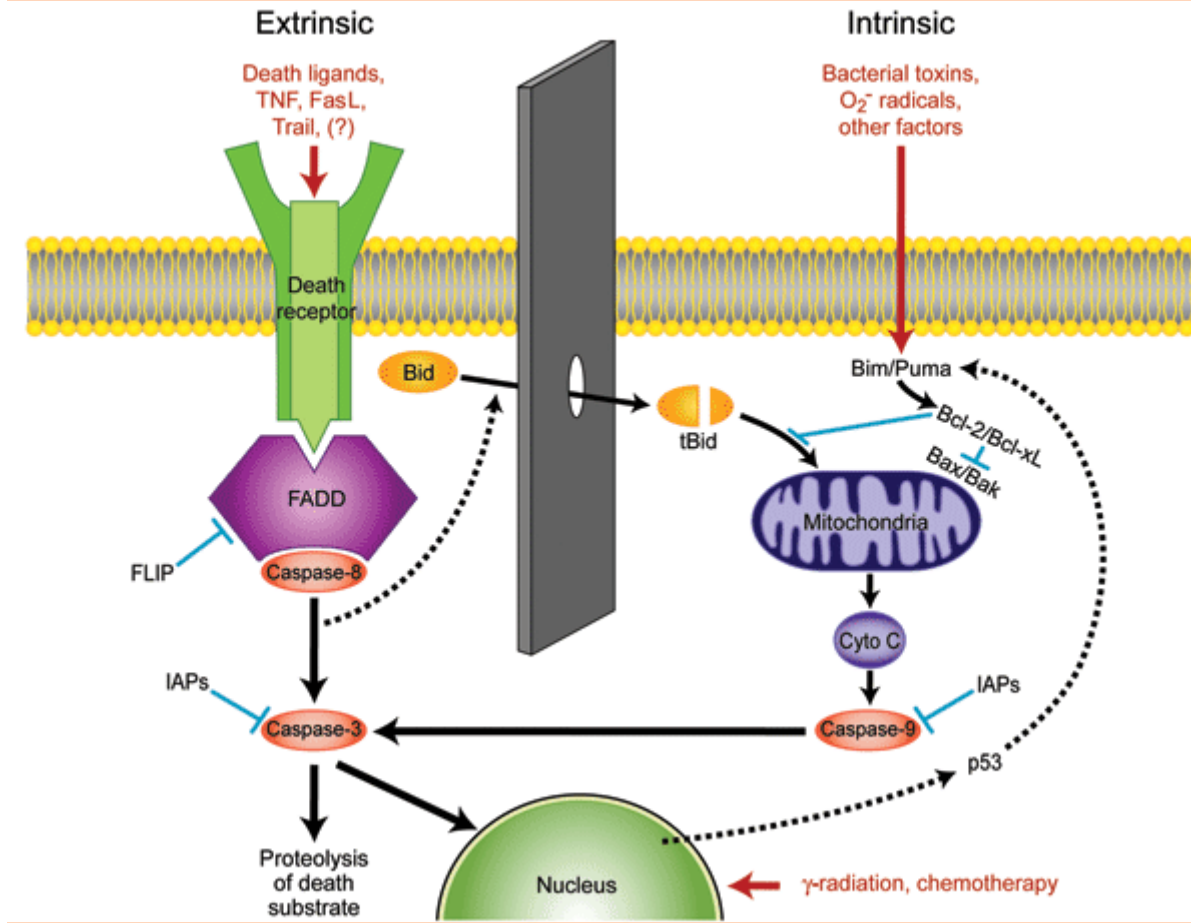


a Granule exocytosis pathway



Medscape®

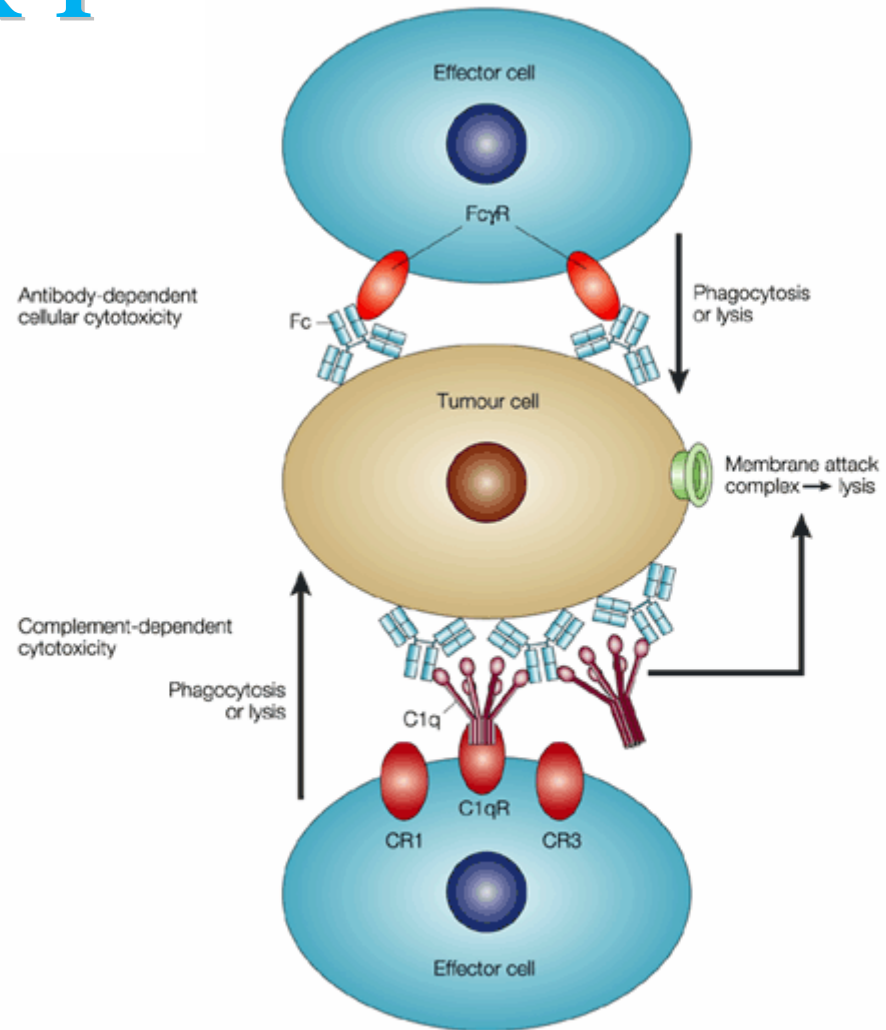
www.medscape.com



Source: Emerg Infect Dis © 2007 Centers for Disease Control and Prevention (CDC)

Nitric oxide

CÉLULAS NK Y ADCC

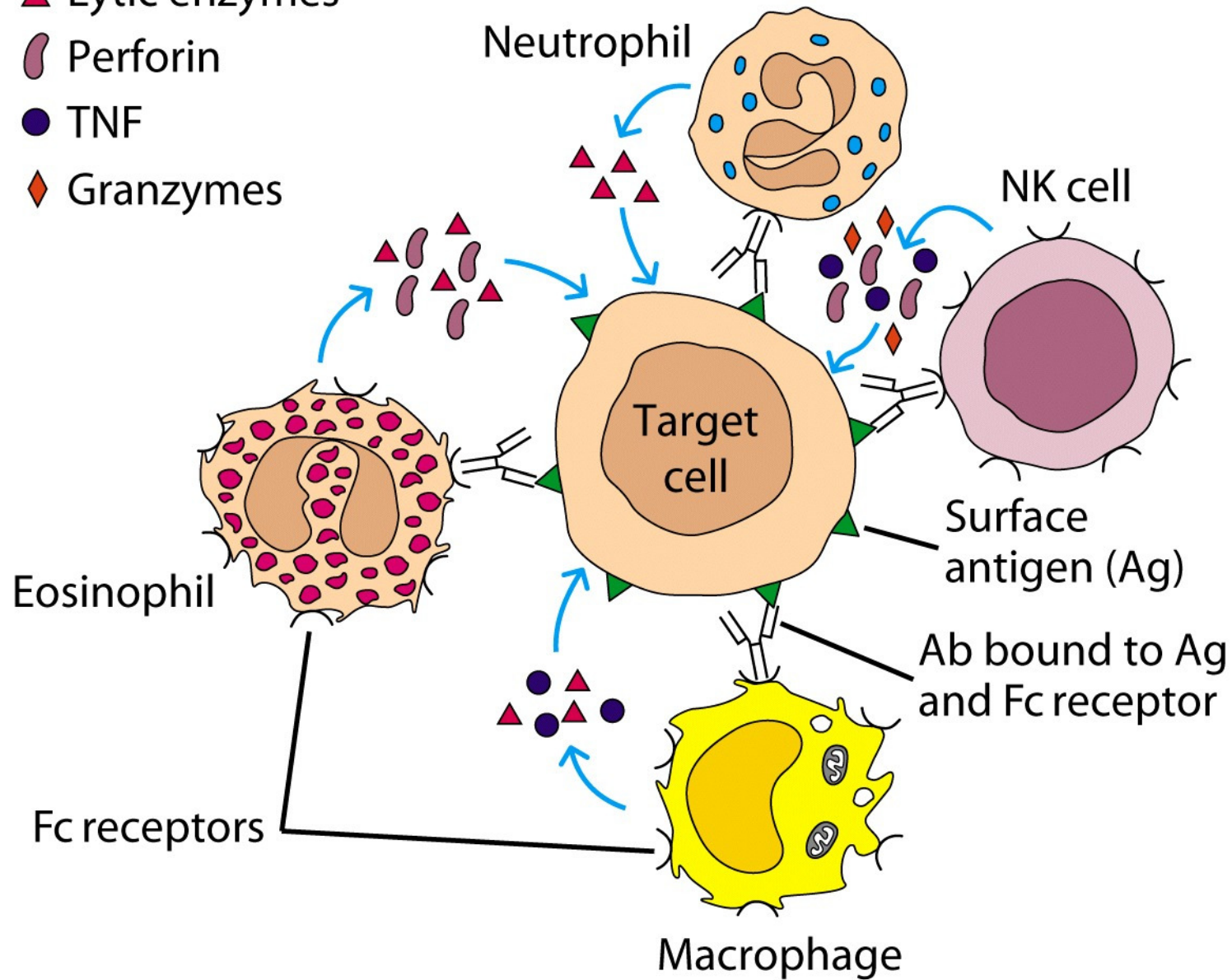


▲ Lytic enzymes

● Perforin

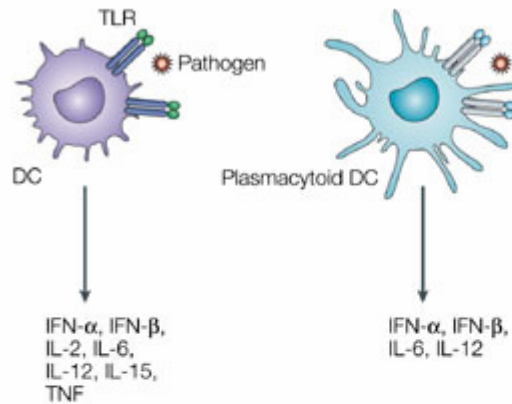
● TNF

◆ Granzymes

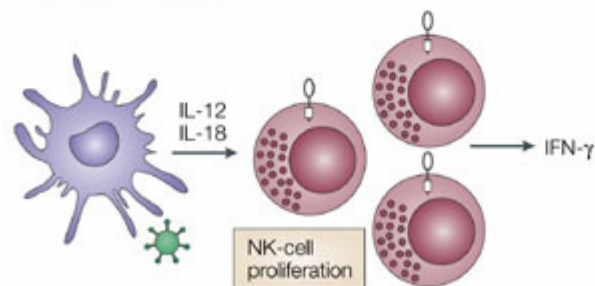


CÉLULAS NK E INFECCIÓN.....

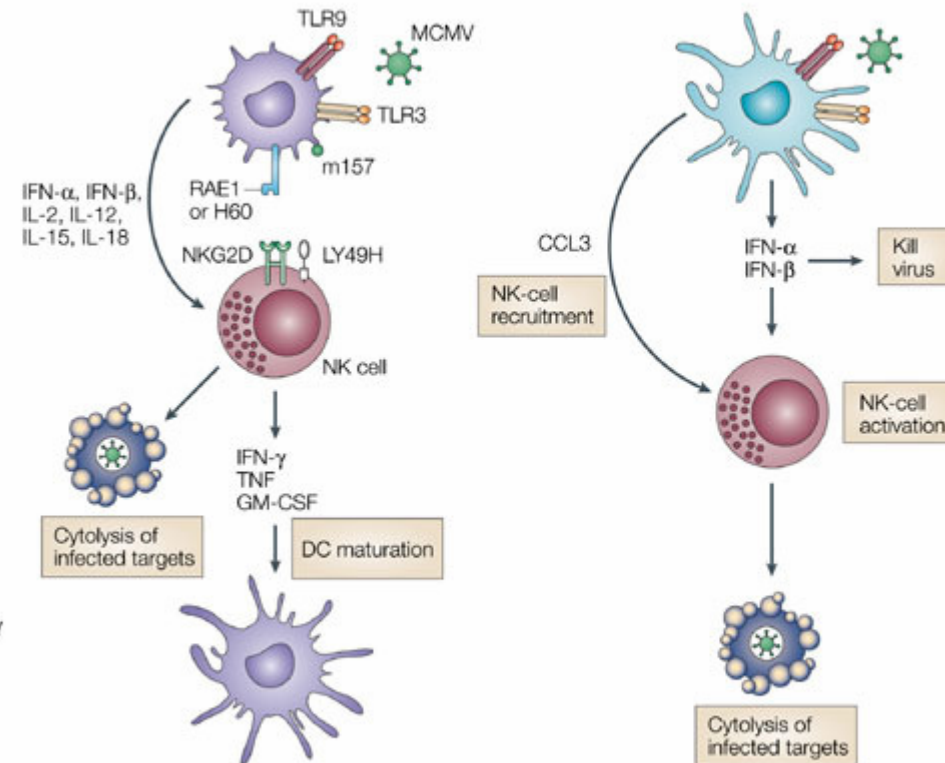
a TLR-mediated activation of DCs



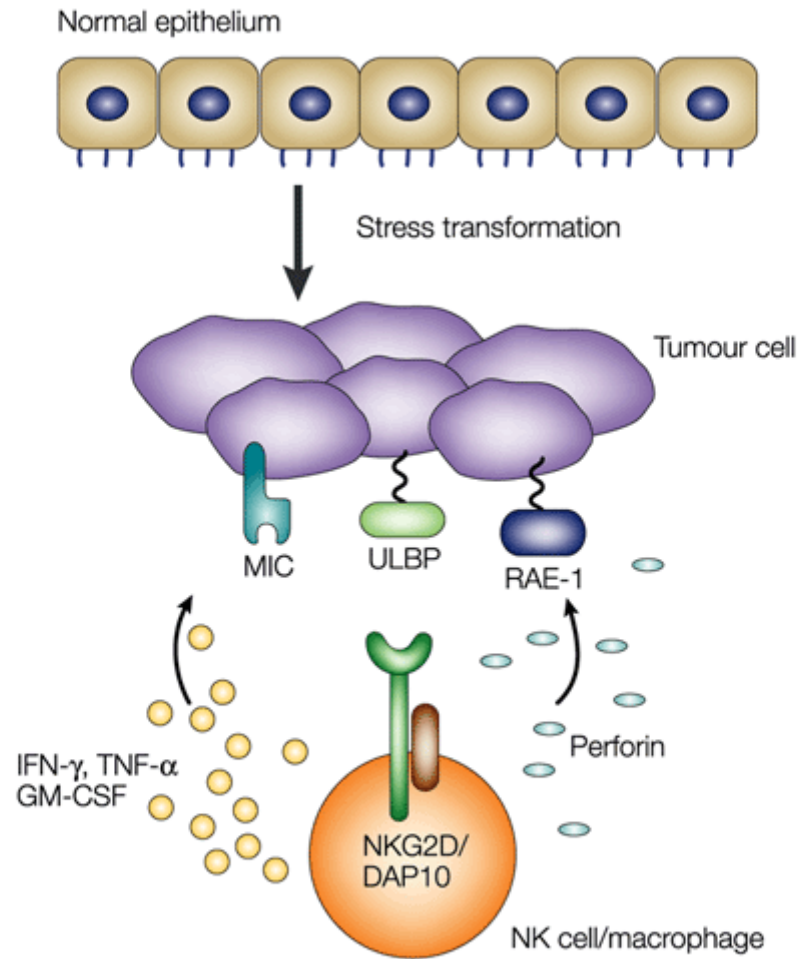
c Late interactions between DCs and NK cells in MCMV infection

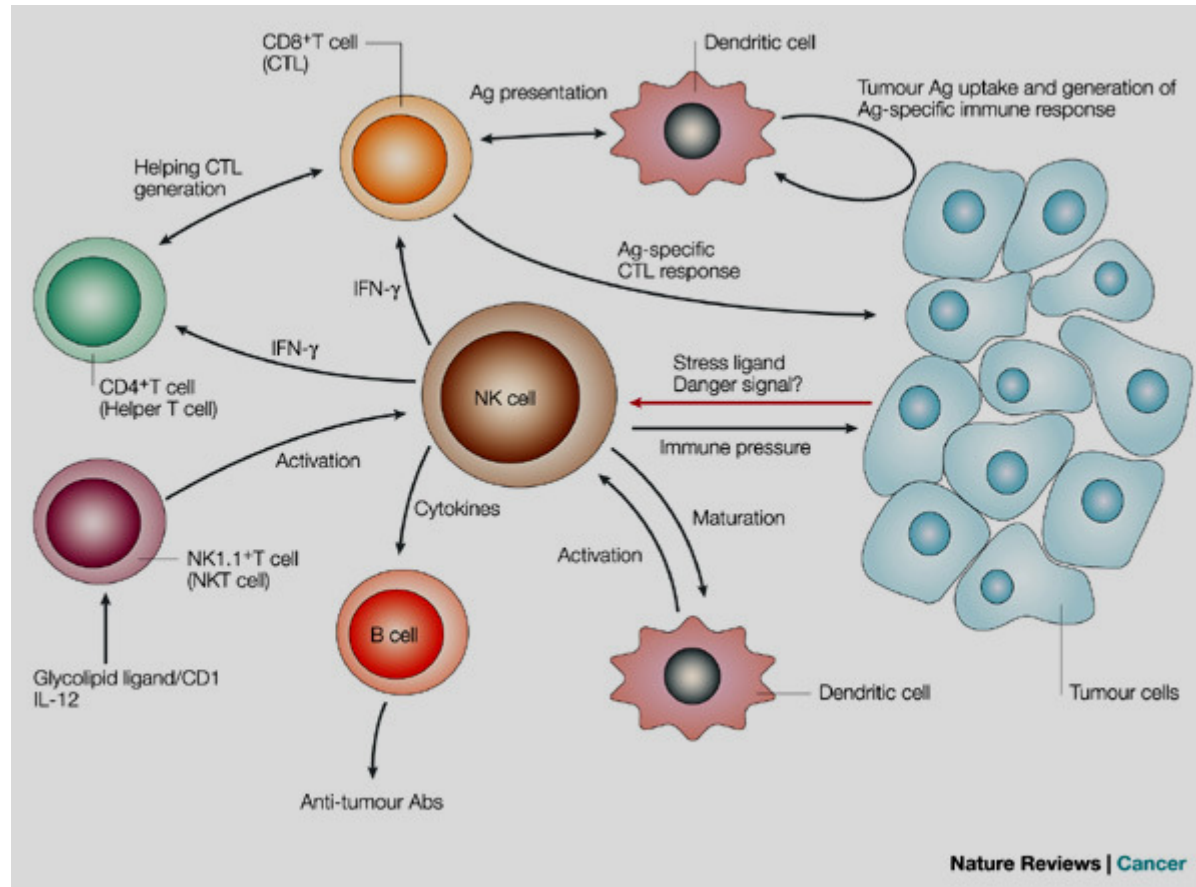


b Early interactions between DCs and NK cells in MCMV infection

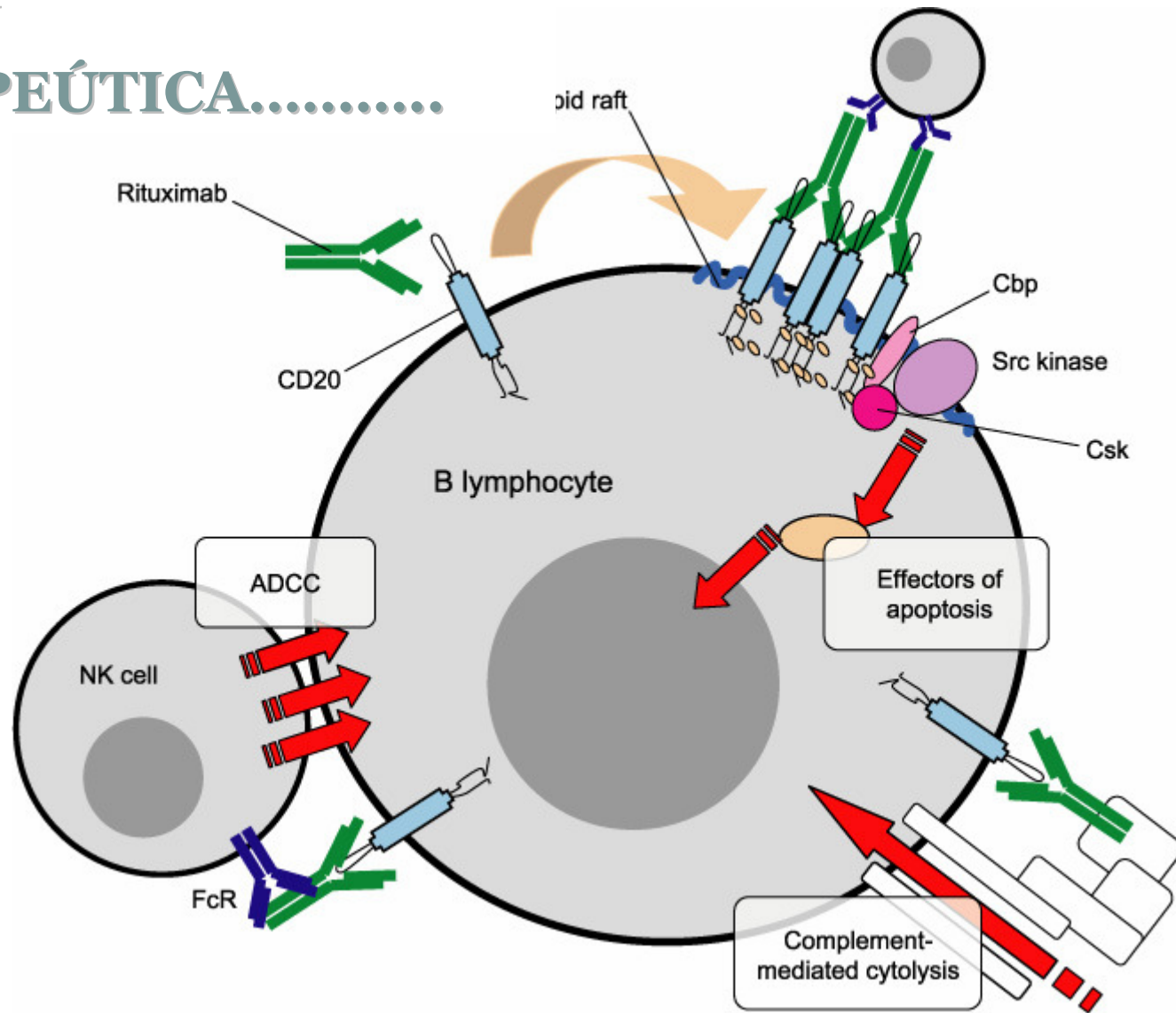


NK Y TUMORES...

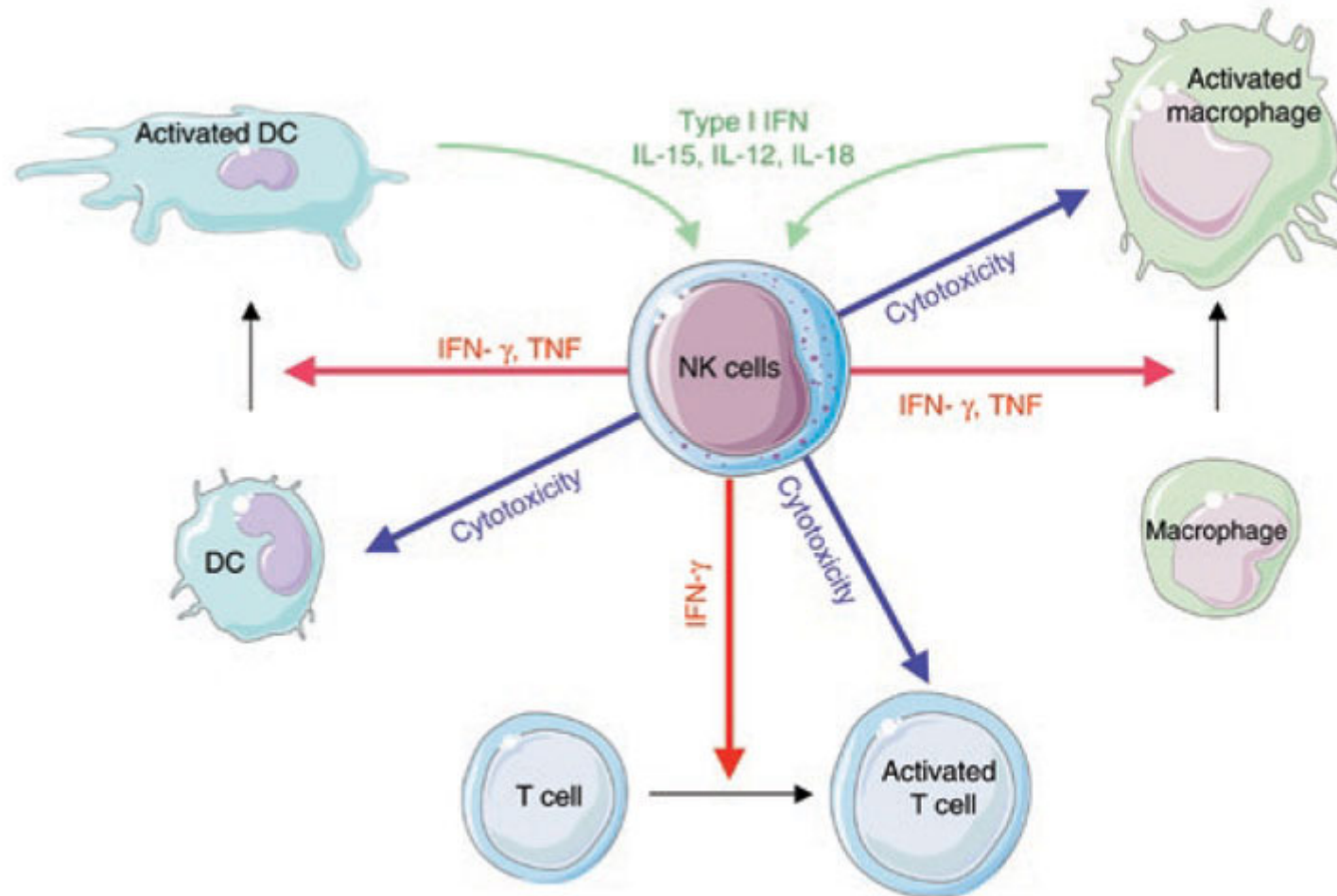


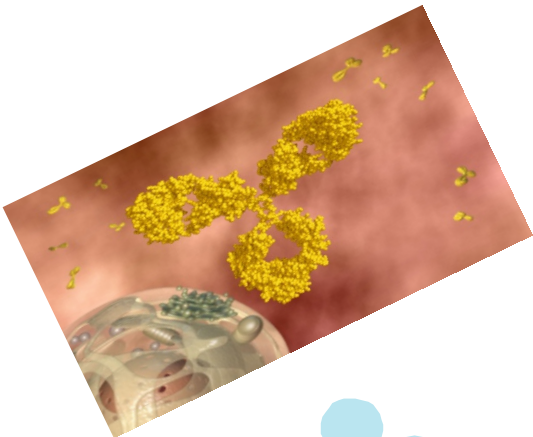


NK EN TERAPEÚTICA.....



FUNCIONES DE LAS CÉLULAS NK...

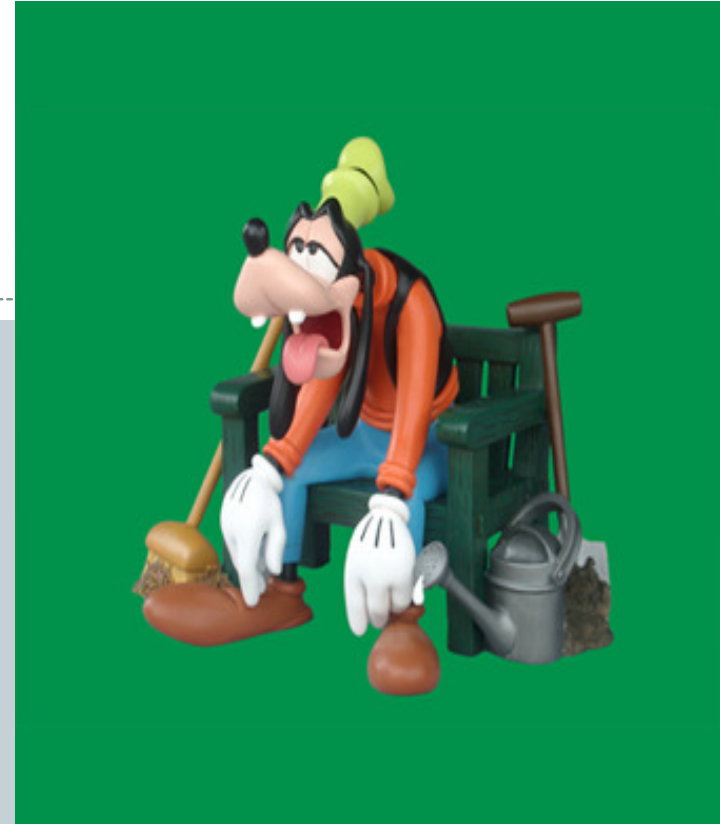


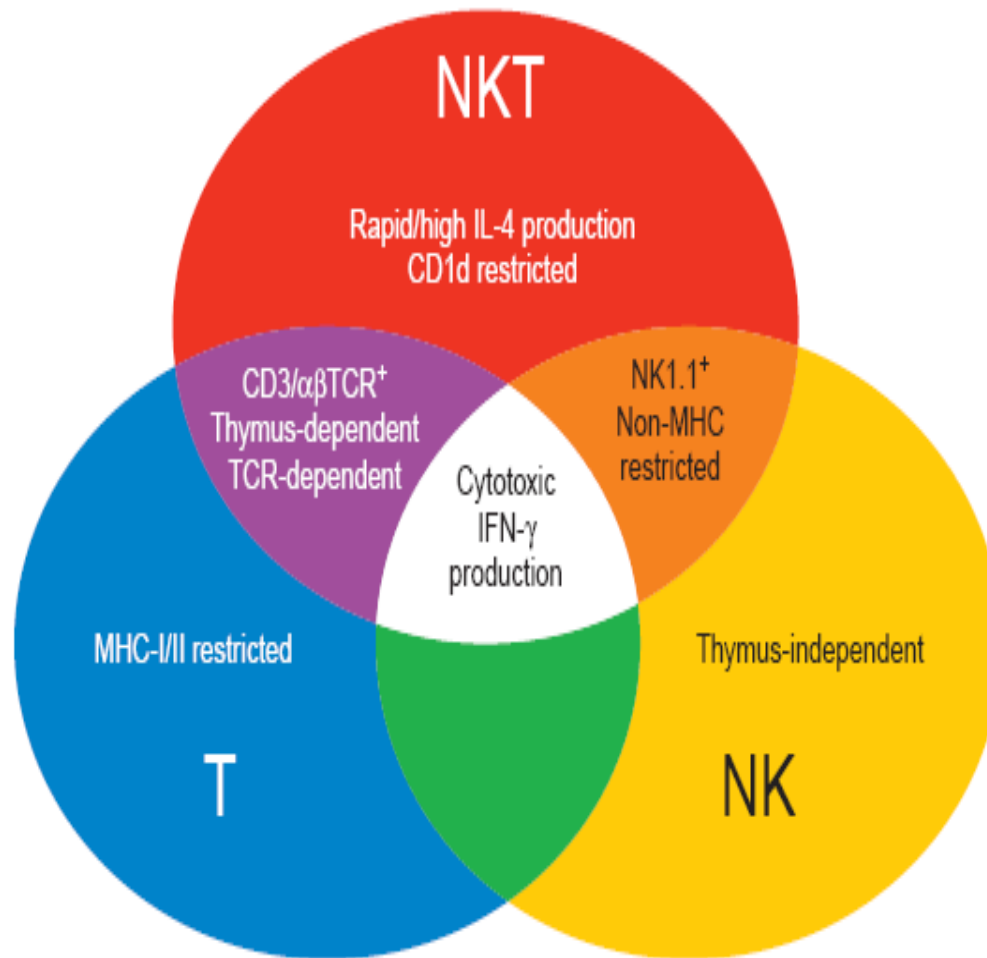


MÁS
CÉLULAS.....



Linfocitos NKT





Immunology Today

Hoy definidas como....



...células que tienen

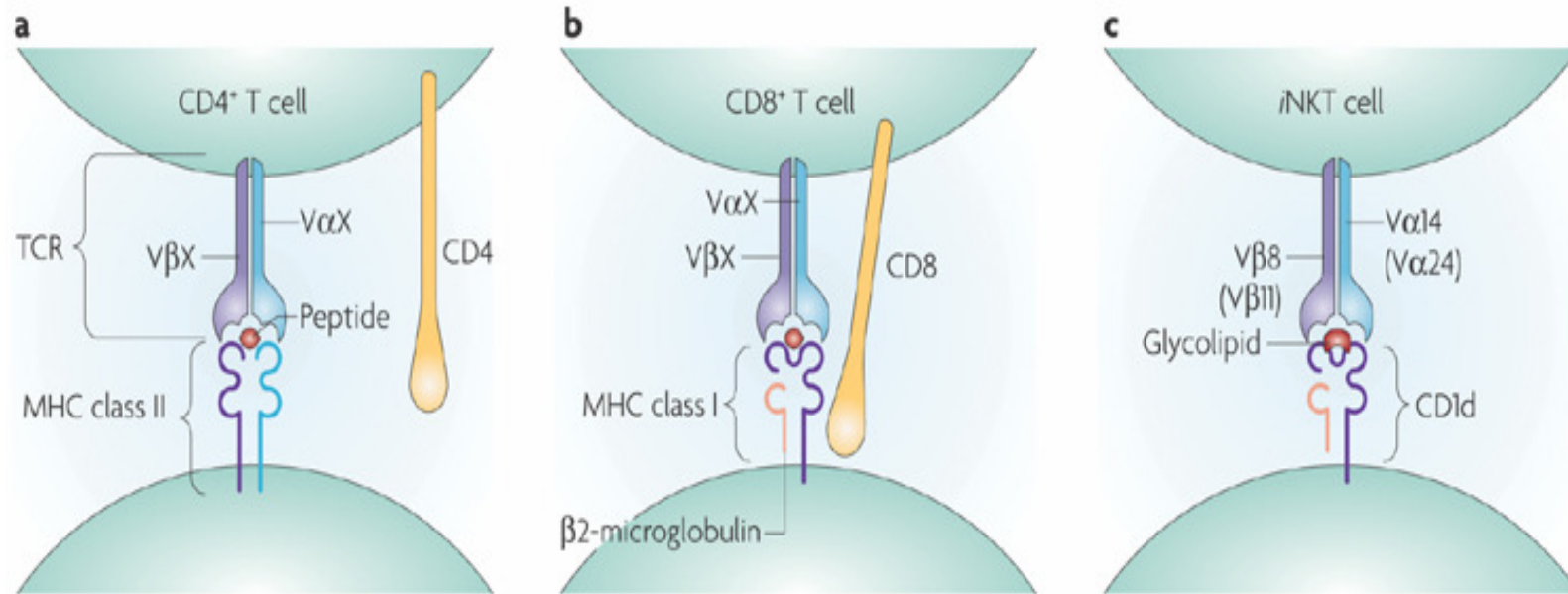
una cadena invariante V α 24-J α 18

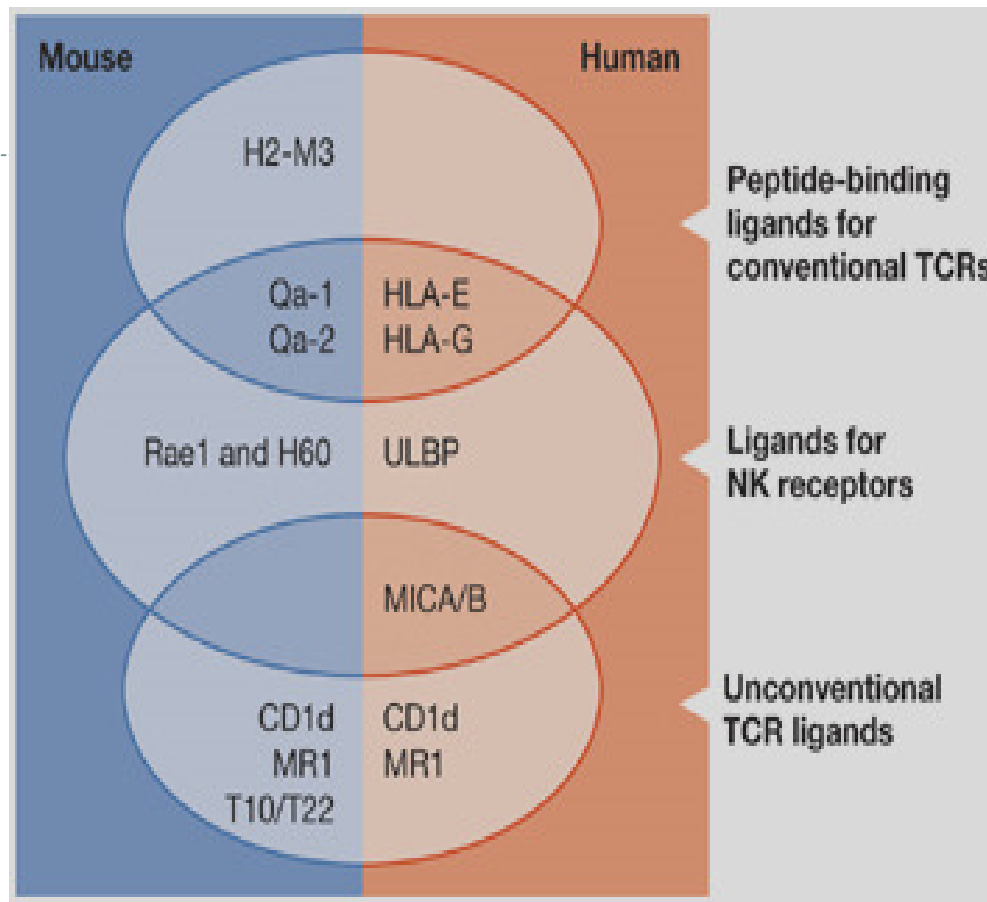
y

reactividad para α -GalCer

Annu. Rev. Immunol. 2005. 26:877–900

RECONOCIMIENTO DE ANTÍGENO POR CÉLULAS T...





Conventional T-cell receptors (TCRs) are those of polyclonal $\alpha\beta$ T cells

Unconventional TCRs correspond to oligoclonal T-cell subsets, such as natural killer (NK) T cells (for CD1d), $\gamma\delta$ T cells (T10/T22, MICA/B) or gut-associated T cells (MR1)

Moléculas MHC- no clásicas.....



Características

- ▣ Son un subtipo de linfocitos T con dos posibles fenotipos: $CD4^+$ y $CD4^- CD8^-$ (DN).
- ▣ Expresan
 1. receptores de células NK
 2. Un TCR semi-invariante, restringido por CD1d.
- ▣ **Se considera que participan en la respuesta inmune innata pues sus TCR son semiinvariantes**
- ▣ Su capacidad de secretar inmediatamente grandes cantidades de citocinas (**IFN- γ , IL-4, TNF**) cuando sus TCR son activados les confiere un papel inmunoregulador.
- ▣ Falta de memoria inmunológica

Distribución

- ✓ **NKT pueden encontrarse en los mismos lugares que las células T, en el ratón.**
- ✓ **La relación de NKT: T varía según los distintos tejidos.**
- ✓ **NKT son más frecuentes en hígado (30–50%), médula ósea (20–30%) y timo (10–20%) .**

Las células iNKT proporcionan cooperación a los LB.....



- ▣ Los Ag naturales presentados por CD1d a las células iNKT se desconocen pero si se ha aislado un glicoesfingolípido de esponjas marinas llamado **α -GalCer**, que fija específicamente CD1d y activa a las células iNKT.
- ▣ Las iNKT son tan eficientes como los linfocitos Tho para promover in vitro la proliferación de linfocitos B autólogos y la producción de Igs.
- ▣ Los dos mayores subtipos de células NKT expresan niveles comparables de CD40L y citocinas, e inducen niveles similares de proliferación de células B.
- ▣ Las células NKT CD4⁺ inducen altos niveles de producción de Igs.

CÉLULAS QUE EXPRESAN CD1



	Group-1-CD1-restricted T cells	CD1d-restricted iNKT cells	CD1d-restricted diverse NKT cells
Antigens	Microbial and self lipids	Microbial and self lipids	Unknown
T-cell population	Clonally diverse	Canonical TCR α but polyclonal	Clonally diverse
TCR	TCR α : diverse; TCR β : diverse	TCR α : invariant V α 14 or V α 24 and J α 18; TCR β : limited V β repertoire with diverse CDR3	TCR α : diverse; TCR β : diverse
Precursor frequency	One per thousands, unique specificity for single antigen	<1% of T cells in humans; 2–50% of T cells in mice; pool of cells that responds <i>en masse</i> to a single antigen	Unknown
Memory	Yes	No	Unknown
Immunity	Adaptive, slow	Innate-like, rapid (hours to few days)	Unknown

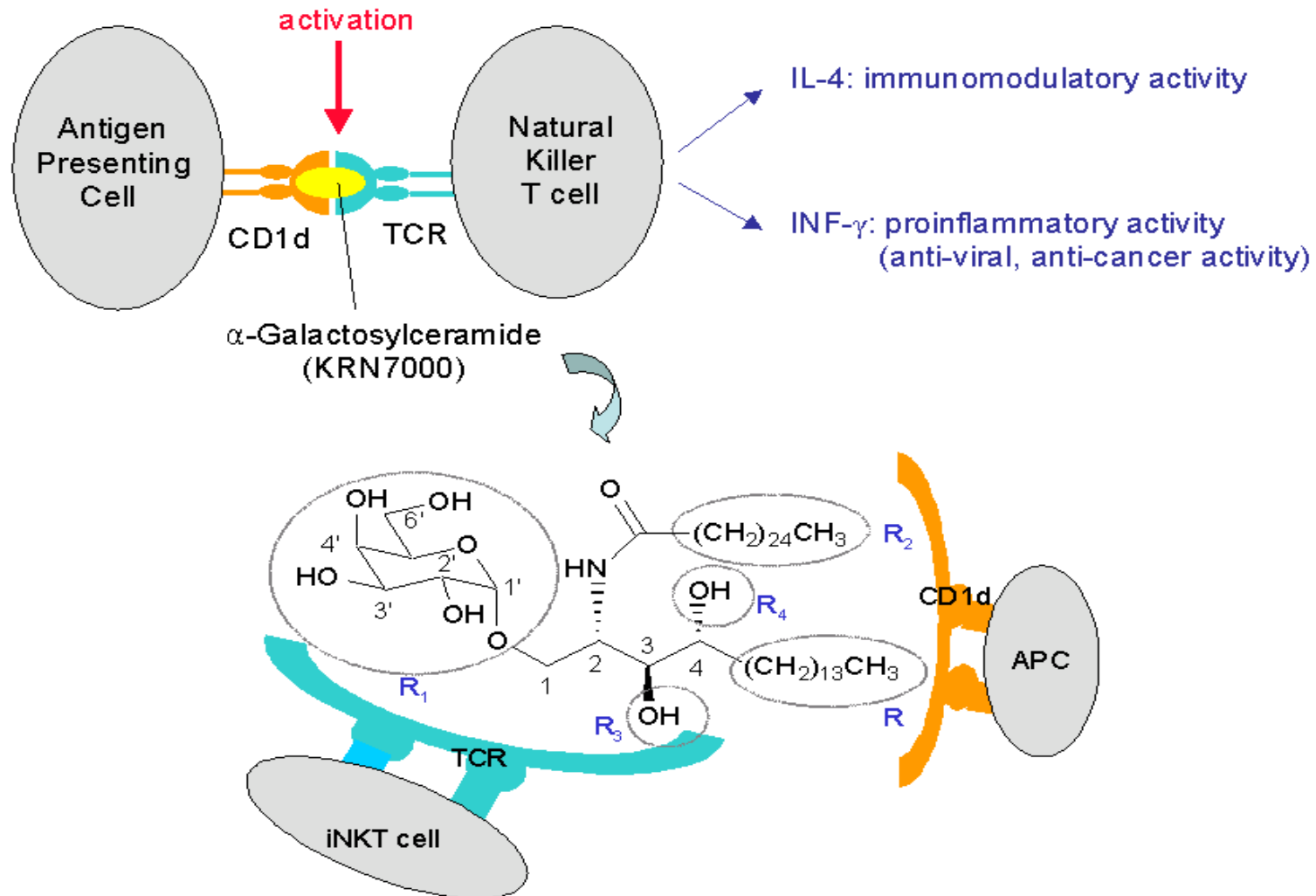
CDR3, complementarity-determining region 3; iNKT cell, invariant natural killer T cell; TCR, T-cell receptor.

Source	Antigen	CD1 isoform
<i>Mycobacterium tuberculosis</i> and other mycobacteria	Mycolic acids	CD1b
	Glucose monomycolate	CD1b
	Sulpholipid (diacylated sulphoglycolipid)	CD1b
	Phosphatidylinositol mannosides	CD1b, CD1d
	Mannosylated lipoarabinomannan	CD1b
	Mannosyl- β 1-phosphomycoketides	CD1c
	Didehydroxymycobactin	CD1a
<i>Sphingomonas</i> spp.	α -Glucuronosylceramide	CD1d
<i>Borrelia burgdorferi</i>	α -Galactosyldiacylglycerol	CD1d
<i>Leishmania donovani</i>	Lipophosphoglycan	CD1d
Mammalian (self)	Phosphatidylinositol	CD1d
	Phosphatidylglycerol	CD1d
	Phosphatidylethanolamine	CD1d
	GM1	CD1b
	GD3	CD1d
	Sulphatide	CD1a, CD1b, CD1c
	Isoglobotrihexosylceramide	CD1d
	Synthetic or marine sponge	α -Galactosylceramide

*@&#!

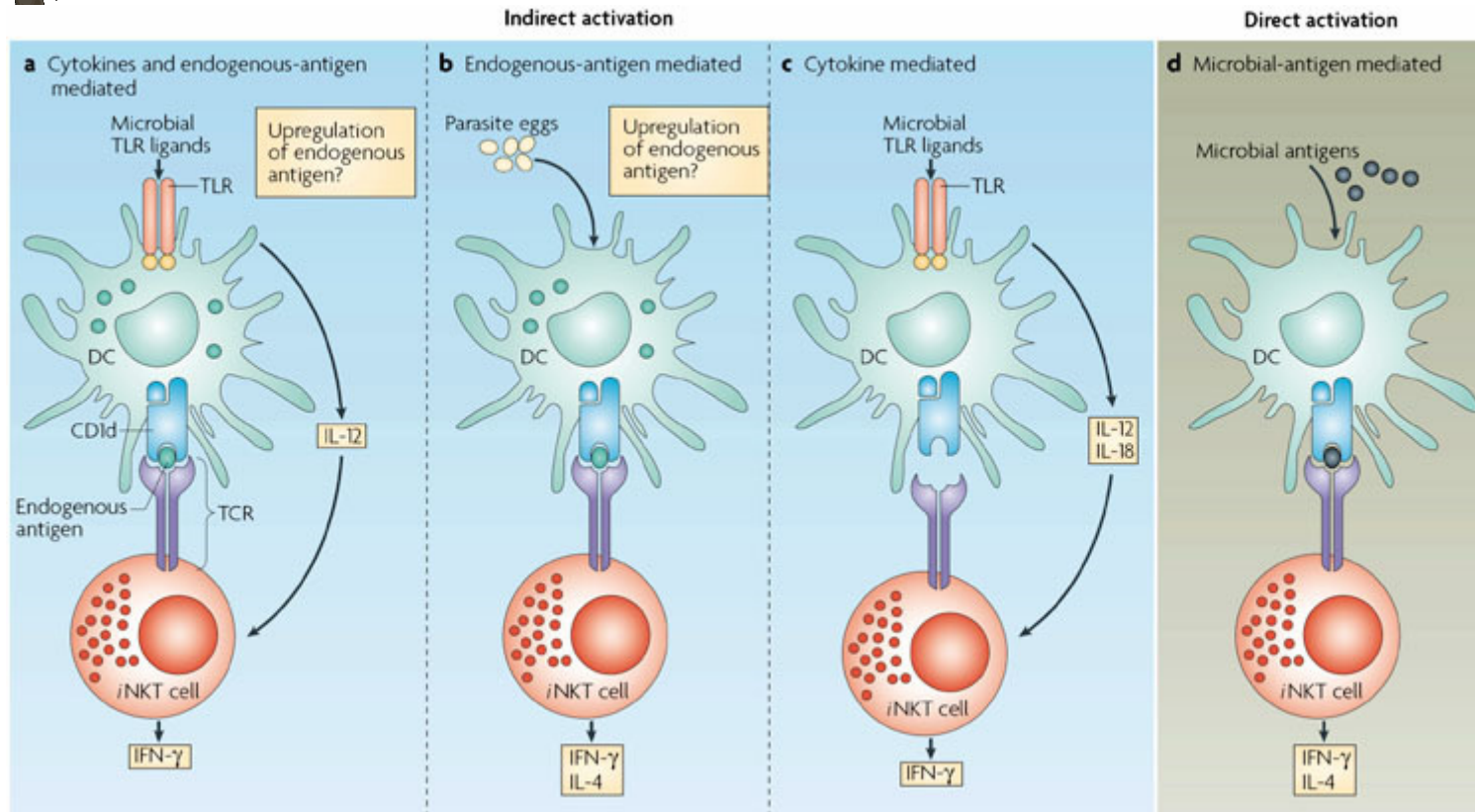


NKT Y FUNCIONES

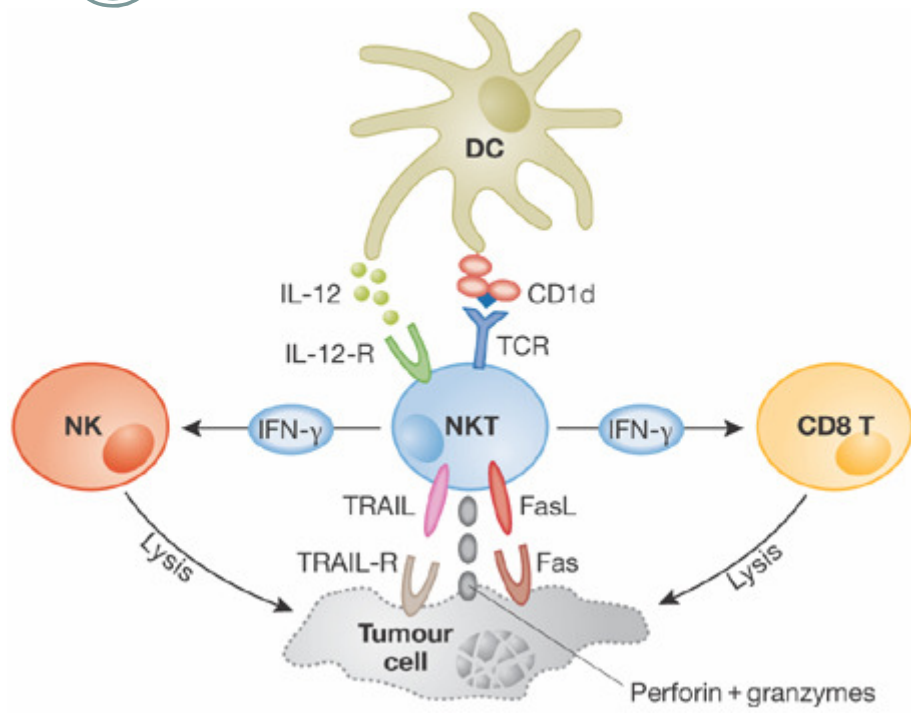
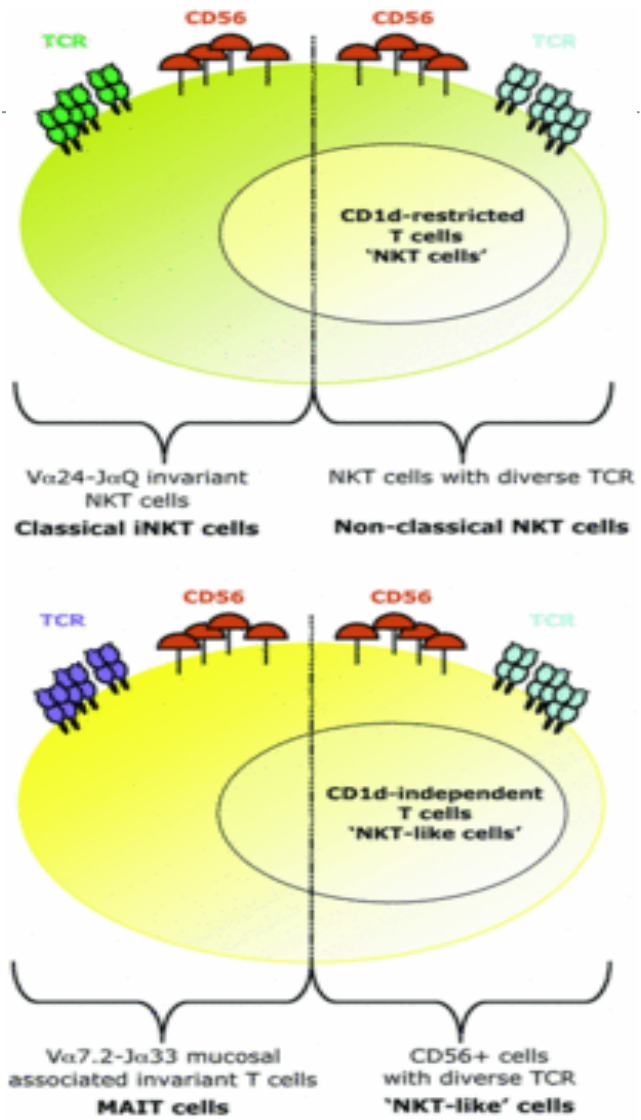




Control de infecciones

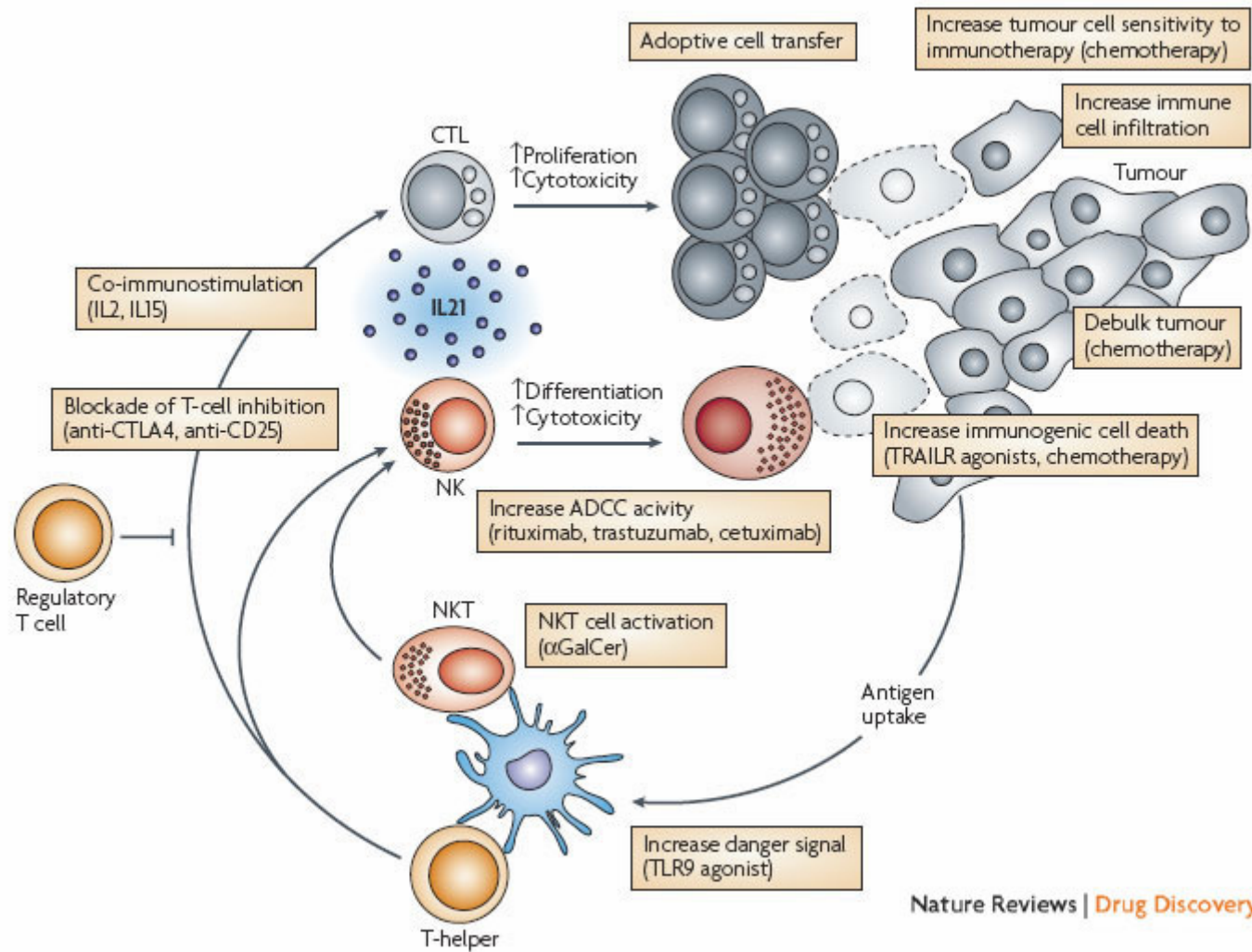


NKT Y CITOTOXICIDAD...





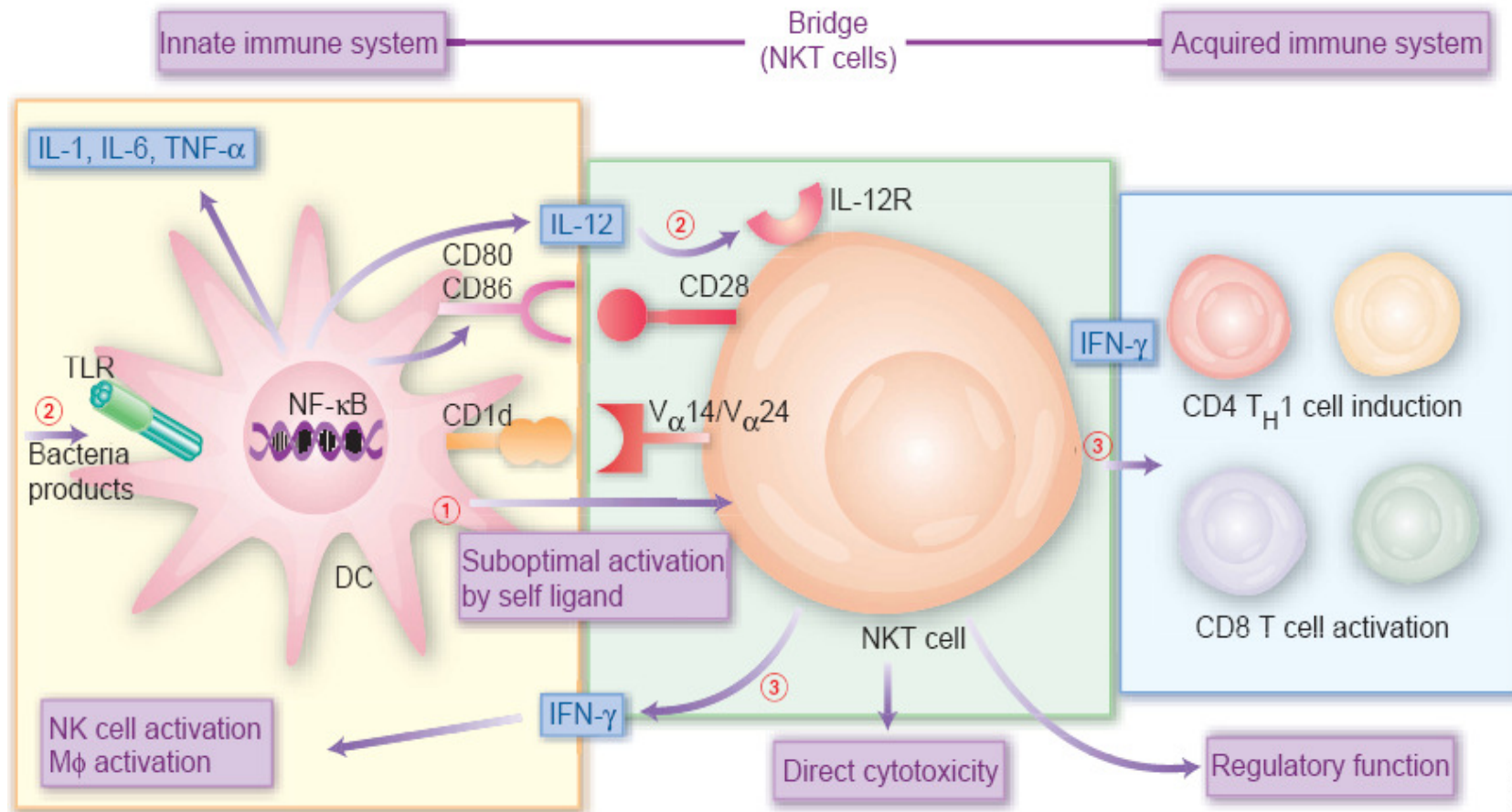
Inmunidad antitumoral



Nature Reviews | Drug Discovery

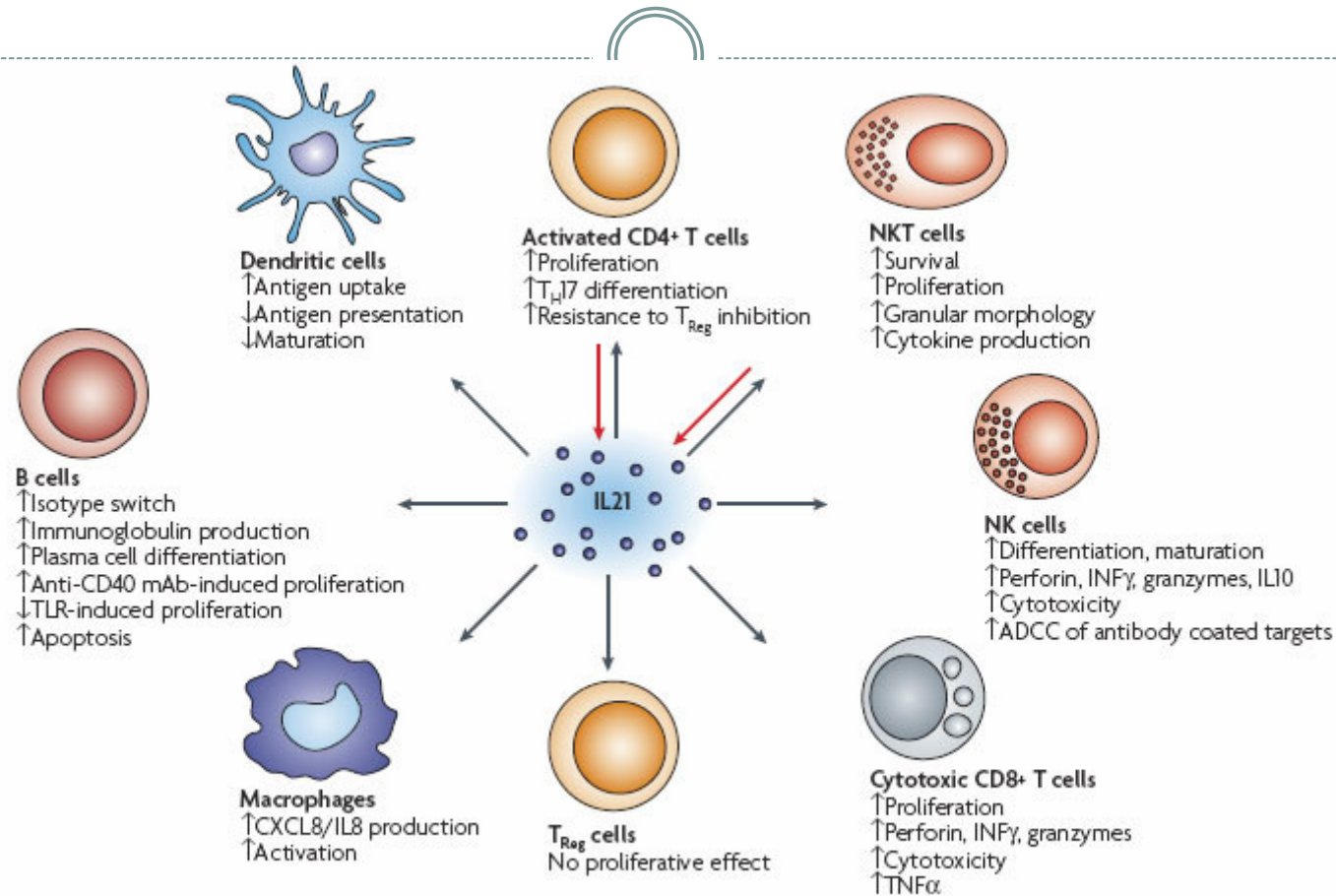


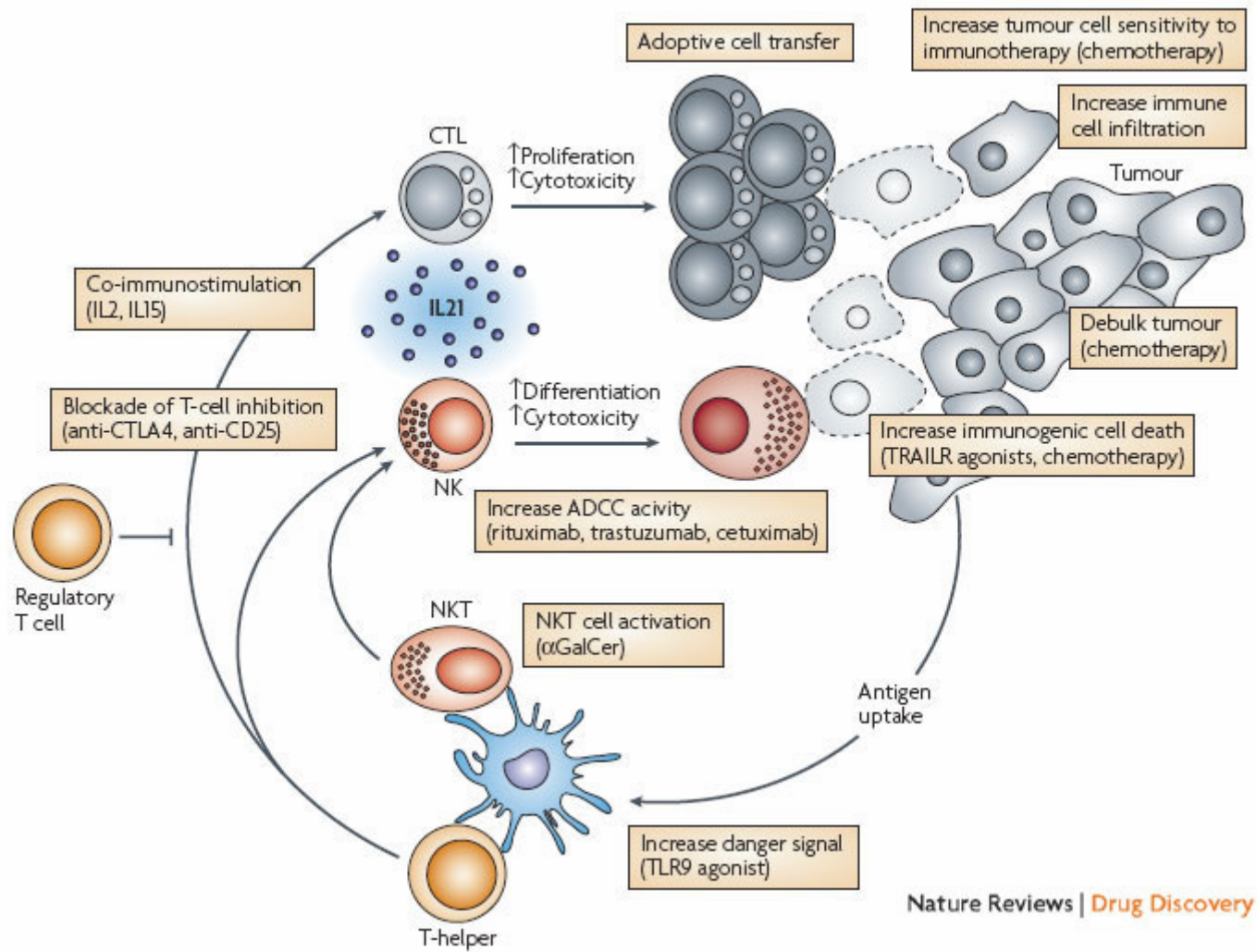
"Bridging" la inmunidad innata y la adquirida...



C.C.

IL-21 y tratamiento para el cáncer





Nature Reviews | Drug Discovery

LINFOCITOS

Tγδ



Two classes of T-cell receptor

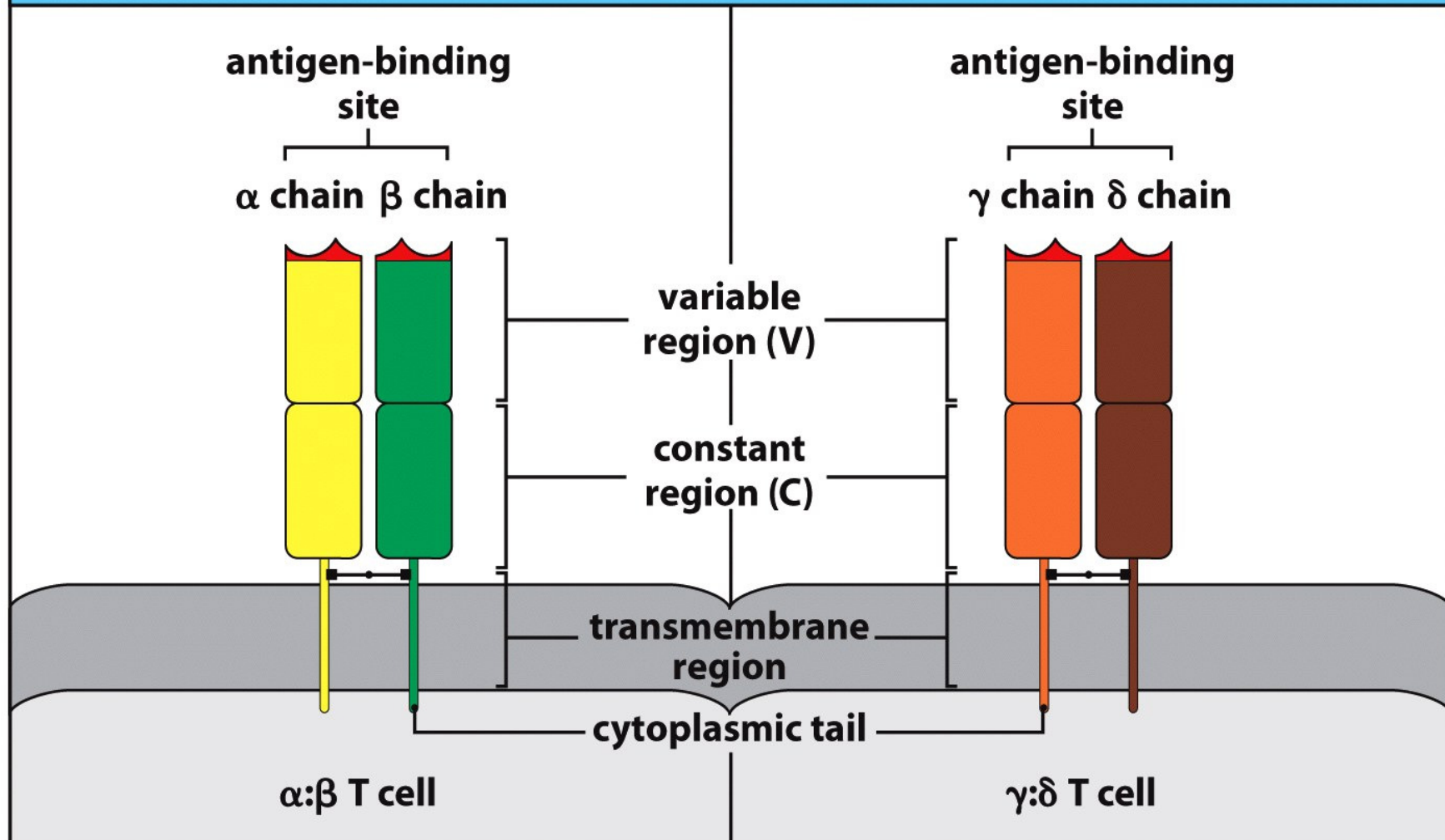


Figure 5.7 The Immune System, 3ed. (© Garland Science 2009)

Characterísticas

Table 1 | $\gamma\delta$ T cells can be distinguished from other lymphocyte lineages

Characteristic	$\alpha\beta$ T cells	$\gamma\delta$ T cells	B cells
Antigen-receptor configuration	CD3 complex + $\alpha\beta$ TCR	CD3 complex + $\gamma\delta$ TCR	Ig
Theoretical receptor number	$\sim 10^{15}$	$\sim 10^{20}$	$\sim 10^{11}$
Antigen recognition	Peptide + MHC	Protein and non-protein	Protein and non-protein
MHC restriction	Yes	Rare	No
Phenotype	CD4 ⁺ or CD8 ⁺	Most are CD4 ⁻ CD8 ⁻ ; iIELs are CD8($\alpha\alpha$) ⁺	CD19 ⁺ CD20 ⁺
Frequency in blood	65–75%	1–5% (25–60% in gut)	5–10%
Distribution	Blood and lymphoid tissues	Blood, epithelial and lymphoid tissues	Blood and lymphoid tissues
Effector capability	CTLs (CD8 ⁺) Cytokine release (T_H1/T_H2)	CTLs Cytokine release ($T_H1 > T_H2$)	Ig production
Function	Immune protection and pathogen eradication	Immunoregulation and immunosurveillance	Humoural immunity

CTLs, cytotoxic T lymphocytes; iIELs, intestinal intraepithelial T lymphocytes; Ig, immunoglobulin; T_H cell, T helper cell; TCR, T-cell receptor. Data adapted from REFS 64,65.

ONTOGENIA

A common double-negative T-cell progenitor gives rise to $\alpha:\beta$ and $\gamma:\delta$ T cells

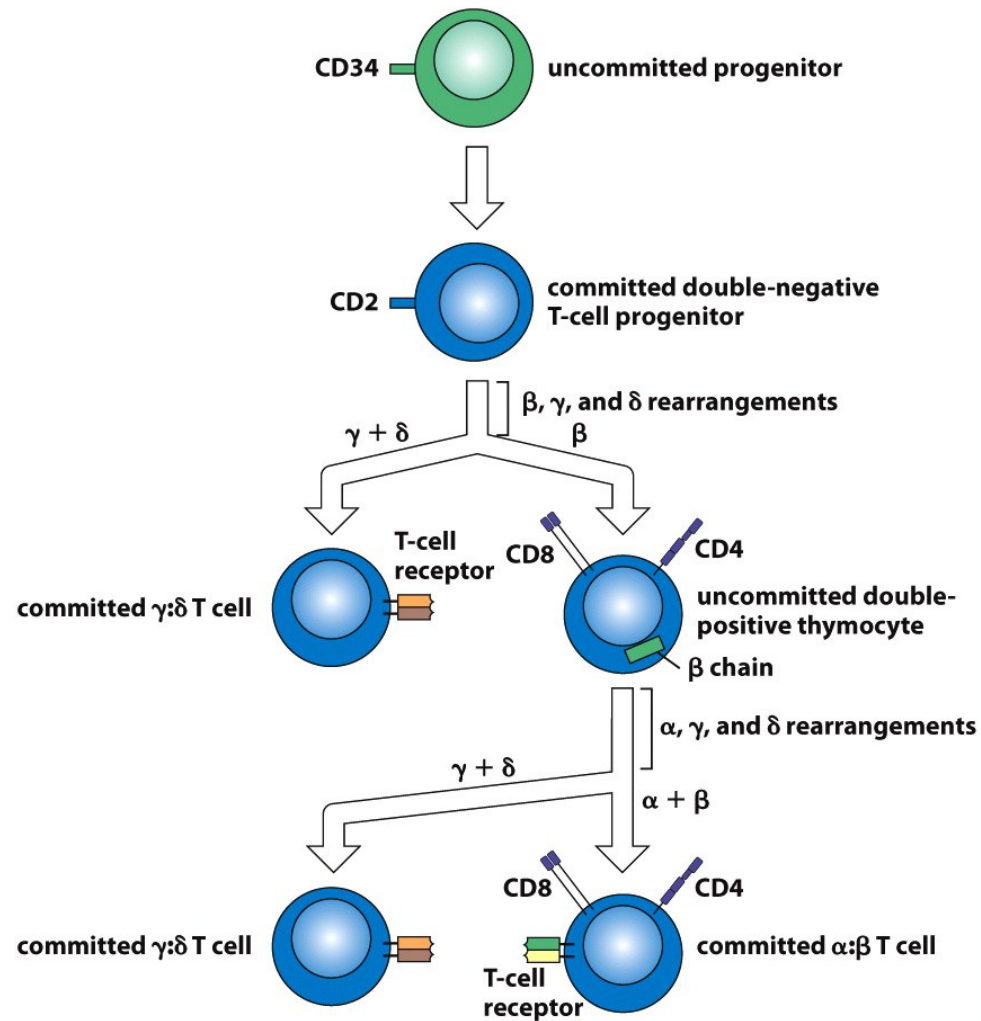
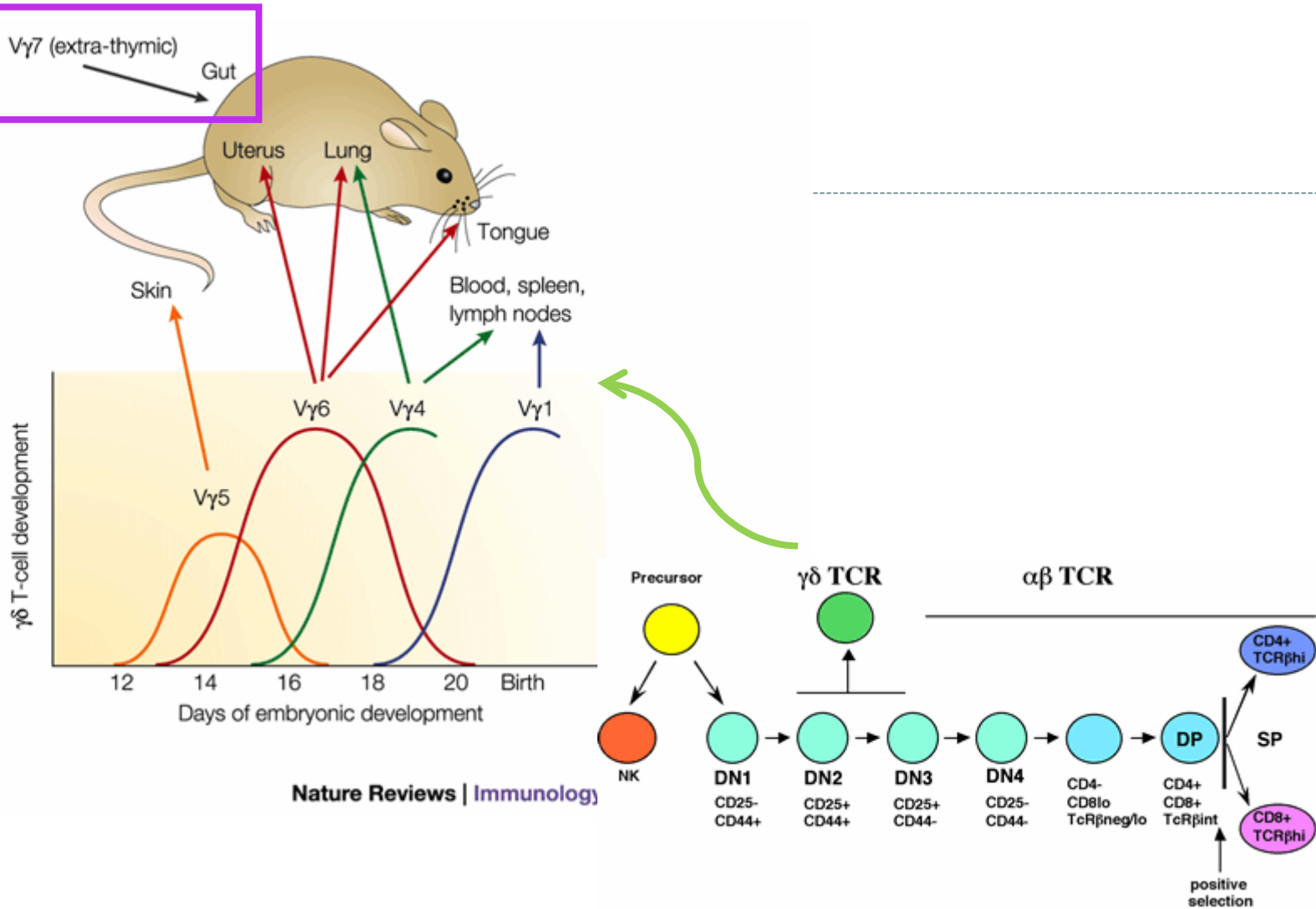
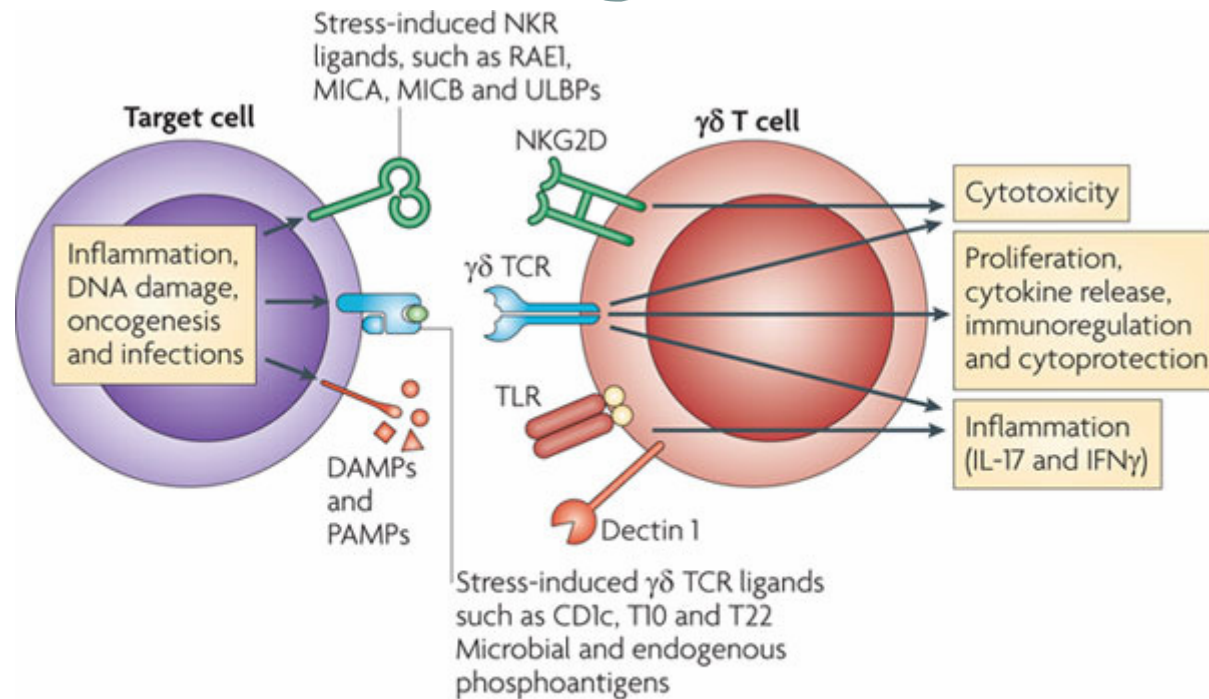


Figure 7.7 The Immune System, 3ed. (© Garland Science 2009)

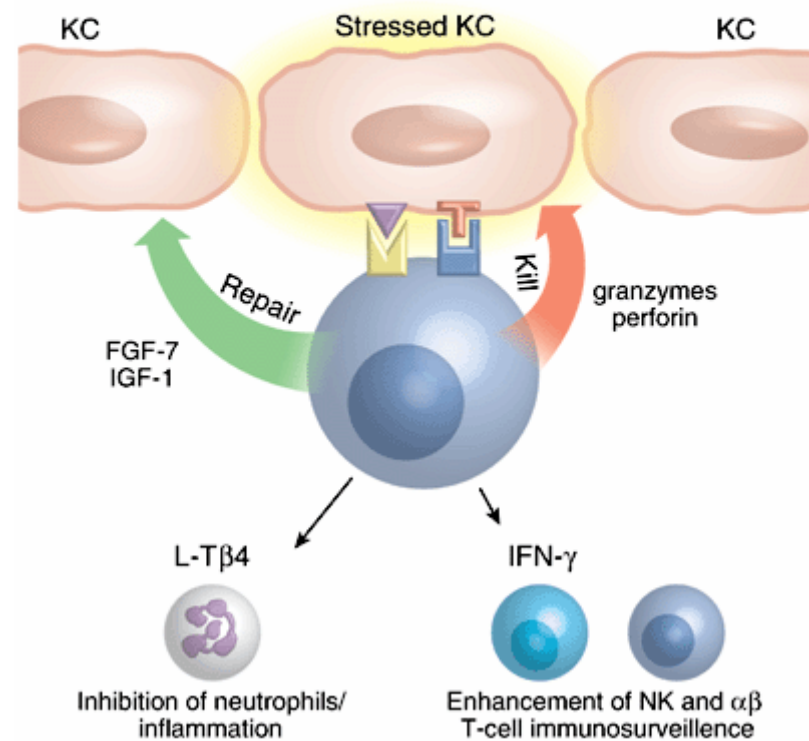
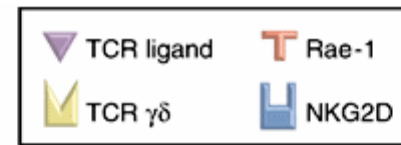


Distribución de los linfocitos T $\gamma\delta$

¿Cómo funciona el linfocito $T\gamma\delta$???



Los linfocitos T $\gamma\delta$ en la piel estresada.....

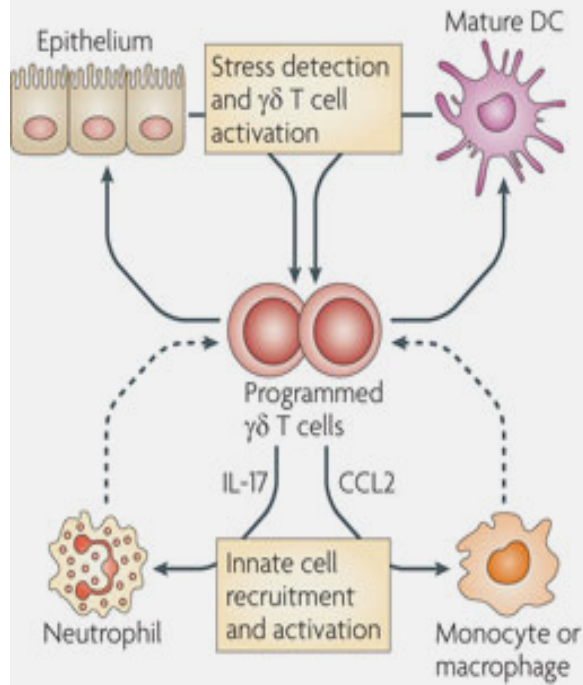


Fibroblast growth factor-VII (FGF-7I); keratinocyte growth factor-1 (IGF-1)

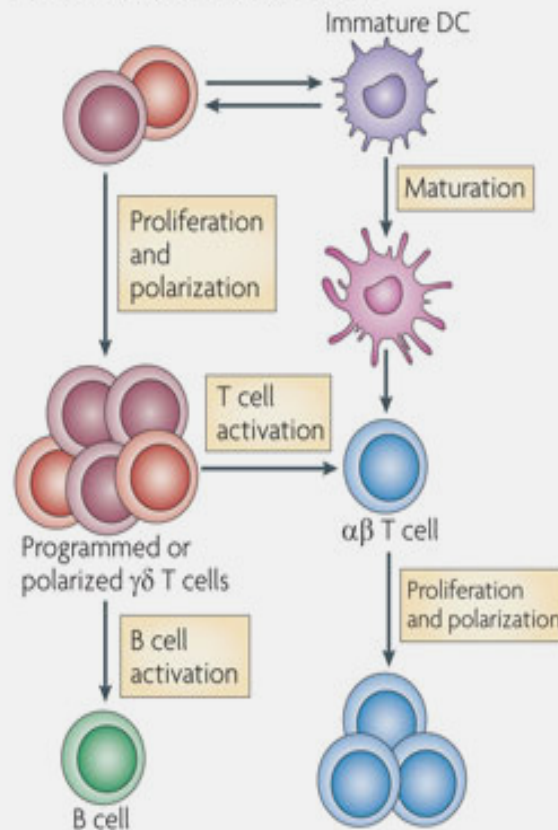
Thymosin β -4 (L β -T4): inhibe la liberación de mediadores oxidativos por los PMNs.

El linfocito $\gamma\delta$ en acción...

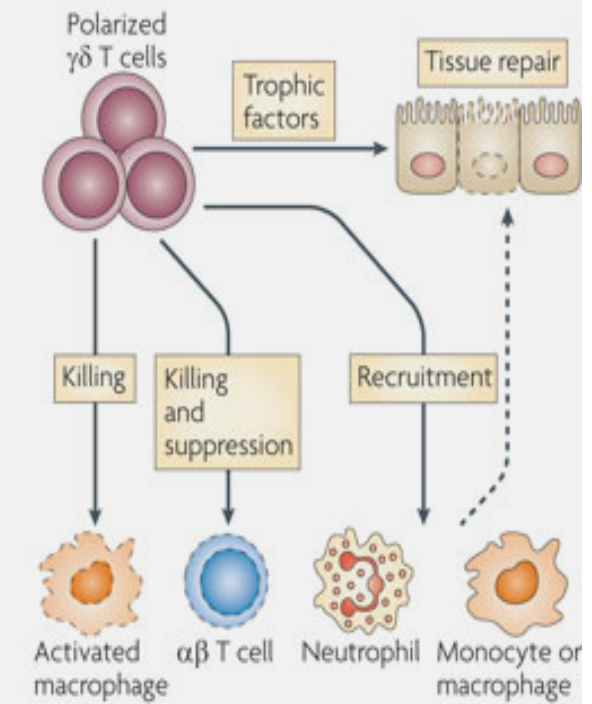
a Early: innate boost



b Intermediate: adaptive boost



c Late: downmodulation of immune responses and tissue repair

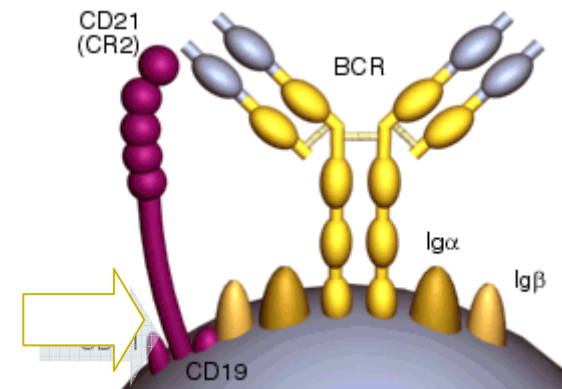


Linfocitos MZB



- ▣ Representan la primera línea de defensa capaz de detectar la presencia de microorganismos en sangre y producir importantes cantidades de anticuerpos neutralizantes en forma rápida para detener la multiplicación bacteriana.
- ▣ Su arquitectura permite un contacto íntimo entre los antígenos y células efectoras. Dentro de los primeros 3 a 4 días de la estimulación antigénica producen grandes cantidades de IgM específica.
- ▣ Producen anticuerpos sin necesidad de recibir coestimulación y **responden preferentemente a antígenos PS de bacterias capsulares.**
- ▣ **Los linfocitos MZB son particularmente dependientes del complemento para diferenciarse a plasmocitos productores de Ig.**

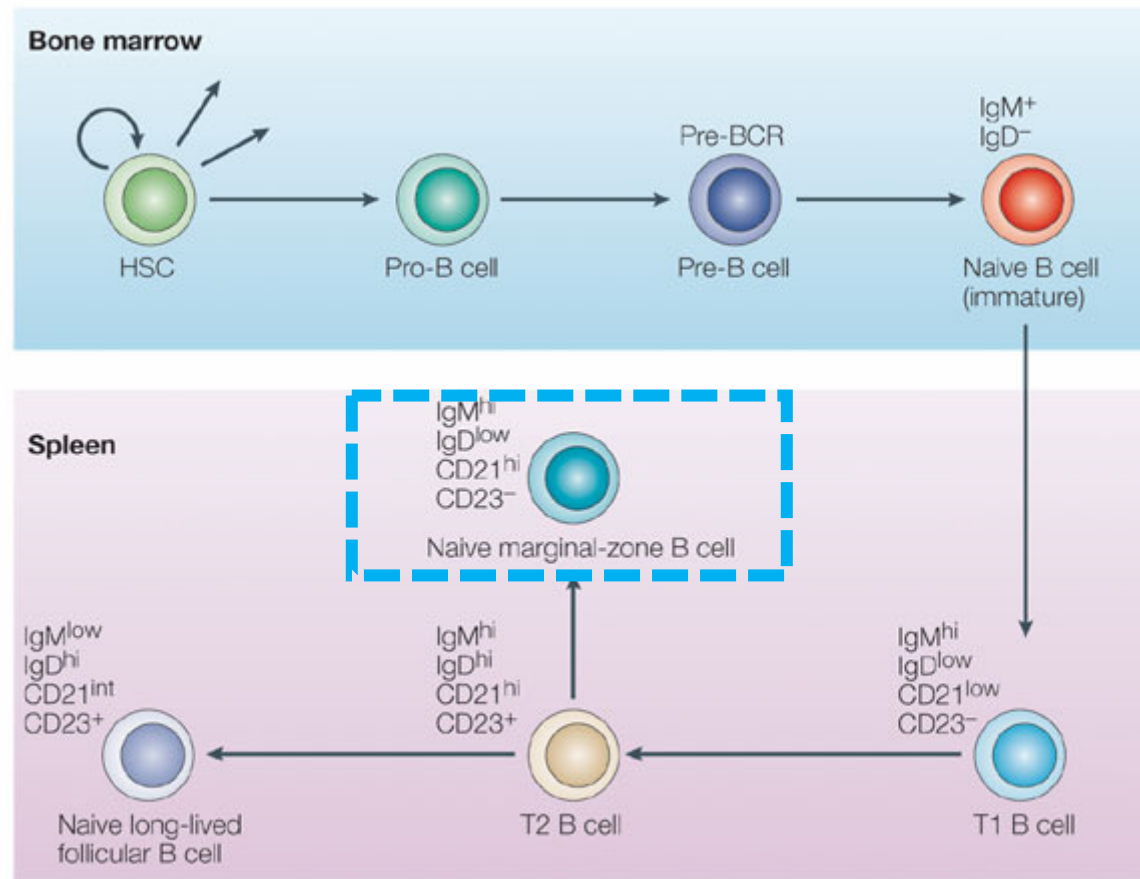
Algunas características





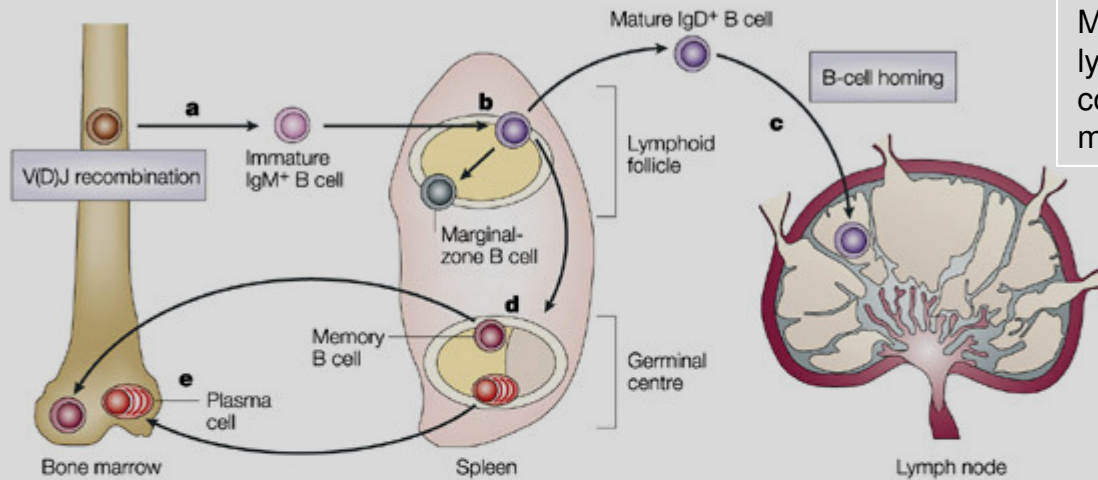
- ▣ **Los niños menos de 2 años tienen una respuesta pobre frente a las infecciones por bacterias encapsuladas como *Streptococcus pneumoniae*, *Neisseria meningitidis* o *Haemophilus influenzae*.**
- ▣ **La protección contra este tipo de bacterias está dada por anticuerpos específicos que permiten el reconocimiento y fagocitosis de las mismas por parte de macrófagos y PMNs.**
- ▣ **La incapacidad de los infantes para producir anticuerpos anti-PS bacterianos parece radicar en la inmadurez de los linfocitos MZB, que expresan bajos niveles de CD21.**

ONTOGENIA DE LAS CÉLULAS MZB...



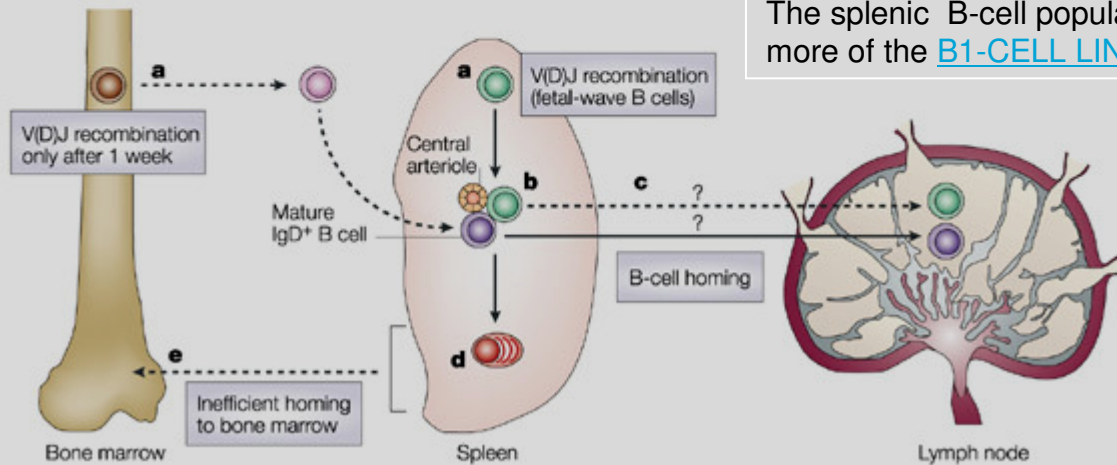
Some cells are driven (possibly by antigen) to become [MARGINAL ZONE B CELLS \(MZB\)](#) that reside in this specialized location (the marginal zone)

Adult human

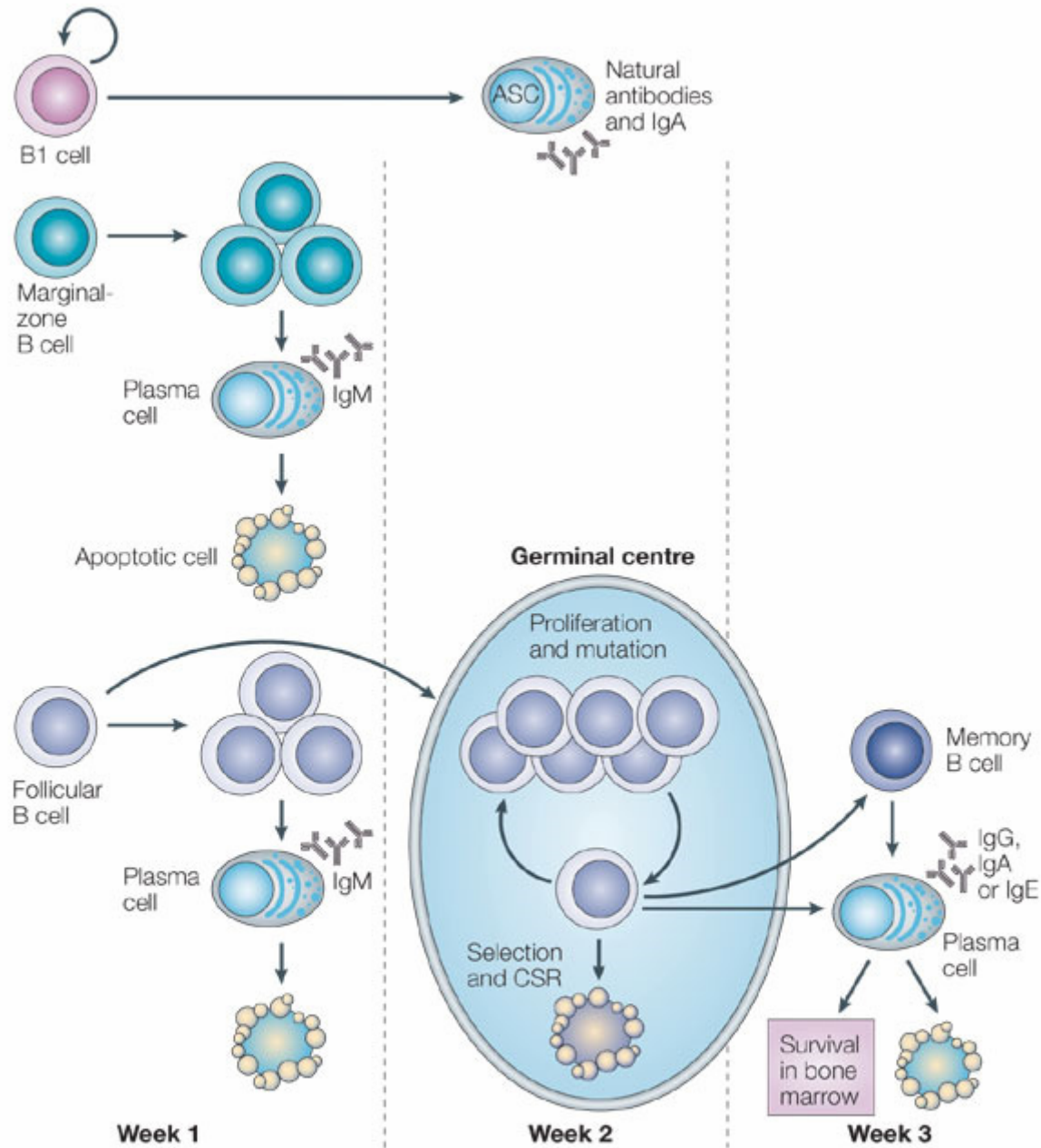


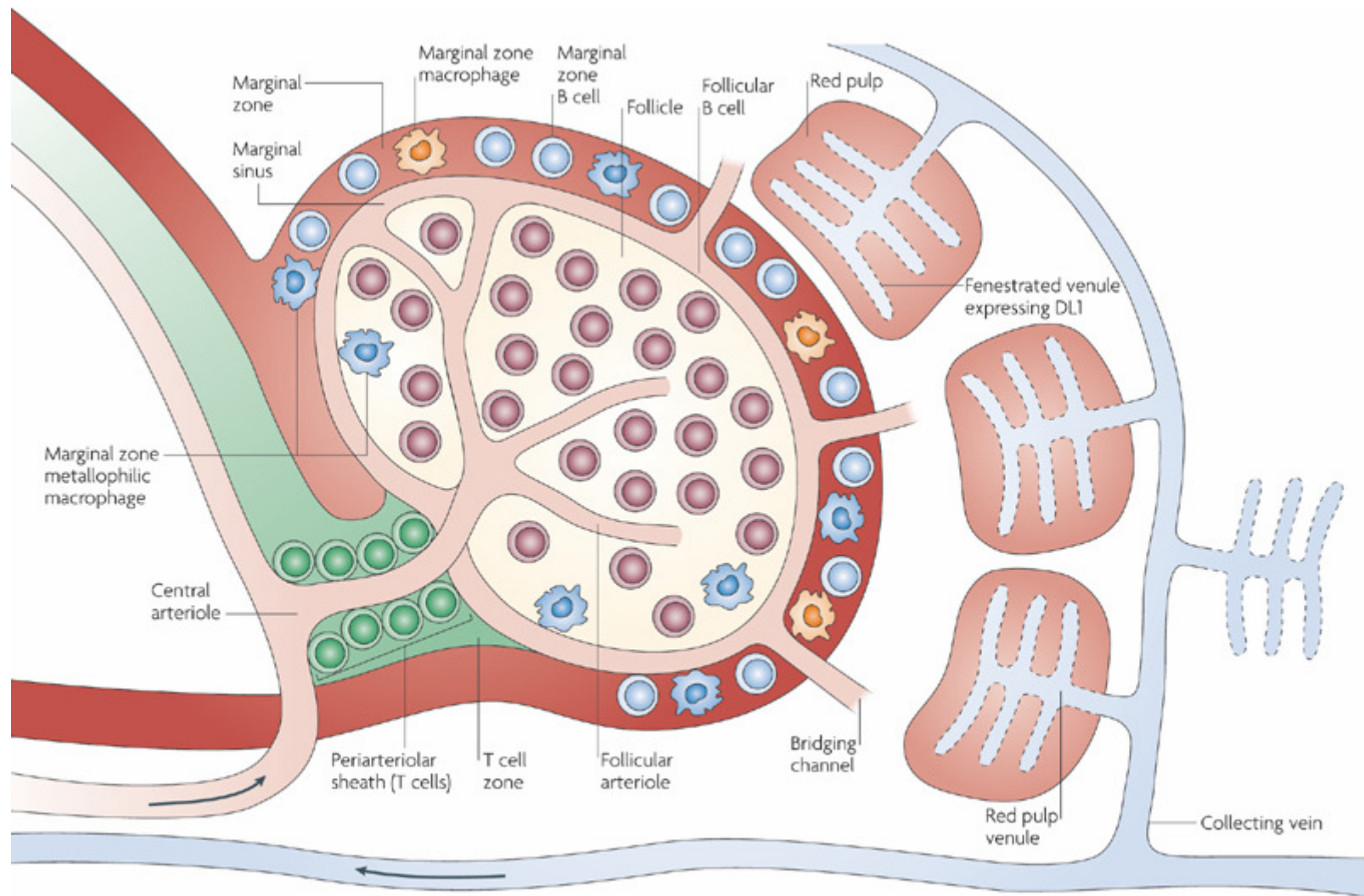
Mature B cells can circulate to other lymphoid organs, where entry is controlled by expression of homing molecules, such as L-selectin.

Neonatal mice



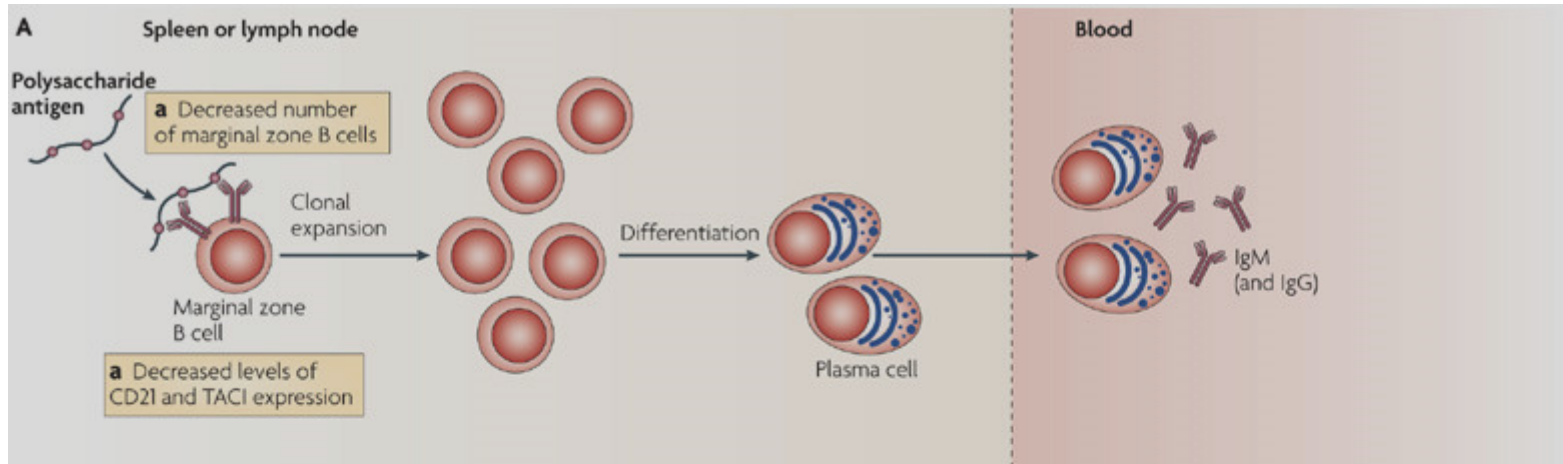
The splenic B-cell population contains proportionally more of the [B1-CELL LINEAGE](#) in neonates.



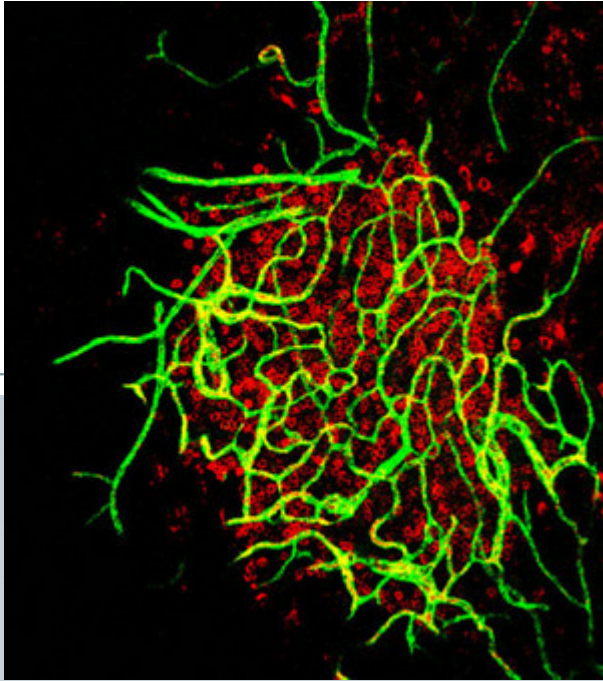


Phenotypes of naïve mature B cell subtypes

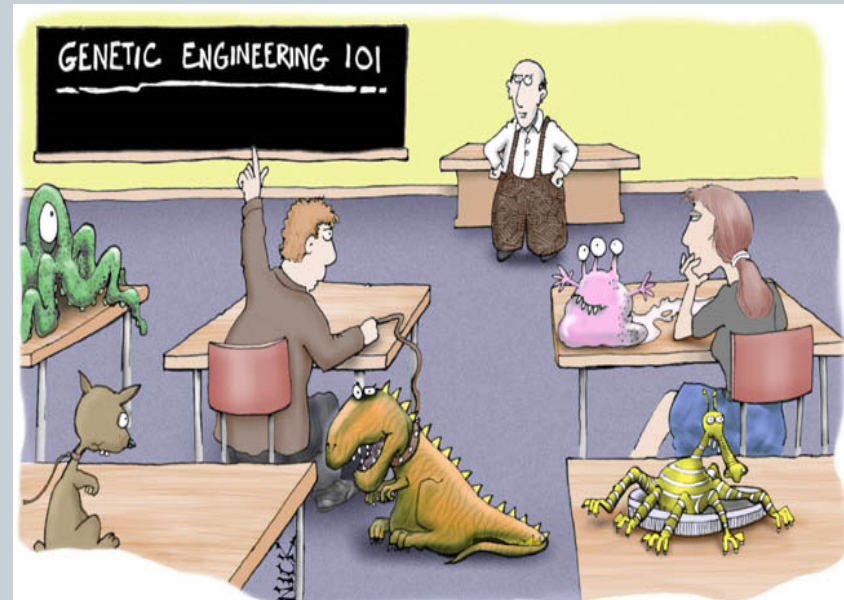
Surface molecule	Type of B cell		
	B-1	MZ	Follicular
IgM	+++	+++	+
IgD	+/-	+/-	+++
CD45R	+ /+++	++	+++
CD21	+/-	+++	++
CD23	++ or -	-	++
CD5	+	-	-
$\alpha_M\beta_2$ integrin	+ or -	-	-
CD9	+	+	-



Polysaccharides reach the marginal zone of lymphoid organs, bind to marginal zone B cells and drive their differentiation to short-lived plasma cells. In early life, a decreased number of marginal zone B cells and decreased levels of expression of CD21 and/or TACI (transmembrane activator and calcium-modulating cyclophilin-ligand interactor) limit the activation capacity of B cells (a), resulting in the generation of fewer plasma cells.

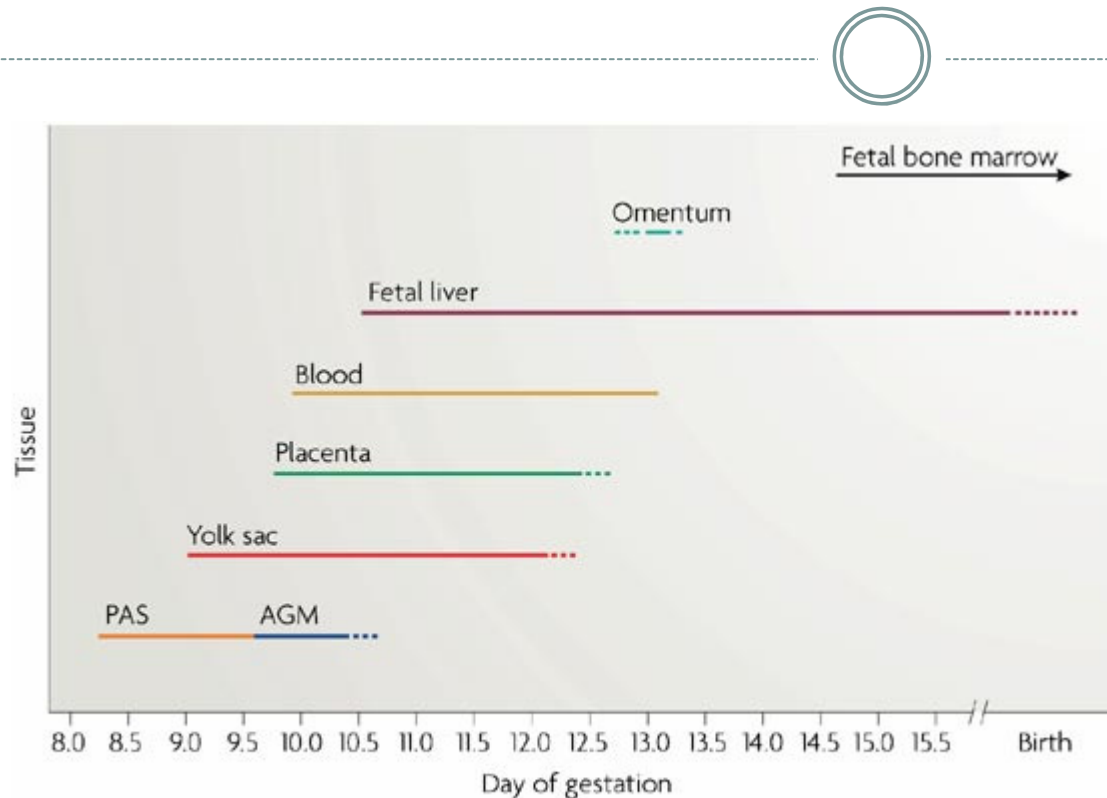


Linfocitos B1



"Okay—is there anybody ELSE whose homework ate their dog?"

LINFOPOYESIS DE CÉLULAS B Y GENERACIÓN DE CÉLULAS B₁



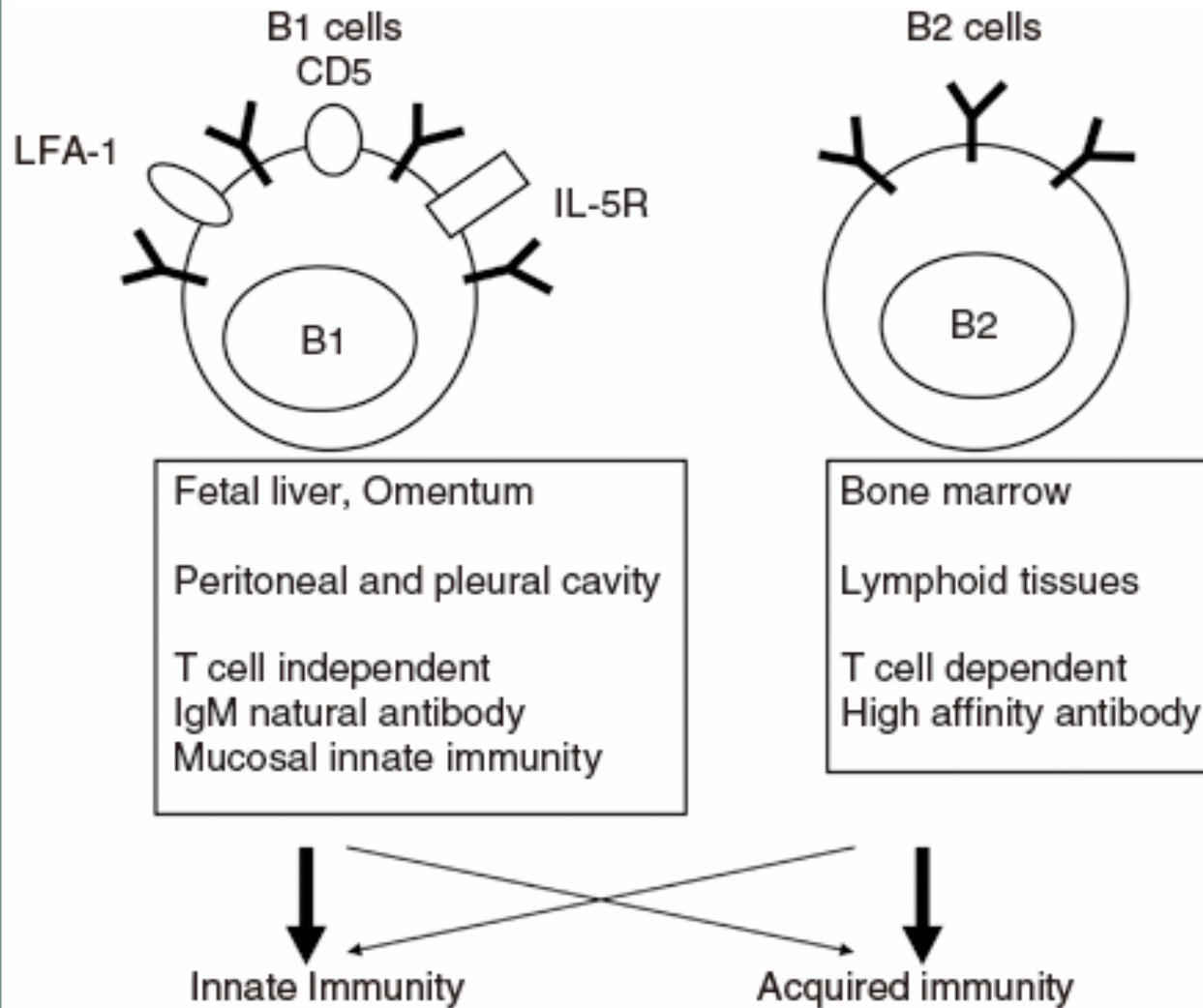
Nature Reviews | Immunology

Para-aortic splanchnopleura PAS: The embryonic tissue formed by the association of the mesoderm and endoderm. It is located on either side of the aorta. The AGM region subsequently develops from the PAS.

Aorta-gonad-mesonephros (AGM). An embryonic site in which the development of definitive haematopoietic stem cells (HSCs) occurs.

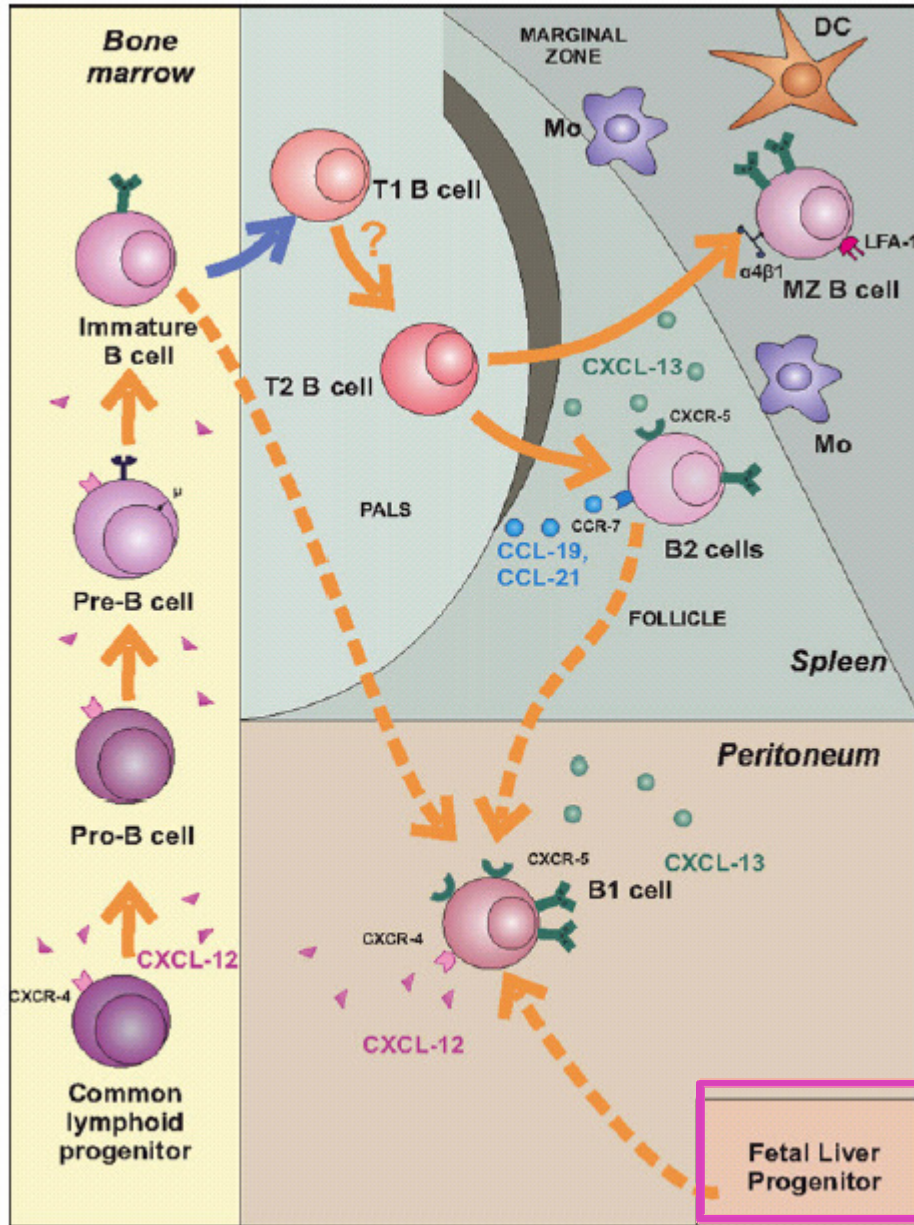
B-1 cells express the B-cell-lineage antigens **CD19** and **CD45R**, although **CD45R** is present at lower levels on B-1 cells than on B-2 cells.

B-1 cells in the peritoneal and pleural cavities can be identified by their unusual **CD11b⁺sIgM^{hi}sIgD^{low}** phenotype and can be further subdivided on the basis of differential expression of the cell-surface antigen **CD5**, into **CD5⁺CD11b⁺sIgM^{hi}sIgD^{low}** B-1a cells and **CD5⁻CD11b⁺sIgM^{hi}sIgD^{low}** B-1b cells.



Omento: lámina constituida por una bicapa de células mesoteliales que conecta el bazo, páncreas, estómago y colon.

- En el humano representan alrededor del 5% de la población total de LB, no así en otras especies (conejos y bovinos).
- **Expresan CD5 aunque no es un componente indispensable del linaje B1.**
- Los anticuerpos producidos por LB1 exhiben escasa afinidad por sus antígenos y en general son multiespecíficos.



CXCL13 is required for B1 cell homing, natural antibody production, and body cavity immunity.

Immunity, Volume16 Issue 1, 67-76, 1 January 2002.

Regulation of B1 cell migration by signals through Toll-like receptors

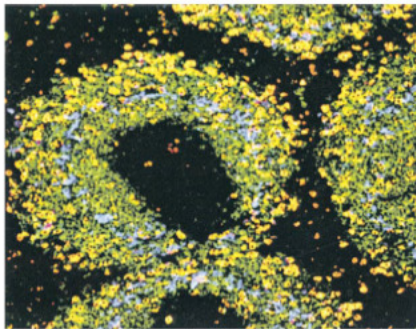
Direct signals through Toll-like receptors (TLRs) induce specific, rapid, and transient down-regulation of integrins and CD9 on B1 cells, which is required for detachment from local matrix and a high velocity movement of cells in response to chemokines.

J Exp Med. 2006 October 30; 203(11): 2541–2550.

Homing de las células B en órganos y cavidades

Células B1 constituyen el 30-50% (1×10^6 cells) de las células B en cavidades peritoneal y pleural.

Células B1 representan 2% (1×10^6 cells) de las células B cells en el bazo, pero raro hallarlas en ganglios linfáticos.



**B-2/follicular
B cells**

MZB

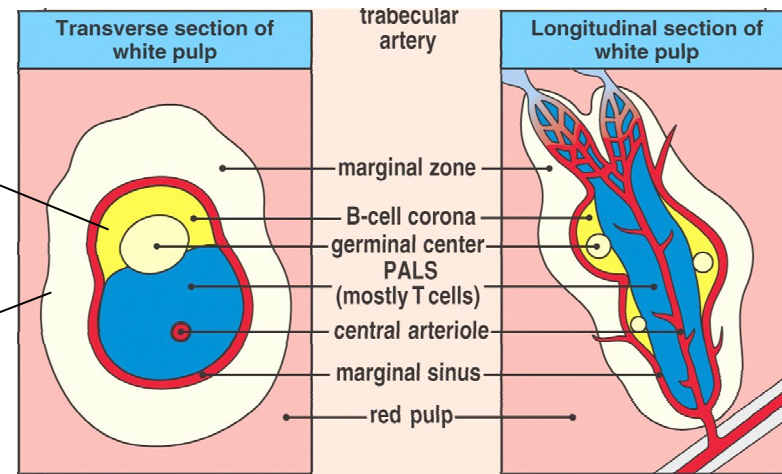
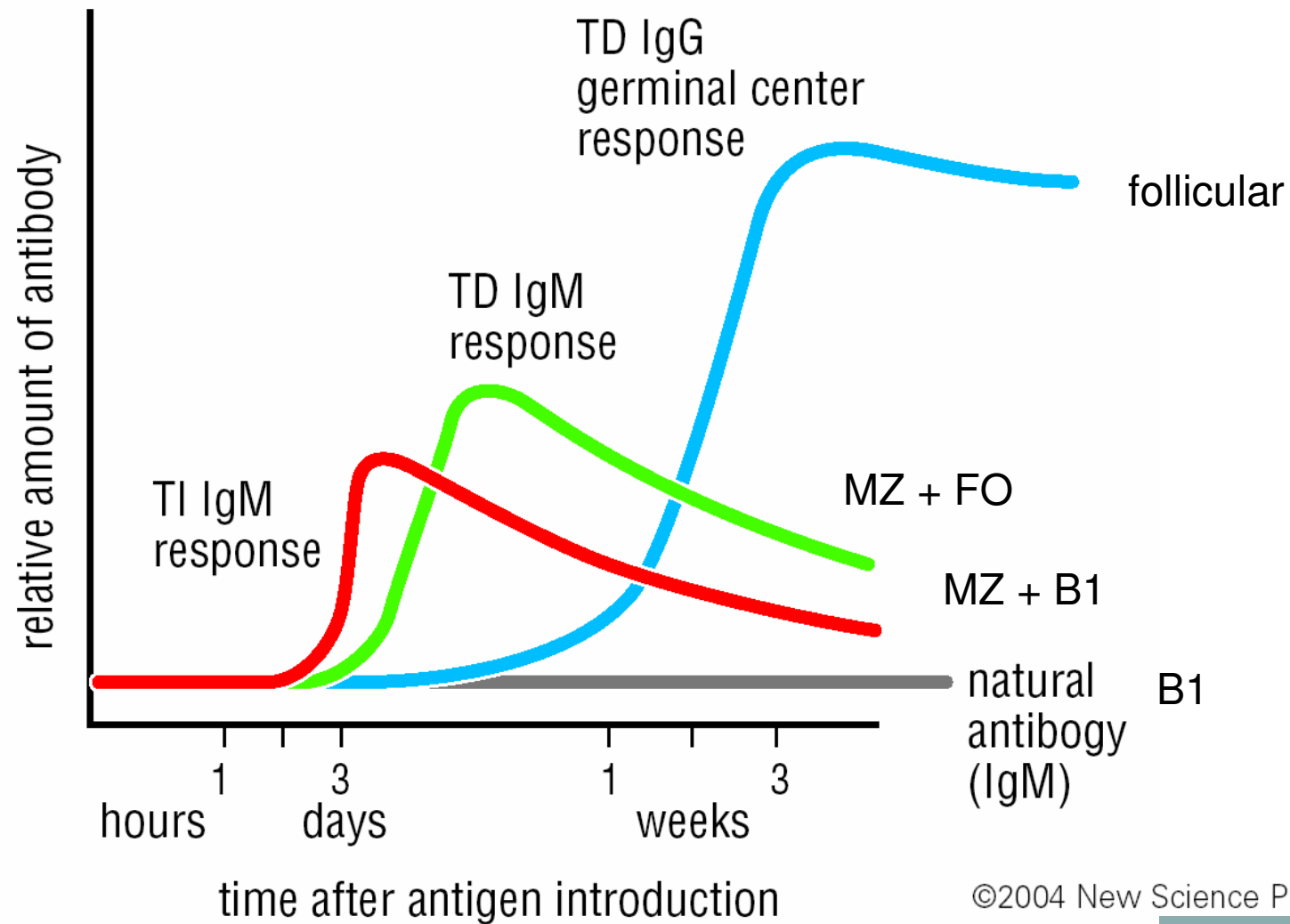


Table 1**Characteristic features of four distinct B-cell subsets.**

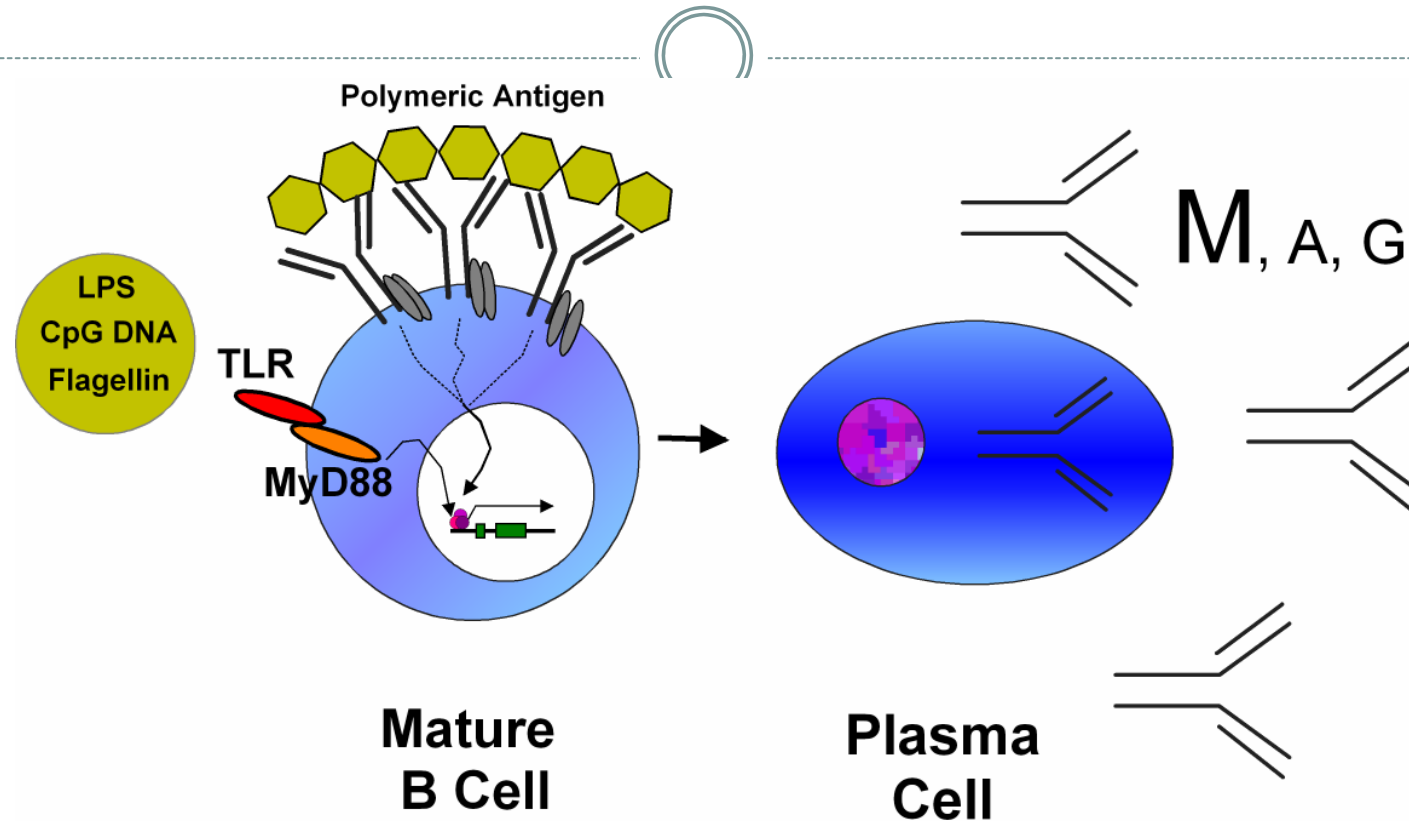
	B-1a	B-1b	MZ	B-2/follicular
CD19	+	+	+	+
CD45R/B220	+	+	++	++
IgM	++	++	+++	+
IgD	+/-	+/-	+/- to ++	++
CD5	+	-	-	-
Mac-1/CD11b	+ (PerC only)	+	-	-
CD43	++	++	-	-
CD21	+	+	+++	++
BCR signaling	+++	++	+	+/-
Notch-2	+?	+?	++	-
BAFF	-	-	-	+
Location	Spleen, PerC	PerC	Spleen	Spleen, lymph node
Development	Mainly fetal	Fetal and adult	Fetal and adult	Mainly adult
BCR diversity	Restricted	Restricted	Restricted	Diverse
Response	T cell independent; carbohydrate	T cell independent; carbohydrate	Blood-borne particulate	T cell dependent; protein
Natural autoantibody	+	+	+	-

Abbreviation: PerC, peritoneal cavity washout cells.

Roles biológicos de los distintos tipos de células B



Respuesta T-independiente



- ▣ **Tipo 1 – Mitógenos (LPS)**
- ▣ **Tipo 2 – Poliméricos (polisacáridos, flagelina bacteriana)**

Recordemos algo importante....

Linfocitos B1

Estímulo???

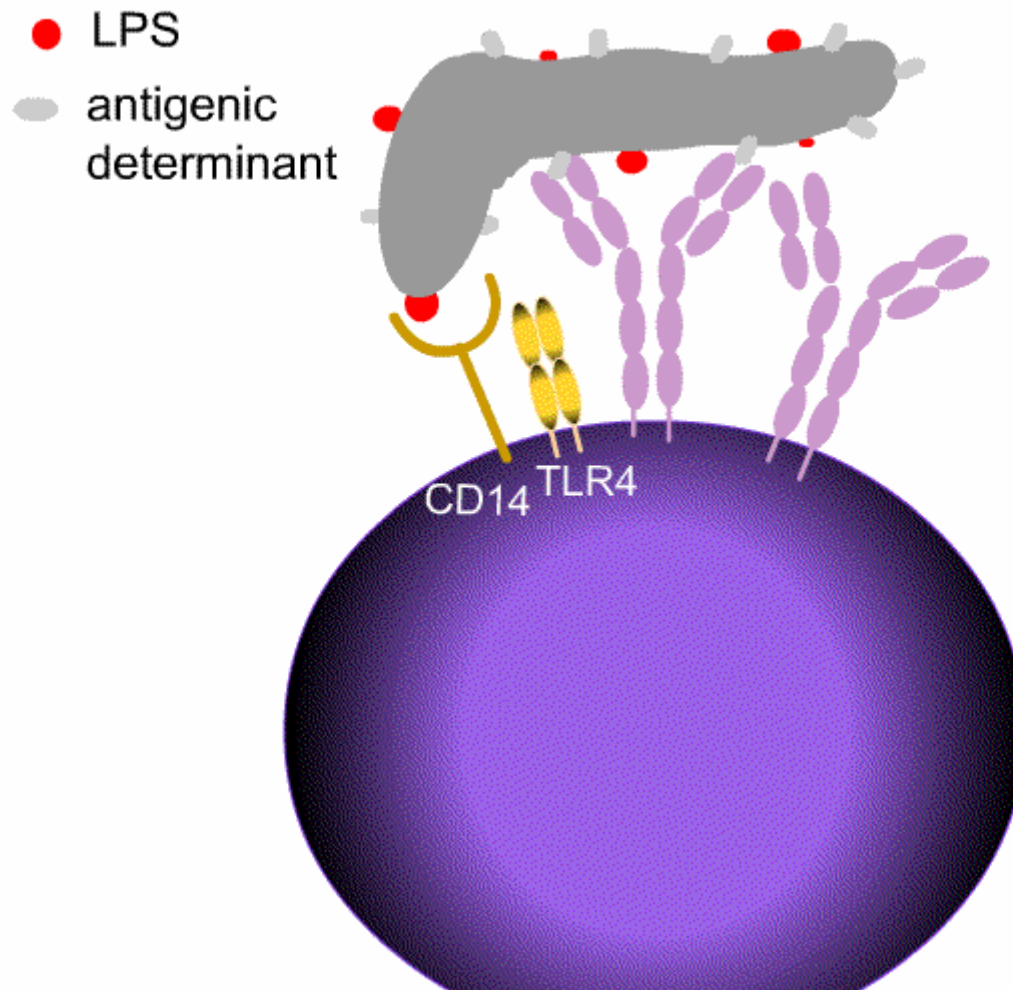
Concentración basal de ANTICUERPOS NATURALES (IgM o IgA).

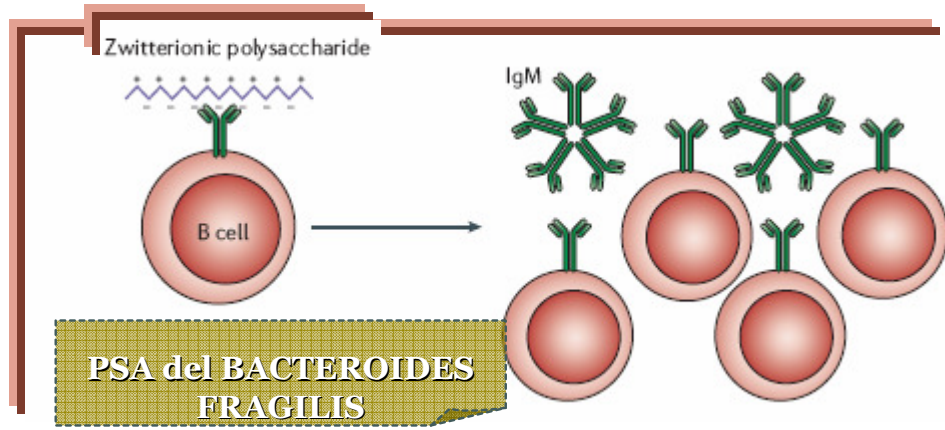
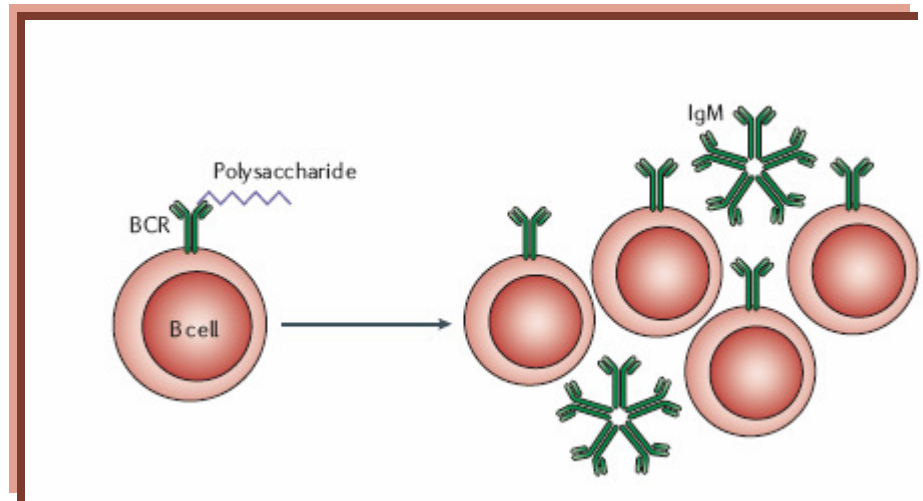
Tipo 1 – Mitógenos (LPS)

Tipo 2 – Poliméricos (polisacáridos, flagelina bacteriana)

Diferenciación a plasmocitos secretores de IgM, IgA o IgG3.

Respuesta TI-I



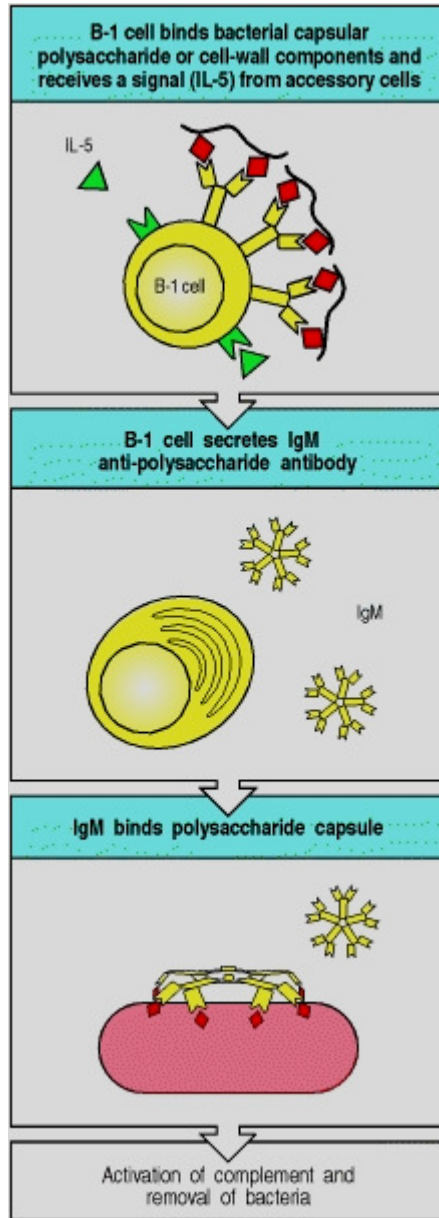


Respuesta

TI-2

- Anticuerpos frente a antígenos TI-2 son de isotipo IgM, IgG3 .
- Células B1 producen IgA en el intestino.
- NO hay MADURACIÓN DE LA AFINIDAD.
- NO hay MEMORIA INMUNOLÓGICA.

Células MZB y B1 median la respuesta temprana TI contra la infección.

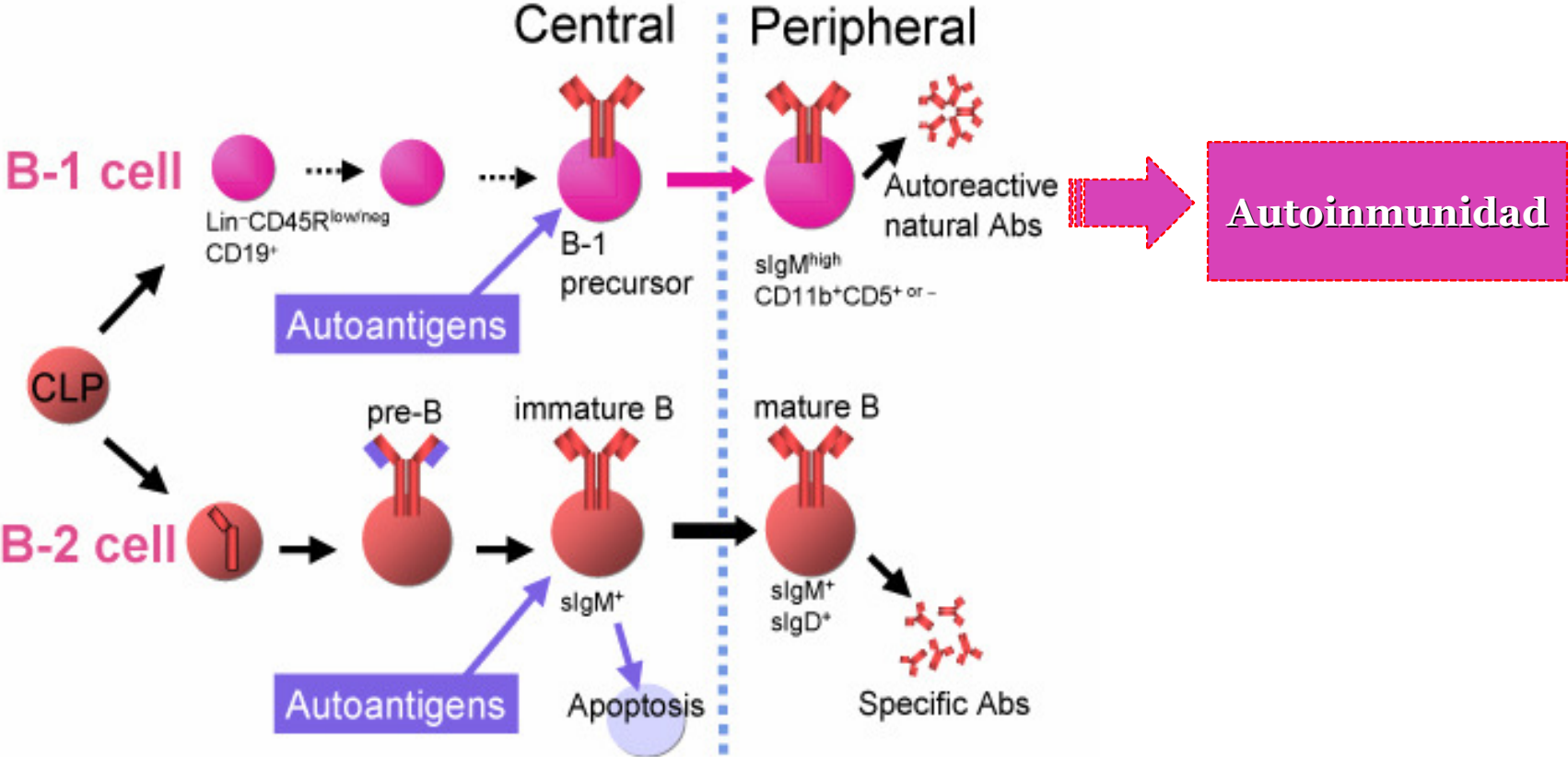


The role of IL-5 for mature B-1 cells in homeostatic proliferation, cell survival, and Ig. production...

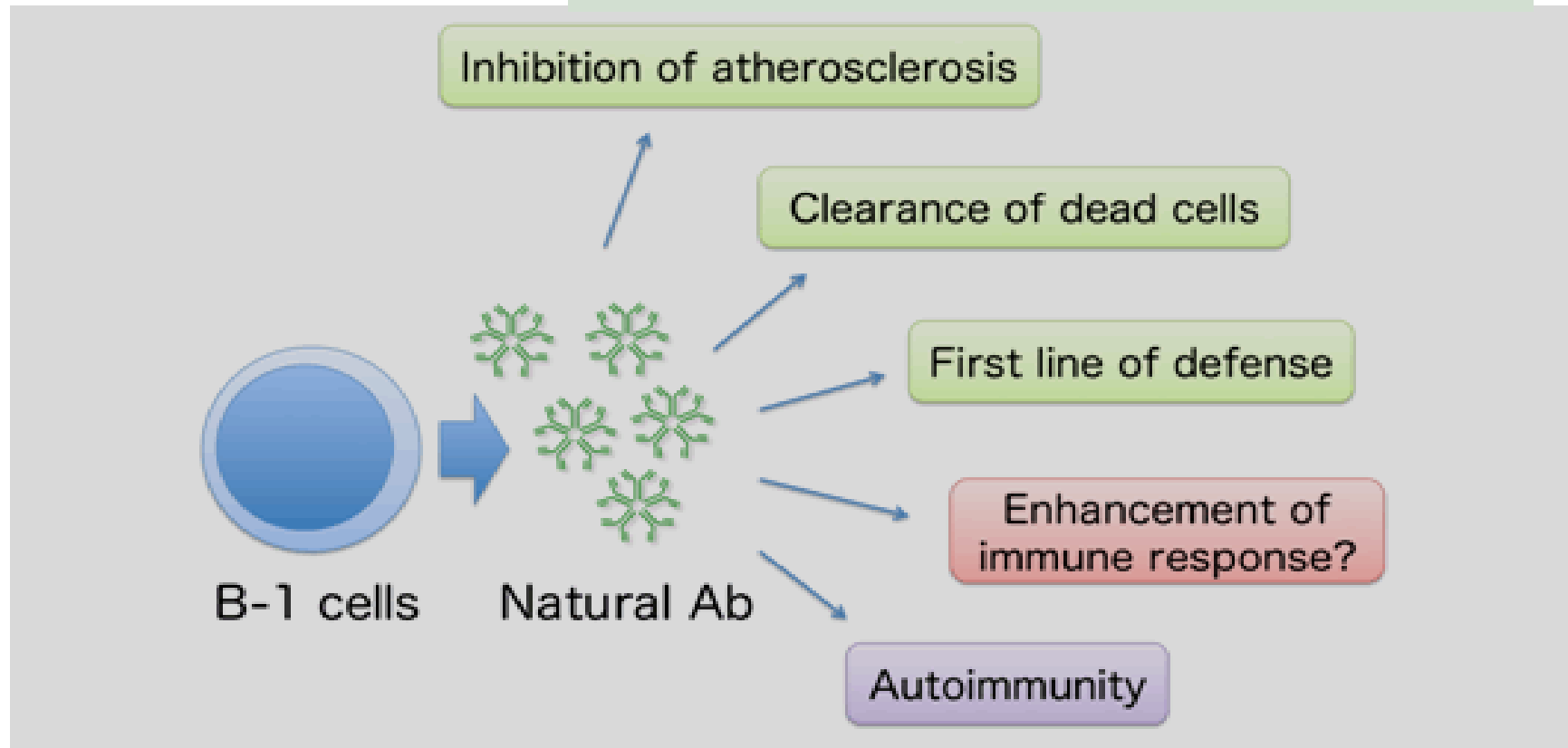
J Immunol. 2004 May 15;172(10):6020-9

B-1 cells constitutively express the **IL-5R alpha-chain** (IL-5Ralpha) and give rise to Ab-producing cells in response to various stimuli, including IL-5 and LPS. The IL-5/IL-5R system plays an important role in maintaining the number and the cell size as well as the functions of mature B-1 cells.

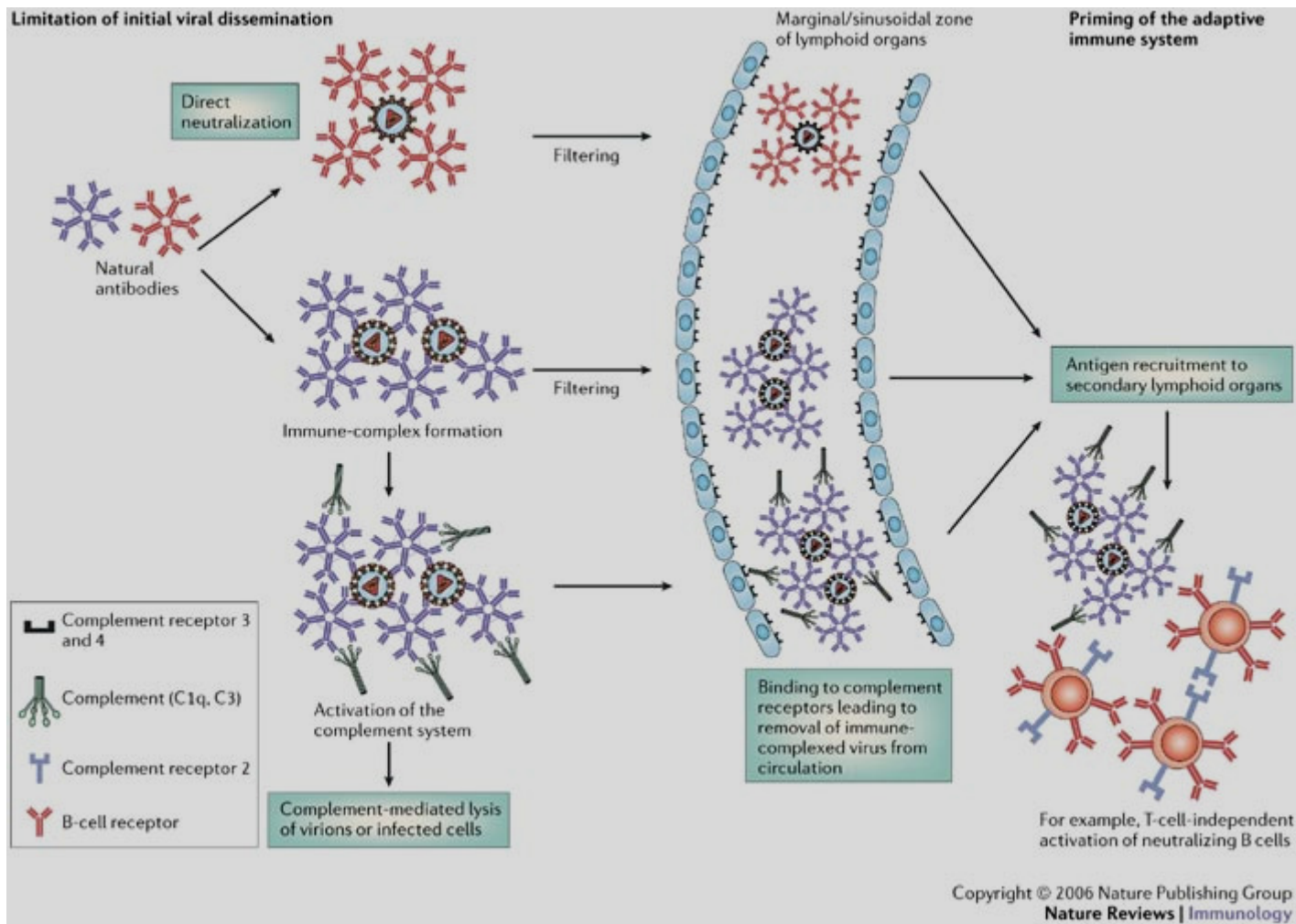
Tolerance in B cells



Clearance de LDL –oxidadas....



Mice that are deficient in B-1 cells are more susceptible to infection with *Streptococcus pneumoniae* because they fail to produce an [antibody](#) against the phospholipid headgroup phosphorylcholine that effectively protects against this organism.



Lo que nos beneficia.....



- ▣ **Son anticuerpos presentes en el suero de individuos normales, generados en ausencia de estímulo antigénico exógeno.**
- ▣ Son capaces de proteger frente a determinadas infecciones.
- ▣ Participan en la depuración de células apoptóticas.
- ▣ Desempeñan un papel en la vigilancia inmunitaria contra los tumores.
- ▣ A nivel intestinal, la IgAs protege la mucosa intestinal de las posibles acciones nocivas de la flora comensal, como la penetración en los tejidos del huésped.



la búsqueda de la perfección
a través del detalle...

