

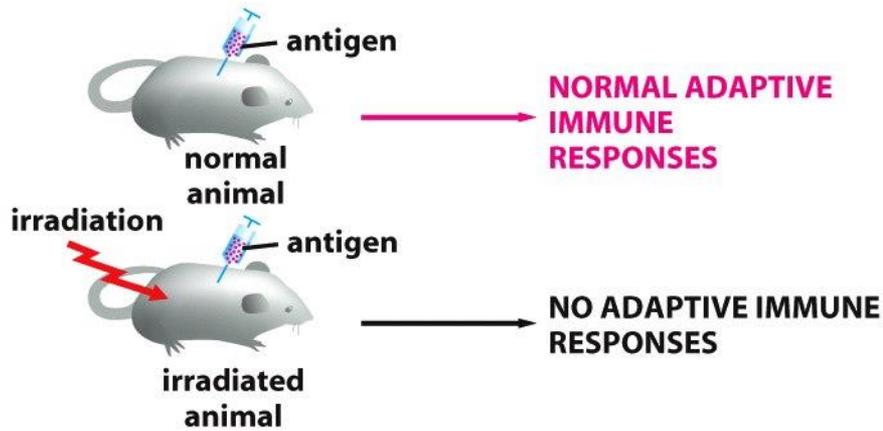
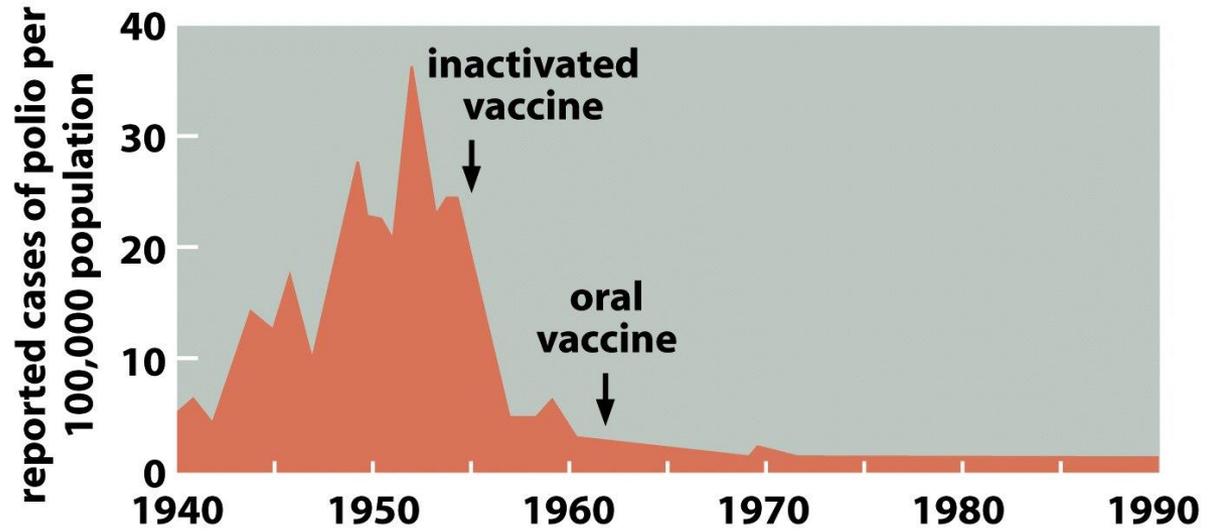


VACCINATION.
DR. JENNER PERFORMING THE FIRST
VACCINATION ON JAMES PHIPPS.
A BOY OF EIGHT, MAY 14, 1774.

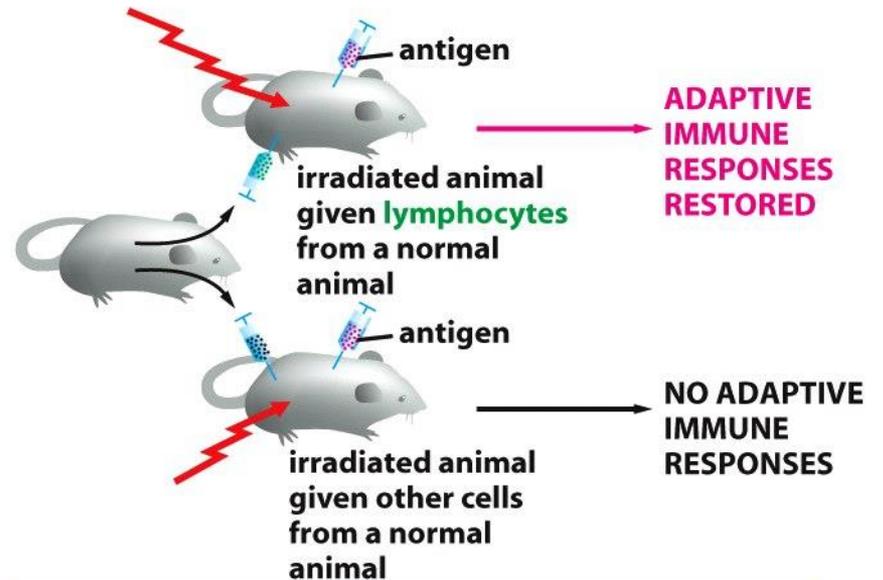
Biología celular de la inmunidad - II

Flavio Zolessi

Inmunidad adaptativa

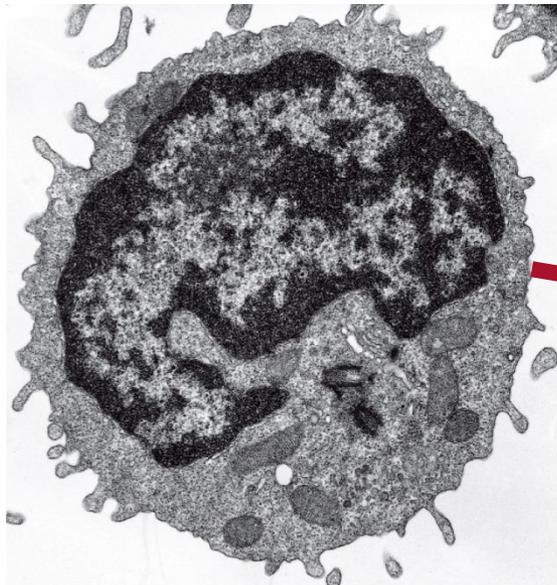
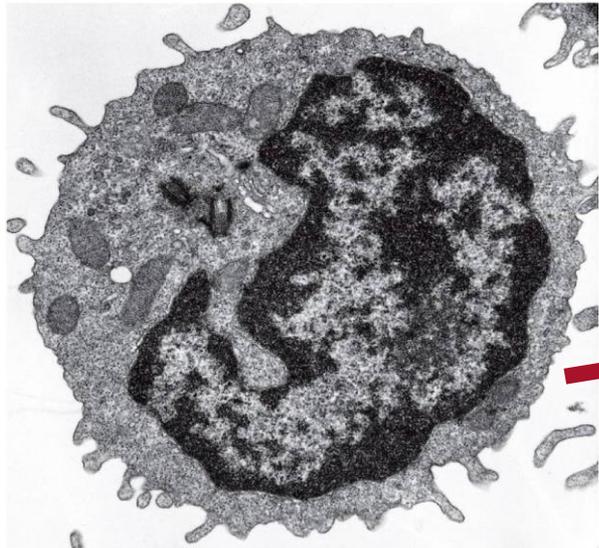


CONTROL



EXPERIMENT

Inmunidad adaptativa: Linfocitos



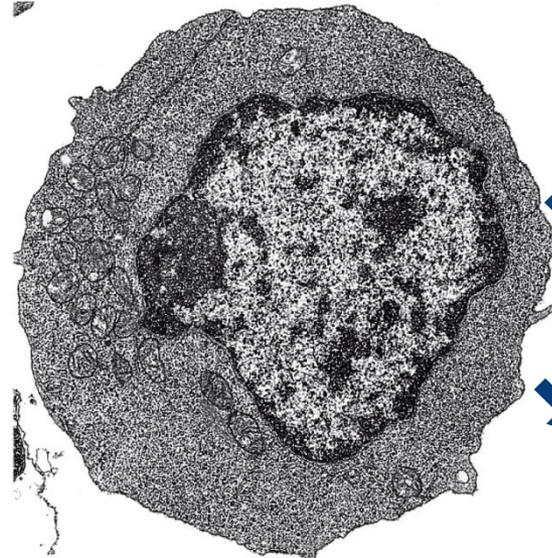
resting T or B cell

1 μ m



effector B cell (plasma cell)

1 μ m



effector T cell

1 μ m

Citotóxicos

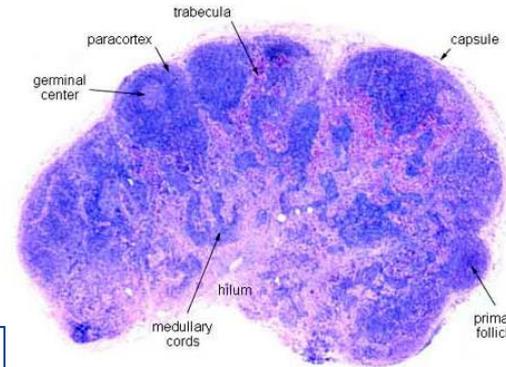
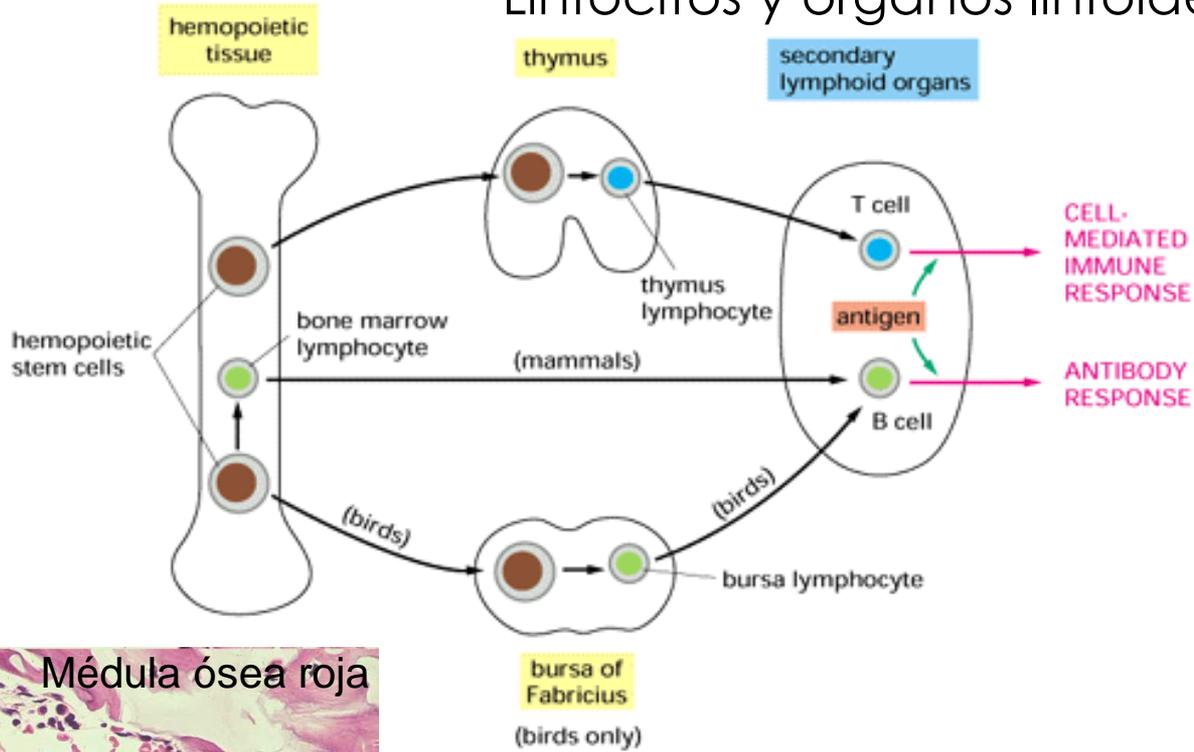


Colaboradores

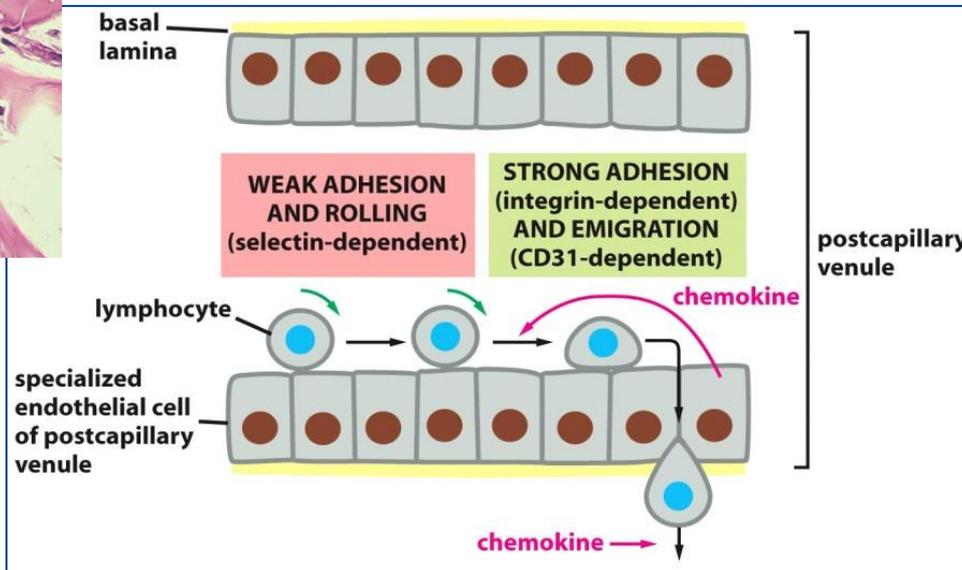
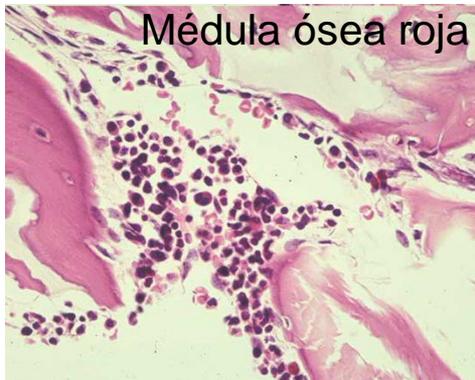


Reguladores
(supresores)

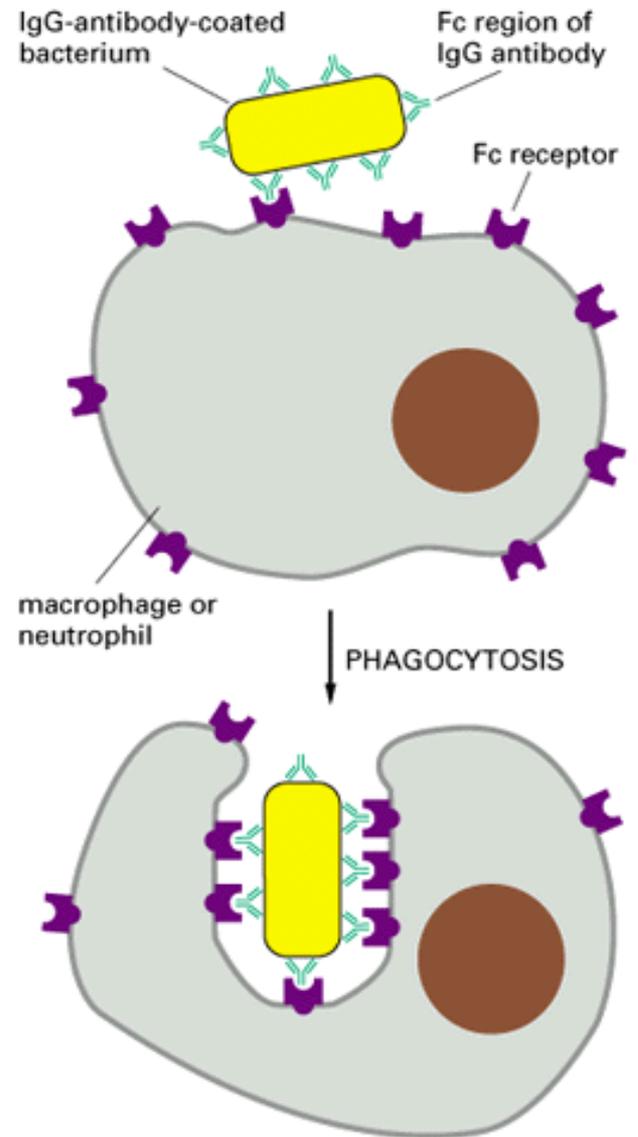
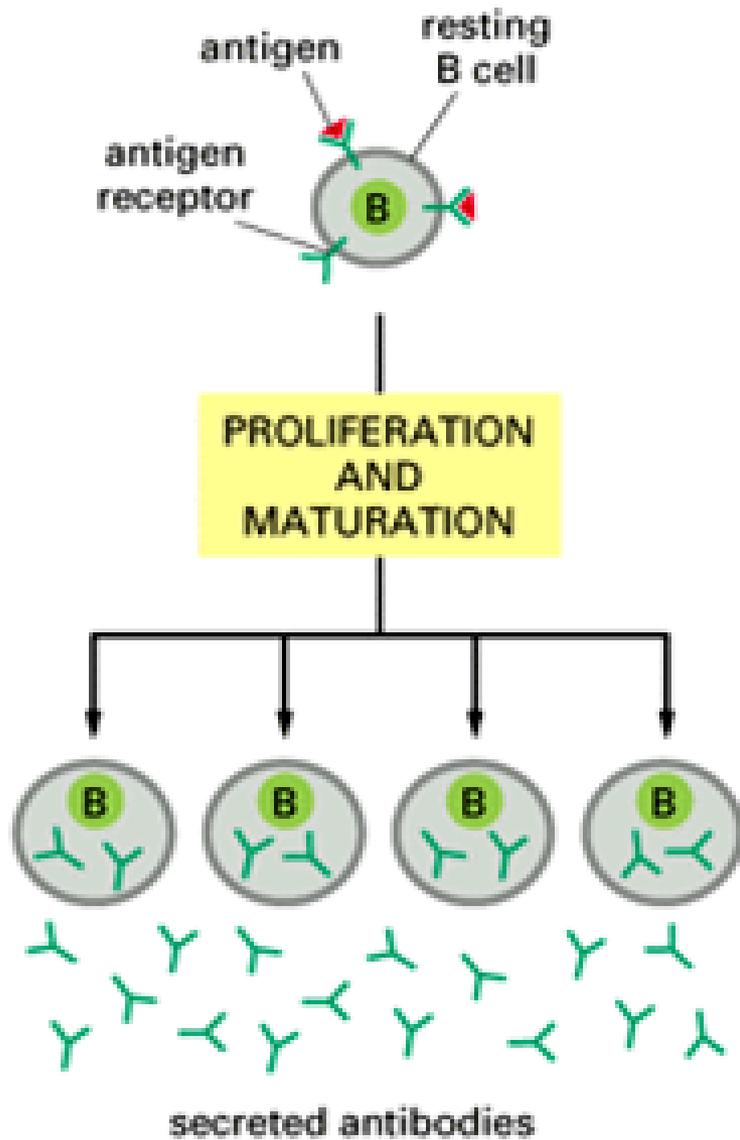
Linfocitos y órganos linfoides



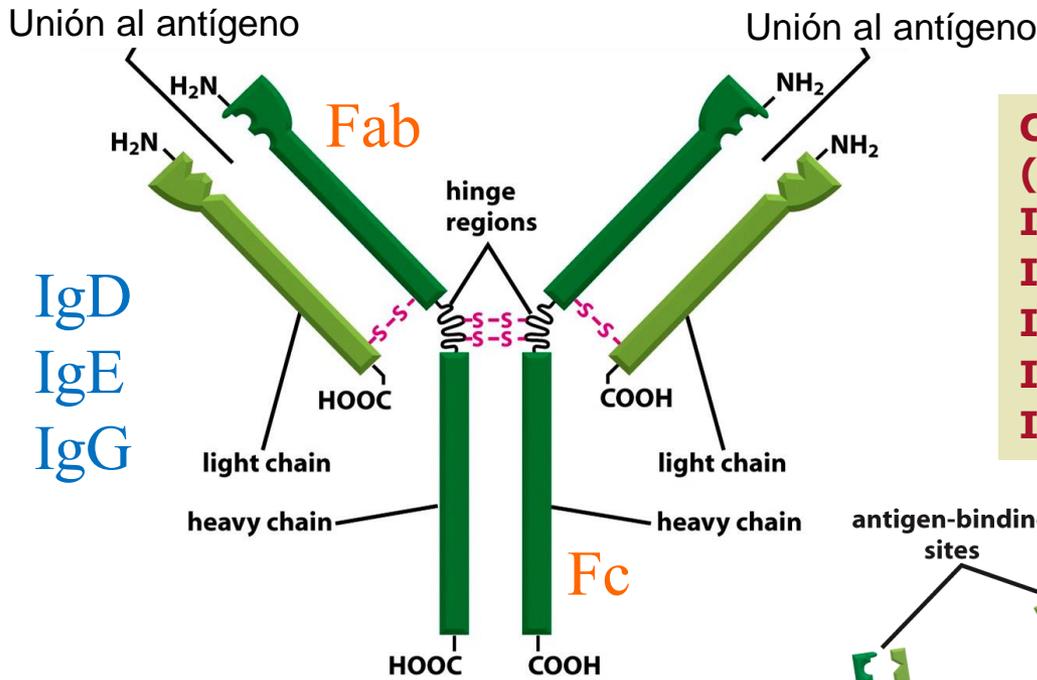
Ganglio linfático



Linfocitos B y anticuerpos



Estructura de los anticuerpos



Cadenas pesadas: (locus único)

- IgA-- α
- IgD-- δ
- IgE-- ϵ
- IgG-- γ
- IgM-- μ

Cadenas livianas: (locus separados)

- κ
- λ

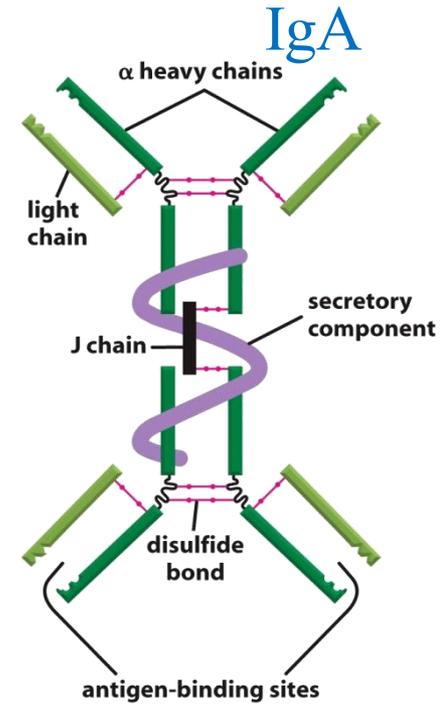
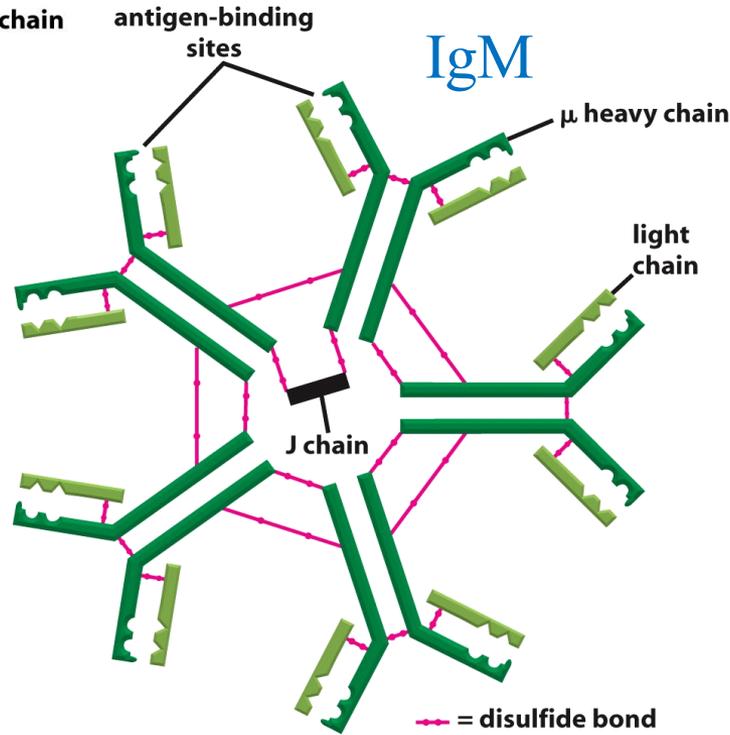
Nobel, 1972



Gerald M. Edelman
(1929 - 2014)



Rodney R. Porter
(1917 - 1985)



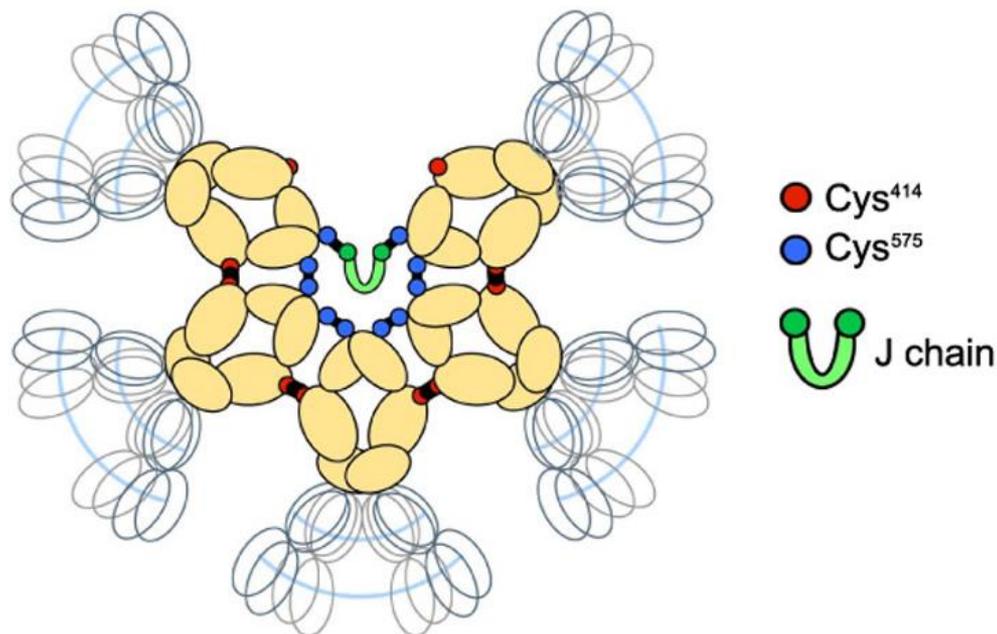
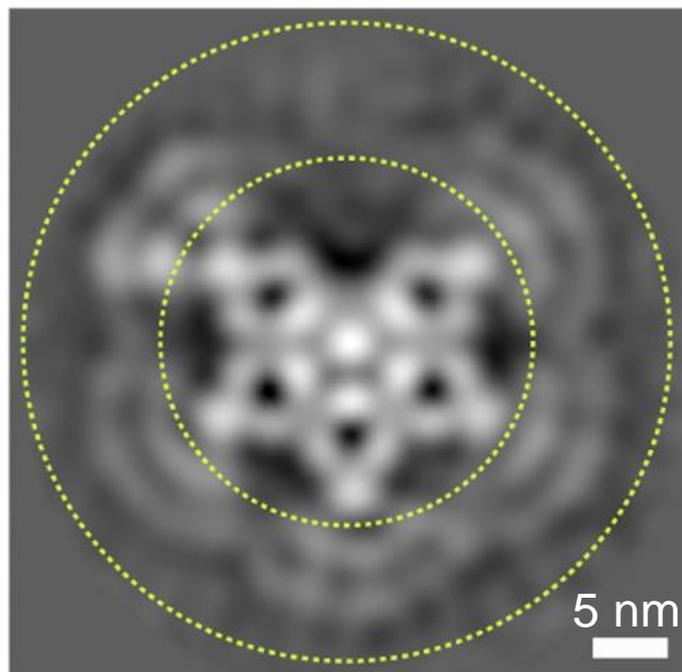
BIOCHEMISTRY

The IgM pentamer is an asymmetric pentagon with an open groove that binds the AIM protein

Emiri Hiramoto¹, Akihisa Tsutsumi², Risa Suzuki¹, Shigeru Matsuoka^{1*},
Satoko Arai^{1†}, Masahide Kikkawa², Toru Miyazaki^{1,3,4†}

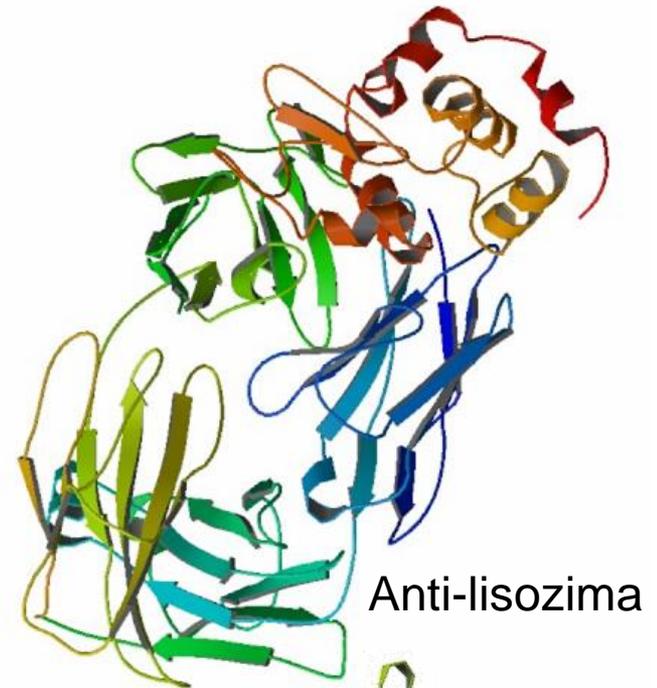
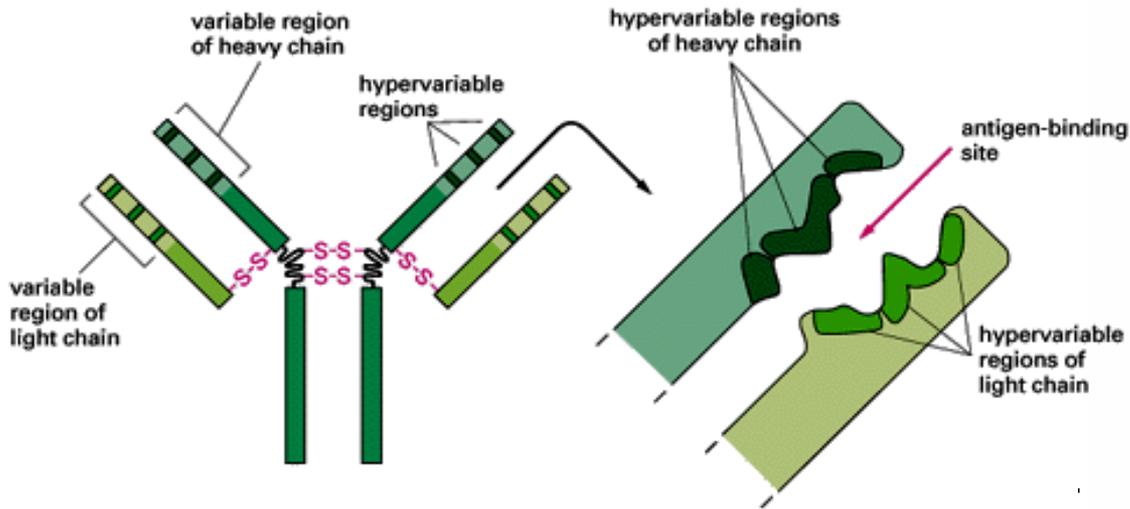
<https://advances.sciencemag.org/content/4/10/eaau1199>

D **Mouse IgM (full length)**

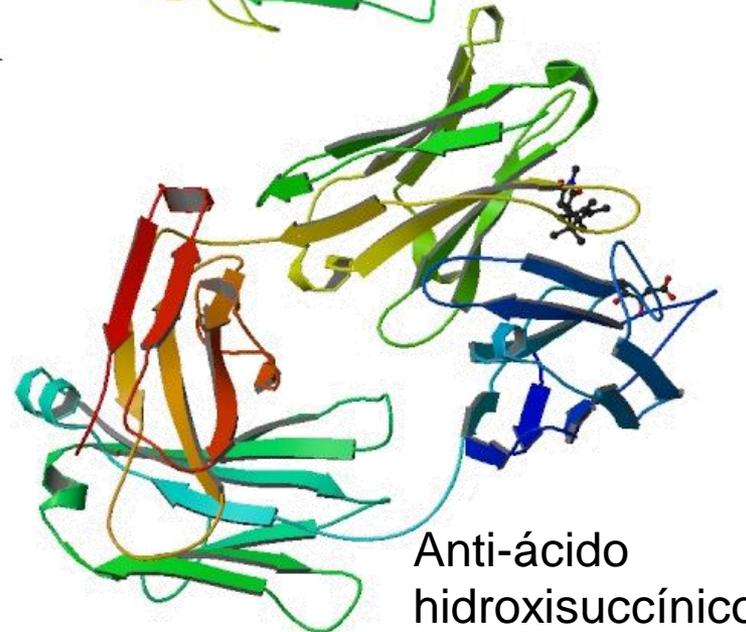
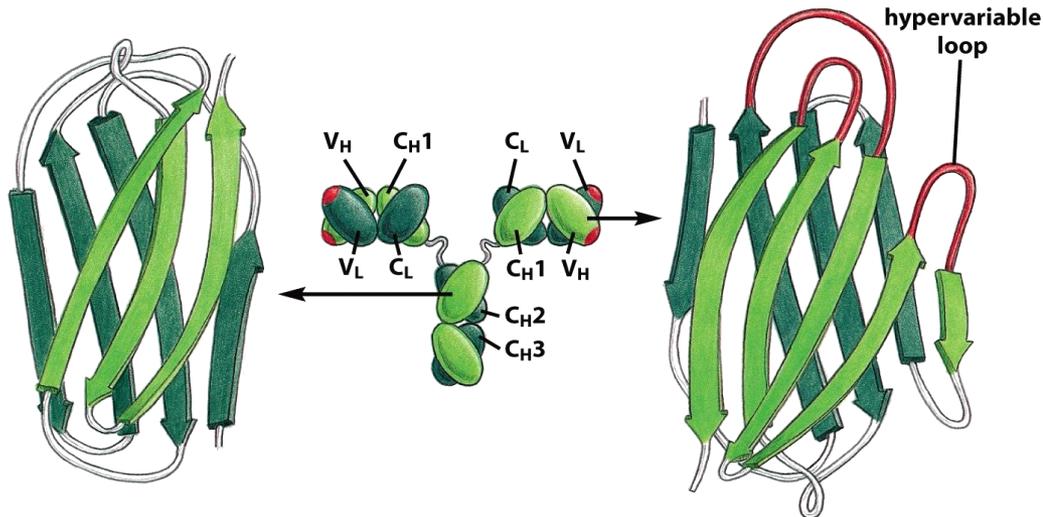


Tinción negativa - MET

Estructura de los anticuerpos

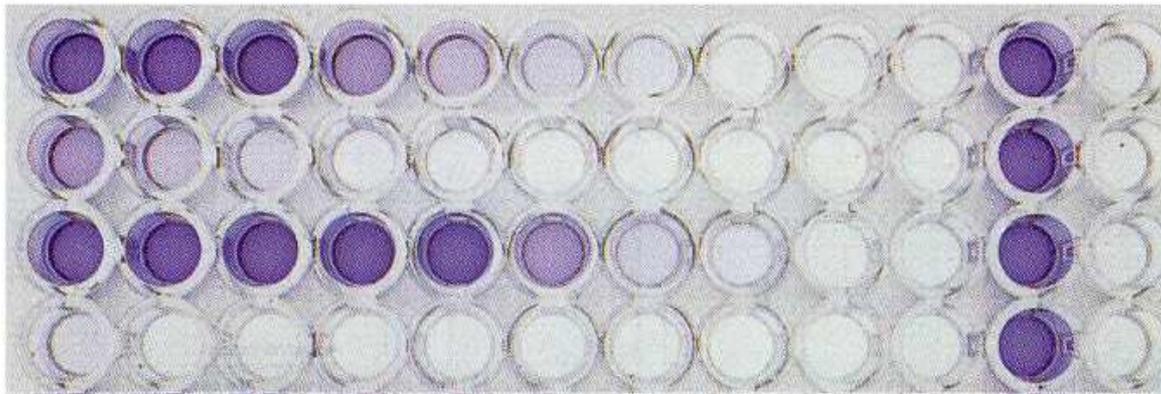
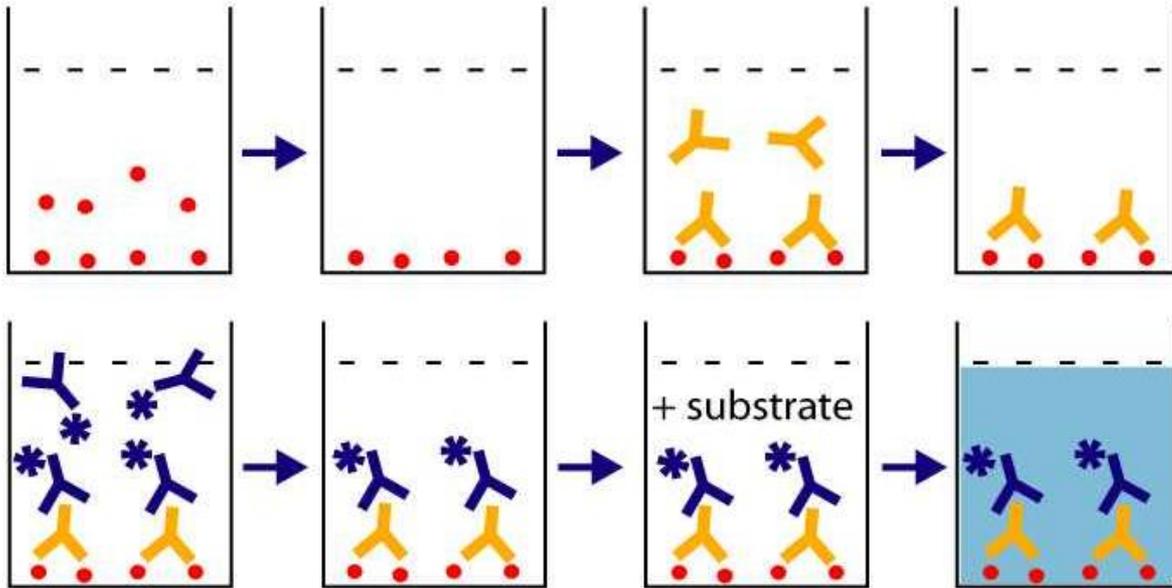


Anti-lisozima

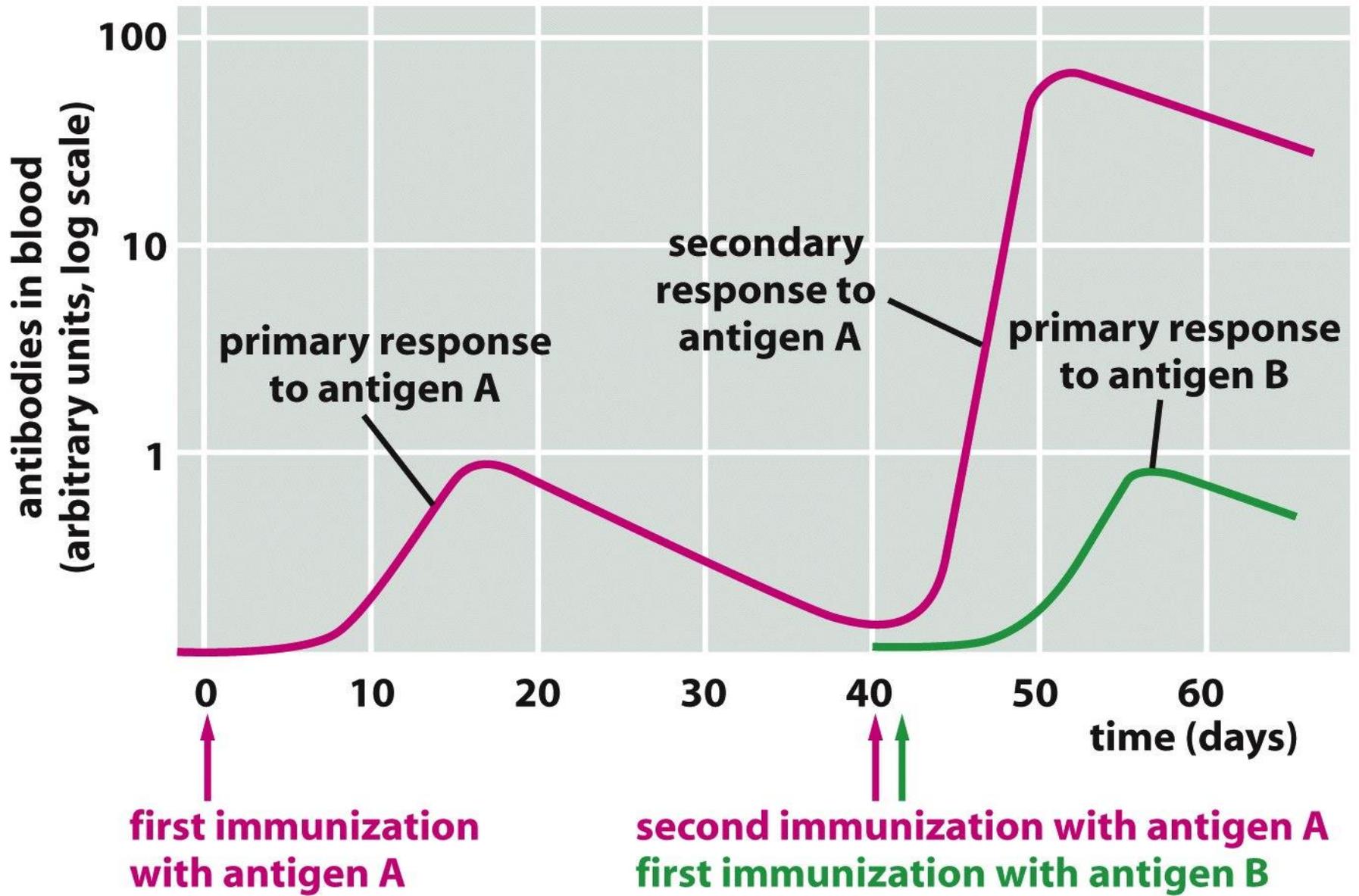


Anti-ácido hidroxisuccínico

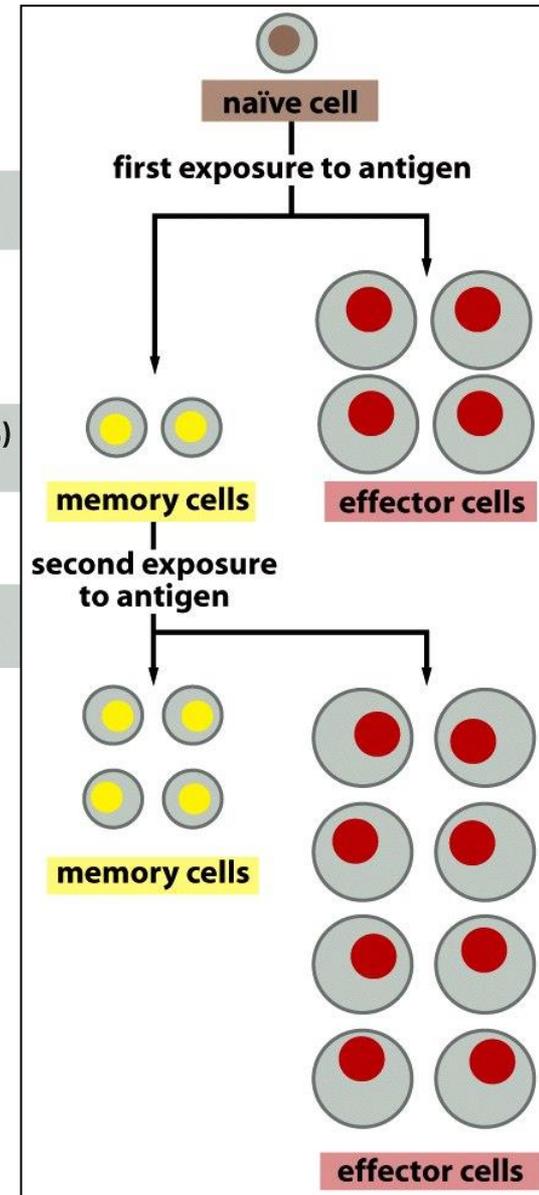
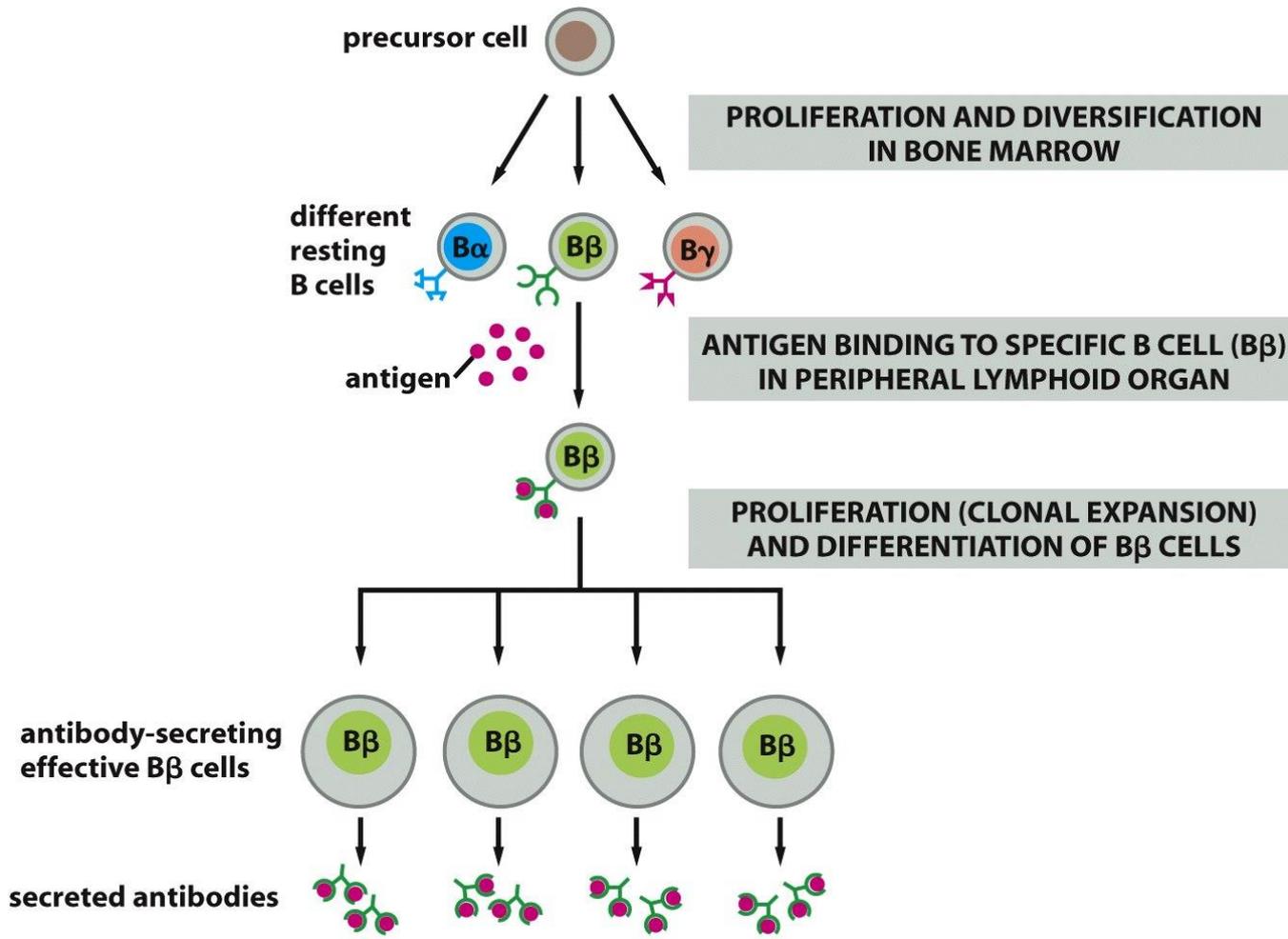
Cuantificación de anticuerpos: ELISA ("Enzyme-Linked ImmunoSorbent Assay")



Respuesta de anticuerpos



Teoría de la selección clonal



Anticuerpos monoclonales

Nature Vol. 256 August 7 1975

Continuous cultures of fused cells secreting antibody of predefined specificity

*MRC Laboratory of Molecular Biology,
Hills Road, Cambridge CB2 2QH, UK*

G. KÖHLER
C. MILSTEIN

The Nobel Prize in Physiology or Medicine 1984

The Nobel Prize in Physiology or Medicine 1984 was awarded jointly to Niels K. Jerne, Georges J.F. Köhler and César Milstein *"for theories concerning the specificity in development and control of the immune system and the discovery of the principle for production of monoclonal antibodies"*.



Niels K. Jerne
Prize share: 1/3



Georges J.F. Köhler
Prize share: 1/3



César Milstein
Prize share: 1/3

Anticuerpos monoclonales:

1- ¿Qué son y cómo se obtienen?

2- ¿Qué aplicaciones tienen hoy en día?

Anticuerpos monoclonales

mouse immunized with antigen X

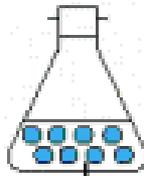


cell making anti-X antibody



B lymphocytes (die after a few days in culture)

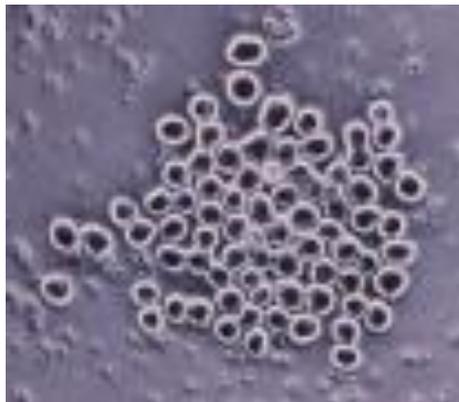
mutant cell line derived from a tumor of B lymphocytes



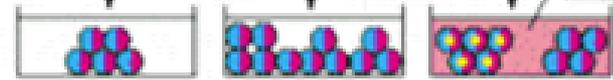
(cells grow indefinitely in normal medium, but die in selective medium)

FUSION

products plated in multiple wells

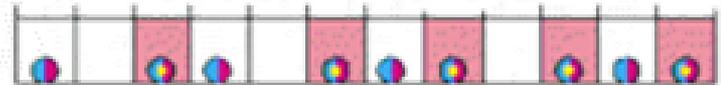


only hybridomas grow on the selective medium



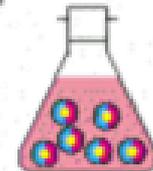
secreted anti-X antibody

test supernatant for anti-X antibody and redistribute cells from positive well at ~1 cell per well

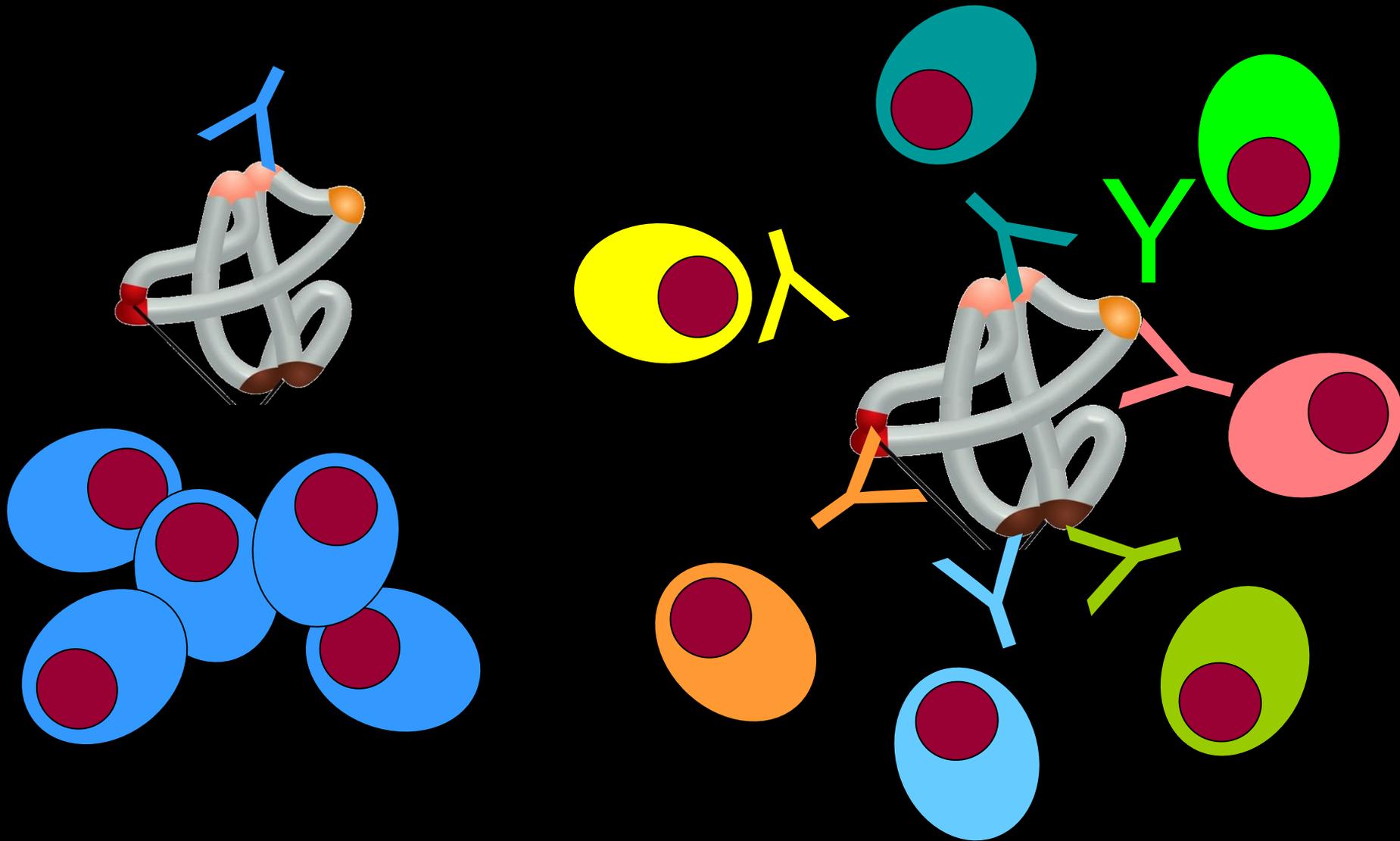


allow cells to multiply, then test supernatant for anti-X antibodies;

positive clones provide a continuing source of anti-X antibody



Epítopes, determinantes antigénicos y respuestas policlonales



Determinantes antigénicos y formación de complejos inmunes

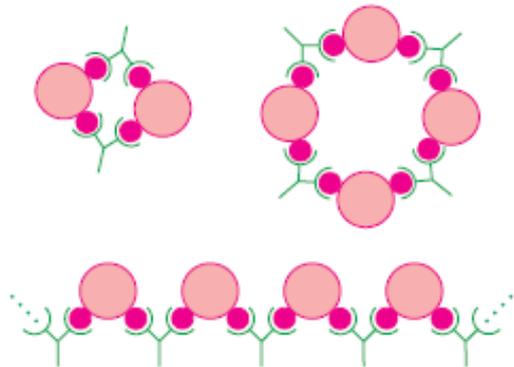
(A)

 one antigenic determinant



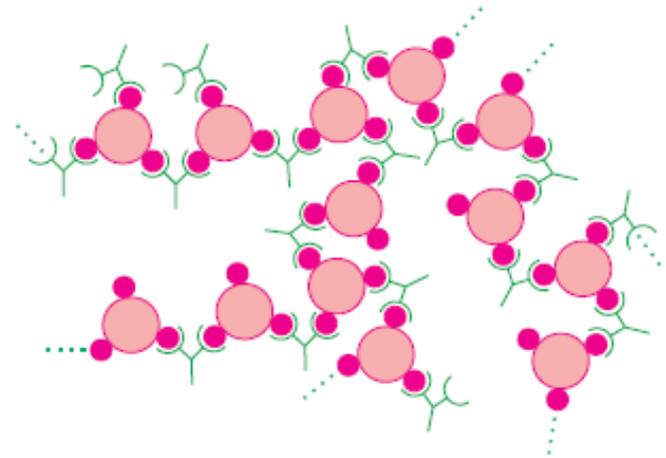
(B)

 two identical antigenic determinants



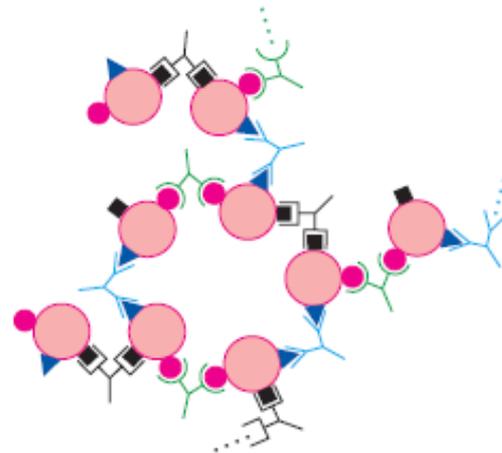
(C)

 three or more identical antigenic determinants



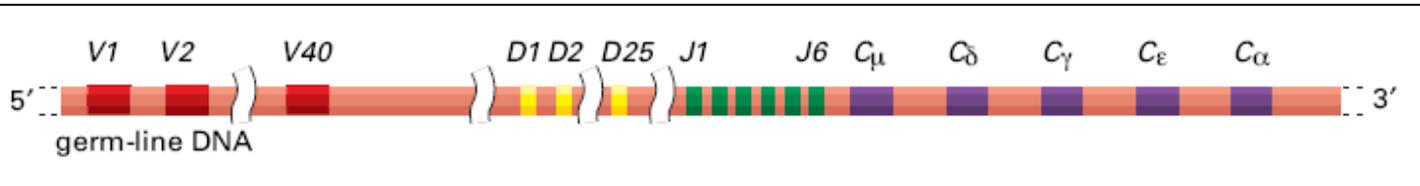
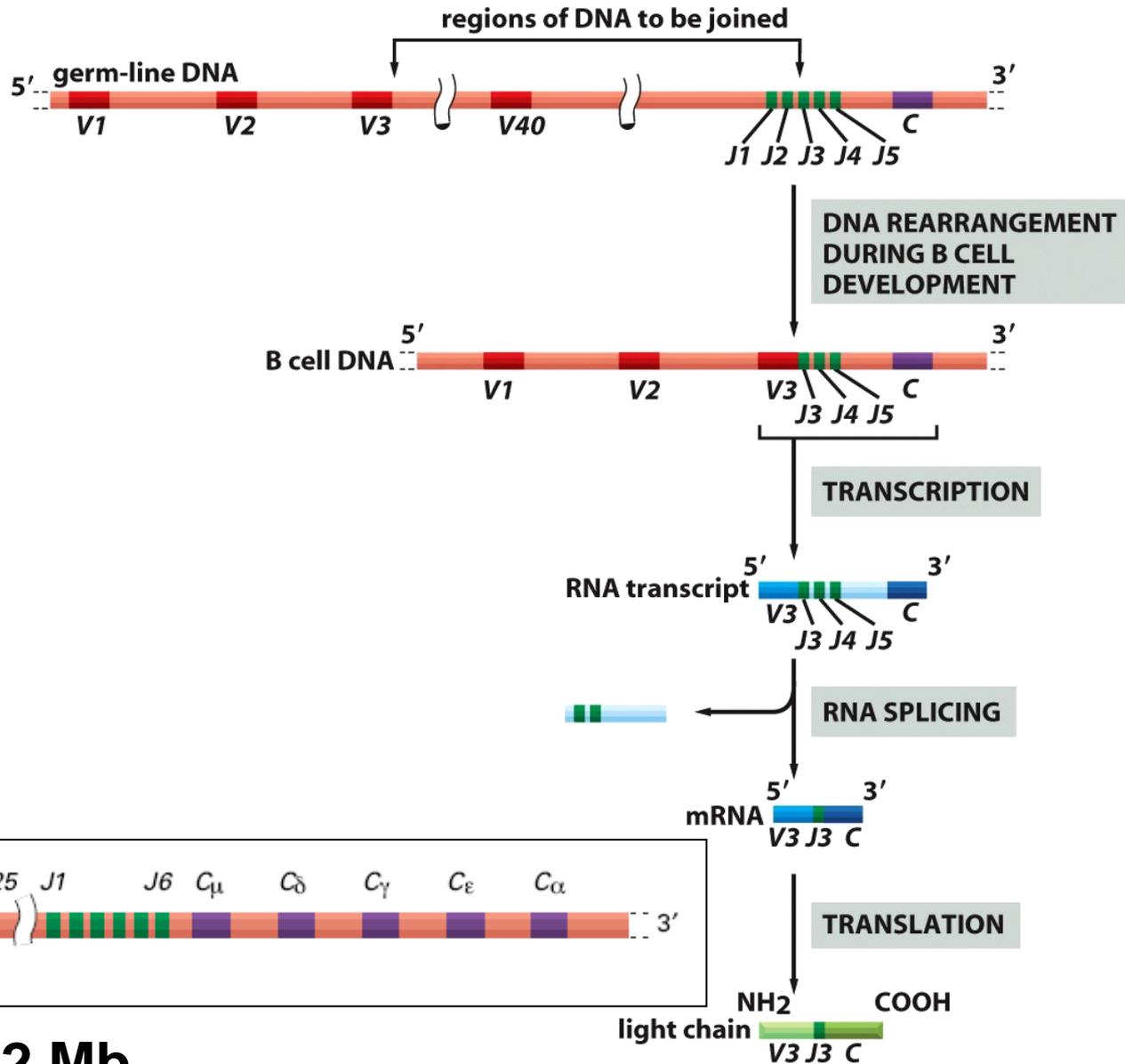
(D)

 three or more different antigenic determinants



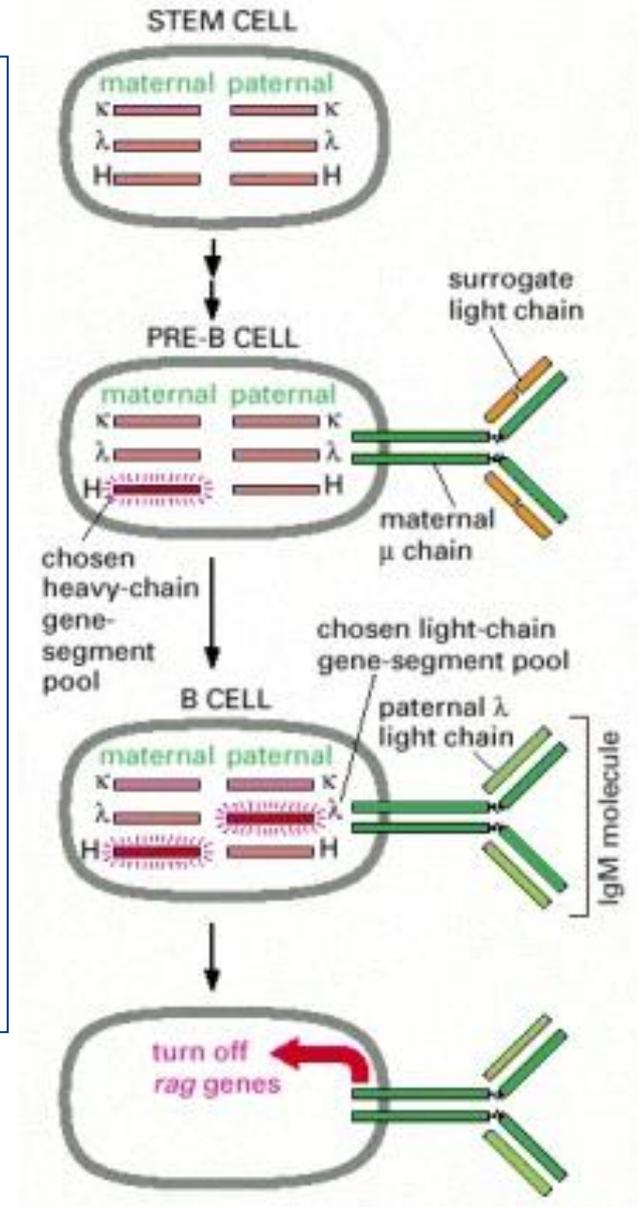
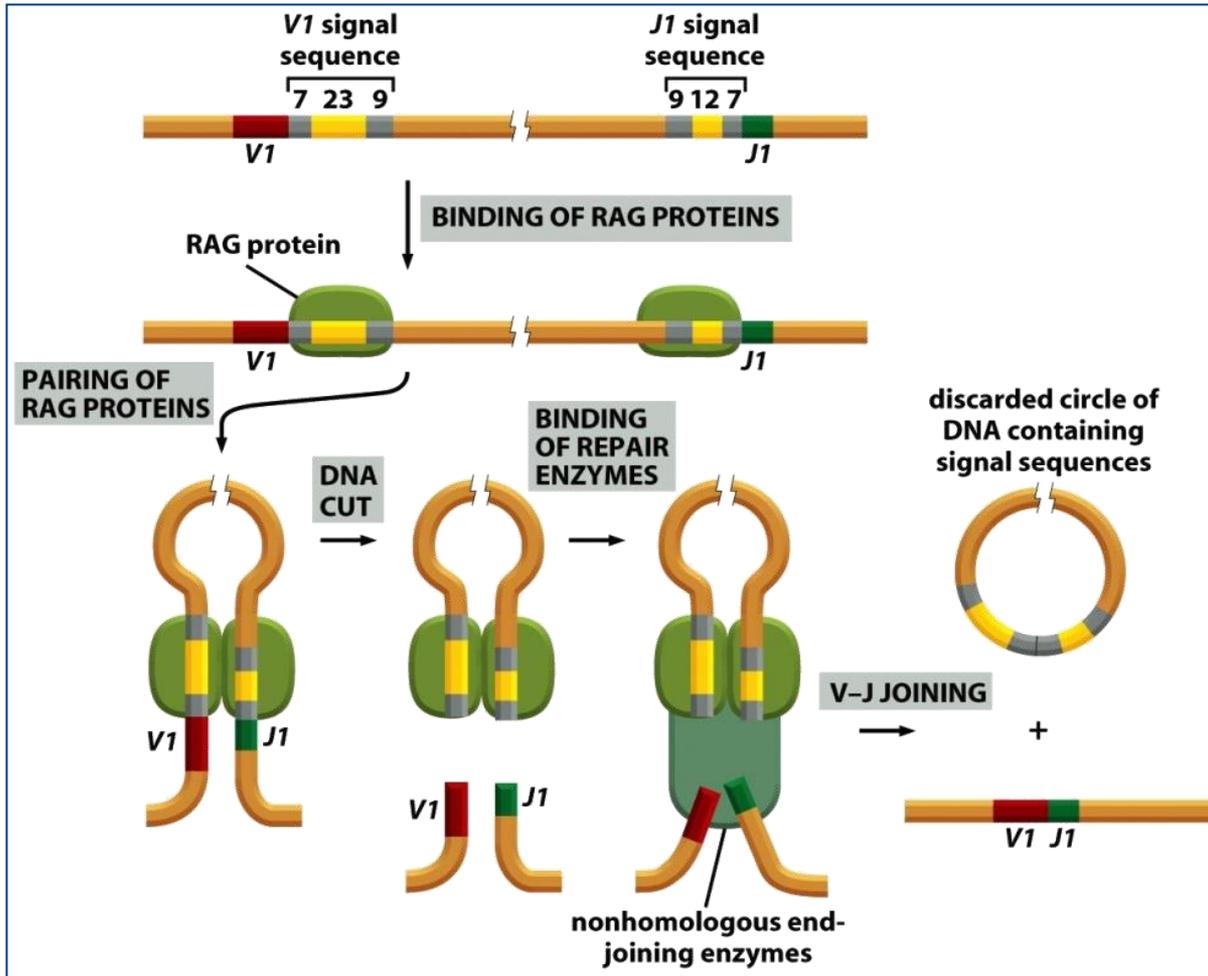
1.000.000.000.000

Generación de la diversidad de anticuerpos

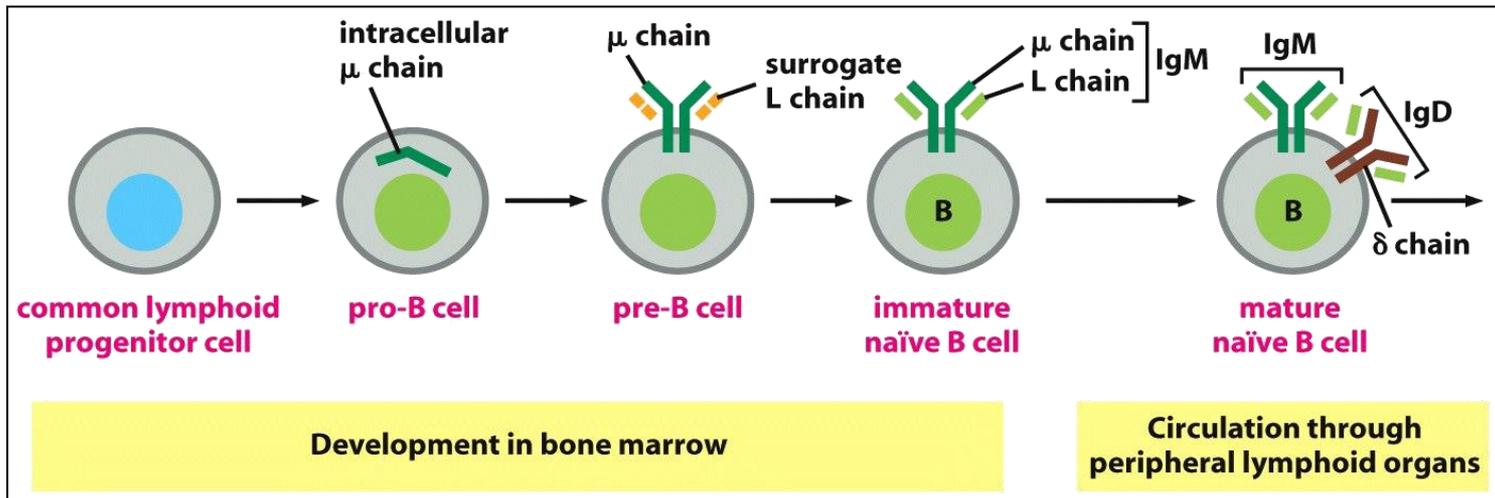
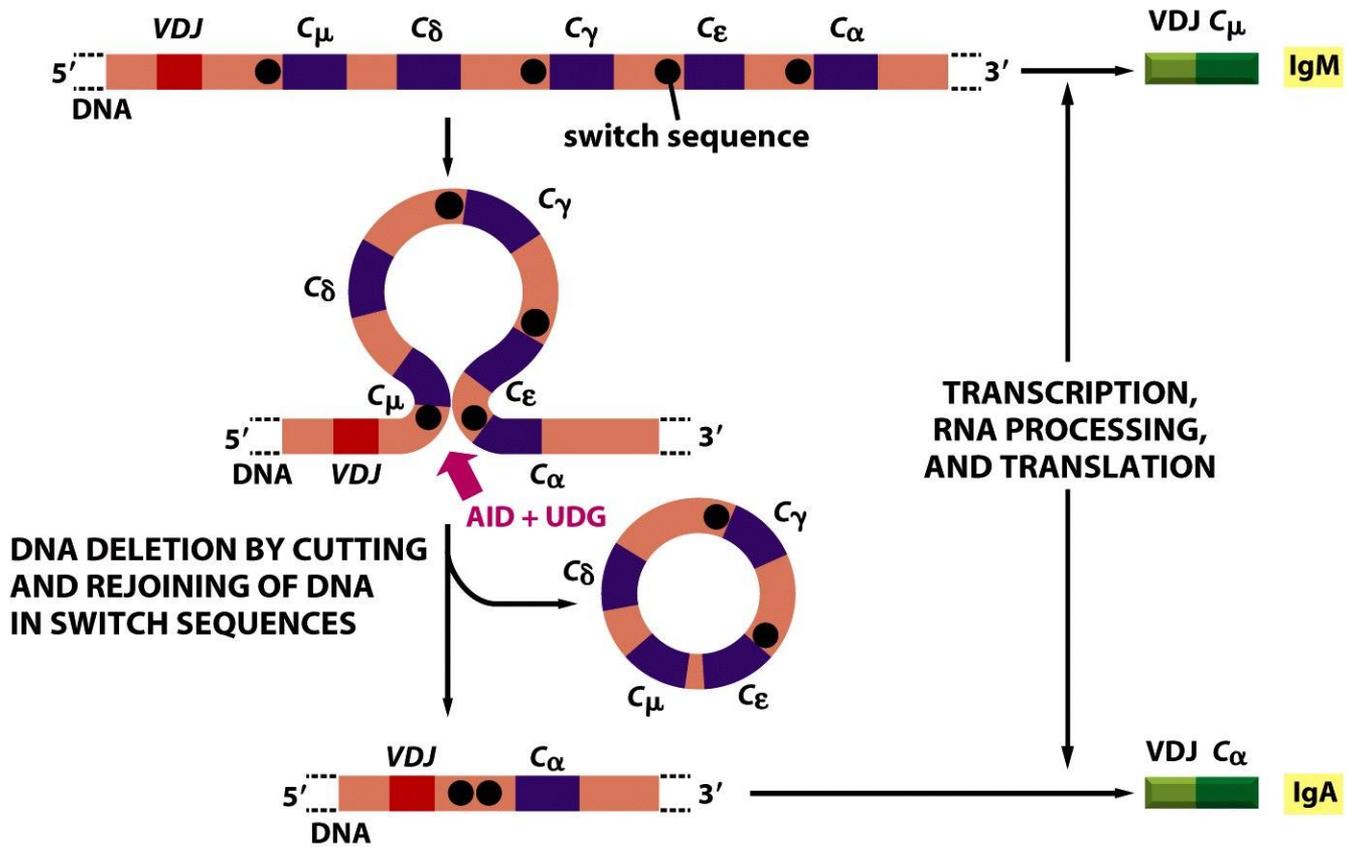


2 Mb

Generación de la diversidad de anticuerpos



Generación de la diversidad de anticuerpos



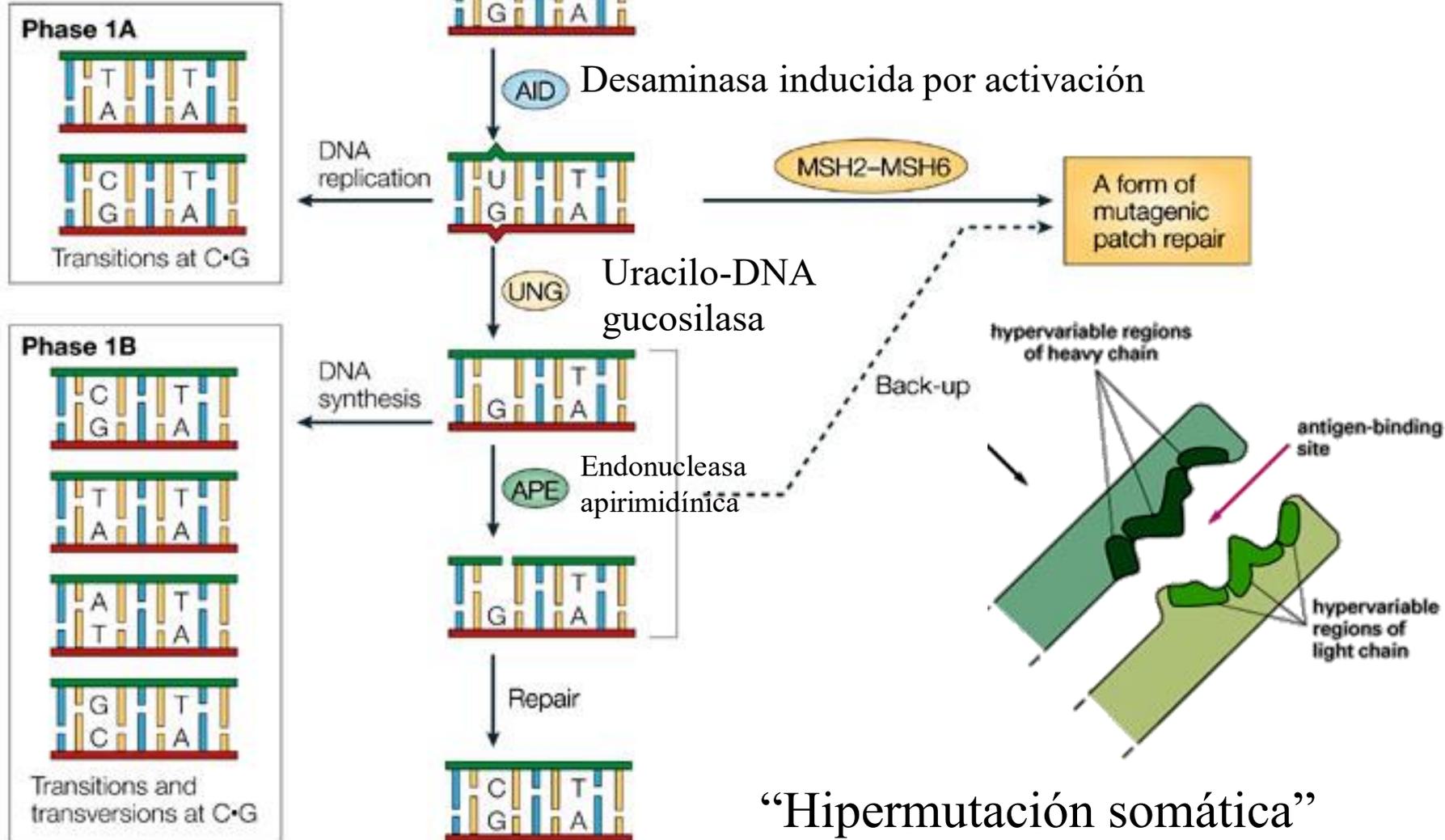
Generación de la diversidad de anticuerpos

Phase 1

Mutations at C•G pairs by deamination of C to U

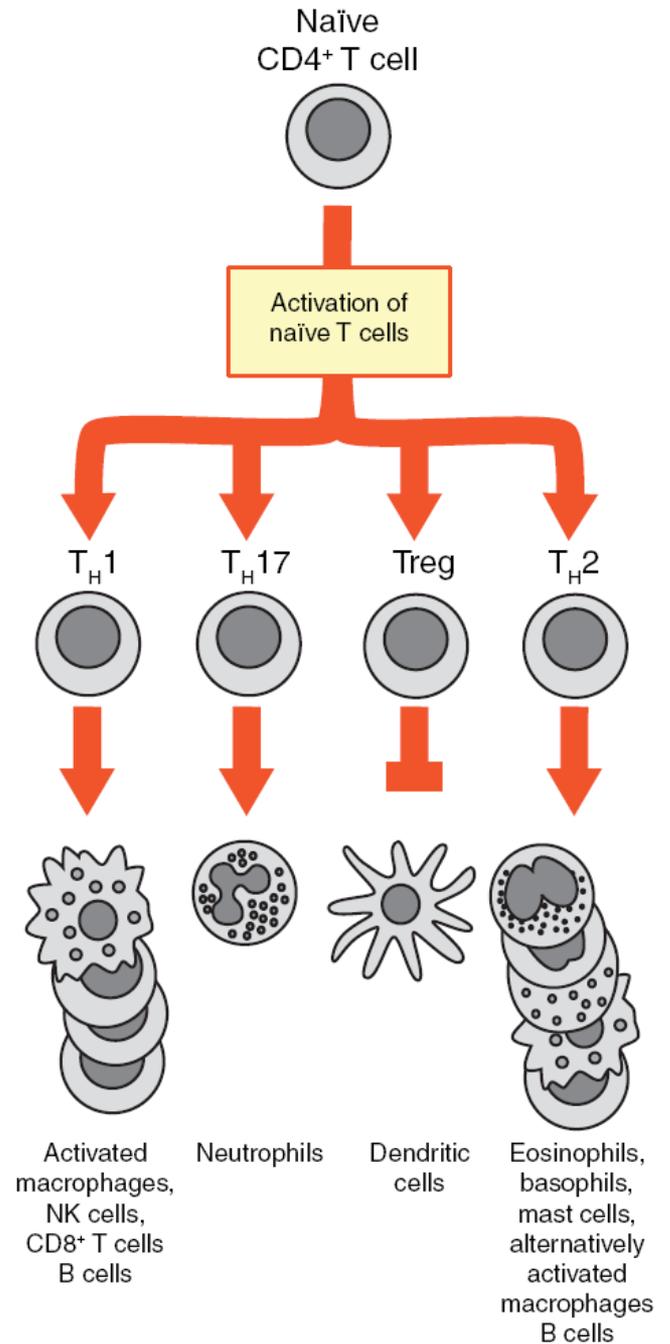
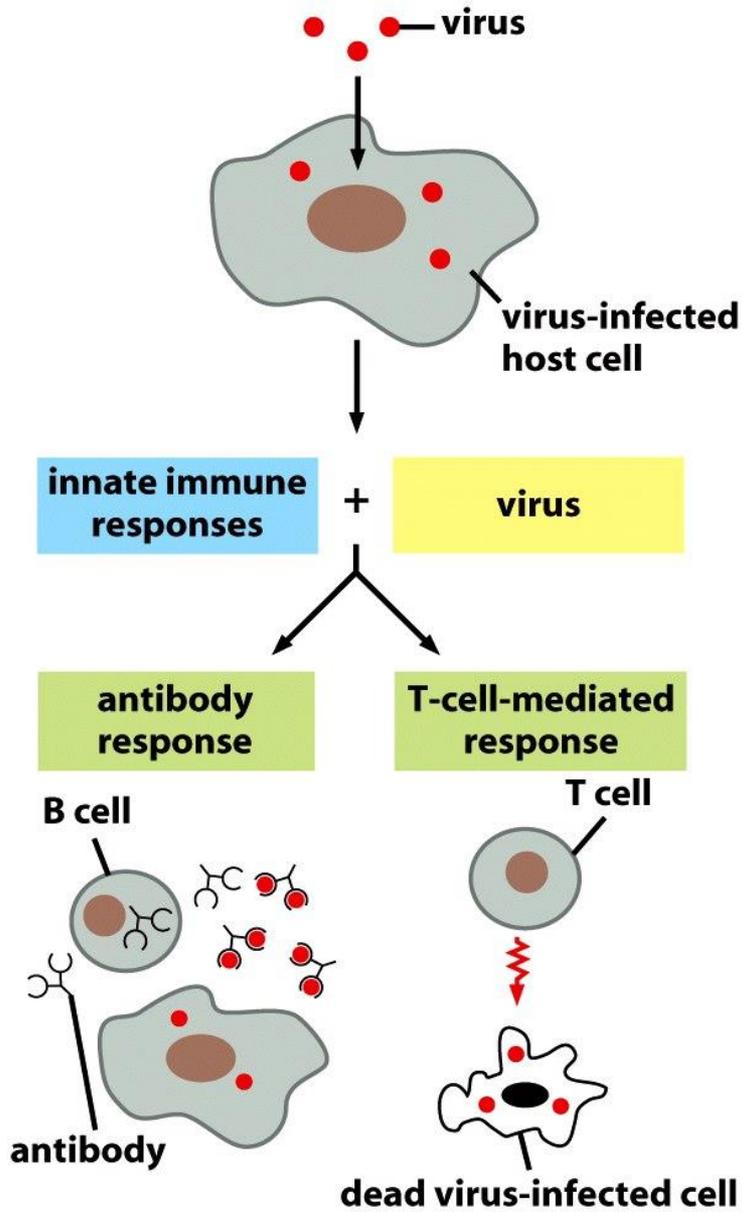
Phase 2

Mutations mainly at A•T pairs (mechanism unknown)

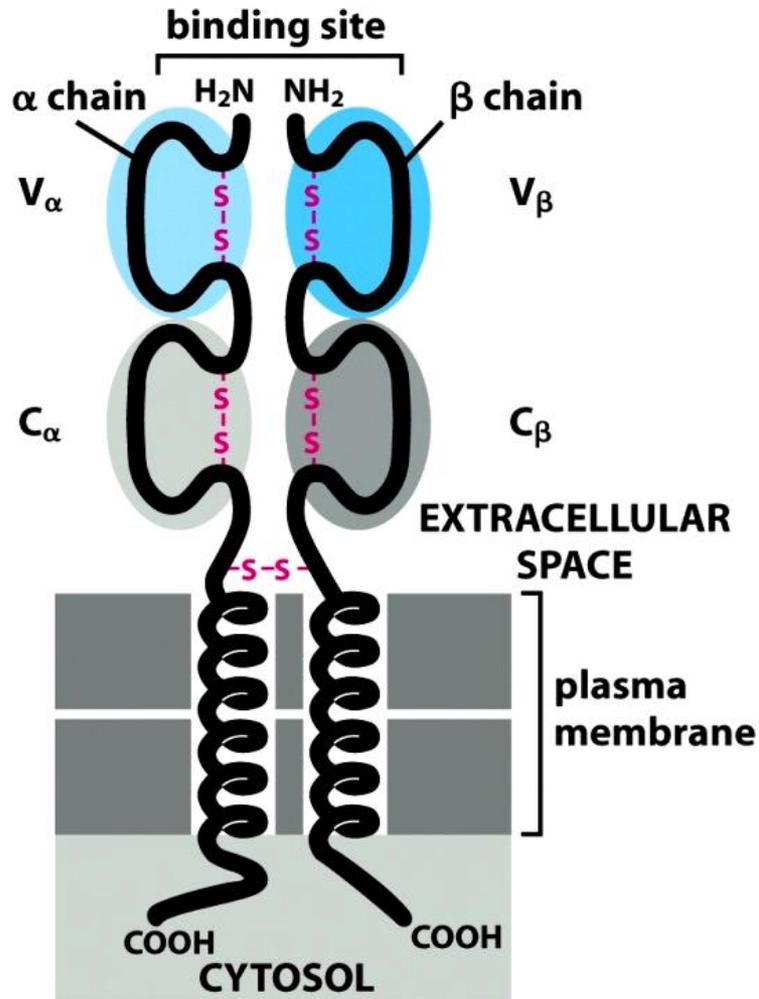


“Hipermutación somática”

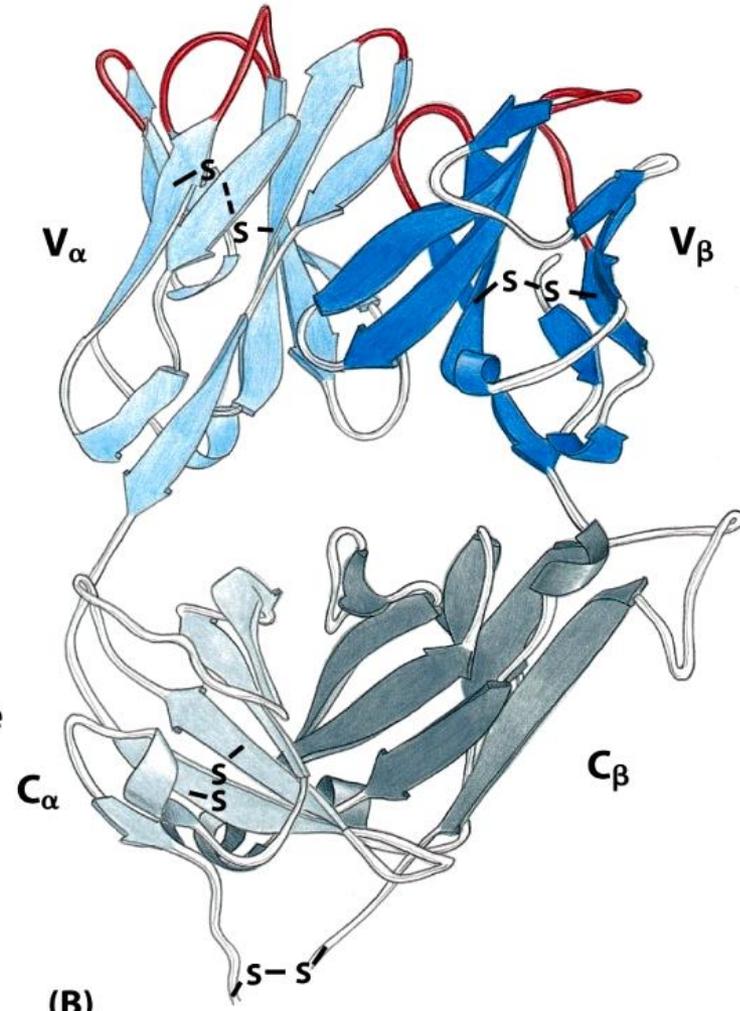
Linfocitos T



El receptor T



(A)

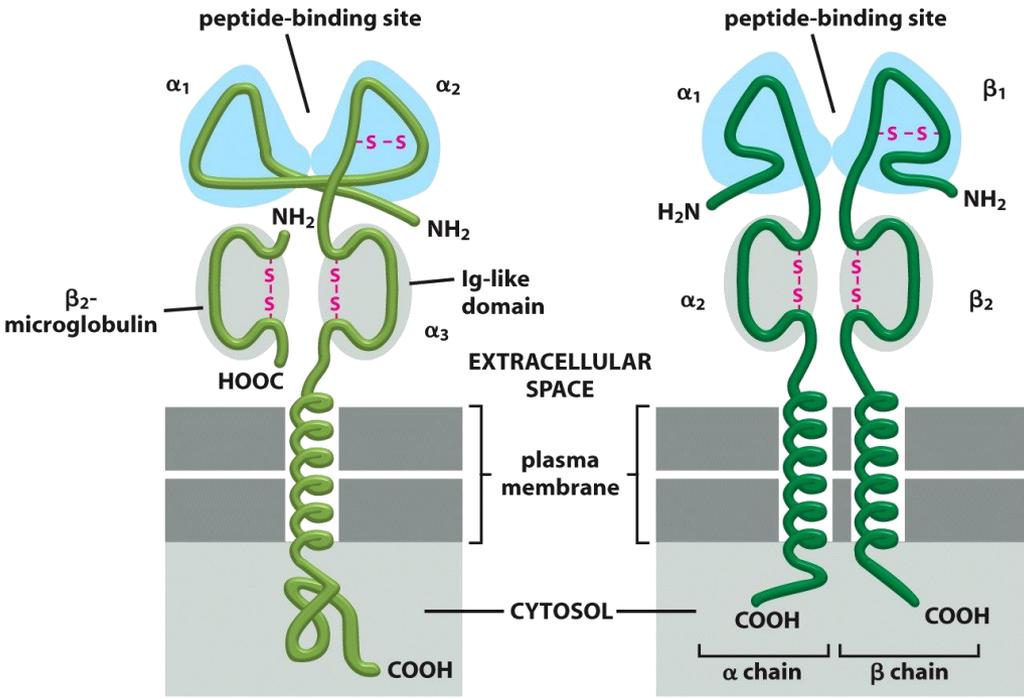
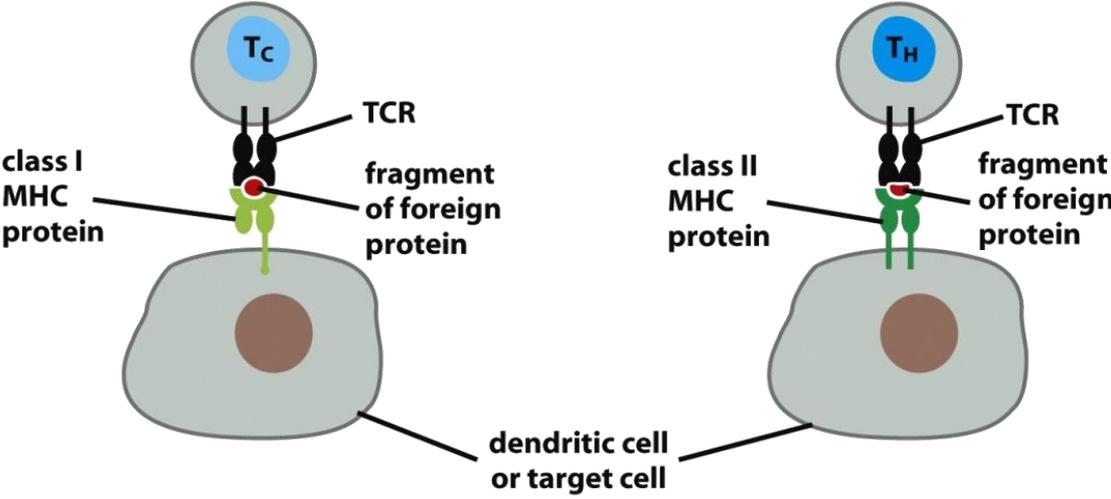


(B)

CYTOTOXIC T CELL

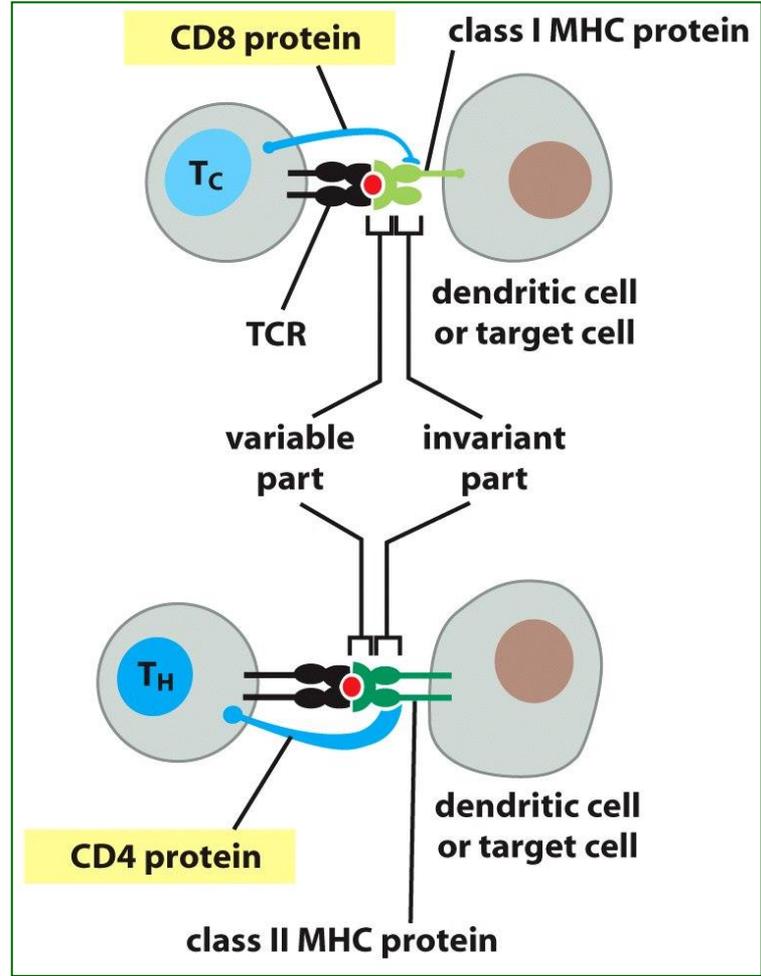
HELPER OR REGULATORY T CELL

Activación de linfocitos T:
Proteínas MHC

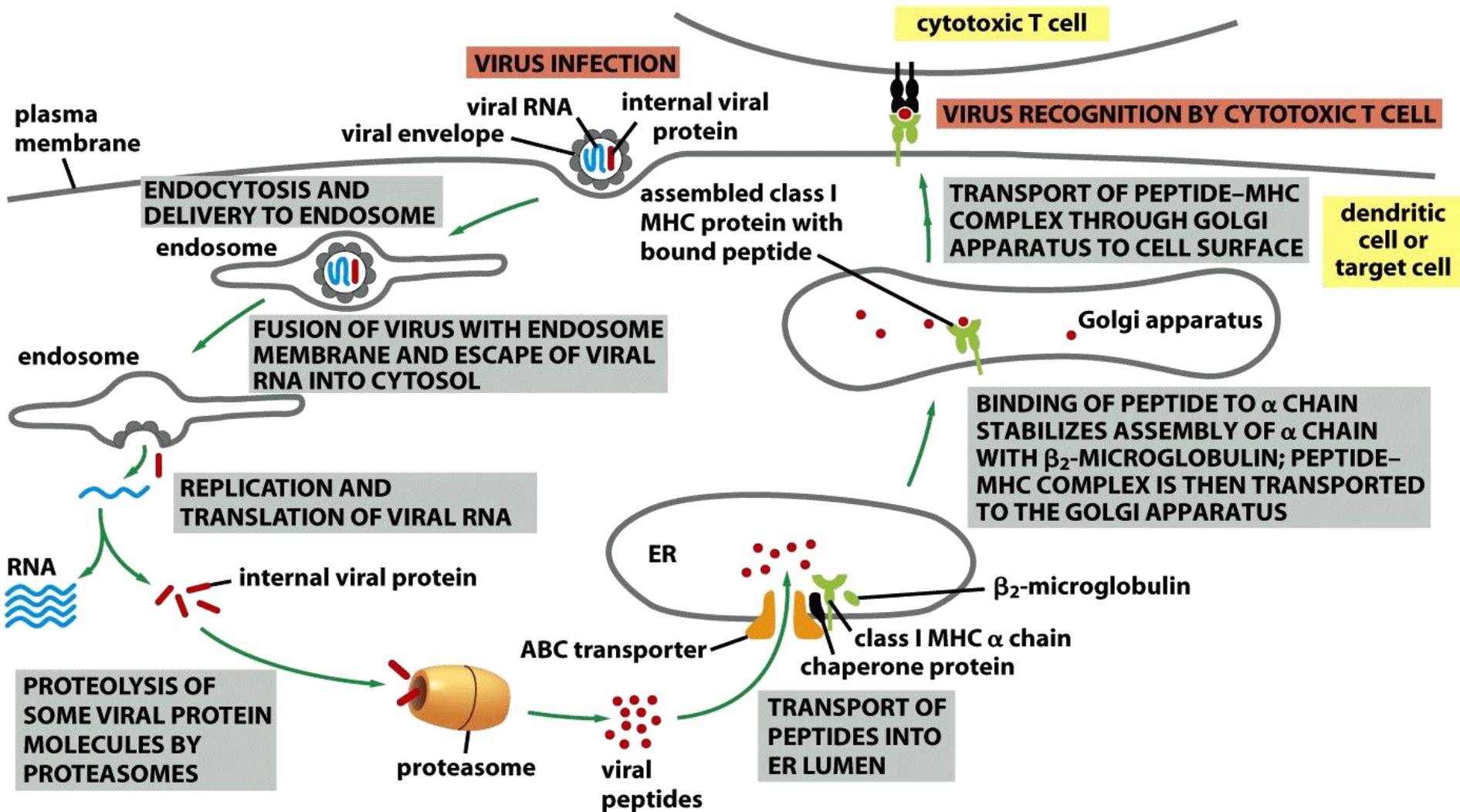


(A) CLASS I MHC PROTEIN

(B) CLASS II MHC PROTEIN

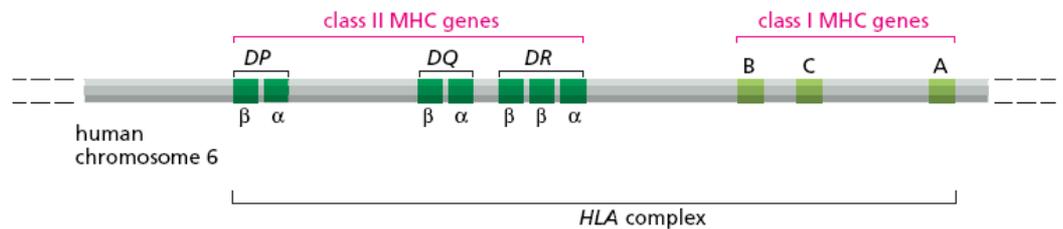
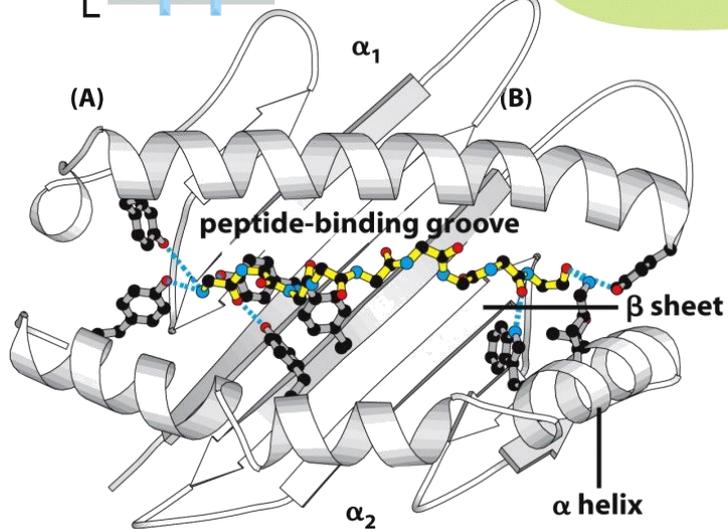
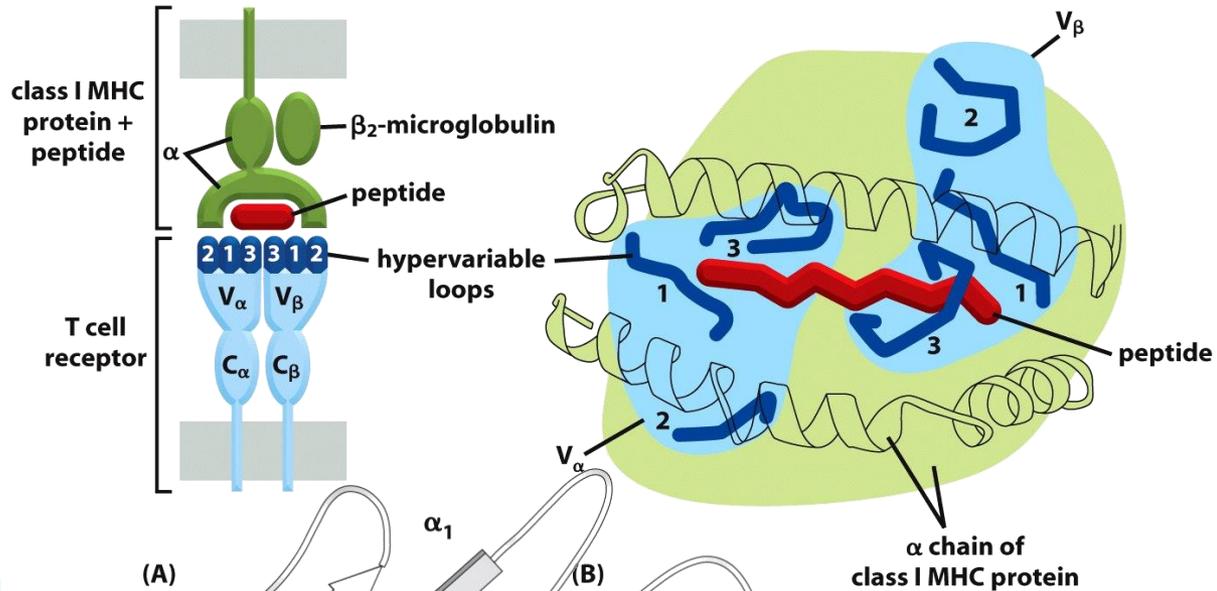
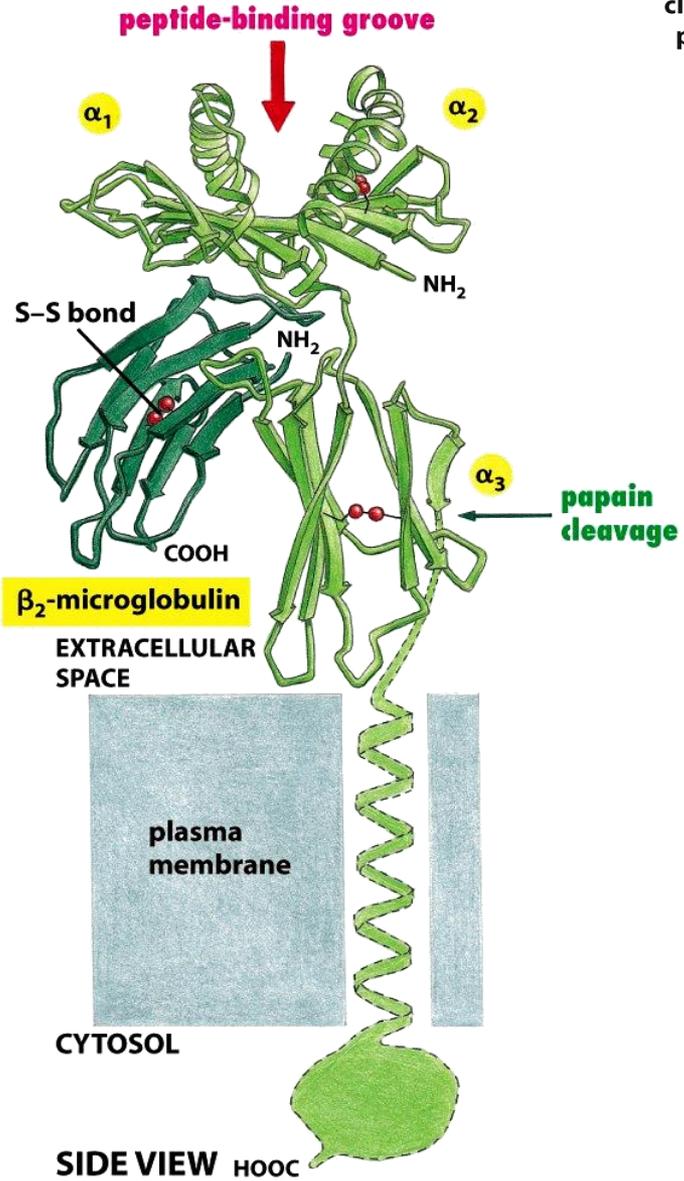


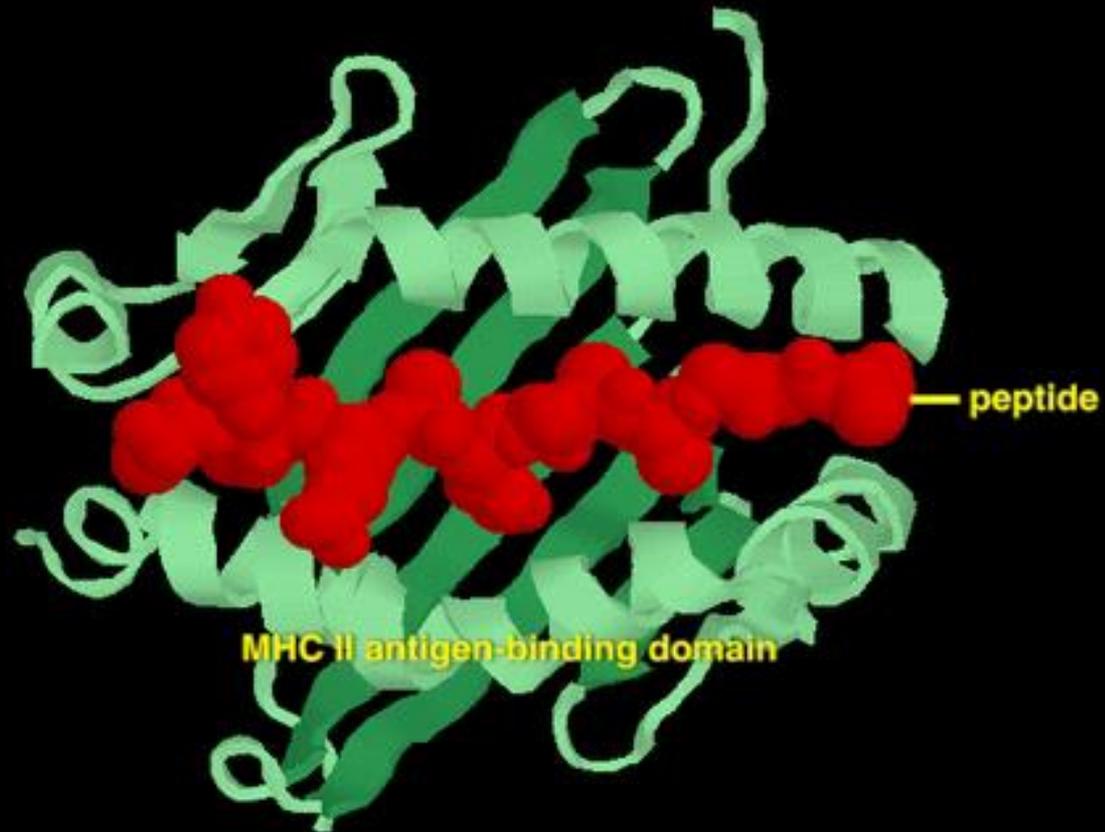
Procesamiento y presentación de antígenos a linfocitos T



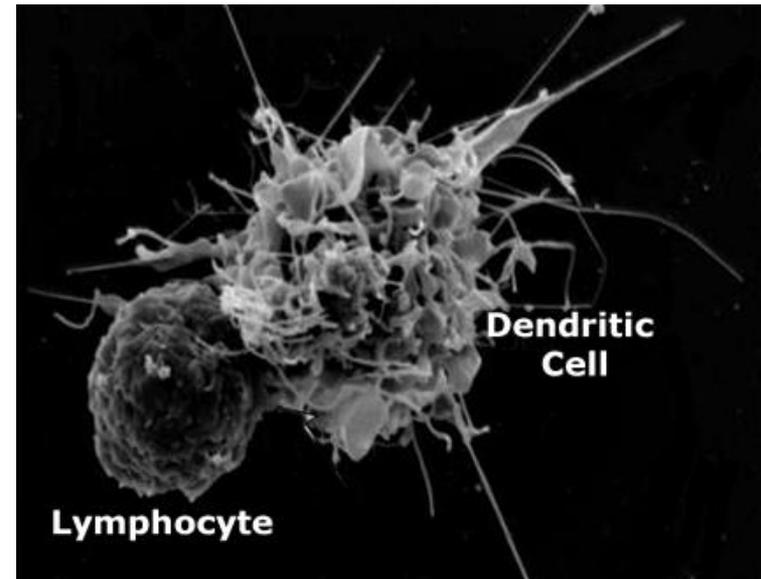
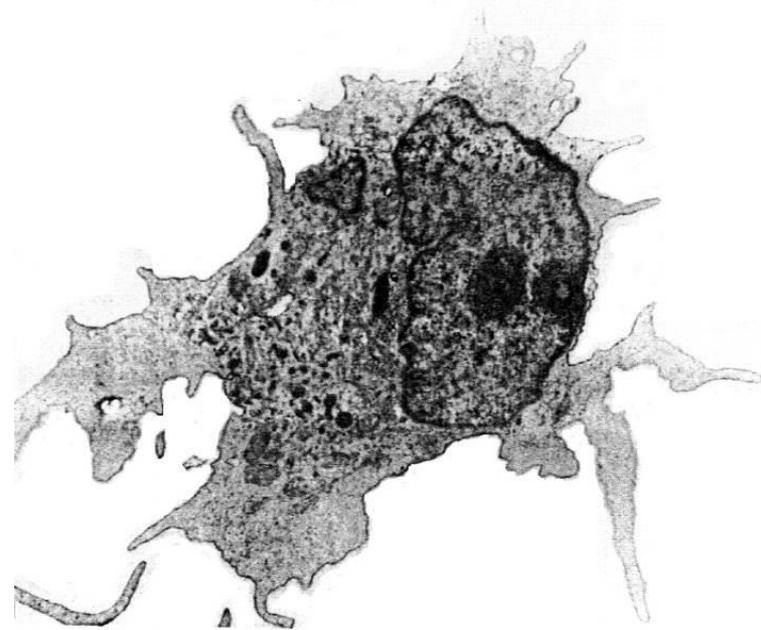
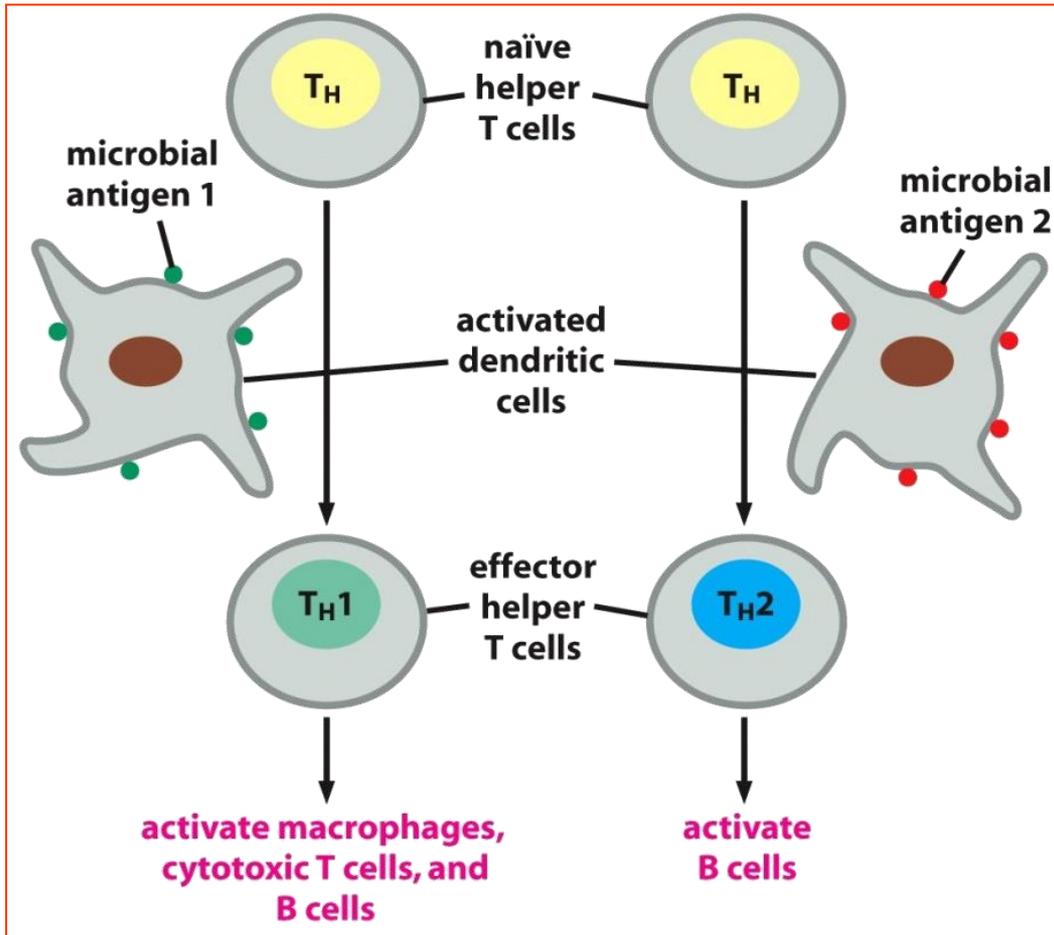
Estructura de los MHC

MHC I

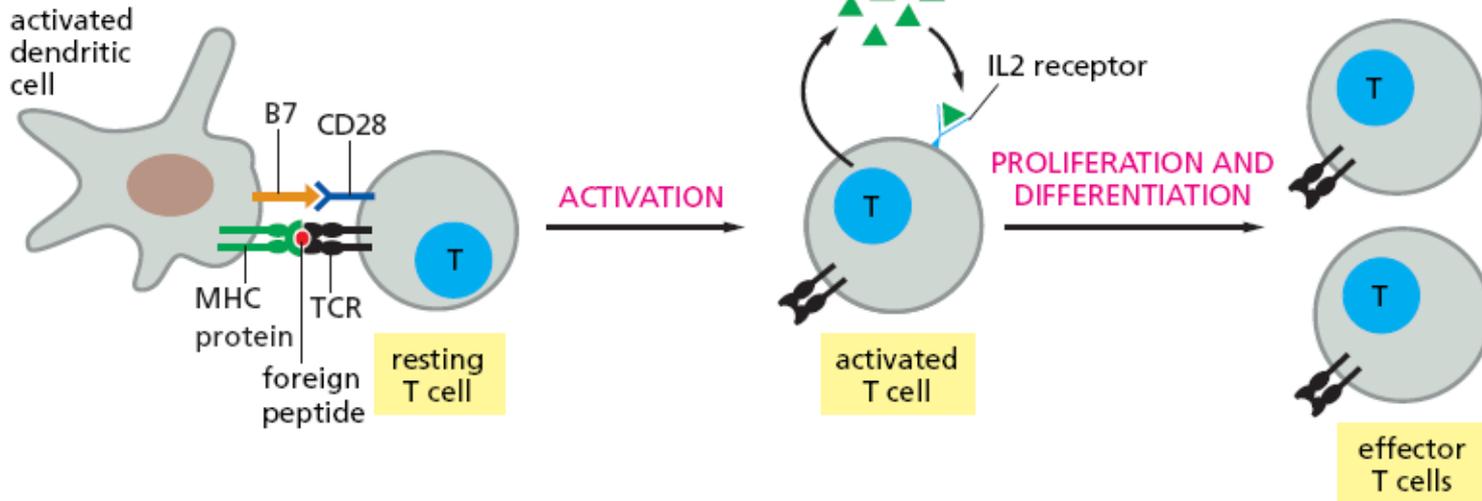
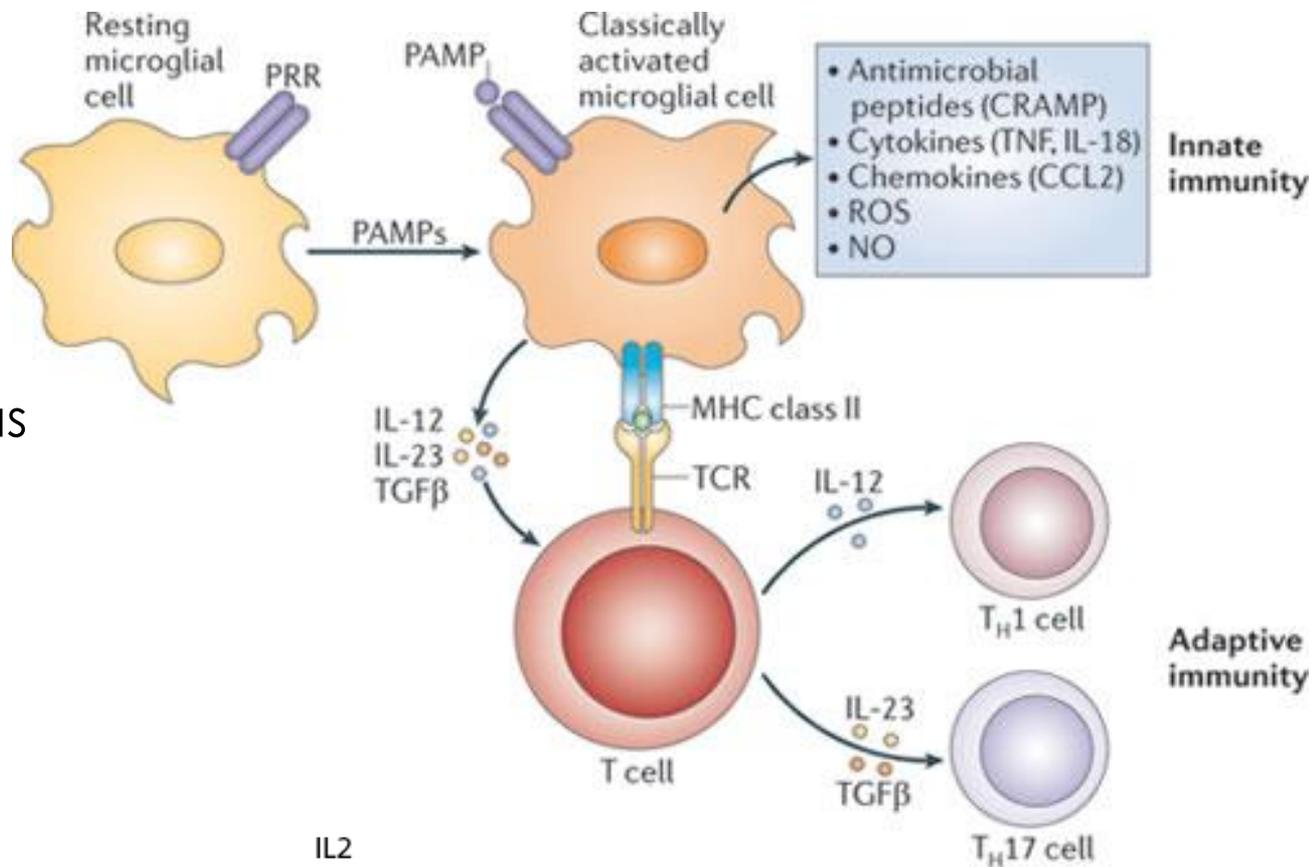




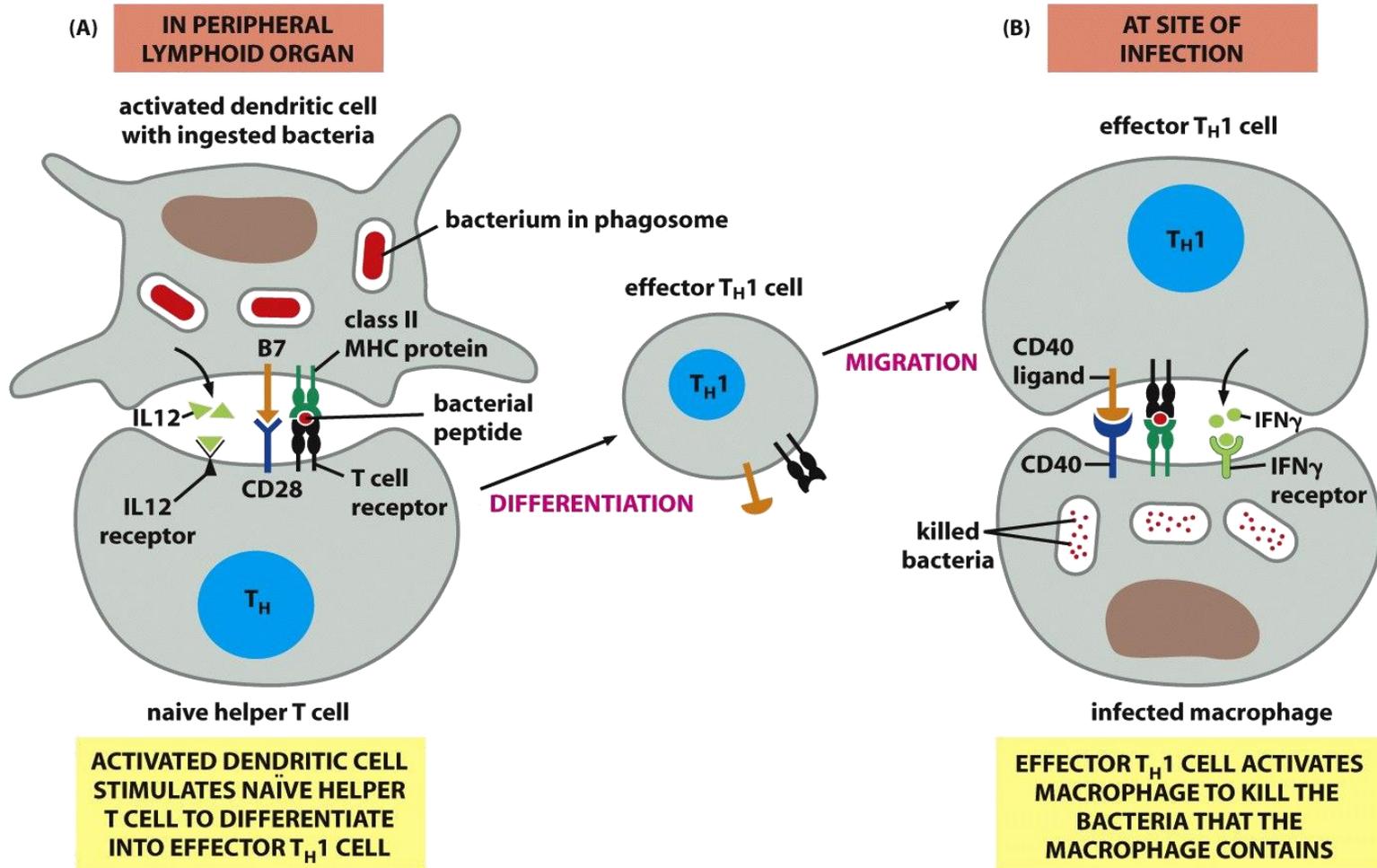
Activación de linfocitos T por células del sistema inmune innato



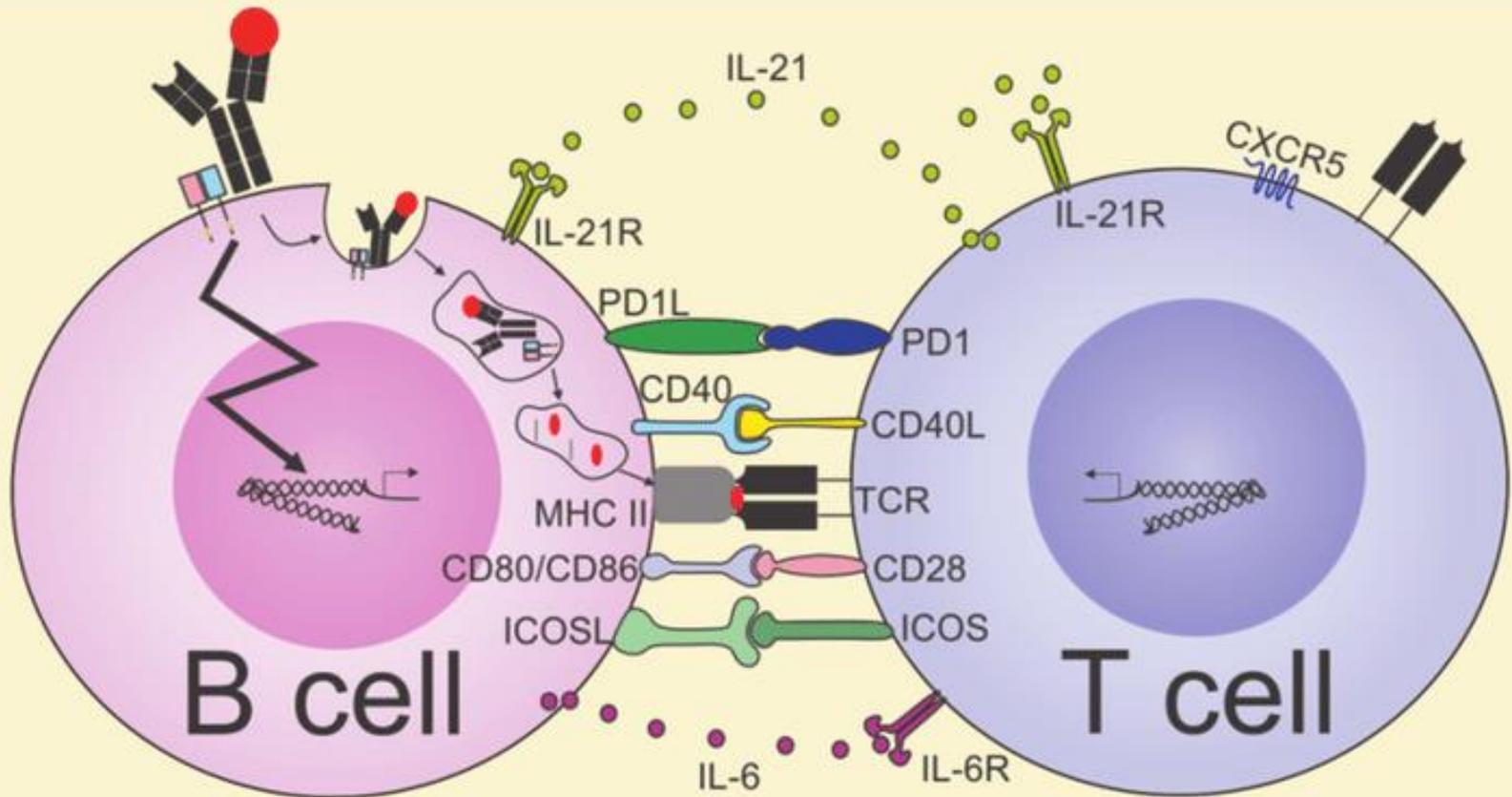
Activación de linfocitos T por células del sistema inmune innato



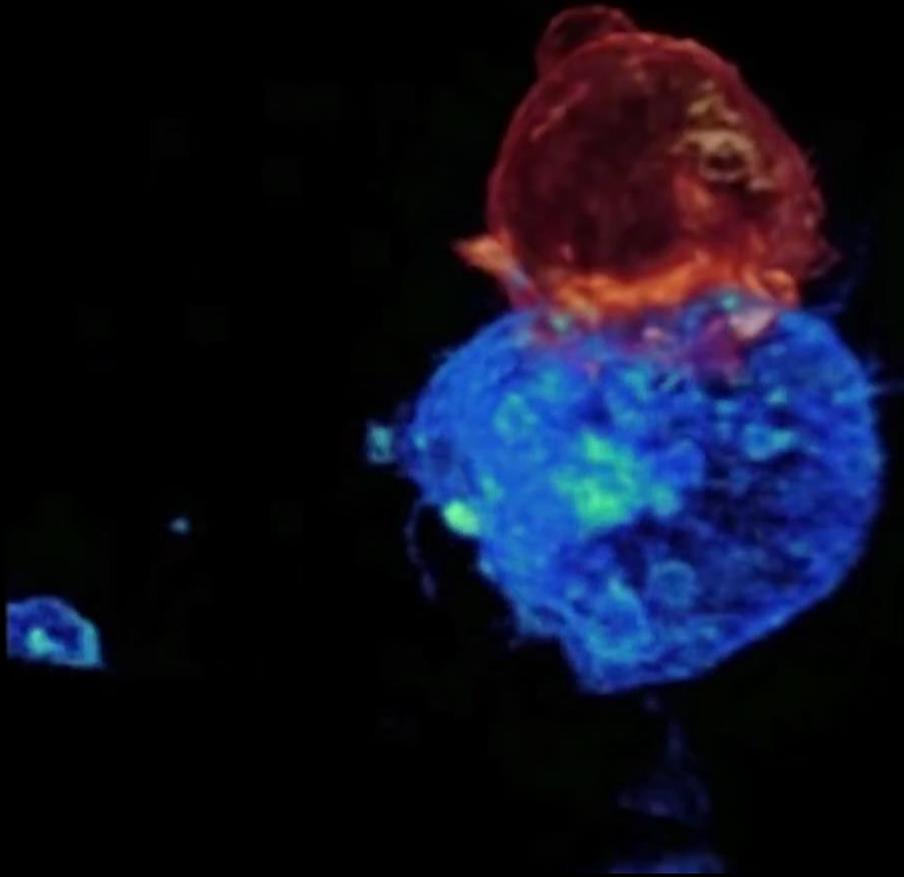
Linfocitos T colaboradores (“helper”): Activación de fagocitos



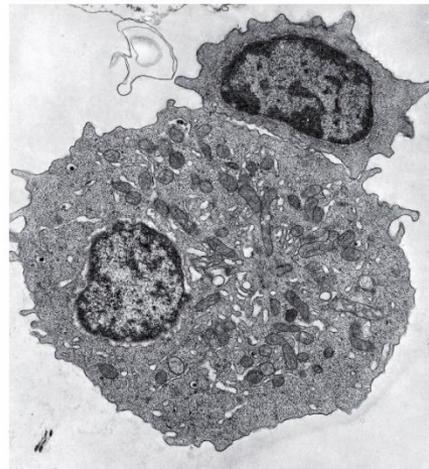
Linfocitos T colaboradores ("helper"): Activación de linfocitos B



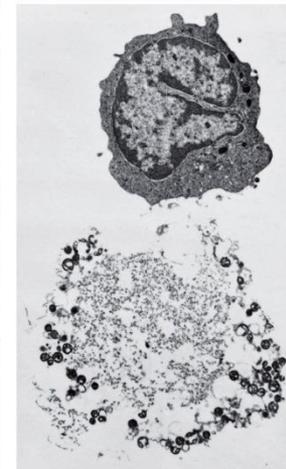
- | | | | |
|---|---|---|--|
|  MHC II |  ICOSL |  CD80/CD86 |  IL-21R |
|  TCR |  ICOS |  CD28 |  IL-21 |
|  Endosomal vesicle |  CD40 |  PD1 |  IL-6 |
|  BCR |  CD40L |  PD1L |  IL-6R |
|  Antigen | |  CXCR5 | |



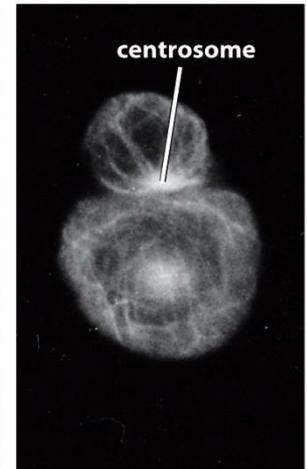
Linfocitos T citotóxicos



(A)



(B)



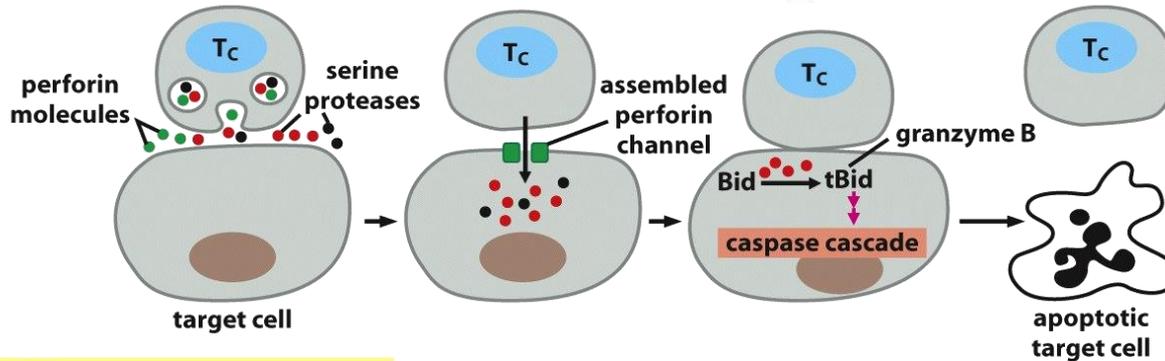
(C)

5 μ m

10 μ m

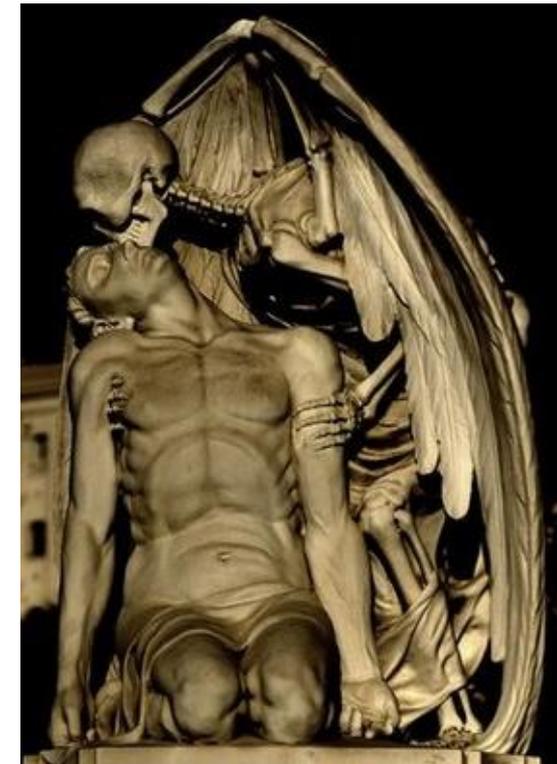
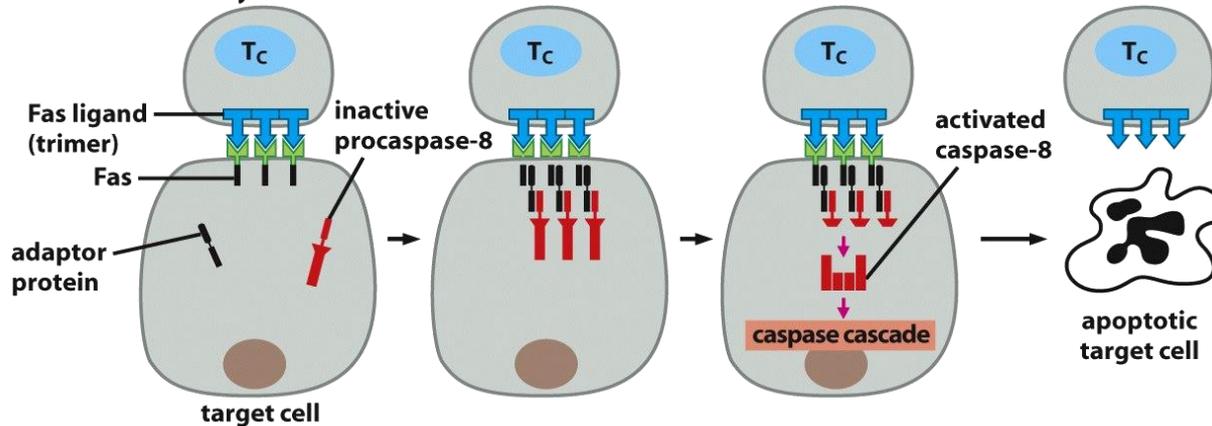
A Perforin-dependent killing

effector cytotoxic T cell



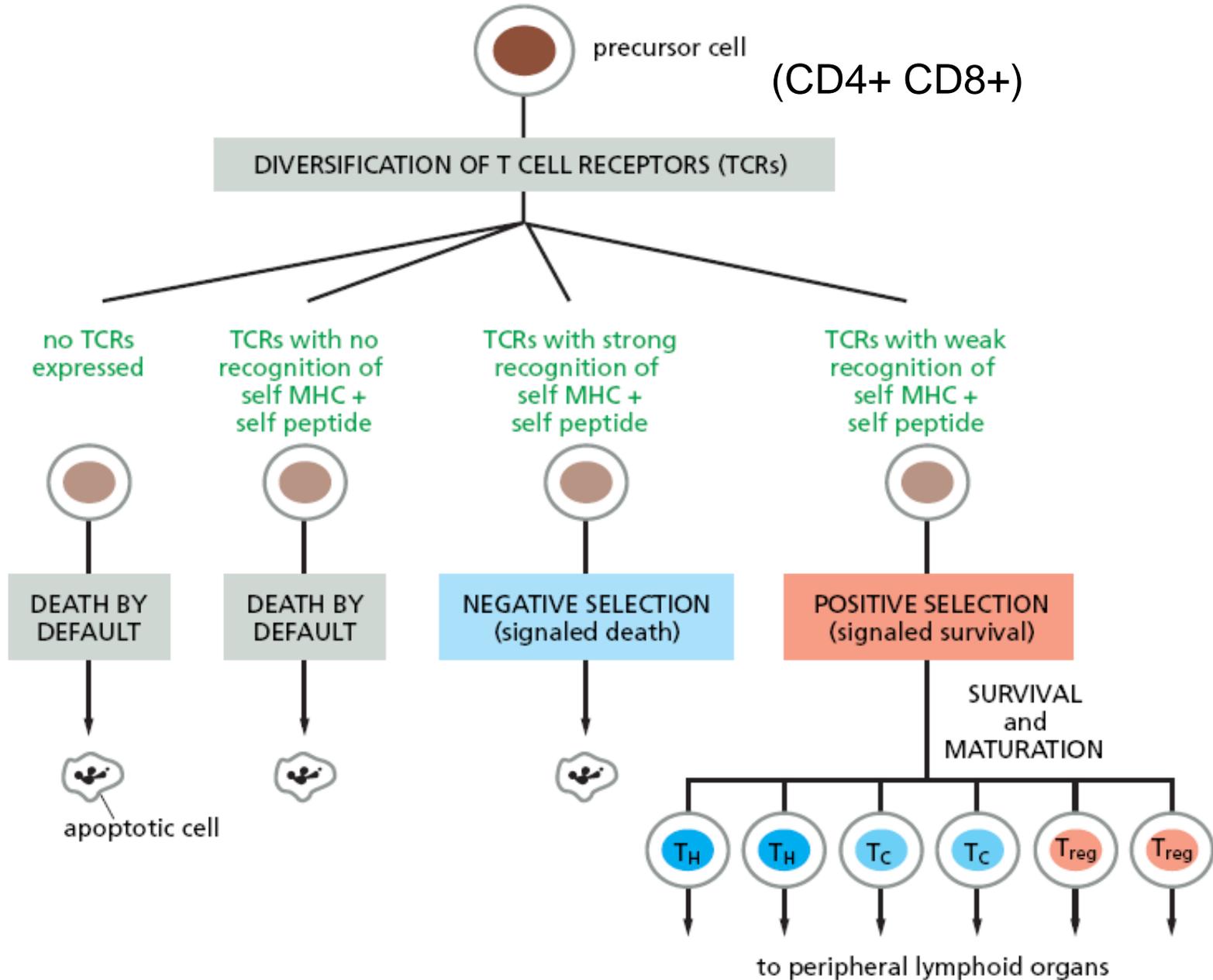
B Fas-dependent killing

effector cytotoxic T cell

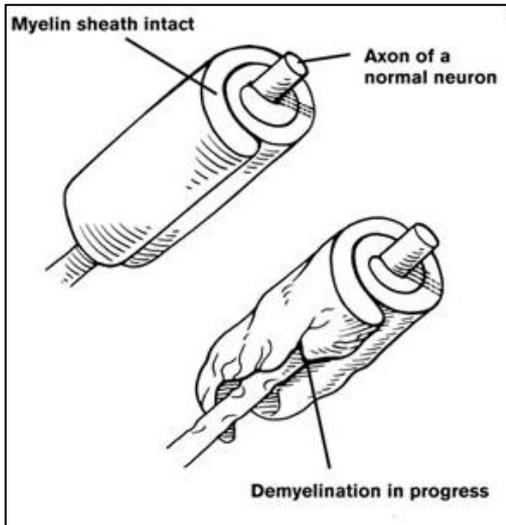
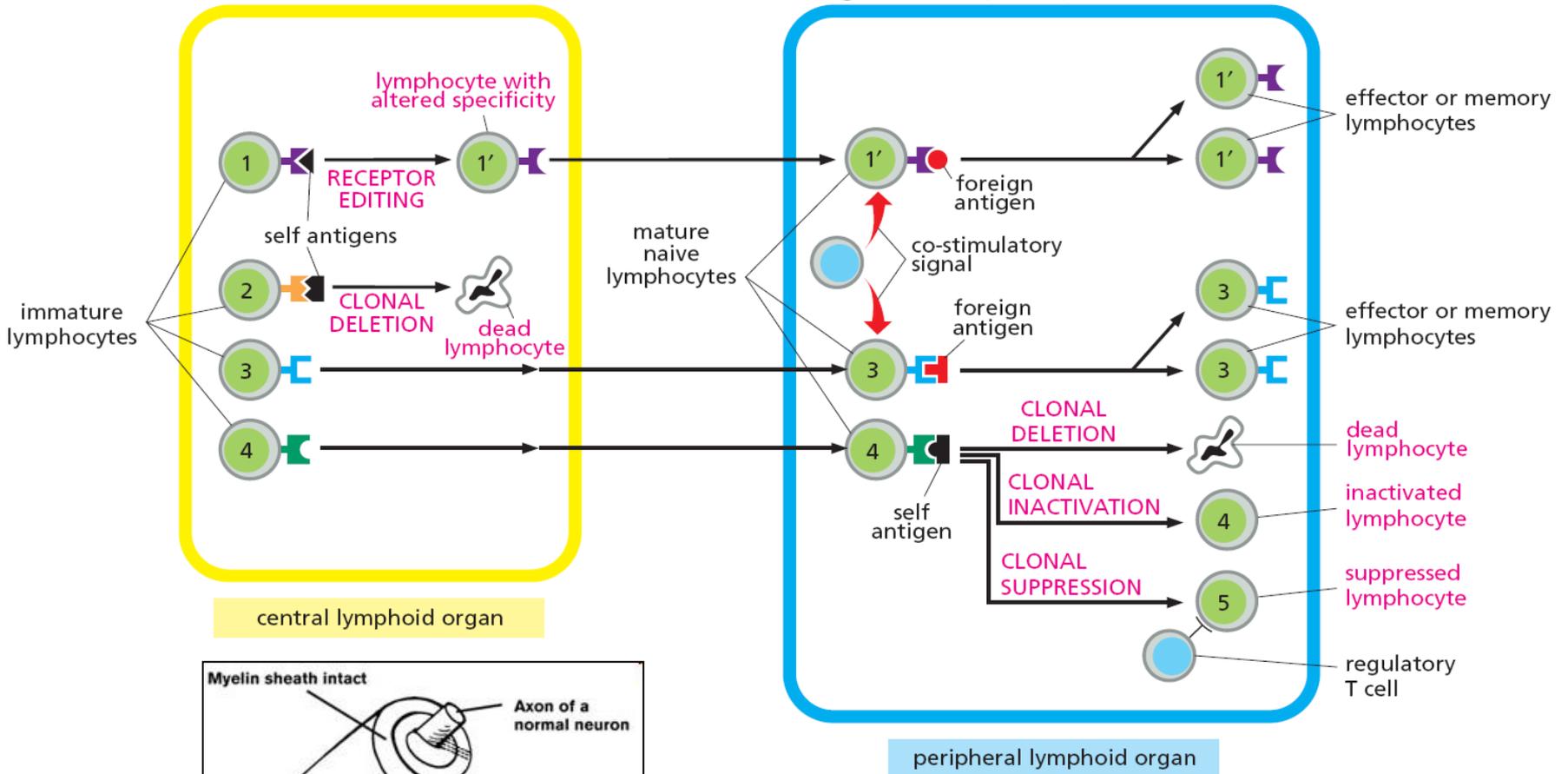


Jaume Barba, 1930
Cementerio Poblenou, Barcelona

Diferenciación de linfocitos T: selección positiva y negativa en el timo

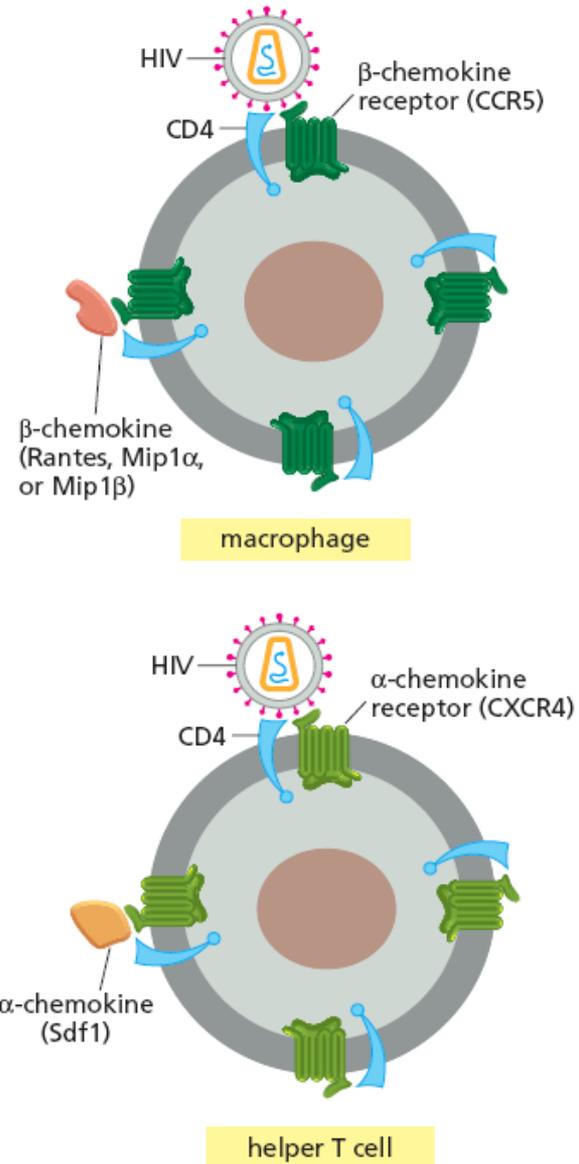
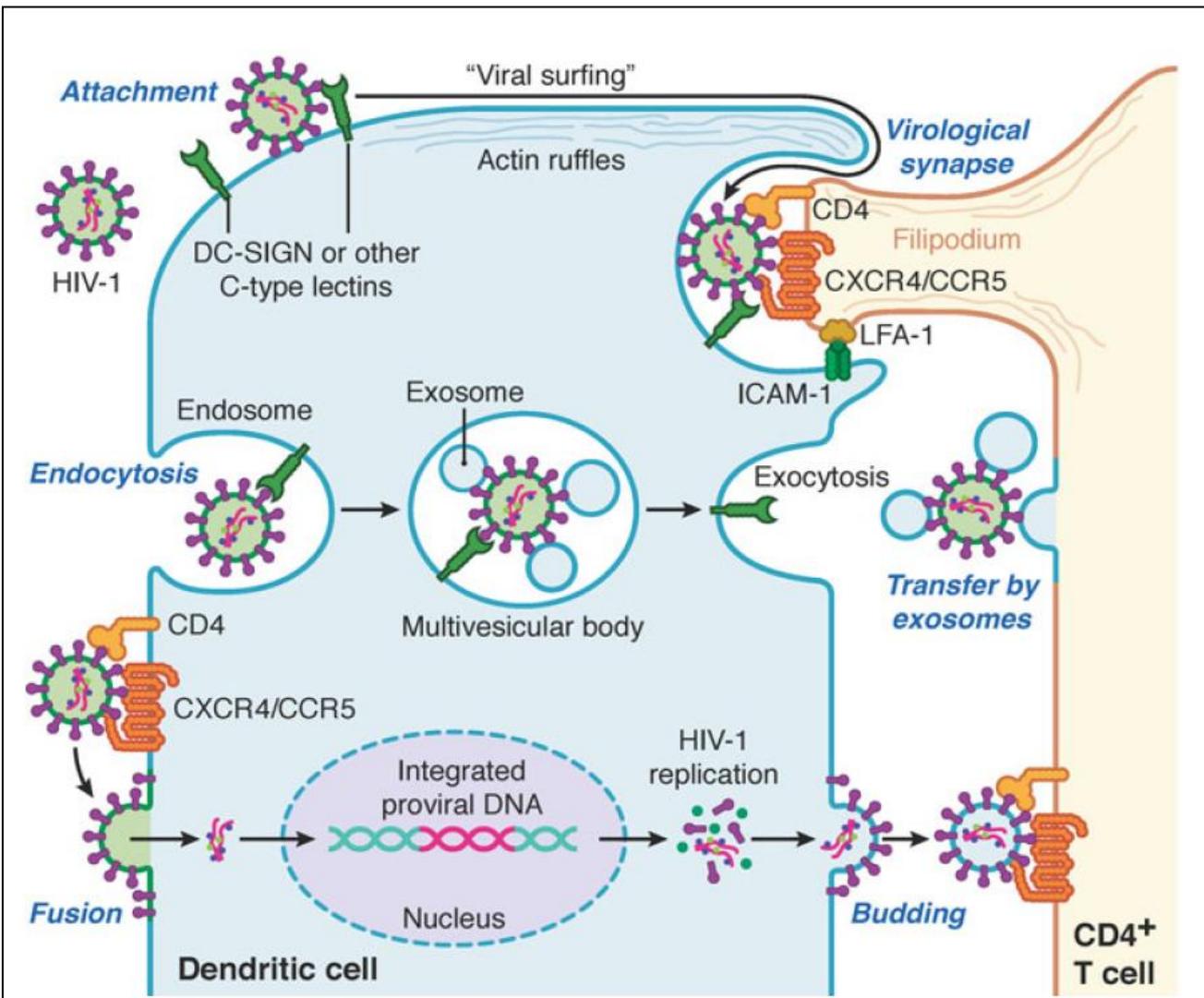


Tolerancia a antígenos propios



Esclerosis múltiple

Infección de linfocitos T CD4+ por HIV





The Cow-Pock — or — the Wonderful Effects of the New Inoculation! — vide. the Publications of the Anti-Vaccine Society.

Pub. June 10, 1805. by H. Humphrey, St. James's Street.

